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ADEQUATE ANALGESIA IN CARING FOR PAEDIATRIC BURNS PATIENTS IN A PERI-URBAN SETTING IN KZN

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A thesis submitted to the College of Health Sciences, University of KwaZulu-Natal, in fulfilment of the requirements for the degree of **Doctor of Philosophy (PhD) Health Sciences**

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Adequate Analgesia in Caring for Paediatric Burns Patients in a Peri-Urban Setting in KZN

As the candidate's supervisor, I AGREE to the submission of this thesis in the form of integrative material for examination.

The chapters are written as a set of discrete research publications, with an overall introduction and final summary.

This is to certify that the contents of this thesis are the original research work of

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Date: 7 October 2020

DECLARATION

I, **SHELLEY WALL**, Student number **211560758**, declare that,

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DEDICATION

This PhD thesis is dedicated to the more than 300 000 children who are burnt in South Africa annually, many of whom suffer more than is necessary due to inadequate analgesia and an inadequate burn care system in South Africa.

It is my hope that this PhD can change, in some small way, and improve the way that these burn-injured children are managed. A burn injury is traumatic enough as it is, but the suffering does not need to be compounded by inadequate analgesia.

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MY FAMILY

Firstly, I am eternally grateful to my husband, **Julian,** for his unwavering support, for always encouraging me to follow my dreams and better myself. Despite working long hours himself, he is always willing to look after our children or do whatever needs to be done to give me the opportunity to study further. To my children, **Elijah and Ava,** you are and will always be my greatest achievements. To my parents, **Peter and Karen,** I would not be where I am today without you. You taught me that I can achieve anything I put my mind to. Success is only worth anything with family to share it with.

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OUR BURN-INJURED CHILDREN

Managing burn-injured children is sometimes such a roller-coaster of emotions. The disappointment of each failed graft and the heart break of each child who dies is counteracted by the joy experienced when a child who has been sick for weeks or even months is standing and singing all of a sudden one day when you walk into the ward; or seeing a child who was on the brink of death following up at the clinic and thriving. Each and every child we have managed has left their mark on me in some way or another…I have learnt so much about myself, about life, about never giving up and about putting everything into perspective from each tiny soul that we have managed.

DRILL (Developing Research Innovation Localisation and Leadership)

Being a DRILL fellow has opened my eyes to a different world. I have learnt so much and grown an incredible amount since my DRILL journey commenced. Thank you to the DRILL PI's Fatima, Petra, Suvira and Doug for their guidance and support and the various workshops they each conducted with the aim of making us all better researchers. Thank you to Nisha, Lungelo, Themba and Prem for all the behind-the-scenes work. Thank you to the other DRILL fellows, in particular **Verusia Chetty,** for your constant support, advice and guidance with writing up this PhD thesis.

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ABSTRACT

This PhD thesis centres on achieving adequate analgesia in caring for paediatric burn-injured patients in KwaZulu-Natal, South Africa. The burden of burn injuries in sub-Saharan Africa is huge. A large number of children in the under-five age group sustain burns in the region annually. Pain is virtually synonymous with burn injuries. All children with burns experience pain, regardless of the cause, size or depth of the burn. This PhD study aimed to improve the care offered to paediatric burns patients by addressing obstacles to adequate analgesia in paediatric burns patients; and to offer a practical, easy to use, locally applicable analgesia protocol which can be used at district, regional and tertiary hospitals alike. The objectives were to identify deficits in the knowledge of doctors in terms of prescribing procedural analgesia for children with burns; to evaluate the use of an alternative analgesic agent, Methoxyflurane, for pain management during dressing changes in an outpatient department; to compare the analgesic requirements of children presenting with acute versus chronic burns; to evaluate the use of an alternative analgesic agent, Methoxyflurane, for pain management during dressing changes for patients admitted to the burns ward; to evaluate obstacles to adequate analgesia in paediatric burns patients; and to develop an analgesia protocol applicable to KwaZulu-Natal and other low-middle-income countries (LMIC), through the consensus of experts in the field. The development of this protocol was conducted in three phases. The first phase involved assessing obstacles to adequate analgesia in paediatric burns patients. The second phase involved assessing Methoxyflurane as an alternative analgesia option in both the inpatient and the outpatient setting; and the final phase involved the addition of Methoxyflurane to our analgesia protocols and reaching an expert consensus that the elements included in the analgesia protocol were applicable to KwaZulu-Natal and other low-middle-income settings. The analgesia protocol for paediatric burns patients has been developed with the local setting and resources as a primary consideration. It was specifically designed to be easy to use, safe in novice hands and locally applicable. In order to ensure that theoretical findings from the study are translated into practices that benefit all burn-injured children, this research should be combined with advocacy efforts.

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ABBREVIATIONS

LMIC	Low-Middle-Income Country
KZN	KwaZulu-Natal
PMB	Pietermaritzburg
TBSA	Total Body Surface Area
PBS	Pietermaritzburg Burn Service
BREC	Biomedical Research Ethics Committee
FLACC	Face, Limbs, Activity, Cry, Consolability
Comfort B	Comfort Behaviour Score
mg/kg/%TBSA	milligrams per kilogram per percentage total body surface area
ICU	Intensive Care Unit
IV	Intravenous
IMI	Intramuscular Injection
PO	Per Os
PTSD	Post-Traumatic Stress Disorder
Hrly	Hourly
ISBI	International Society for Burn Injury
POCIS	Pain Observation Scale for Young Children
mg/kg/days admitted/TBSA	milligrams per kilogram per days admitted per total body surface area
SA	South Africa

OPERATIONAL DEFINITIONS

Burn-injury

A burn injury is injury to tissues caused by contact with dry heat (fire), moist heat (steam or liquid), chemicals, electricity, lightning, or radiation. (1)

Paediatric

Paediatric is defined as of, or relating to, the care of children.(1) For the purposes of this study, children 12 years and under were considered as paediatric patients.

Analgesia

Analgesia is defined as the reduced sensibility to pain, without loss of consciousness and without the sense of touch necessarily being affected.(2) There are various different modalities to provide pain relief. In the context of this study, analgesia is the provision of medication to relieve pain.

Background Pain

Background pain is a result of the thermal tissue injury and it is the pain the patient experiences while at rest. It is usually of low to moderate intensity.(3)

Background Analgesia

Medication to relieve background pain.

Procedural Pain

Procedural pain is a result of wound debridement, dressing changes and/or rehabilitation activities. It is usually brief but intense pain. (3)

Procedural Analgesia

Procedural analgesia is the use of analgesic or dissociative medications during diagnostic or therapeutic procedures to relieve anxiety and pain. Procedural analgesia is widely practiced outside of the operating theatre by non-anaesthetists.(4)

RESEARCH OUTPUTS

A. PEER-REVIEWED PUBLICATION LIST

Wall SL, Clarke DL, Allorto NL. Analgesia protocols for burns dressings: Challenges with implementation, Burns (2019), https://doi.org/10.1016/j.burns.2019.04.012

Wall S, Bangalee V. The ketamine crisis: Does South Africa have a plan B? South African Med J. 2019; 109(12):911–3. https://doi.org/10.7196/SAMJ.2019.v109i12.14188

Wall SL, Clarke DL, Nauhaus HM, Allorto AL. Barriers to Adequate Analgesia in Paediatric Burns Patients. SAMJ. October 2020; 110(10):1032-1035. https://doi.org/10.7196/SAMJ.2020.v110i10.14519

Wall SL, Clarke DL, Allorto NL. A comparison of analgesia requirements in children with burns: Do delayed referrals require higher procedural analgesia doses? Burn Open [Internet]. 2020;4 (3):103–9. Available from: https://doi.org/10.1016/j.burnso.2020.04.001

Wall SL, Clarke DL, Smith, MTD, Allorto NL. Use of methoxyflurane for paediatric patients in a regional burn service outpatient clinic. Southern African Journal of Anaesthesia and Analgesia, 26(5): 240–244. https://doi.org/10.36303/SAJAA.2020.26.5.2311

Wall, S., Allorto, N., & Chetty, V. (2021). Reaching consensus on an analgesia protocol for paediatric burn patients in a resource-scarce South African community. South African Family Practice, 63(1), 7 pages. https://doi.org/10.4102/safp.v63i1.5193

B. CONFERENCES

INTERNATIONAL

Oral Presentation: "Analgesia Protocols for Burns Dressings: The Lack of Efficacy without Constant Re-enforcement" – International Society for Burn Injury Conference, **Delhi**, **India** (December 2018)

Poster Presentation: "Analgesia Protocols for Burns Dressings: Challenges with Implementation" – European Burn Association Conference, **Helsinki**, **Finland** (September 2019)

Oral Presentation: "Analgesia Protocols for Burns Dressings: Challenges with Implementation" – Australia-New Zealand Burn Association Annual Scientific Meeting, **Hobart**, **Tasmania** (October 2019)

NATIONAL

Oral Presentation: "A Comparison of Analgesia Requirements in Children with Burns: Do Delayed Referrals Require Higher Procedural Analgesia Doses?" Cape Town International Trauma Conference, **Cape Town, South Africa.** (November 2019

CHAPTER 1

INTRODUCTION

1.1. OVERVIEW OF THE THESIS

This manuscript has been prepared in accordance with the College of Health Science guidelines for PhD by research. [Appendix 1] The chosen method for submission of this study is 'a thesis by manuscript'. The guidelines dictate that, for this method of submission, the candidate may have at least three papers as the prime author that have not yet been published but are in the form of manuscripts; at least two of these papers must constitute original research. This PhD comprises one published editorial, three published manuscript, one manuscript accepted for publication and one submitted and awaiting second round review. This manuscript consists of ten chapters.

Chapter 1: This chapter provides an overview of the current literature which served as motivation for this research. The study's aims and objectives are set out.

Chapter 2: This chapter explores the theoretical and conceptual frameworks which inform the foundation of this research study approach. It summarises the methodology of each stage of the research.

Chapter 3: This chapter is presented in the form of a published study. It outlines the results of a study conducted to ascertain doctors' knowledge regarding analgesia for paediatric burns patients and to determine compliance with prescribed analgesia protocols.

Wall SL, Clarke DL, Allorto NL. Analgesia protocols for burns dressings: Challenges with implementation. Burns (2019), doi:10.1016/j.burns.2019.04.012

Chapter 4: This chapter is presented in the form of a published editorial, outlining issues regarding the shortage of ketamine and the grave impact this will have on procedural analgesia for burns dressings. It provides further motivation for the need for an alternative analgesia option.

Wall SL, Bangalee V. The ketamine crisis: Does South Africa have a plan B? S Afr Med J 2019; 109(12):911-913. doi: 10.7196/SAMJ.2019.v109i12.14188

Chapter 5: This chapter is presented in the form of a manuscript, submitted for publication, which assesses whether delayed referral to a burn service and inadequate analgesia from the time of a burn injury results in increased procedural analgesia requirements.

Wall SL, Clarke DL, Allorto NL. A comparison of analgesia requirements in children with burns: Do delayed referrals require higher procedural analgesia doses? Burn Open [Internet]. 2020;4 (3):103–9. Available from: https://doi.org/10.1016/j.burnso.2020.04.001

Chapter 6: This chapter is presented in the form of a manuscript, submitted for publication, which explores barriers to adequate analgesia in paediatric burns patients.

Wall SL, Clarke DL, Nauhaus HM, Allorto AL. Barriers to Adequate Analgesia in Paediatric Burns Patients. SAMJ. October 2020; 110(10):1032-1035.

Chapter 7: This chapter is presented in the form of a manuscript, submitted for publication, which investigates the use of an alternative analgesia option, Methoxyflurane, in a busy regional burn service outpatient clinic.

Wall SL, Clarke DL, Smith MTD, Allorto NL. Use of Methoxyflurane in a regional burn service outpatient clinic. SAJAA, Accepted for publication

Chapter 8: This chapter is presented in the form of a manuscript, submitted for publication, outlining the results of an expert consensus panel conducted to assess the analgesia protocol for paediatric burns patients developed from this PhD.

Wall SL, Allorto NL, Chetty V. Reaching consensus on an analgesia protocol for paediatric burn patients in a resource-scarce South African community. South African Journal of Family Practice. Manuscript under round 2 of review

Chapter 9: This concluding chapter presents a general synthesis of the results of this thesis. Limitations of the research are highlighted and recommendations for future research are offered.

1.2. BACKGROUND AND CONTEXT OF THIS RESEARCH

ANALGESIA IN PAEDIATRIC BURNS

Introduction

Burn injuries in developing countries are an endemic health issue.(5) Low- and middle-income countries (LMICs) account for 70% of burn-injuries and 90% of burn-related fatalities globally.(6)(5) The highest incidence of burns per capita world-wide, occurs in Africa.(7,8) Poverty, over-crowding and illiteracy all contribute to this public health dilemma in resource-poor environments. Lack of appropriately trained staff, appropriate equipment and resources all pose a major limitation on access to burn care in LMICs.(6)

The burden of burn injuries on sub-Saharan countries, especially amongst children, is huge. In children in the under-five age group, it is estimated that between 300 000 and 17.5 million children sustain burn-injuries annually in the region(9,10) The incidence of death from a burn in this age group in the WHO AFRO region is double that of children under 5 world-wide. It is estimated the 3.2% of the South African population will sustain a burn injury annually and 3200 of these patients require specialist burn care.(11,12) As is the case with the rest of Africa, there is little literature regarding the exact incidence of burn injuries in South Africa. This is likely due to the lack of national burn registries to collect accurate data. KwaZulu-Natal is no different and there are no studies published on the incidence of burn injuries in the province. A study in rural KwaZulu-Natal revealed that 70% of the burns occur in children under twelve years of age.(13) In a more urban setting, in Pietermaritzburg, 51% of burns admitted occur in children under three years of age.(14)

Pain is virtually synonymous with burn injuries. All children with burns experience pain, regardless of the cause, size or depth of the burn.(15) The course of their injury, treatment and recovery is fraught with anxiety and pain. Despite long-standing acknowledgement of the adverse sequelae of poorly controlled pain on children, inadequate pain control remains inadequate world-over.(15,16) Burn pain is exceptionally difficult to manage due its dynamic nature.(15) Burn-injury related factors, health practitioner-related factors and system-related factors all contribute to the challenge in managing burn pain.(17,18) There is a complex relationship between pain and anxiety in burns patients.(19) Anxiety is a major factor in escalating levels of pain in burns children; therefore, management of both pain and anxiety in burn-injured patients is paramount, as the one can perpetuate the other. (20,21) Non-compliance with treatment, resulting in delayed healing, can result from under-treated pain. (15) It has

long been recognised that inadequate pain control can have adverse physiological and emotional sequelae. However, pain control remains inadequate across the globe. (15,16,20,21) Burn pain is dynamic and needs to be constantly reassessed. There is great inter- and intra-individual response of burns patients to analgesic drugs.(22) Not only do different patients respond differently to analgesic drugs, but the same patient can respond differently to the same drugs depending on which phase of the hypermetabolic response to the burn that the patient is in.(23) This all culminates in the challenge of achieving adequate analgesia in burn-injured patients. It has been claimed that burn pain is the most complex to treat among all aetiologies of acute pain.(3)

In studies done in Kwa-Zulu Natal, it was demonstrated that less than 40% of doctors in district hospitals were administering procedural analgesia for dressing changes.(24) Another study in the same setting revealed that less than half of the doctors were prescribing the correct dosages of medications for background analgesia and that the burns patients were being under-dosed and, as such, receiving inadequate analgesia.(25) The management of pain in children in particular poses an even greater challenge due to a combination of factors. These include, but are not limited to, a lack of education on the management of pain and the management of burns, the inexperience of those prescribing the analgesia and those administering it, poor objective pain assessment and poor communication between the child, the family and the hospital staff.(26)(27)

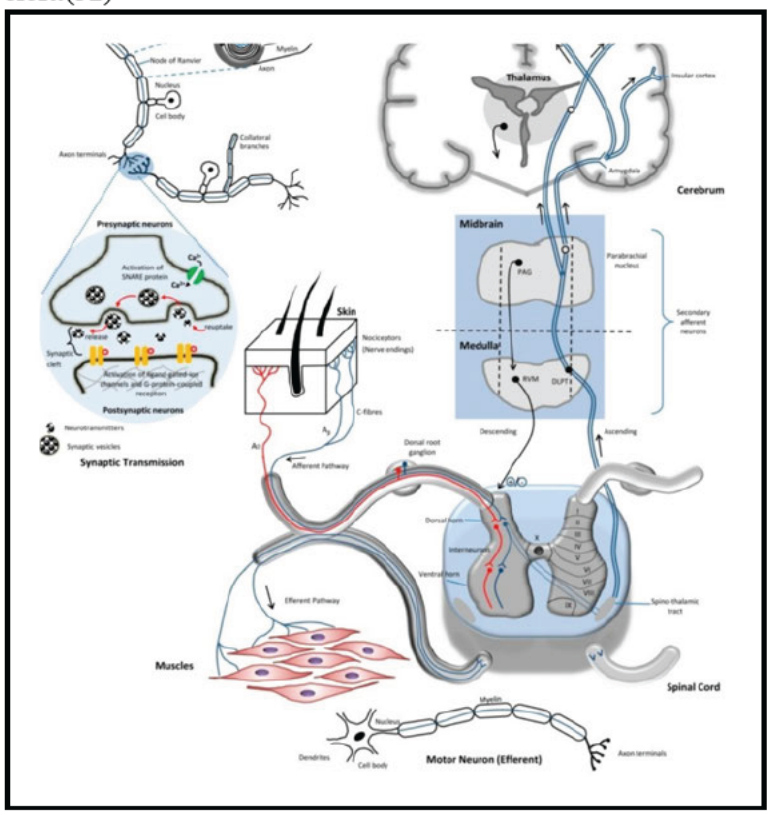
The Physiology of Burn Pain

Acute pain associated with acute burns and other tissue injury is transmitted by peripheral nociceptors. Peripheral nociceptors are the peripheral endings of primary sensory neurons. Their cell bodies are in the dorsal root of the spinal cord and trigeminal ganglia. Other sensory receptors in the skin contain specialised transducing structures; however, peripheral nociceptors do not, and they essentially exist as free nerve endings. (21) The basic pathways of the transmission of pain are depicted in figure 1.1.

There is a decrease in the threshold for subsequent excitation of spinal neurons following the intense barrage of incoming pain stimuli associated with a burn. This may also be associated with a greater response to subsequent stimuli and an expansion of receptive fields. (28) The increased pain sensitivity or ‘hyperalgesia’, which often follows a significant burn injury, is likely due to all of these adaptive changes. If the hyperalgesia is limited to the area of the injury, it is characterised as ‘primary’ hyperalgesia; and if it extends to areas adjacent to the burn injury, it is ‘secondary’

hyperalgesia. (29) It appears that sensitisation of both peripheral nociceptors and the spinal neurons is required for primary hyperalgesia, whereas sensitisation of the spinal neurons alone can result in secondary hyperalgesia.(30,31)

Figure 1.1: Basic pathways of the transmission of pain and the synaptic transmission in synaptic cleft.(32)



Local and systemic responses, including fever, anorexia and pain in the injured (primary hyperalgesia) and uninjured areas (secondary hyperalgesia), result from any large burn (>20% TBSA). Until recently, this sensation was thought to occur by the transmission of impulses via nerve impulses from the injured region to the spinal cord and the brain.(33) Other mechanisms have been suggested by more recent evidence. Acute pain is relieved well by drugs which silence sensory nerves. Drugs effective for acute pain are less effective once inflammation sets in. A rapid and long-lasting increase in the pro-inflammatory signalling molecule in the brain, especially interleukin-1B in the CSF, is caused by local inflammation at the site of the burn. The hypersensitivity to pain is strongly inhibited by blockers of interleukin 1B (e.g. COX-2 inhibitors). (33,34) The use of COX-2 inhibitors will have anti-inflammatory, antipyretic effects, but also anti-hyperalgesic effects, by acting on both local and central sites.(21)

Opioids act on the central nervous system to provide analgesia. Although postsynaptic inhibition of neurotransmitter release may occur, the principal result of activation of the opioid receptor is reduced neurotransmission, mainly by presynaptic inhibition of neurotransmitter release. Activation of descending antinociceptive pathways originating in the midbrain periaqueductal grey matter results in the analgesia which is caused by microinjection of opioids at various sites in the CNS. The transmission of nociceptive messages from the spinal cord is inhibited by this analgesia.(35) Profound analgesia, which can be effective in relief of burn pain, is produced by the injection of opiates at the spinal cord level. (21)

Some studies have demonstrated that nociception can occur, or be modulated, at the peripheral nerve terminal as well.(36) Opioid receptor-mediated analgesia manifests considerable plasticity. It is not a simple on-off phenomenon. The cell bodies of the nociceptors in the dorsal root ganglion synthesise opiate receptors. These are then transported both centrally and peripherally within the ganglions. (37) The release of endogenous ligands by immune cells infiltrating inflamed tissue results in peripheral activation of opioid receptors. (31,36) Injury can upregulate or activate the opioid receptors. This can either directly decrease neurotransmitters, or inhibit the release of excitatory neurotransmission such as substance P, and thereby modulate the perception of pain. (36,37) Some reports describe the use of peripheral opioids to treat inflammation-induced pain through the installation of small quantities of opiates locally, directly into the region of injury. This has not been tested for extensive burns, but has been found to be useful for localised burn pain. (38) The importance of the peripheral opioid receptors is confirmed by the finding that large doses of topical lignocaine significantly relieved burn pain. (39)

Acute administration of opioids can result in analgesia and side effects. However, tolerance and dependence typically develop after chronic administration. It has recently been recognised that tolerance can also develop acutely.(40) Acute tolerance can lead to hyperalgesia. The development of the hyperalgesic state and the transmission of signals interpreted as pain are triggered from the activation of N-methyl-D-aspartate (NMDA) receptors in the CNS after noxious stimuli. (41) Opioid-induced hyperalgesia can be prevented by the administration of the NMDA antagonist, ketamine. This also overcomes tolerance to analgesics.(42)

Methoxyflurane has been shown to be effective against burn pain. (43,44) Methoxyflurane increases gap junction closing times and decreases junction channel opening times thus inducing a reduction in

junctional conductance.(45) It increases the fluidity of the lipid membrane activating calcium dependent ATPase in the sarcoplasmic reticulum. Methoxyflurane binds to the glutamate receptor, the glycine receptor, the GABA receptor and the large conductance Ca^{2+} activated potassium channel.(45) It is the culmination of all of these that results in pain insensitivity and generalized muscle relaxation.(46)

Various studies from first world countries have compared the use of methoxyflurane and ketamine for minor procedures, including burns dressings. (44,47,48) Methoxyflurane was assessed to have many advantages over ketamine, namely, the fact that methoxyflurane can be self-administered and no IV access is required.(47,48) While ketamine is exceptionally effective, safe ketamine use requires monitoring and an extended recovery period, which can be challenging in a limited-resource setting with little or no monitoring equipment available. (49) Another challenge with ketamine is the prolonged recovery time.(48) This is a challenge in a setting where patients have to travel far for clinic or hospital visits and delayed recovery and ambulation may result in a challenge returning home post-procedure.

Complications of Pain

A massive sympathetic outflow mediated by the hypothalamus characterises the altered physiological condition which exists in a large burn of greater than 20% of the total body surface area. (50) An extreme surge in catecholamines; insulin; growth hormone; antidiuretic hormone; aldosterone; glucagon; thyroxine and interleukins are part of the neurohormonal response to burns and surgery. There is a direct correlation between the magnitude of the injury and the extent of the stress response. Increased morbidity and mortality are associated with higher plasma levels of stress response markers. (51,52)

An attempt to attenuate the physiologic impact of pain is made with the liberal use of narcotics and anxiolytics. By reducing the neuroendocrine activation of regulating hormones, the stress responses to trauma and surgery can be blunted. This can be achieved with sufficient doses of opioids.(53) The actual growth and architecture of the brain may be affected by significant stress-related neuroendocrine changes. This can have a lifelong impact on arousal and the processing of emotional stimuli. (54,55)

Over 50% of burn-injured children display some post-traumatic symptoms and as many as 25-33% eventually develop post-traumatic stress disorder (PTSD). Mood, anxiety, sleep, conduct, elimination, learning and attentional disorders may all develop in a child with burns. (56,57) If pain and anxiety are effectively managed, this can reduce the risk of developing PTSD. This is essential, as recent evidence suggests that once post-traumatic symptoms become persistent, they become refractory to treatment. (56)

Inadequate pain control can result in fear, which in turn leads to poor compliance with rehabilitation therapies. There is also an increased incidence of chronic pain.(58) In combination, the poor pain control and the psychosocial trauma of the pain itself may result in sleep disturbances. Lack of sleep causes further exacerbation of the pain. (58) There is an association between poorly controlled pain, sleep disturbances and poor wound healing (15,59,60)

Assessment of Pain

Pain is often exceptionally difficult to assess in children, particularly in younger children and infants who are not able to accurately verbalise their experiences. Analgesia needs to be continually reviewed as the pain experienced by children varies significantly. The combination of the difficulty children have in expressing their pain, and the difficulty that health care professionals have in interpreting the information conveyed by children, are the major contributing factors to poor pain control in children.(15)

The objectives of pain assessment are three-fold:

1. to detect the presence of pain;
2. to estimate the impact of this pain;
3. to determine the impact of interventions designed to relieve pain. (61)

Pain in infants and younger children is assessed using behavioural observations. In children over four years of age with sufficient cognitive and language abilities to be accurate, self-report measures can be used. A variety of scoring systems have been developed which link facial muscle movement, body movement (especially limb withdrawal to painful signals) and vocalisations, in particular crying, to a variety of emotional states, such as pain. (62–67)

Two widely used tools for assessing pain in children are the 'FLACC tool' and the 'Faces Ladder Scale'. Both are easy simple and easy to use.

FLACC Tool (Face, Legs, Activity, Cry and Consolability): This is a behaviour tool where the child should be observed for 2 – 5 minutes, taking note of the face, legs, activity, cry and consolability. The five categories should be assessed on a scale of 0 – 2 and the overall score will be 0 – 10. (68,69) Kochman et al. have validated the FLACC tool as an appropriate tool to assess acute pain in children between the ages of six months and five years. (70)

Faces/Ladder Scale: The Wong-Baker FACES Pain Rating Scale is recommended for children over three years of age. (71) The child should be made to understand that the smiling face means no pain and the distressed face indicates severe pain. The child should then indicate where on the scale they are experiencing pain.

The COMFORT behaviour scale (COMFORT-B) is a scoring system adapted from the original COMFORT scale. The original COMFORT scale was developed and validated for use in the intensive care setting for ventilated children between the ages of birth and 18 years.(72) It was developed for use in the intensive care unit and is a measure of physiological and behavioural domains.(72) The scale was adapted to make it applicable to non-ventilated patients by the addition of the item 'crying'. The adapted scale was named the 'COMFORT Behaviour Scale', or the 'COMFORT-B Scale". (73) The validity and reliability of the COMFORT-B Scale has been tested in burn-injured children under the age of five years and was found to be a clinically useful pain scoring system. (74)

Table 1: Comparison between FLACC Score, COMFORT-B Score and Wong-Baker FACES Pain-rating Scale (75)

Pain Scale	Score Type	Age group	Scoring	How to Score	Clinical Utility	Validated Uses
FLACC Score(68)	Behavioural scale	2 months – 7 years	0-10	5 categories including: facial expression, leg movement,	Simple, quick, no assessment of	Procedural pain; Post op pain, ventilated and non-ventilated critical care

				activity, cry, and consolability. Score of 0-2 assigned to non-verbal signs in each category	physiological variables.	paediatric patients
COMFORT-B Score(72–74)	Behavioural scale	2 months to 3years	6-30	6 categories including: alertness, calmness, respiratory response (for vented children) or cry(for spontaneously breathing children), physical movements, facial tension, and muscle tone. Must observe the patient for 2 full minutes and then scored 1 to 5 in each category	More laborious to perform	Critically ill children ages 0 to 10 years for pain Tested for use of assessment of sedation in critically ill children ages 0 to 16

Wong-Baker FACES Pain Rating Scale(76)	Self-report Scale	3 years and older	1-10	There is a chart with a face at each even number with facial expressions ranging from least painful to most painful and child is asked to choose which face corresponds to how they are feeling.	Easy and quick.	Pain in children 3 and up.

Management of Burn Pain

The pain which burn-injured patients experience can be divided into three categories:

1. background pain;
2. procedural pain; and
3. chronic/neuropathic pain

It is important to recognise that patients will need different analgesia strategies to deal with each of these three categories of pain. The management of pain should be presumptive and pre-emptive. (15) Physical, emotional and family distress can all be reduced by both pharmacological and psychological pain-relieving interventions. A multidisciplinary team can help to integrate the pharmacological and non-pharmacological modalities of pain management.(15)

Regular analgesia, given at the correct dose and correct intervals, can manage background pain well. Procedural pain may be more complex to manage as it is difficult to assess and, as such, is frequently under-treated. Procedural pain requires more intense analgesia. Anticipatory anxiety before future procedures and a lower pain tolerance threshold can result from poor pain management. (15) This is

known as wind-up pain, and patients who have received inadequate analgesia during initial procedures may require higher doses of analgesia than would otherwise have been needed.

Chronic pain is not well understood, and the causes are often multi-factorial. Neuropathic pain is one cause of chronic pain. Nerve damage, abnormalities in nerve regeneration and reprogramming of the central nervous system may all contribute to neuropathic pain. (77) Chronic pain can be challenging to manage as conventional treatment modalities are often ineffective. For sympathetically mediated pain, adjuvant treatment such as clonidine and anticonvulsants are often effective. Psychological intervention to promote better coping strategies should also be employed.(15)

Lack of Burn Care Training

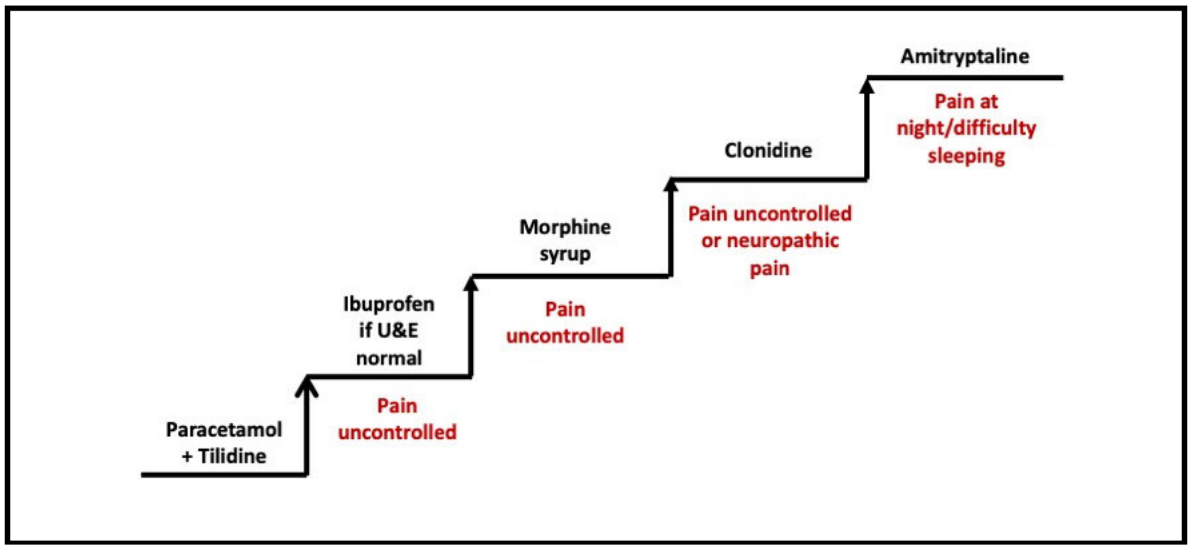
Historically, both undergraduate and postgraduate medical training programmes have placed a low educational emphasis on pain management.(27) There is an even greater deficit in burn training in undergraduate and post-graduate training, which places burn-injured patients at an even greater disadvantage. (17,78) This inadequate education in burns and pain management culminates in healthcare professionals who are managing patients with severe pain, yet lacking the appropriate knowledge, training and skills to effectively and adequately manage pain in burn-injured patients .

Analgesia the PMB Way

The PBS manages pain by means of an analgesia protocol which forms part of the burns protocols called “Burn Care: The PMB Way”. This protocol was developed in collaboration with burn surgeons and aneasthetists to make it safe for use by healthcare professionals with limited experience managing burns patients. It took into consideration local availability of drugs and the limited monitoring equipment.

Background analgesia for children is prescribed in a stepwise fashion. Initially, patients are given paracetamol and tilidine. If the renal function is normal and pain remains inadequately controlled, ibuprofen is added. Should the pain remain uncontrolled, oral morphine is added. Clonidine is then added of pain control is still inadequate or if there is neuropathic pain. If patients are experiencing pain at night or are having difficulty sleeping at night, amitryptalline is prescribed. This is summarized in Figure 2.

Figure 1.2: Stepwise escalation of analgesia: The PMB way



The cornerstone of the analgesia protocol for procedural sedation has always been ketamine. In the wards, ketamine for dressing changes is administered orally. The patients are given the oral ketamine in conjunction with midazolam 30 minutes prior to dressing changes. Should the patient still be in pain, the patient is given half of the oral ketamine done intramuscularly and at the next dressing, the initial dose and the additional ketamine dose is prescribed as the first analgesia dose. In the outpatient clinic, due to the need for a more rapid onset of the procedural analgesia, ketamine is given intramuscularly. Due to intermittent shortages of ketamine, the long recovery time, which is not ideal in an outpatient setting and the fact that safe administration of ketamine requires monitoring, which is not always available in our setting, we sought an alternative option for procedural analgesia for dressing changes.

The "Burn Care: The PMB Way" protocols are freely available, and their use is promoted in all hospitals referring to the PBS. The uptake of these protocols is variable. We endeavour to improve not only the protocols themselves but the uptake of the protocols as well.

Conclusion

Burn pain is experienced differently by each child. Constant reassessment of pain and adjustment of analgesia strategies is vital to achieve adequate analgesia. It must be recognised that background pain, procedure pain and chronic pain are separate entities and must be managed individually. Suboptimal pain management can result in multiple complications, which can potentially be avoided by addressing pain and anxiety from the time of the burn injury. A multidisciplinary team to integrate both pharmacological and nonpharmacological modalities of pain management is invaluable in the

management of burn pain and anxiety. There is a relative paucity of locally relevant data on analgesia in the paediatric burn population in South Africa. This study aims to identify obstacles to burn injured children receiving adequate analgesia in South Africa. The knowledge acquired can then be used to address these obstacles and ultimately improve the pain management of this group of children.

1.3. PROBLEM STATEMENT

Pre-existing work done in western KwaZulu-Natal has identified that there are gaps in the care and management of burn-injured patients. These gaps include:

1. lack of capacity to manage burns patients at regional level resulting in overwhelmed tertiary level services (79,80)
2. lack of management and analgesia protocols in many centres managing burns (80)(81)
3. lack of dedicated dressing area (80)

The causes of these deficits are multifactorial. However, systematic failures contribute significantly. Frequently, peripheral hospitals are unaware of the protocols which do exist and fail to implement existing protocols. Pain resulting from inadequate analgesia is an indicator of a systems failure in the management of these patients. This study aims to identify the obstacles which prevent burns patients from receiving adequate analgesia and to use this information to drive quality improvement programmes designed to address these deficits in pain management.

1.4. RESEARCH QUESTION

What is a feasible approach to optimise pain management for burn-injured children in KwaZulu-Natal (KZN)?

1.5. RESEARCH AIM AND OBJECTIVES

Aim: To determine a feasible pain management protocol for burn-injured children in KwaZulu-Natal (KZN)

Objectives:

1. to identify deficits in the knowledge of doctors working in western KwaZulu-Natal in terms of prescribing procedural sedation for children with burns over a six-month period;
2. to compare the procedural analgesia requirements of children presenting with burns at the Pietermaritzburg Burn Service acutely, versus those with a delayed referral, for a one-year period from 1 July 2018 to 30 June 2019;

3. to evaluate obstacles to patients getting adequate analgesia in terms of healthcare practitioner-related factors, system-related factors and burn-related factors, from December 2018 to May 2019.
4. to evaluate the use of an alternative analgesic agent, Methoxyflurane, for pain management during dressing changes in an outpatient burn clinic in a regional hospital in KwaZulu-Natal over a two-month period from January to February 2019; and
5. to gain expert consensus on a feasible analgesia protocol for burn-injured children through a modified Delphi survey.

1.6 CONCEPTUAL OVERVIEW

This study aimed to provide an alternative approach to provide improved pain control in burn-injured children in KwaZulu-Natal. Pain management in burn injured patients is exceptionally challenging. There is a complex interplay of numerous factors which all contribute to children with burn injuries receiving inadequate analgesia in KwaZulu-Natal. Achieving adequate analgesia in paediatric burns patients requires the identification of obstacles to these patients achieving inadequate analgesia in the first place. Figure .1 reflects the intersection of these obstacles in a problem analysis.

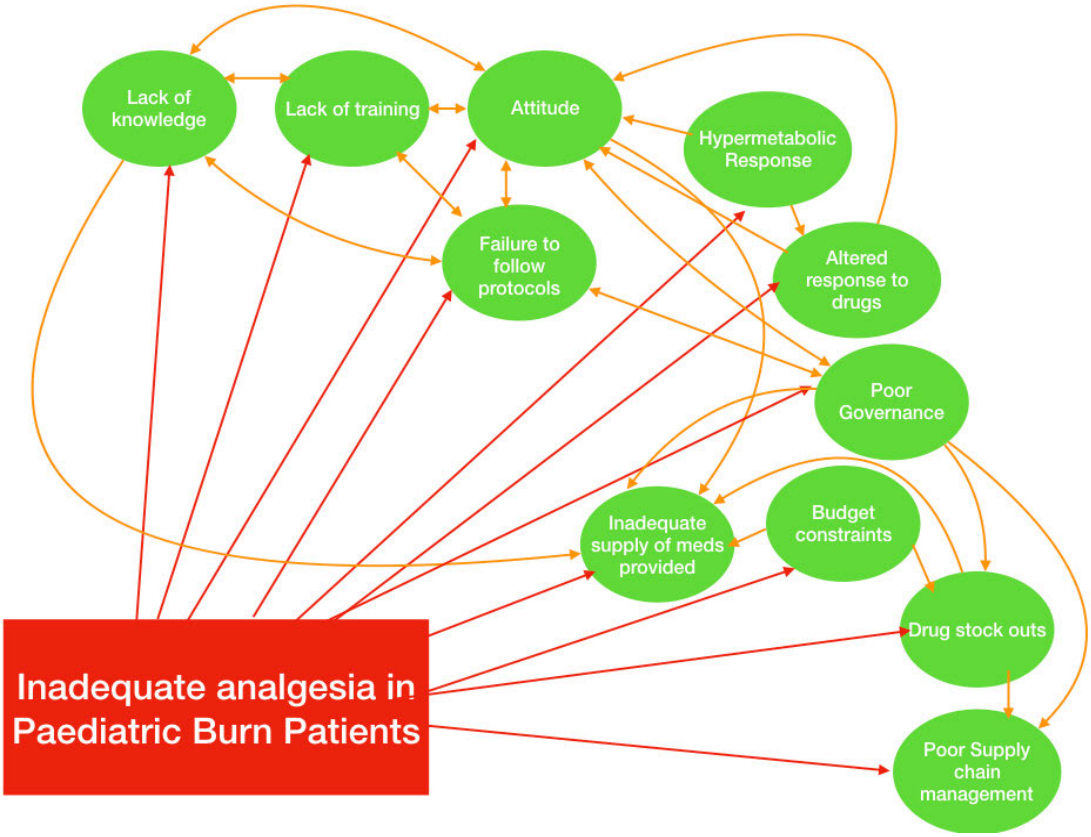
Factors contributing to inadequate analgesia can broadly be categorised into:

1. Healthcare practitioner-related factors
2. System-related factors
3. Burn-injury related factors.

A lack of knowledge and training on the part of healthcare practitioners results in an attitude that burn injuries are ‘just painful’.(82) This then results in failure to follow analgesia protocols. The hypermetabolic response results in altered responses to drugs, including analgesia.(82) A lack of understanding of the impact of the hypermetabolic response and the impact on the pharmacodynamics and pharmacokinetics of analgesics further compounds the interpretation of doctors that burn injuries are ‘just painful’, as patients do not respond in the same manner as non-burned patients to all analgesic drugs. There is, regularly, an inadequate supply of analgesia medication due to incorrect prescribing of medication; due to a lack of knowledge of analgesia in burns on the part of the doctor and; even when medication is correctly prescribed, due to budget constraints, there are frequently drug stock-outs; or inadequate volumes of drugs are supplied to patients in order to supply more

patients with at least some analgesia, as opposed to some getting adequate volumes and other patients receiving no analgesia at all due to limited stock.(18)

Figure 1.3: Problem analysis of reasons for inadequate analgesia in paediatric burns patients.



The intersection of the factors influencing the inadequate analgesia in children with burn injuries were considered in the conceptual framework for this study. Figure 2.2 shows the conceptual framework that was used in the development of this study.

Burn-injury related factors that contribute to inadequate analgesia include the hypermetabolic response to the burn. The resultant altered pharmacodynamic and pharmacokinetic responses to drugs, including analgesics, influence the efficacy of analgesic drugs in these patients.(82) The hypermetabolic response and altered response to drugs is not a modifiable factor in improving

analgesia in paediatric burns patients. Improving doctors' knowledge regarding these altered drug reactions, however, is modifiable, and this would result in different prescribing practices in terms of analgesia, which will result in improved pain control for burn-injured patients.

A low educational emphasis is placed on pain management in both undergraduate and postgraduate training.(27) There is an even greater deficit in the training of burns treatment at all levels.(17,78) This lack of training and knowledge in analgesia, in particular in burns, results in doctors prescribing inadequate analgesia for burn-injured children, which we demonstrated in this study.(24) There is a common misconception that burn injuries 'are just painful'. There is an expectation that burn pain during dressing changes in not controllable. (82) This contributes to less of an attempt being made to control pain as the healthcare workers exist in a culture where burn patients in pain is acceptable and even expected.

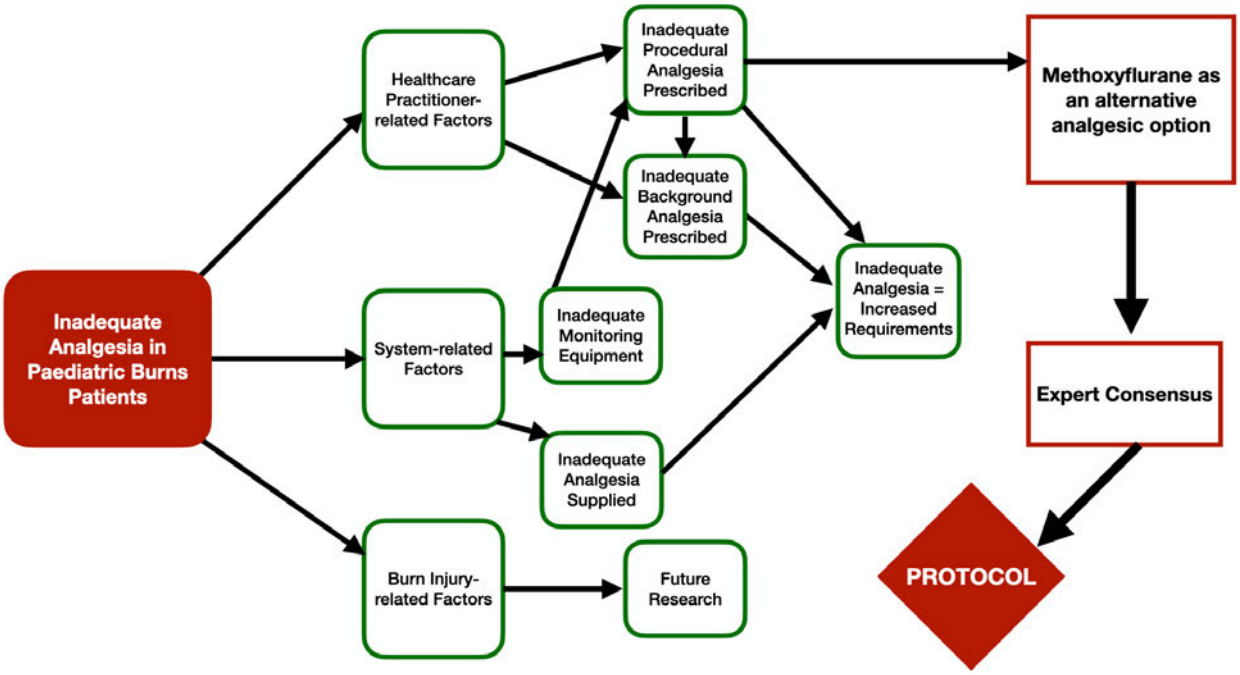


Figure 1.4: A conceptual framework for obstacles to adequate analgesia in paediatric burns patients

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Inadequate analgesia can have negative physiological and emotional sequelae. The development of anxiety, wind-up, allodynia and hyperalgesia is a consequence of inadequate analgesia.(83) This study demonstrated that patients who receive inadequate analgesia from the time of their injury, require much higher doses of analgesia than patients who receive adequate analgesia from the outset. This difference is statistically significant.(84)

There are numerous system-related factors which contribute to inadequate analgesia provision for paediatric burns patients. Through the development of the 'PMB Way Burns Protocols'- which include analgesia protocols, and strict adherence to these protocols, we have developed a culture that does not accept children in pain. These protocols dictate the analgesia that is prescribed to patients. This study has demonstrated that there is a statistically significant difference ($p<001$) between the volume of paracetamol and ibuprofen prescribed and the volume supplied to patients to take home.(25) The result of this is that the patient's medication is depleted before their next appointment at the hospital. These interruptions in adequate analgesia can result in neuropathic pain and complex pain syndromes.

The reasons for the inadequate supply of analgesia are multifactorial. Contributing factors are drug stock-outs, budget constraints and possibly also a lack of knowledge on the part of the pharmacist regarding the importance of analgesia in these patients, even after discharge and acute management.

The obstacles to achieving adequate analgesia in paediatric burns patients are numerous. Many doctors in the peripheral hospitals were uncomfortable using ketamine as a procedural analgesic. This may be in part due to the fact that only 8% of them were aware of the correct dose of Ketamine. (24) This, combined with the fact that hospitals in our setting seldom have monitoring equipment to be used following Ketamine administration, which also makes doctors reluctant to use it, and the current international Ketamine shortage. Ketamine is also not without side effects despite life threatening adverse events being exceptionally rare.(85) Vomiting, agitation, hypoxia and apnoea have all been well described with ketamine use.(85) We endeavoured to find an alternative analgesic agent for dressing changes in our setting which was effective but required minimal or no monitoring. While other options are available such as fentanyl, midazolam, propofol or combinations of these, they all posed similar concerns as ketamine. For rapid onset of action administration was via intramuscular or intravenous route, which was still painful for burn-injured children who were already traumatized by their burn itself, they required monitoring to be administered safely and availability of these drugs in our setting was also a concern. This was the motivation to trial Methoxyflurane. The use of methoxyflurane for burns dressings in the outpatient clinic results in the avoidance of ketamine and the risk of these side effects.

Methoxyflurane is not a new drug, it has been used for procedural analgesia since the 1960s.(86) It has been prescribed for burns dressings in children since the 1970s.(87–91) Methoxyflurane has been found, by various authors to be efficacious in this population.(88–92) Methoxyflurane has various other advantages besides it's analgesic properties. It has been demonstrated to have mood-modifying effects, retrograde amnesia, minimal sedation, lack of the need for a painful intramuscular or intravenous injection and lack of the need for starvation prior to administration. There was a concern regarding renal dysfunction and methoxyflurane use however, there was no evidence of methoxyflurane-induced renal toxicity, either clinical or biochemical when used for procedural analgesia at low doses for a short duration. (43,93,94) Multiple exposures of methoxyflurane have not been shown to have any adverse effects. (88–91) There is a paucity of literature on the use of Methoxyflurane in burn-injured children in our setting.

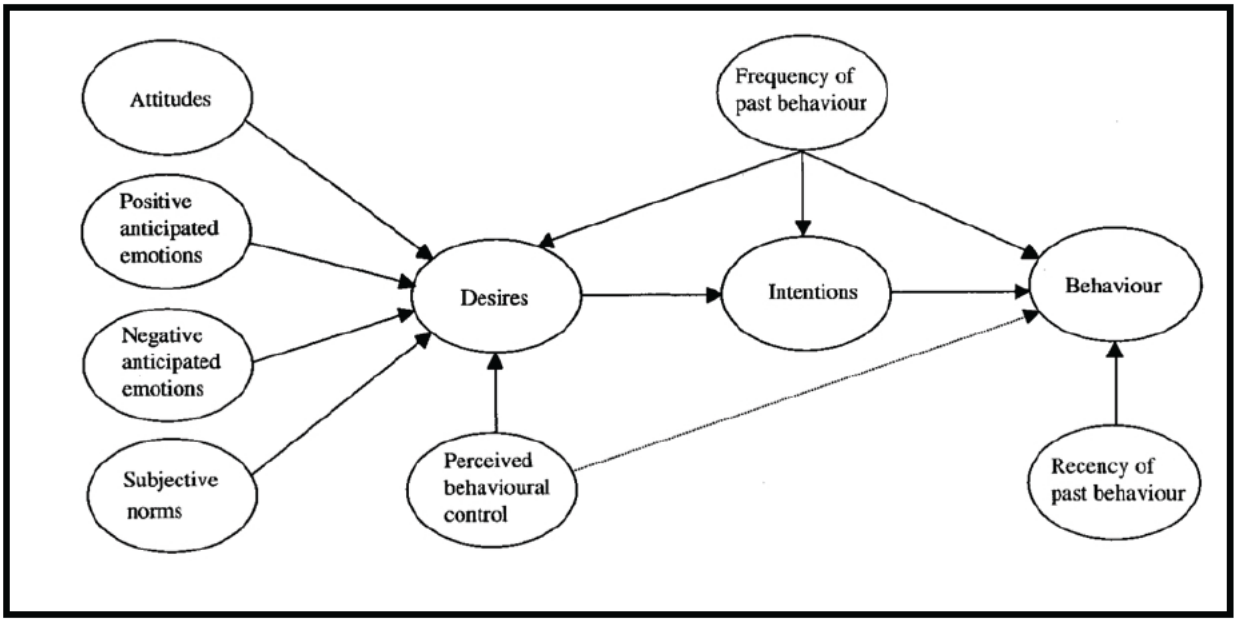
Methoxyflurane was added to our outpatient analgesia protocol. It proved to provide adequate analgesia for dressing changes in 60% of children presenting to the burns outpatient clinic. Methoxyflurane was added to the analgesia protocols which form part of the 'PMB Way Burns

Protocols'. An expert consensus was conducted in the form of a modified Delphi survey. Experts agreed that Methoxyflurane should be included in the analgesia protocol as part of procedural analgesia for burn dressings in both the inpatient and outpatient settings.(25)

1.7 THEORETICAL FRAMEWORK

The model of goal-directed behaviour is the theoretical framework which underpinned this research. (95) This model is an extension of the theory of planned behaviour.(96) This model suggests that the frequency of past behaviour is a predictor of desires, intentions and behaviours. The recency of past behaviour is a predictor of behaviour alone. It also speaks to attitude and emotions playing a role in desires, and consequently in intention, and subsequently in behaviour. This model can be seen in Figure 2.3.

Figure 1.5: The Model of Goal-Directed Behaviour



Healthcare practitioners' attitudes and previous negative experiences with burns patients greatly influence their likelihood of prescribing analgesia and their assessment of the adequacy of analgesia. The attitude that burn pain during dressings is not controllable affects doctors' prescribing practices of analgesia.[1] In many healthcare institutions, due to the fact that children have their dressings changes

with inadequate analgesia, these children scream for the duration of the dressing change. Negative experiences, such as children screaming in pain with every dressing change, is more likely to drive doctors to avoid burns dressings. It promotes the practices of doctors prescribing an initial dose of analgesia and then leaving the ward, with no assessment of the adequacy of the analgesia, and no additional analgesia doses should adequate analgesia not have been achieved. The misconception that burns 'are just painful' influences the doctors' intention to provide adequate analgesia as they are expecting that the patients are going to be in pain. The more frequently burns dressings are changed with inadequate analgesia, the faster inadequate pain control becomes the norm.

Instilling a culture of adequate analgesia, where a child screaming in pain during dressing changes is considered unacceptable, will promote burns dressings in a more positive light. The children will not be screaming in pain. The doctors will be more likely to ensure adequate analgesia for all future dressings. Their desire will be to have pain-free children. Their intention will be to provide sufficient analgesia to avoid the child screaming in pain.

CHAPTER 2

METHODOLOGY

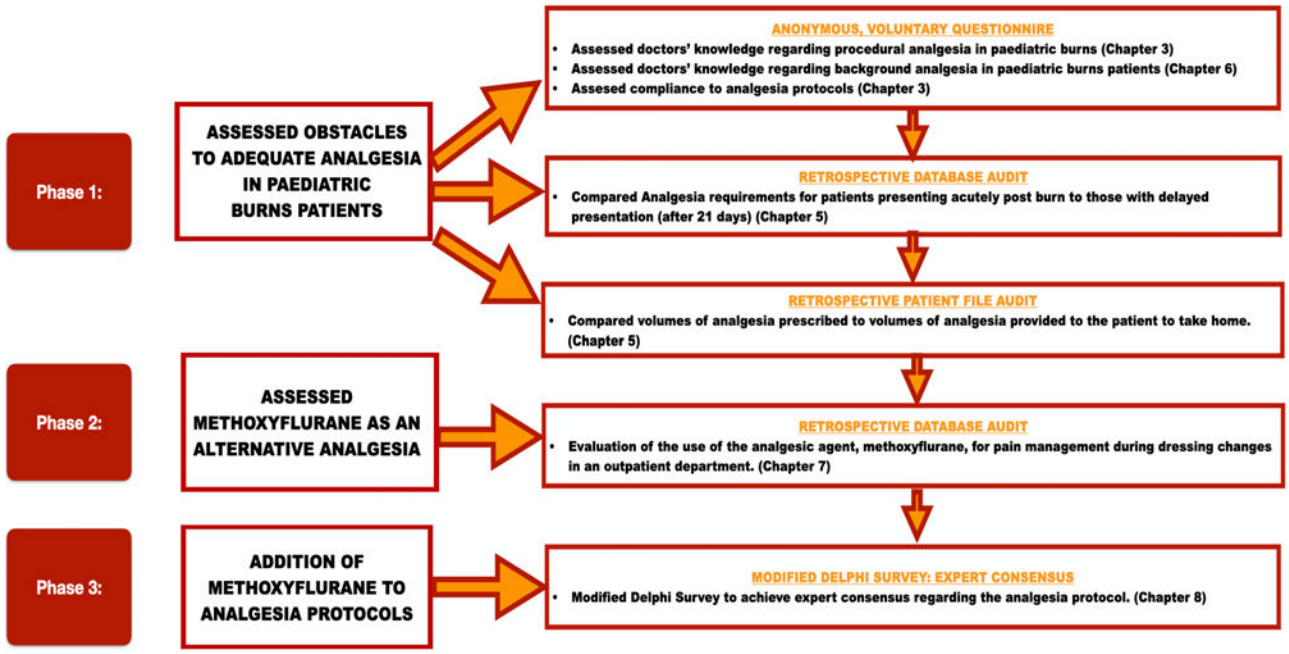
2.1 INTRODUCTION

The methodology of each stage of the research is summarised and the methodological approach, framed by a positivist view, will be described in this chapter.

2.2 OVERVIEW OF METHODS

This study was conducted using quantitative methods. An overview of the methods is given in Figure 2.4. The phases of the study are described below and are further described in more detail in each chapter.

Figure 2.1: Overview of Methods



Phase 1: The first phase of this study was identifying obstacles to adequate analgesia in paediatric burns patients. This was done in three stages.

Phase 1.1: An anonymous, voluntary questionnaire.

This phase of the study was conducted through an anonymous, voluntary questionnaire. All medical officers and registrars working in the PBS, and all of the doctors working in the referral district hospitals who were encountered during outreach visits, were invited to complete the questionnaire. Questions relevant to the analgesia protocol and questions thought to be relevant to testing knowledge of analgesia for burns dressings were included in the questionnaire. The intention was to highlight practical knowledge or lack thereof. Information regarding demographics, including the level of hospital where the doctor worked and the number of years' experience working as a doctor was collected. The questionnaire also evaluated the use of procedural analgesia, including drugs, dosages and the assessment of the adequacy of analgesia. Information regarding background analgesia, such as choice and frequency of drugs, was also collected. The questionnaire is included as Appendix 3.

Phase 1.2: A retrospective database analysis

Data regarding the total Ketamine dose for the duration of the patient's admission is routinely collected as part of the burns database. Data for children under the age of 12 years admitted to the PBS for a one-year period was reviewed. Age, admission weight, total ketamine dose and route of Ketamine administration were analysed. Days admitted were calculated from the date of admission and the date of discharge. Delay from the time of the burn to admission was calculated from the date and time of admission. Children admitted to the paediatric intensive care unit at any time during their stay, or those who demised, were excluded from the study. Children with missing data on the database were also excluded.

These patients were divided into two groups: those referred to the PBS early (prior to 21 days post-burn) and delayed referral (those referred 21 days or more post burn). The total ketamine use in mg/kg was compared between the two groups, taking number of days admitted and the total body surface area (TBSA) of the burn into account during the statistical analysis.

Phase 1.3: A retrospective patient file audit

An audit of the outpatient folders of children attending the burns clinic for a two-month period was conducted. Prescribing information such as drugs prescribed, dosage, drug frequency, duration of the prescription for analgesia and the volume of the analgesia medication supplied to the patient was recorded. The difference between the volume prescribed and the volume of medication supplied to the patients was calculated and statistical analysis was then performed on this data.

Phase 2: A retrospective database review

Data during dressing changes are routinely recorded as part of the burns registry. A retrospective review of data for a two-month period was undertaken, after the addition of Methoxyflurane as the first line analgesia option for use in the paediatric outpatient clinic. All children under the age of 12 years were included in the study. Methoxyflurane was administered at a concentration of 0.2-0.4% with a soft silicone mask for all dressing changes. The adequacy of analgesia was assessed using the Face, Limbs, Activity, Cry, Consolibility (FLACC score). Ketamine had been administered at 5mg\kg intramuscularly if the child refused the mask, thereby preventing administration of the Methoxyflurane; or if Methoxyflurane was not achieving adequate analgesia (FLACC scale score of 3 or more)

Phase 3: Introduction of Methoxyflurane into the 'PMB Way' analgesia protocols

Phase 2 of this study demonstrated that Methoxyflurane is a viable alternative analgesia option and can form a useful addition to the analgesia armamentarium of a doctor managing burns. As a result of this, Methoxyflurane was added to our analgesia protocols. The protocol was then subjected to a consensus study in the form of a modified Delphi survey to achieve consensus from experts in the field of burn management in LMIC's.

2.3 ETHICAL CONSIDERATIONS

The study protocol received full ethical clearance from the University of KwaZulu-Natal, South Africa, (BREC Reference: BE594/18) [Appendix 2]. All studies were individually detailed in the single ethics clearance application for the PhD study. All patients presenting to the Pietermaritzburg Burn Service sign consent for their data to be collected on the burns registry. The burns registry has class approval granted by the Biomedical Research and Ethics Committee, University of KwaZulu

Natal (BCA106/14), which is renewed annually. Parents or guardians sign consent on behalf of minors for the burns registry.

2.4 STUDY SETTINGS

This study was conducted within the Pietermaritzburg Burn Service (PBS). The PBS is managed by two burns surgeons and operates across the regional (Edendale Hospital) and tertiary (Greys Hospital) hospitals in Pietermaritzburg. There are 40 dedicated burns beds across the metropolitan area. Thirty of these, including six high care beds, are at Edendale Hospital; and ten of these beds are at Greys Hospital. The PBS provides support to 19 district hospitals in the western third of KwaZulu-Natal Province. Annually, the patient load consists of 500 - 600 patients who are managed as inpatients, and a further 500 patients who are managed exclusively as outpatients.

2.5 RECRUITMENT AND SELECTION OF PARTICIPANTS

Phase 1.1

All doctors encountered during outreach visits and all those working in the Pietermaritzburg Department of Surgery were invited to complete a voluntary, anonymous questionnaire regarding their experience and knowledge of analgesia in paediatric burns patients.

Phase 1.2:

As part of the burns database, data regarding the total Ketamine dose for the duration of the patient's admission was routinely collected. Data from all children under 12 years was collected for a one-year period and total Ketamine doses were compared. The total Ketamine use was recorded in mg/kg/ %TBSA (milligrams per kilogram per percentage of total body surface area burn), which allowed for a comparison of the analgesic requirements of patients with acute burns, as opposed to those with a delayed presentation.

Phase 1.3:

A retrospective chart review of all children presenting to the outpatient clinic for a two-month period was done. The prescribed volume of the analgesia was compared to the actual volume provided to the patient to take home.

Phase 2:

Data regarding dressing changes was routinely collected as part of the burns database. Information recorded included patient demographics, details of the burn injury and wound, medication administered, and pain and anxiety responses. The study used data from all children presenting to the outpatient clinic for a two-month period, to evaluate the efficacy of an alternative analgesic agent, Methoxyflurane.

Phase 3:

Methoxyflurane was added to the paediatric burns analgesia protocol and a two-round modified Delphi survey was conducted to achieve consensus regarding the protocol.

2.6 DATA ANALYSIS

The statistical analysis is briefly described below and is described in more detail in each chapter.

Phase 1.1:

Descriptive statistics were used to describe the information collected. Where applicable, Chi-Square tests were used to compare the category variables.

Phase 1.2:

A Mann-Whitney-Wilcoxon test was conducted to compare the acute referral and the delayed referral groups. A Fisher's exact test was then conducted to determine whether the total Ketamine dose (mg/kg/days admitted/TBSA) was affected by the mechanism of injury. A Fisher's exact test was also conducted to assess whether TBSA played a role in the total Ketamine dose (mg/kg/days admitted/TBSA).

Phase 1.3:

A Wilcoxon signed-rank test was used to compare the volume of analgesia prescribed to the volume of analgesia supplied.

Phase 2:

Descriptive statistics were used to describe the information collected.

Phase 3:

An expert panel of doctors managing burn injuries in LMICs engaged through a modified Delphi survey. The survey tool was developed using the analgesia protocol. The information sheet and first round questionnaire are included as Appendix 3. Consensus was determined by an a priori threshold of 80% of agreement on analgesia protocol. This was repeated until consensus was reached.

2.7 CONCLUSION

This study was conducted using a quantitative methodology. The theoretical framework which underpinned this research was that of the goal-directed behaviour model. This study was conducted in three main phases which were derived from the conceptual framework of this study.

CHAPTER 3
IDENTIFICATION OF DEFICITS IN DOCTORS' KNOWLEDGE

3.1 SUMMARY

This chapter is presented in the form of a published study, presenting and discussing the results of a questionnaire conducted to demonstrate the lack of knowledge of doctors regarding procedural analgesia for burns dressings for paediatric burns patients and the lack of compliance with protocols by doctors in the referral hospitals. This was central to this PhD research as it demonstrated that a lack of knowledge on the part of the doctors managing these patients in the peripheral hospitals, with regards to procedural analgesia for paediatric burn-injured patients, and a lack of adherence to protocols, each present an obstacle to adequate analgesia in paediatric burns patients. The authors identified a discrepancy in knowledge between staff in an academic burns centre and those in peripheral referral hospitals and recommend that ongoing efforts are directed toward changing the culture of district institutions and strengthening attempts to standardise care across the region.

3.2 PUBLICATION DETAILS

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DOI Number	10.1016/j.burns.2019.04.012

3.3 JOURNAL DETAILS

Burns is a peer-review journal. Burns focuses on the clinical, scientific and social aspects of burn injuries. The journal covers the prevention of the injury, the epidemiology of burns, and all aspects of treatment, including the development of new techniques and the verification of existing ones. Regular features include clinical and scientific papers, state of the art reviews and descriptions of burn-care in practice. It is a SCOPUS-listed journal with an impact factor of 2.247 (2018 Journal Citation Reports – Clarivate Analytics, 2019)

3.4 PUBLICATION TIMELINE

The first draft of this article was submitted to Burns on 23 December 2018. Reviewers' and editorial feedback was received on the 30 January 2019 and 4 April 2019; with all comments and queries responded to on the 14 March 2019 and 6 April 2019. The final manuscript was accepted and slated for publication on 11 April 2019 and was published online on 21 June 2019 and published in print in November 2019.

3.5 CONTRIBUTION DETAILS

The candidate conceptualised, developed and wrote the paper. Professor Clarke and Dr Allorto provided assistance with the conceptualisation of the paper and contributed significant editing of the draft and final manuscript. The statistical analysis was also done by the candidate.

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Analgesia protocols for burns dressings: Challenges with implementation

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ABSTRACT

Background: The aim of this study is to compare doctors' knowledge regarding analgesia in paediatric burns patients in a setting where analgesia protocols are provided but not reinforced to a setting where the same protocols are used but with constant re enforcement from burns surgeons.

Methods: We reviewed questionnaires completed anonymously by doctors managing burns children in the Pietermaritzburg (PMB) Hospital Complex and the referral hospitals.

Results: The questionnaire was completed by 43 doctors with 53% of the participants working in the referral hospitals. Procedural sedation was given by 98% of doctors. All PMB doctors giving procedural sedation used ketamine compared to 39% in the referral hospitals, which was statistically significant ($\chi 2 = 18.237$; $p < 0.001$). Eighty percent of PMB doctors were aware of the correct doses of ketamine and compared to 8% of referral doctors. This was statistically significant ($\chi 2 = 21.778$; $p < 0.001$). When assessing the adequacy of analgesia, all of the doctors from PMB used a scoring system or clinical impression. In the referral doctor group, 54% used a scoring system, 38% used the child screaming as an indicator of inadequate analgesia.

Conclusion: We have identified a discrepancy in knowledge between staff in an academic burn centre and those in peripheral referral hospitals. This discrepancy translates into differences in quality of burn analgesia which patients receive. Ongoing efforts must be directed towards changing the culture of district institution and strengthening attempts to standardize care across the region.

1. Introduction

Pain is virtually synonymous with burn injuries and all children with a burn will experience pain, regardless of the cause, size or depth of the burn [1]. Pain control remains inadequate globally, despite the longstanding recognition that inadequate pain control can have adverse physiological and emotional sequelae on children [1 4]. There is little in the literature on analgesia in paediatric burns patients in South Africa. Although specialist burn services in South Africa generally use analgesia protocols, the management of pain in district hospitals is less well structured. Inadequate training in the management of burn related pain, combined with a poor understanding of how the hypermetabolic response alters pharmacodynamics suggests that the quality of care of burns patients is heterogenous and may vary according to the level of hospital.

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0305 4179/

In South Africa, patients with burns which would be referred to specialist centers in high income countries, are often managed at district level institutions by junior and or inexperienced staff. In light of this the Pietermaritzburg Burn Service (PBS) has developed analgesia protocols to standardize and facilitate care in both the district and referral institutions. The protocol was developed by a team of surgeons and anaesthetists with extensive local knowledge regarding drug availability as well as clinical experience with burn dressing changes. The doctors in the referral hospitals are either junior or if they are senior lack training in burns. The PBS protocol was intended to be safe and practical as dressing changes are done in wards and out patient clinics with little to no electronic monitoring. Ketamine has a proven track record in terms of safety in our setting and is readily available. The protocol was implemented in the PBS and distributed to all district hospitals referring to the PBS. This project focuses on the success of implementation of the protocol and aims to identify and quantify any discrepancy in the quality of burn care between patients in the two different settings.

Clinical guidelines or protocols have become prominent in clinical practice over the past three decades [5]. Protocols, can benefit both patients and health care providers in the sense that they improve health outcomes, and promote distributive justice by advocating for improved service delivery and highlighting under recognized and marginalized health prob lems and clinical services. In addition, they provide clinical decision support to health care workers by providing firm recommendations and guidance to inexperienced clinicians [5,6]. Protocols promote standardization of care and this is especially relevant in conditions where direct supervision by senior clinicians is not possible. There are limitations to protocols and these revolve around the impact the inherent biases and clinical experience of the group developing the guidelines, have on the recommendations [7]. In addition the inappropriate application of protocols by inexperienced staff may be problematic. Protocols can be exceptionally useful to inexperienced healthcare professionals.

2. Methodology

The Pietermaritzburg Burn Service (PBS) operates across the regional (Edendale Hospital) and Tertiary (Greys Hospital) Hospitals in Pietermaritzburg. The Burn Service consists of two burns surgeons who have access to 40 beds in the metropolitan dedicated to burns patients. Thirty of these beds, with six high care beds are at Edendale Hospital and ten beds are at Greys Hospital. The patient load annually consists of 500 600 patients who are managed as inpatients and a further 500 patients who receive exclusively outpatient care. The PBS provides support to 19 district hospitals in the western third of Kwa Zulu Natal Province. This is a deeply rural area and the PBS delivers support via a combination of direct outreach visits as well as a number of secure social media platforms which allow for direct confidential sharing of patient images and clinical details. All burn patients in western KZN are discussed with or seen by the two burn surgeons. Burns in western KZN are managed according to "The PMB Way Burns Protocols". These are available physically and electronically throughout all the hospitals in western KZN.

All medical officers and registrars working in the PBS have access to "The PMB Way Burns Protocols" (Table 1) which includes analgesia protocols (Table 1). They are directly supervised by the two burn surgeons and undertake a three month rotation in the burns service. The presence of the burn surgeon ensures constant reinforcement of the burns proto cols. The analgesia protocols should be adhered to for every dressing change in both the wards and in the clinic. The staff in the referral hospitals manage a wide spectrum of diseases and only care for burns patients occasionally. These hospitals have "The PMB Way Burns Protocols" available to them, however they do not have the benefit of content reinforcement and clinical structure provided by the burns consultants.

This study was conducted through an anonymous, volun tary questionnaire which was completed over a six month period, from June to November 2018. All medical officers and registrars working in the PBS were invited to complete the questionnaire and all doctors working in the referral district hospitals, who were encountered in outreach visits were invited to compete the questionnaire. Questions which were thought relevant to testing knowledge of analgesia for burns dressings and relevant to the analgesia protocol were included in the questionnaire. The questions were intended to highlight practical knowledge or lack thereof. The questionnaire collected information regarding demographics including the level of hospital where the doctor worked and the number of years of experience as working as a doctor. It also evaluated the use of procedural sedation, including drugs and dosages and the assessment of adequacy of analgesia.

Data was collected on to an excel spreadsheet. In terms of the analysis of the data, continuous variables are presented as means (±SD) and categorical variables are presented as frequencies (%). Chi square Tests are used to compare groups where the sample size allowed. Due to the limited sample size available in the group of Pietermaritzburg doctors, further statistical analysis was not always possible, in this case simple statistics is used. All analyses were performed using SPSS version 25.

3. Results

Results are summarised in Tables 2 and 3. When assessing the adequacy of analgesia, 58% (11/19) of the doctors from Pietermaritzburg used a scoring system, either the FLACC score [11] or the Universal Pain Score (Faces) [12] to assess if the patient was in pain. Forty two percent (8/19) used clinical impression to assess pain. In the referral doctor group, 54% (13/24) used a scoring system (FLACC or FACES) to assess for pain, 38% used the child screaming as an indicator of inadequate analgesia and three doctors (8%) admitted to using no system at all to assess for adequacy of analgesia. One hundred percent of the doctors working in the PBS provided an initial dose of analgesia followed by a top up dose as required. Only 75% of the doctors in the referral hospitals provided top up doses of analgesia with 25% of them providing a single dose of analgesia regardless of its efficacy.

Table 1 – "The PMB way analgesia protocols".

	Background analgesia and sedation		
	Drug	Paediatric	Adult
IV access/ICU/high care	Ketamine	1 mg/kg IVI titrations quick on set quick offset	1 mg/kg IVI titrations quick on set quick offset
Ward	Ketamine	5 mg/kg/per os	5 mg/kg/per os
Dose 1	Midazolam	0.25 mg/kg per os mixed to gether 20 30 min to work	2.5 5 mg per os mixed together 20 30 min to work
Ward	Ketamine	half the previous dose ketamine	100 mg ketamine IMI
Dose 2 (for pain score >3)	NO Midazolam	IMI 5 10 min onset	5 10 min onset
Ward	Ketamine	half the previous dose ketamine	100 mg ketamine IMI
Dose 3 (for pain score>3)	NO Midazolam	IMI	
	The final total dose of Ketamine given at the procedure must be written as the script for the following dressing change, do not leave the inadequate dose as the prescription		
Clinic	Ketamine OR	5 mg/kg IMI	5 mg/kg IMI
	Methoxyfluorane OR	0.5 mls inhaled	1 2 mls inhaled
	Morphine		10 15 mg IMI
Emergency department	Ketamine	5 mg/kg IMI	5 mg/kg IMI
	Morphine		0.05 mg/kg IVI
	Fentanyl		50 100mcg IVI
	Background analgesia and sedation		
	Drug	Paediatric	Adult
	These are oral doses unless otherwise stated		
Mandatory	Paracetamol (syrup = 120 mg/ 5 ml)	15 mg/kg 6 hrly	1 g 6 hrly
Mandatory	Tilidine (1 drop = 2.5 mg)	1 mg/kg 6 hrly	
Mandatory	Tramadol		50 100 mg 6 hrly
Add if pain not controlled and for donor site pain	Ibuprofen (100 mg/5 mls)	10 mg/kg 8 hrly	400 mg 8hrly
	Consider contraindications: Curling's ulcer, acute kidney injury, comorbidities		
Consider if >15%TBSA/pain still uncontrolled	Morphine syrup 1 mg/ml	Start at 0.2 mg/kg 6 hrly Increase frequency up to 2 hrly then increase dose by 25%, consider infusion	0.2 mg/kg 6 hrly Increase frequency up to 2 hrly then increase dose by 25%, consider infusion
Add if pain not controlled OR neuropathic pain	Clonidine (25mcg tablets that cannot be broken)	25mcg 8 hrly increase to maximum 50mcg 8 hrly	75mcg 8hrly increase in increments of 25mcg per dose up to 150mcg 8hrly
Add if pain at night/ difficulty sleeping	Amitryptiline		25 mg nocte, can be increased to 50 and then 75 mg nocte
	Background analgesia and sedation		
	Drug	Paediatric	Adult
For neuropathic pain and or severe itch	Pregabalin 75 or 150 mg tabs mixed into suspension for paeds	start at 25 mg 12hrly, increase in 25 mg increments to max 75 mg 12 hrly	start at 75 mg 12 hrly, increase to max 150 mg 12hrly
	Gabapentin 100 mg or 300 mg tablest	10 mg/kg 8hrly, increments of 100 mg/dose up to 600 mg 8 hrly	300 mg 8 hrly, increase up to 600 mg 8 hrly
Add if neuropathic pain and no gabapentin/pregablin	Tegretol 200 mg tabs		200 mg 12 hrly increase to max 1200 mg/day (400 mg 8 hrly)
If itch and no pregaba/ gabapentin	Allergex	0.1 mg/kg start 12hrly, can be increased to 8 hrly	4mg 8 hrly
	Pyridoxine		25 mg daily
For ICU patients/large TBSA burns (MORPHINE mixed as a 1 mg/ml solution ie. 10 mg in 10 mls or 50 mg in 50 mls)	Morphine IVI Remember this needs to be weaned and not stopped suddenly! (wean the infusion rate then move to bolus dosing and increase the dose interval over time)	0.1 mg/kg loading dose then 0.1 mg/kg/h infusion increase to effect, reload and increase rate by 0.05 mg/kg	0.1 mg/kg loading dose then 0.1 mg/kg/h infusion increase to effect, reload and increase rate by 0.05 mg/kg
For PTSD OR anxiety OR opioid withdrawal	Valium	2.5 mg nocte, titrate to effect can be increased to 8 hrly	5 mg nocte, titrate to effect can be increased up to 5 10 mg 4 hrly
For Delirium	Haloperidol		2.5 5 mg 8 hrly

Table 2 – Demographics.

	PBS	Referral	Overall
Number of participants (%)	20 (47%)	23 (53%)	43 (100%)
Mean years qualified as a doctor (±SD)	7.2 (±3.0)	9.6 (±7.3)	8.6 (±5.9)

Table 3 – Procedural analgesia.

	PBS	Referral	Overall	Statistically significant difference
Procedural Sedation Given	100% (20/20)	96% (22/23)	98% (42/43)	
Ketamine use (%)	100% (20/20)	39% (9/23)	67% (29/43)	$x^2 = 18.237$; $p < 0.001$
Midazolam use	65% (13/20)	17% (4/23)	40% (17/43)	
Correct dose of Ketamine known	80% (16/20)	8% (2/23)	42% (18/43)	$x^2 = 21.778$; $p < 0.001$
Aware there is no maximum Ketamine dose	50%(10/20)	4% (1/23)	26% (11/43)	

4. Discussion

Although adequate analgesia is an essential part of burn management there are wide variations in practice across the world. A recent survey by the American Burn Association found that opioids and benzodiazepines are the mainstay of the burn wound analgesia in the United States. This is simply not practical or safe in our setting. Although multimodal distraction has also been described with good results it is too expensive for a low income country. Ketamine is cheap, safe, practical and effective and remains the cornerstone of our protocols [8 10].

The "FMB WAY" has had a dramatic effect on the culture of burns care in our center and we have nurtured a culture which does not tolerate or ignore children in pain. Unfortunately, we have been less successful in transmitting this same culture to our district hospitals as evidenced by the fact that there appears to be a statistically significant difference in the knowledge and understanding of analgesia and in compliance to the available analgesia protocols between the group of doctors in the PBS and those in the referral institutions.

After multiple outreach visits to the hospitals who refer to us, it became apparent that the protocol was not being adhered to. In some cases, the doctors were aware of the protocol but were not adhering to it as they were uncomfortable using ketamine, which is the cornerstone of the protocol and in other cases they were not aware of the protocol. At the time of the questionnaires being completed, all of the hospitals did have ketamine and dormicum.

There is a misconception that burns are just painful and that there is not much concern about tailoring analgesia to individual patients. Although we acknowledge that ideally pain management should be tailored to the individual patient, a high turnover of doctors in the referral hospitals, varying levels of experience of the doctors administering the analgesia for the burns patients and the fact that some of these doctors very seldom manage burns patients, we feel that managing pain according to a protocol is the safest option to ensure that patients receive adequate analgesia. There is a dedicated burns service which the doctors have constant access to should they wish to discuss their patient and they can then get advise tailored to their patient should the protocol analgesia not offer adequate analgesia. Pain assessment in children is challenging. Staff often ignore or do not recognize the subtle signs of pain and only consider a child to be in pain when they are screaming. Doctors who do not use some form of assessment of adequacy of analgesia are less likely to give top up doses of analgesia as necessary.

Kochman et al. have shown the FLACC score to be an appropriate observational tool to assess acute pain in children between the ages of 6 months and 5 years, however, this study was not specific to the burn population [13]. We use the FLACC score as we are most familiar with it. It is one of three scores recommended in the ISBI (International Society for Burn Injury) guidelines [14]. The other two scales, the COMFORT B [15] and the POCIS scales, however, have been validated in the setting of children with burns [16] and could be useful additions to our protocol.

It is often also very challenging to differentiate between anxiety and pain, especially in children. Part of our protocol includes the addition of an anxiolytic if we suspect that difficult pain control may be due to anxiety.

The challenge remains the implementation of such protocols and a number of obstacles to their widespread adoption have been described in the literature. Grol and Grimshaw describe the complexity of change management even when the issue is clearly clinically beneficial such as hand hygiene. Attitudes amongst health care workers need to be challenged. These include: dressings changes in burn injured patients are just a painful experience, it is the nature of the injury, this is how it has always been done. There is a very real possibility that health care providers suffer from compassion fatigue themselves. Without strong local champions it is difficult to change an organisational culture. In the PBS strong and dynamic leadership has re enforced the implementation of the protocols.

The failure to implement protocols in the district hospitals in multi factorial. High turnover of staff prevents the development of any sort of institutional memory in remote district hospitals. It is not possible to visit every one of these peripheral hospitals in the beginning of each year to reintroduce the protocols each year.

5. Conclusion

We have identified a discrepancy in knowledge between staff in an academic burn center and those in peripheral referral hospitals. This discrepancy translates into differences in quality of burn analgesia which patients receive. Ongoing efforts must be directed towards changing the culture of district institution and strengthening attempts to standardize care across the region.

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Conflict of interest

The authors declare that they have no conflict of interest.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.burns.2019.04.012.

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3.6 CONCLUSION

Protocols for patient management have become increasingly popular in recent years. They aid healthcare practitioners who only occasionally manage certain conditions and help to standardize care. There are, however, numerous challenges in implementing protocols for patient management. The PBS consists of two burn surgeons who constantly reinforce the PMB way protocols in Pietermaritzburg and as such, a culture which does not accept burn-injured patients in pain has been fostered. There is only intermittent reinforcement of the PMB Way protocols for the referring hospitals when they contact the PBS burns surgeons to refer burns patients and it is evident from this study that the same culture of does not exist in the regional hospitals. There is also a very fast turnover of doctors in the referring hospitals which prevents institutional memory and contributes to lack of adherence to burns protocols. Less than 10% of the doctors in the referring hospitals were aware of the correct dose of ketamine and, while this was not measured in the questionnaire, there seems to be a fear when it comes to using ketamine in the wards. This is likely in part due to lack of experience using Ketamine and secondly due to a lack of monitoring equipment for the dressing changes. Due to the fear of ketamine and the lack of monitoring, methoxyflurane would offer a solution to procedural sedation in these settings. The use of the entire 3ml vial is considered safe in adults and children alike so there is no issue in terms of dosing and no additional monitoring is required. This paper highlights a deficit in the knowledge of doctors with regard to analgesia required for burns dressings and a lack of compliance to existing analgesia protocols. Anecdotally, it seems as if these doctors fear ketamine, firstly due to lack of experience using it and secondly, potentially due to a lack of monitoring equipment. The served, in part as a motivation to find an alternative analgesia option to ketamine.

CHAPTER 4

THE KETAMINE CRISIS IN SOUTH AFRICA

4.1 SUMMARY

This published editorial highlights the versatility of Ketamine and its vital role in procedural analgesia for dressing changes for burns patients. It describes the issues surrounding the shortages of drugs in South Africa, specifically focusing on the Ketamine shortage. This editorial suggests alternatives to the use of Ketamine, one of which is Methoxyflurane. The issue of the Ketamine shortage is one of the obstacles to adequate analgesia in paediatric burns patients. The use of Methoxyflurane is central to this PhD.

4.2 PUBLICATION DETAILS

Title	The Ketamine crisis: Does South Africa have a plan B?
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4.3 JOURNAL DETAILS

The South African Medical Journal (SAMJ) is a peer-reviewed, internationally indexed journal published monthly. It is accredited by SciELO SA and Science Citation Index (Web of Science (WoS) Core Collection).The SAMJ is a general medical journal publishing leading research impacting clinical care in Africa. The journal is intending to capture the spectrum of medical and health sciences, grouped by relevance to the country's burden of

disease. The journal carries research articles and letters; editorials; clinical practice and other medical articles and personal opinion; South African health-related news; obituaries and general correspondence.

4.4 PUBLICATION TIMELINE

The first draft of this article was submitted to SAMJ on 1 June 2019. Reviewers' and editorial feedback was received on the 26 June 2019 with all comments and queries responded to on the 27 June 2019. The final manuscript was accepted and slated for publication on 10 July 2019 and was published online on 27 November 2019 and published in print in December 2019.

4.5 CONTRIBUTION DETAILS

The candidate conceptualised, developed and wrote the paper. Dr Bangalee provided assistance with the conceptualisation of the paper and contributed significant editing of the draft, final manuscript and revisions.

CLINICAL ALERT

The ketamine crisis: Does South Africa have a plan B?

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South Africa (SA) has a high incidence of deaths from trauma and injuries. Trauma has been identified as one part of the quadruple burden of disease afflicting the country. This article is concerned with the management of burns, which 3% of the population suffer from annually. Ketamine, acknowledged for its versatility and safety profile, remains a critical component in the medical arsenal of anaesthesiologists and clinicians treating both acute and chronic pain. In the management of burn-injured patients in particular, ketamine is the cornerstone of many analgesia protocols. However, issues pertaining to shortages of this medicine in SA warrant concern and discussion, particularly in view of the high reliance of doctors on ketamine for first-line procedural analgesia in the management of burns in both adult and paediatric patients. This article attempts to highlight the issues related to ketamine shortages, which often have significant clinical, safety, operational and research implications.

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In excess of 1 million people suffer from burns in Africa annually.[1] Across the African continent, burns account for 18% of hospital admissions and have a mortality rate of 6 - 10%.[1] According to a 2017 Medical Research Council report,[2] South Africa (SA)'s annual burn mortality rate of 8.5/100 000 is substantially above the world average of 5/100 000. The same report stated that 3% of the SA population suffer from burns annually, and that of these burns, 20% are classified as moderate to severe. Moreover, ~161 children are severely burned in accidents in the home every month in SA, and because of inadequacies in the burn care system, 6 of these children will die. A World Health Organization report on burns in March 2018[3] claimed that annually in SA, USD26 million is spent on burn care for patients burned in cooking incidents from kerosene (paraffin) stoves.[3] The socioeconomic impact of this situation is worsened by indirect costs due to inability of these patients to return to work, resulting in their requiring disability grants, and their need for prolonged care for deformities caused by the burns.

Defining the problem

From the point of initial injury and throughout rehabilitation, the management of pain in burn patients is an area of major concern, with several clinicians attesting to burn pain being the most difficult of any of the acute pain aetiologies to treat.[4] In addition to pain related to the burn, the curative and rehabilitative therapies compound the difficulty of pain control, as these interventions, which include dressing changes, excision and grafting, and physical therapy, cause pain that is often equivalent to or worse than the pain of the initial burn injury.[4] Studies have shown that good pain management and control is associated with better wound healing, sleep, participation in activities of daily living, quality of life and recovery.[5,6] For the above reasons, pain management forms the foundation of burn care.

The benefits of ketamine are numerous. Since its first clinical use in 1970, ketamine has continued to remain a critical component of the medical arsenal of anaesthesiologists and clinicians treating both acute and chronic pain, in particular finding a growing use in the management of adult and paediatric burns.[7] Over the past two decades, several studies have investigated the additional antidepressant and anti-inflammatory effects of ketamine.[7-9] The appeal of ketamine in the clinical setting is its versatility as a result of its unique ability to induce three clinical outcomes, i.e. narcosis, analgesia and amnesia. There is currently no other medicine used in clinical practice that can provide these three effects simultaneously.[7] Apart from its rapid onset of action, it does not induce hypotension and there is minimal risk of airway loss because the pharyngeal and laryngeal reflexes are only slightly impaired. It also rarely induces bronchospasm, which makes it particularly useful in asthmatic patients as well as in children. Its increasing portfolio of use coupled with its safety profile have cemented its place in a plethora of management protocols in the South African Standard Treatment Guidelines.[10,11]

In the operating theatre, ketamine can be used for the induction and maintenance of anaesthesia. Because it does not induce hypotension, it is especially useful in cases where haemodynamic control is required.[12] Ketamine is also used in various settings outside the operating room, such as procedural sedation for dressing changes, splinting, line changes and fracture reductions. Ketamine shortages therefore pose a threat to doctors and patients alike in the SA healthcare system, demanding national attention from all those practising in the field.

The impact of ketamine shortages is far reaching, as this drug is the safest, most practical option for procedural sedation for minor procedures in wards and outpatient departments in hospitals with either no theatre facilities or limited theatre time. When it is not possible to do simple procedures safely in the ward, they need to be done in theatre. Theatre time is a scarce and costly resource in our environment.

This dilemma ultimately affects the quality of patient care, as every situation in which ketamine is out of stock has a measurable human impact. From the perspective of patients and their families,

medicine shortages result in wasted time and work days, money lost on pointless travel, poor retention and follow-up for chronic diseases, untreated diseases, and most importantly a loss of confidence in the public health system.[13]

At the bedside, doctors' frustration due to medicine shortages is shared by pharmacists, who are required to make complex decisions and provide recommendations to doctors based on a limited availability of options. The failing balance of supply (pharmacist) and demand (doctor) often results in strained relationships between these two members of the healthcare team in the clinical setting. Hospital pharmacists are required to find alternatives, leading to the administration of second- and third-line medicines that may be inferior in quality or outcome. In the case of ketamine specifically, alternative treatments may not be readily available and in addition may require additional training and resources for their safe use. Alternative regimens further raise the risk of dosage errors if healthcare practitioners are not familiar with the dosing and administration required for these products. This lack of training and knowledge associated with using alternatives leads to adverse effects, unforeseen complications, and effectiveness issues that negatively affect costs and place an added strain on an already overburdened healthcare budget. From a clinical and ethical standpoint, shortages of a medicine like ketamine, which has multiple indications in the healthcare sector, require tough decisions to be made on which patient populations will be given priority for a medicine that is in short supply.

Alternatives to ketamine

One potential alternative to ketamine is methoxyflurane. It is a short-acting inhalational analgesic agent with a rapid onset of action. The analgesic effects manifest after 6 - 8 breaths, and once inhalation is ceased, the analgesic effects wear off within a few minutes. It has been well described in the management of acute pain and a variety of procedures including dressing changes and dental procedures. Although studies in the adult population predominate, there are studies proving it to be safe and efficacious in the paediatric population with minimal side-effects.[14] One of the disadvantages of methoxyflurane is that it is currently not widely available in the public health sector. It is more expensive than ketamine, and the majority of doctors are reluctant to use medications that they are unfamiliar with, which also limits its use.

Other alternatives for procedural sedation, such as the combination of propofol and fentanyl, are also limited by lack of availability in certain state facilities. The safety of such combinations in the hands of healthcare workers inexperienced in procedural sedation, and in view of the lack of monitoring equipment in these facilities, is questionable.

Why is there a ketamine shortage?

The reasons for the ketamine shortage are not entirely clear. Some of the global reasons provided by manufacturers include an increased demand for ketamine and manufacturing delays. There are currently only two registered ketamine products on the SA market (both of which are generics), which further contributes to the lack of a viable supply chain. In general, generic injectable medications are most commonly affected by shortages, owing to the costly and complex production processes related to their manufacture and the fact that they have smaller profit margins than branded medications, so there is a lack of interest on the part of manufacturers in producing the line. Furthermore, backlogs at the South African Health Products Regulatory Authority with regard to both new medicine and generic medicine registration limit the available alternatives.

In addition to manufacturing issues related to ketamine shortages, logistics and supply chain challenges are contributing factors. Maintaining an adequate inventory in the midst of a drug shortage is a difficult task, leading some providers and organisations to stock up on medicines in anticipation of a shortage, which increases costs and risks wasted inventory.[12] While the National Department of Health is aware of the problem, and there have been several studies attesting to medicine shortages, it is evident that procurement and distribution of medical supplies remain inadequate in SA.[15] Supply issues have also been linked to inadequate training and the inability of personnel to manage medicine supplies, report shortages, and respond appropriately to prevent their recurrence.[16] Additionally, challenges in the healthcare system related to shortages of healthcare workers, weak oversight and management, and inadequate monitoring and evaluation of clinical data have been reported as further contributing factors.

Conclusions

In a nutshell, ketamine is exceptionally user-friendly for relatively untrained clinicians in resource-limited settings, and any shortage of this drug should therefore be grounds for grave concern. Although there are a small number of alternatives to ketamine for the management of burn pain, the viability of these options in the public health sector is dubious. Unfortunately, the ketamine issue is not an isolated one. Several essential medicines used in surgical patient care and critical care settings in SA are frequently out of stock or in short supply. This article aims to start the conversation and the thinking about identifying reasons for the shortages and finding solutions to this problem to ensure that we have a plan B. The solution will require a multidisciplinary effort from each level of the healthcare system (districts, province and the National Department of Health). Failure to address the ketamine shortage before stocks are completely depleted will have far-reaching effects across our healthcare system.

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4.6 CONCLUSION

Ketamine has been the cornerstone of many procedural analgesia protocols world-over. However, it is not without its challenges. It has a long recovery time, and this is a challenge when used in busy outpatient settings. Patients should be monitored following the administration of ketamine. In LMIC's there is often little or no monitoring equipment available for dressing changes. While ketamine is used in various LMIC settings without being monitored, this is not best practice. In terms of risk benefit ratio and the risk of wind-up pain and chronic pain syndromes from inadequate analgesia, the risk of using ketamine without monitoring is often deemed to outweigh the benefits of adequate procedural analgesia/sedation for dressing changes.

There has on occasion been a shortage of ketamine worldwide. This was one of the catalysts for the PBS considering alternative options to ketamine for procedural analgesia for dressing changes. There are various options which can serve as alternatives to ketamine. One of these options is propofol and fentanyl. While this is an effective alternative in a HIC, these drugs are also often in short supply in LMICs. Despite the limited supply of these drugs in LMICs, another hindrance to their use is the fact that monitoring patients following the administration of these drugs is arguably even more important than with the use of ketamine. The most practical drug as an alternative to ketamine in LMICs is Methoxyflurane. It has a rapid onset of action, rapid recovery time, does not require monitoring and can largely be self-administered.

CHAPTER 5

HIGHER ANALGESIA REQUIREMENTS FOR DELAYED REFERRALS

5.1 SUMMARY

This chapter is presented in the form of a manuscript, submitted for publication and currently under review. From the previous study, presented in Chapter 3, we demonstrated that analgesia protocols are poorly adhered to in the hospitals who refer to the PBS and there is a lack of knowledge regarding analgesia for paediatric burns patients. This study builds on the assumption that patients at the referring hospitals receive inadequate analgesia. It goes on to compare the procedural analgesia requirements for dressing changes of patients who are managed at the PBS where the analgesia prescribed is strictly according with the analgesia protocols (so the assumption is adequate analgesia), with those who were managed for three or more weeks at the referral hospitals, where the assumption is inadequate analgesia. This study demonstrates that patients with delayed referrals require more ketamine to achieve adequate procedural analgesia than those referred acutely. The reasons for this are multifactorial, but one possible explanation is inadequate analgesia in the acute phase of the burn, underpinning the importance of adequate analgesia from the time of the injury.

5.2 PUBLICATION DETAILS

Title	A comparison of analgesia requirements in children with burns: do delayed referrals require higher procedural analgesia doses?
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5.3 JOURNAL DETAILS

Burns Open is an open access, peer reviewed international journal. It aims to promote the exchange of information in burn care among all interested in the field of burn care. The journal accepts clinical and bench studies, ideas and innovations, and description of techniques and case reports and series. It publishes articles related to the incidence and epidemiology of burns and burn disasters; the investigation of underlying pathophysiology of injury; the treatment of burn wounds and other skin conditions, including rehabilitation and reconstruction; and outcomes of burn management. Burns Open is an open access journal linked to Burns and currently does not have any available impact factors.

5.4 PUBLICATION TIMELINE

The first draft of this paper was submitted to Burns Open on 28 January 2020. The journal e-mailed proof of submission on the same day. The paper is currently under review.

5.5 CONTRIBUTION DETAILS

The candidate conceptualised, developed and wrote the paper. The candidate also conducted the statistical analysis. Professor Clarke and Dr Allorto provided considerable assistance with the conceptualisation of the paper as well as with editing of the draft and final manuscripts.

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A comparison of analgesia requirements in children with burns: Do delayed referrals require higher procedural analgesia doses?

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ABSTRACT

Background: Our clinical impression is that delayed referrals require more analgesia than children referred to our service acutely. Previous work demonstrated poor uptake of analgesia protocols at district hospitals with probable inadequate background and procedural analgesia, which may account for this. The purpose of this study was to compare analgesia requirements for dressing changes of paediatric patients referred to us acutely versus those children with delayed referral (i.e. more than 21 days post injury). Our hypothesis is that paediatric patients with delayed referral require higher doses of ketamine when taking length of stay and total body surface area (TBSA) of the burn into account.

Methods: Data for children under 12 years, admitted to the Pietermaritzburg Burn Service (PBS) from the 1 July 2017 until 30 June 2018 was reviewed. Total ketamine dose during admission, weight, days admitted and TBSA were analysed. The total ketamine use in milligram per kilogram per days admitted per TBSA (mg/kg/days admitted/TBSA) was calculated. Statistical analysis was performed to compare the total ketamine dose between the acute and delayed referral groups.

Results: One-hundred-and-ninety-seven patients were included. Patients were divided into two groups, the acute group including those referred to the PBS early (prior to 21 days post-burn) and the delayed referral group (those referred 21 days or more post burn). The acute group consisted of 167 patients and the chronic group 30 patients. There is a statistically significant difference between the total ketamine dose (mg/kg/days admitted/TBSA) for the acute referral and delayed referral groups ($p = 0.01$). The median total ketamine dose (mg/kg/days admitted/TBSA) of the acute referral group was 0.27 (Range: 0–7.05) and the median total Ketamine dose (mg/kg/days admitted/TBSA) for the delayed referral group was 0.41 (range: 0.1–3.89).

Conclusion: Patients with delayed referrals require more ketamine to achieve adequate procedural analgesia than patients referred acutely. Inadequate analgesia in the acute phase of the burn may influence this, underpinning the importance of adequate analgesia right from the time of the injury.

1. Introduction

Globally, pain control in burns patients remains inadequate despite longstanding recognition that inadequate pain control can have adverse physiological and emotional sequelae [1–4]. Inadequate analgesia as background as well as procedural, can contribute to the development of anxiety, wind up, allodynia and hyperalgesia [5]. It is difficult to distinguish each syndrome clinically, as they can all be perceived as acute somatic pain during a dressing change and in our practice, this equates to giving more procedural analgesia. Further, the dissociative effect of ketamine can also be perceived as pain by the inexperienced doctor. Ongoing inadequate background analgesia may also contribute to the development of neuropathic pain. This also perpetuates the escalation of procedural analgesia requirements.

Our clinical impression is that children with burn wounds managed at district hospitals for a number of weeks initially, require higher procedural analgesia doses compared to those that have been more acutely admitted to our service. Our previous work demonstrating poor uptake of analgesia protocols at these district hospitals with the potential development of complex pain syndromes is one explanation for our impression due to the probable inadequate background analgesia as well as procedural analgesia [6]. The purpose of this study was to compare the analgesia requirements for dressing changes of paediatric patients between acute referrals and delayed referrals, where delayed is defined as a burn wound that was referred more than 21 days form time of burn. Our hypothesis for this study was that burn-injured

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paediatric patients with delayed referral require higher doses of ketamine when taking length of stay and total body surface area of the burn into account.

2. Setting

The city of Pietermaritzburg is the largest city in western Kwa Zulu Natal Province. It has a population of a million people and drains the rural western third of the Province. The Pietermaritzburg Burn Service (PBS) consists of two burns surgeons who operate across the regional (Edendale Hospital) and Tertiary (Greys Hospital) Hospitals of Pietermaritzburg. The Burn Service has access to 40 beds dedicated burns beds. Ten beds are at Greys Hospital and the remaining thirty beds, including six high care beds, are at Edendale Hospital. Annually the patient load of the PBS consists of 500–600 inpatients (adults and children). Exclusive outpatient care is provided to a further 500 patients (adults and children). There are 19 rural district hospitals which the PBS supports. All patients treated by the PBS are entered onto a burns database. This has class approval granted by the Biomedical Research and Ethics Committee, University of Kwa-Zulu Natal (BCA106/14).

In our service, a combination ketamine and midazolam is administered to all children undergoing dressing changes in both the in-patient and out-patient setting. In-patients receive the ketamine for their dressings in the ward where minimal monitoring equipment (saturation and heart rate) is available. A doctor is present for every dressing change, both to administer the ketamine and to monitor for adequacy of analgesia and to provide additional doses of ketamine as required. The patient is given an initial dose of ketamine, should the analgesia be inadequate an additional dose of ketamine is given. For the next dressing change, the total ketamine dose given at the previous dressing change (the initial dose plus the additional dose) is given as the initial dose of ketamine. This may, however, lead to rapidly escalating doses of ketamine being administered. Only the ketamine can be given as a repeat dose and midazolam remains as a single dose given with first dose of ketamine. Patients are discharged when the wounds are healing, are unlikely to require any further surgery and when they are satisfactorily compliant with mobilization and or splinting.

3. Methods

Analgesia for dressings was prescribed as per out analgesia protocol (Appendix 1). In-patients received oral ketamine and midazolam 30 min prior to the procedure with an additional intramuscular dose of ketamine should adequate analgesia not have been achieved. The additional dose was given at half of the initial oral dose. Pain scores were recorded using the Face, Legs, Activity, Cry, Consolability (FLACC) scale to assess adequacy of analgesia [7]. If the initial dose of ketamine was insufficient to achieve adequate analgesia, the initial dose plus the additional doses are prescribed as the initial dose for the next dressing change. The protocols are adhered to for every dressing change.

Data regarding the total ketamine dose for the duration of the patient's admission is routinely collected as part of the burns data base. This study focused only on children who were admitted as in-patients to our service receiving ketamine only for procedural analgesia and not background analgesia. Data for children (<12 years old) admitted to the PBS from the 1 July 2017 until 30 June 2018 was reviewed. Age, admission weight and total ketamine dose were analysed. The date of admission and date of discharge were used to calculate the days admitted and the date and time of burn and the date and time of admission were used to calculate the delay from time of burn to admission. Children who were admitted to paediatric intensive care unit at any time during their admission were excluded as ketamine is used as an infusion for background analgesia. Children who demised during admission were excluded from the study as well as children with missing data on the database.

The patients were divided into two groups, those referred to the PBS early (prior to 21 days post-burn) and those with a delayed referred (those referred 21 days or more post burn). The total ketamine use in milligram per kilogram per days admitted per TBSA (mg/kg/days admitted/TBSA) was calculated. Statistical analysis was then performed using R Studio Version 1.1.463 [8]. A Mann-Whitney-Wilcoxon test was conducted to compare the acute referral and the delayed referral groups. A Fisher's exact test was then conducted to determine whether the total ketamine dose (mg/kg/days admitted/TBSA) was affected by mechanism of injury. A Fisher's exact test was also conducted to assess whether TBSA played a role in the total ketamine dose (mg/kg/days admitted/TBSA).

4. Results

There were 275 children admitted during the 1 year period under review. One-hundred-and-ninety-seven children met the inclusion criteria. Data for these children was evaluated. The patients referred early consisted of 167 patients and those with a delayed referred were 30 patients. The two groups are described in Table 1.

The mean delay from burn to admission in the late referral group was 48.2 days with a range of 21–230 days delay and a median of 29.5 days. The early referral group of patients presented from scene within an hour of the burn up to 19 days post burn injury.

A Mann-Whitney-Wilcoxon Test was performed to compare the total ketamine (mg/kg) per days admitted per TBSA. There was a statistically significant difference (W = 1778.5, p = 0.01) between

Table 1
Comparison between the acute and delayed referral groups.

	Acute Burn Group	Chronic Burn Group
No in group	167	30
Median Age	2.17 years (Range: 0.17 10.58)	4.80 years (Range: 0.83 10.42)
Gender		
Male	93 (56%)	15 (50%)
Female	74 (44%)	15 (50%)
Median Days Admitted	14 (Range: 1 105)	9 (Range: 5 23)
Median Delay from Burn to Admission (Days)	0 (Range: 0 19)	29.5 (Range: 21 230)
Mechanism of Burn:		
Hot Water Scald	114 (68%)	16 (53%)
Flame	23 (14%)	11 (37%)
Electrical	10 (6%)	2 (7%)
Other	20 (12%)	1 (3%)
Median TBSA	11.0 (Range: 1 50)	4.5 (Range: 1 40)
Median Ketamine Dose (mg/kg/days admitted/TBSA)	0.27 (Range: 0 7.05)	0.41 (Range: 0.1 3.89)

the acute referral and delayed referral groups. The median total ketamine dose (mg/kg/days admitted/TBSA) of the acute referral group was 0.27 (range: 0–7.05) and the median total Ketamine dose (mg/kg/days admitted/TBSA) for the delayed referral group was 0.41 (range: 0.1–3.89). The comparison between the total ketamine doses between the acute and delayed referral groups can be seen in the boxplots in Fig. 1.

In order to determine whether mechanism of injury played a role in the total ketamine dose required, a two-sided Fisher's exact test was conducted for each of the groups. This test revealed that in the acute group there was a statistically significant difference in the total ketamine dose (mg/kg/days admitted/TBSA) required, depending on the mechanism of injury ($p = 0.003$, Fisher's exact test). However, in the delayed referral group, when considering mechanism of injury, the difference in total ketamine dose required was not statistically significant ($p = 0.15$, Fisher's exact test). In both the acute and delayed referral groups the electrical injuries required more than double the total ketamine dose than the other mechanisms of injury. Figs. 2 and 3 show the comparison of the total ketamine doses between the different mechanisms of injury for the acute and delayed groups respectively.

Statistical analysis using a two-sided Fisher's exact test confirmed that in the acute group there was a statistically significant difference in total ketamine dose (mg/kg/days admitted/TBSA) depending on the TBSA ($p = 0.006$, Fisher's exact test). Again, however, in the delayed referral group, there was no statistically significant difference in the total ketamine dose when taking TBSA into account. ($p = 0.87$, Fisher's exact test). The total ketamine dose over the spectrum of TBSA is demonstrated for the acute and delayed referral groups in Figs. 4 and 5 respectively.

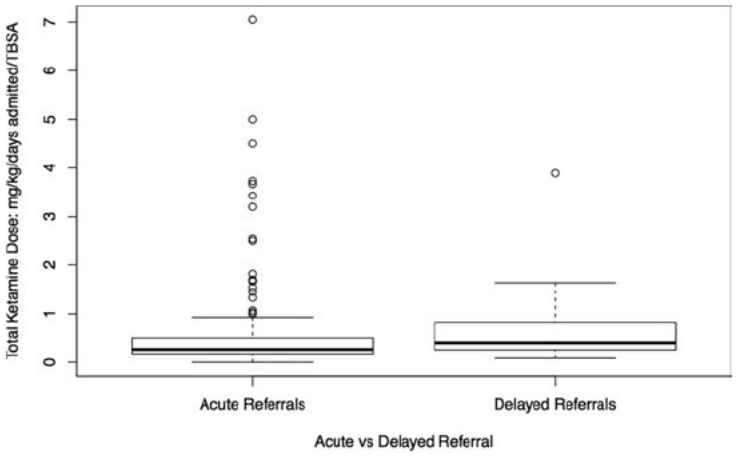

Fig. 1. Comparison of total ketamine dose between acute & delayed referrals.

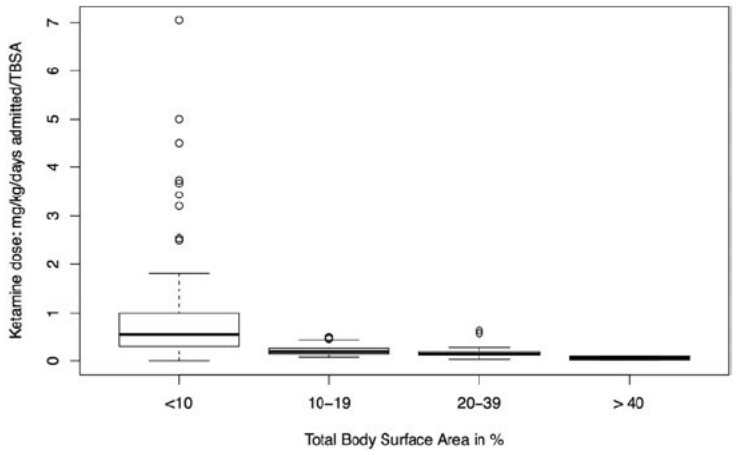

Fig. 2. Acute group comparison of total ketamine dose across the TBSA spectrum.

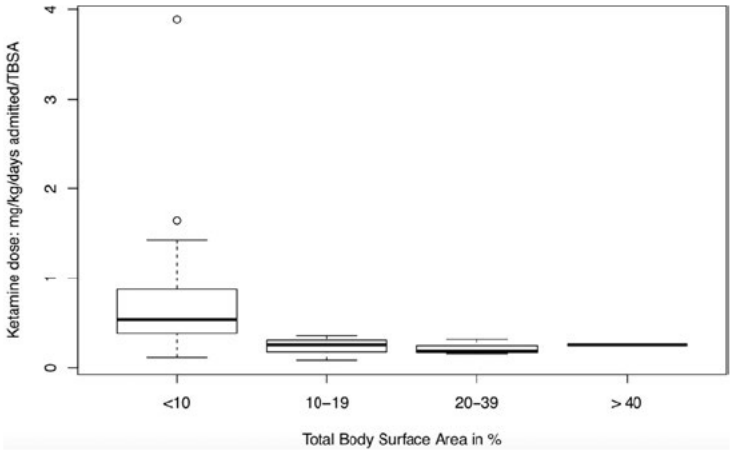

Fig. 3. Delayed referral group comparison of total ketamine dose across the TBSA spectrum.

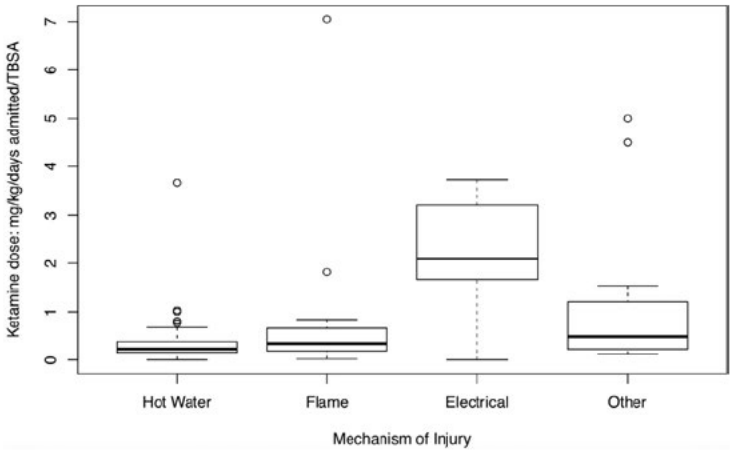

Fig. 4. Acute group comparison of total ketamine dose to mechanism of injury.

5. Discussion

Pain is virtually synonymous with burn injuries and all children with a burn will experience pain, regardless of the cause, size or depth of the burn [1]. Burn pain is dynamic and needs constant reassessment. Anxiety is a major factor which can escalate the level of pain in child with a burn therefore requires direct management in its own right. Pain and anxiety have a poorly understood symbiotic relationship in children [1,2]. Poorly controlled pain and anxiety also have a physical and physiological impact which may result in delayed healing [1,9]. Pain has a significant impact on the development of long-term sensory problems and may precipitate debilitating long-term psychological conditions and chronic regional pain syndromes [10]. Patterson et al showed that pain during hospitalisation was a stronger predictor of psychological adjustment following burn injury than size of the burn or length of hospitalisation [11]. Despite this, pain is often inadequately treated and there are numerous factors which contribute to this inadequate pain control. Medical staff are concerned with possible addiction and other secondary effects of opioids and burn pain is frequently under-estimated [12]. There is a misconception that burn injuries "are just painful". The expectation is often that burn pain simply cannot be controlled [13]. It has also previously been shown that, even with access to existing protocols, there is poor compliance to these protocols [6].

It is well established that chronic pain is far more complex to manage than acute pain and conventional analgesia strategies remain ineffective against chronic pain. Moa et al. describe it as "Managing chronic pain is to fight a "war" not a "battle" [14]. Our study highlights that patients who present with burn wounds

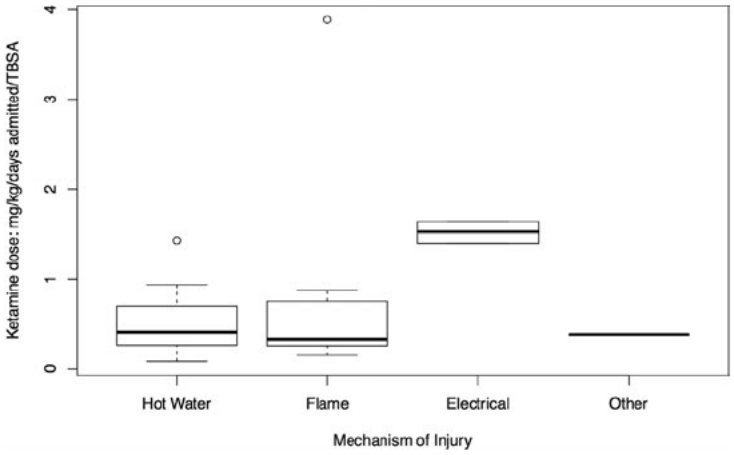

Fig. 5. Delayed referral group comparison of total ketamine dose to mechanism of injury.

referred late require higher doses of ketamine for dressing changes to achieve adequate analgesia when compared to those who were referred or presented early. One explanation for this is having not received adequate analgesia from the outset of the management of their injury. This is in keeping with Patterson et al.'s findings that there is great value in controlling acute pain during hospitalisation of burns patients [11]. Potential deficits in background analgesia may be contributory to the increase analgesia requirements but this was unmeasured in this study.

Previous studies done in our area have shown that only 38% of the doctors in the peripheral hospitals referring to us give ketamine for dressing changes [6]. Of this 38%, only 8% knew the correct dose of ketamine [6]. This is the basis for our assumption that patients managed at the peripheral hospitals for prolonged periods of time are managed with inadequate analgesia. We feel that the inadequate analgesia contributes to the development of wind up pain in these patients and this is the reason that they require so much more analgesia than patients managed with strict analgesia protocols from the time of their injury.

In this study, the mechanism of injury was not entirely equally distributed in the two groups. The mechanism of injury had a statistically significant effect on analgesia requirements in acute burns and this was due to the fact that partial burns, which are more typical with certain mechanisms, are more painful and would therefore require more analgesia. In the delayed group, however, the mechanism no longer had a statistically significant effect on the analgesia requirements. This is due to the fact that all partial burns had healed by the 21 day cut off for an acute referral and all delayed referrals were deeper burns, regardless of their mechanism. We, therefore, do not feel that the discrepancy in mechanism of injury between the groups played any role in the increased analgesia requirements demonstrated by the delayed referral group.

In both the acute and delayed referral groups, electrical injuries required more than double the total ketamine dose (in mg/kg/days admitted/TBSA). This finding was not surprising as it is well established that disproportionate pain is common after electrical burn injuries [15,16]. Pain following electrical injuries is difficult to manage and, regardless of analgesia modality used, pain is often not satisfactorily relieved [17]. This is likely due to the direct nerve injury, scar tissue formation around nerves, and neuropathy from post-injury tissue edema that occurs as a result of the heat generated by the electrical current [18,19].

The TBSA in the acute group was larger than the delayed referral group. This is because patients with large burns are usually referred early. Doctors in the peripheral hospitals are more likely to manage smaller burns themselves at district level hospitals and only refer when the wounds are not healing. The patient admitted as a late referral with 40% TBSA, was a patient being managed at another regional hospital without specialist burn surgeons and 23 days after admission the patient deteriorated and was transferred the patient to us. Patients with smaller burns being managed in peripheral hospitals with inadequate analgesia can still develop anxiety, wind up and chronic pain syndromes. This could account for the delayed referral group requiring significantly higher doses of ketamine despite the average burn size in that group being much smaller than the TBSA of the acute group.

In the acute referral group, there is a statistically significant difference in the ketamine requirements depending on the TBSA. However, this is not the case in the delayed referral group. The TBSA has no significant influence in the delayed group and as such, TBSA does not account for the increased analgesia requirements of the delayed referral group.

Management of background pain, neuropathic pain and anxiety would also influence needs during the dressing change, but data is more difficult to collect and has not been included in this cohort. It is highly likely that background analgesia is also poorly addressed in the hospitals outside of the PBS for the same reasons as poor protocol compliance. This is further compounded by lack of drugs available in the state sector such as clonidine and gabapentin. Typically, paracetamol, tilidine, non-steriodal anti-inflammatories and morphine would be available.

6. Conclusion

Burn-injured patients with a delayed referral require more ketamine to achieve adequate analgesia than patients referred acutely. Inadequate analgesia in the acute phase of the burn may influence this, therefore adequate analgesia right from the time of the injury is imperative.

7. Patient consent

The data for the paper was drawn from an existing database. We do get consent from all patients to store their data on the database.

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Conflict of interest

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

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Appendix 1

"Pietermaritzburg Burn Service (PBS) Analgesia Protocols"

Background Analgesia and Sedation			
	Drug	Paediatric	Adult
IV access/ICU/high care	Ketamine	1 mg/kg IVI titrations Quick onset quick offset	1 mg/kg IVI titrations Quick onset quick offset
Ward Dose 1	Ketamine Midazolam	5 mg/kg/per os 0.25 mg/kg per os mixed together 20–30 min to work	5 mg/kg/per os 2.5–5 mg per os Mixed together 20–30 min to work
Ward Dose 2 (for pain score >3)	Ketamine NO Midazolam	Half the previous dose ketamine IMI 5–10 min onset	100 mg ketamine IMI 5–10 min onset
Ward Dose 3 (for pain score >3)	Ketamine NO Midazolam	Half the previous dose ketamine IMI	100 mg ketamine IMI
	The final total dose of Ketamine given at the procedure must be written as the script for the following dressing change, do not leave the inadequate dose as the prescription		
Clinic	Ketamine OR	5 mg/kg IMI	5 mg/kg IMI
	Morphine	–	10–15 mg IMI
Emergency Department	Ketamine	5 mg/kg IMI	5 mg/kg IMI
	Morphine	–	0.05 mg/kg IVI
	Fentanyl	–	50–100 mcg IVI

Background Analgesia and Sedation			
	Drug	Paediatric	Adult
	These are oral doses unless otherwise stated		
Mandatory	Paracetamol (syrup = 120 mg/5 ml)	15 mg/kg 6 h	1 g 6 h
Mandatory	Tilidine (1 drop = 2.5 mg)	1 mg/kg 6 h	–
Mandatory	Tramadol	–	50–100 mg 6 h
Add if pain not controlled and for donor site pain	Ibuprofen (100 mg/5 ml)	10 mg/kg 8 h	400 mg 8 h
	Consider contraindications: Curling's ulcer, acute kidney injury, comorbidities		

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5.6 CONCLUSION

This chapter builds on the work conducted in chapter 3. This previous work in chapter 3 demonstrated a lack of compliance to analgesia protocols and a deficit of knowledge with regards to analgesia for burn injured patients. The working assumption is that as a result of this, patients with burn injuries in general, receive inadequate analgesia in the peripheral hospitals. Our clinical impression was that patients who were referred to us after a substantial time at the base hospitals required for more analgesia to control their pain than those who we had managed from the outset with strict compliance to the analgesia protocols. This was the basis for the paper presented in this chapter.

The reasons for delayed referral in our setting are multi-factorial. One of these reasons is inadequate training in burns and as such, not recognizing the need to refer until the wound has not healed months down the line. |in general most large burns are referred early as people more easily identify these patients as requiring a higher level of care. The delayed referrals are generally smaller deeper burns which were not identified to be deep burns until they did not heal. Other potential reason for delayed presentation to the PBS is patients not following up due to financial constraints and the cost of transport to the healthcare facility and, less commonly, it may be due to limited beds and theatre time at the PBS and we advise on management while awaiting a bed and theatre time.

Patients who do not receive adequate pain relief from the time of the first dressing change can experience wind up pain.(97,98) As a result they experience the pain of the dressing change more intensely each dressing change. This culminates in a much higher dose of analgesia requirement for subsequent dressings changes. The aim of this paper was to demonstrate this effect and to highlight the importance of procedural sedation for burns dressings. Education in burn care in general will aid in the earlier referral of patients and education focused specifically on the provision of analgesia will contribute to adequate analgesia for burns patients while they await transfer.

CHAPTER 6

BARRIERS TO ADEQUATE ANALGESIA IN PAEDIATRIC BURNS PATIENTS

6.1 SUMMARY

This paper explores the barriers to adequate analgesia in paediatric burns patients. It firstly highlights deficits in the prescribing habits of doctors regarding analgesia for burn-injured patients; and secondly demonstrates that, even when adequate doses of analgesia are prescribed for paediatric burns patients, the volume the patient is sent home with is inadequate, resulting in the medication running out prior to the next follow-up appointment. This paper offers recommendations for overcoming these barriers to adequate analgesia for paediatric burns patients.

6.2 PUBLICATION DETAILS

Title	Barriers to Adequate Analgesia in Paediatric Burns Patients
Authors	S.L. Wall, D.L. Clarke, N.M. Nauhaus, N.L. Allorto
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6.3 JOURNAL DETAILS

The South African Medical Journal (SAMJ) is a peer-reviewed, internationally indexed journal published monthly. It is accredited by SciELO SA and Science Citation Index (Web of Science (WoS) Core Collection).The SAMJ is a general medical journal publishing leading research impacting clinical care in Africa. The journal is intending to capture the

spectrum of medical and health sciences, grouped by relevance to the country's burden of disease. The journal carries research articles and letters; editorials; clinical practice and other medical articles and personal opinion; South African health-related news; obituaries and general correspondence.

6.4 PUBLICATION TIMELINE

The first draft of this article was submitted to SAMJ on 26 November 2019. Reviewers' and editorial feedback was received on the 17 December 2019 with all comments and queries responded to on the 7 January 2020. The final manuscript was accepted and slated for publication on 9 January 2020. The paper was published on 1 October 2020.

6.5 CONTRIBUTION DETAILS

The candidate conceptualised, developed and wrote the paper. Professor Clarke and Dr Allorto provided assistance with the conceptualisation of the paper and contributed significant editing of the draft and final manuscript. The statistical analysis was also done by the candidate.

Barriers to adequate analgesia in paediatric burns patients

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Background. All children with burn injuries experience pain at some time during their management and recovery. Burn pain is challenging to manage, owing to a combination of factors. The process of achieving adequate analgesia involves the correct scripting of medication based on the doctor's knowledge, the correct fulfilling of that script, and patient compliance.

Objectives. To assess two components of this process, correct scripting of medication based on the doctor's knowledge and the correct filling of that script, to highlight potential barriers to adequate analgesia for burn-injured patients being followed up at an outpatient department. Patient compliance was out of the scope of this study.

Methods. The study was conducted in the Pietermaritzburg Burn Service (PBS) in Pietermaritzburg, South Africa, and was undertaken in two parts. The first part was conducted through an anonymous, voluntary questionnaire completed by doctors working in hospitals referring to the PBS. The aim of the questionnaire was to identify deficits in knowledge of doctors regarding background analgesia for burn-injured children. The second part was conducted through an audit of the outpatient folders of children attending the PBS outpatient clinic to identify discrepancies between analgesia prescribed and analgesia supplied to the patient.

Results. Thirty-six doctors completed the questionnaire. While nearly all the doctors prescribed background analgesia, just over half (58%) prescribed paracetamol, and of those, only half prescribed the correct dose. Half of the doctors prescribed tilidine, and only half of them knew the correct dose. Forty-seven percent of the doctors prescribed both paracetamol and tilidine for background analgesia. The outpatient folders of 59 children attending the outpatient clinic were audited. Fifty-three patients were prescribed paracetamol. There was a statistically significant difference between the paracetamol volume prescribed and the volume supplied ($p<0.0001$). Twenty-four patients were prescribed ibuprofen. There was a statistically significant difference between the ibuprofen volume prescribed and the volume supplied ($p<0.0001$).

Conclusions. Burn-injured children commonly receive inadequate analgesia in our setting. The reasons for this are multifactorial. The correct dose and the correct drugs for burn-related background pain are deficits in the knowledge of doctors who deal with this common problem. Furthermore, even if the correct drug and dose are prescribed, the correct volume of medication is often not issued by the pharmacy. This study highlights barriers to achieving adequate analgesia in children with burns being managed as outpatients. Potential strategies to overcome barriers include improving education with regard to pain management and burns at an undergraduate and postgraduate level, and improved supply chain management.

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The most frequent complaint of burn-injured patients is pain.[1] All children with burn injuries will experience pain at some time during the course of their management and recovery. Burn pain is exceptionally challenging to manage[2] owing to a combination of factors, including burn injury-related factors, healthcare practitioner-related factors and system-related factors.[3,4] The burn injury-related factors influencing pain management encompass the dynamic nature of burn pain, which requires ongoing reassessment of the pain and adjustments in the analgesia regimen, altered metabolism of analgesics due to the hypermetabolic response, and the complex interaction between pain and anxiety that is inevitable in burn-injured patients.[5,6]

The Pietermaritzburg Burn Service (PBS) prescribes analgesia according to the PBS burns protocols (Appendix A, http://samj.org.za/public/sup/14519.pdf). These protocols are also provided to the hospitals that refer to the PBS. It has previously been shown that in the referring hospitals there is a lack of knowledge regarding procedural analgesia and variable penetrance of analgesia protocols in the management of patients with burn injuries.[7] We believe that this also translates into a lack of knowledge regarding background analgesia (pain relief aimed at constant burn-related pain, not associated with procedures). This lack of knowledge combined with a common misconception of healthcare practitioners that burn wounds 'are just painful' leads to inadequate pain control for burn patients.[8]

It is our impression that another factor contributing to inadequate pain control in patients being followed up in the outpatient department is that they are not being supplied with enough medication to last until their next follow-up visit. Consequently, their medication is depleted before their next appointment. As a result, it is difficult to break the cycle of pain, which can lead to the development of complex pain syndromes.[9] Various system-related factors contribute to this inadequate supply of medication: stock-outs of drugs, budgetary constraints, lack of resources, and possibly lack of knowledge, on the part of the pharmacists issuing the medication, of the complexity of burn pain and how imperative adequate pain control is in the healing and overall wellbeing of these patients.[4,10]

Objectives

The process of achieving adequate analgesia involves the correct scripting of medication based on the doctor's knowledge, the correct fulfilling of that script, and patient compliance. The objective of this

study was to assess two of these components: correct scripting of medication based on the doctor's knowledge and the correct filling of that script, to highlight potential barriers to adequate analgesia for burn-injured patients being followed up at an outpatient department. Patient compliance was out of the scope of this study.

Methods

The PBS operates across the regional (Edendale Hospital) and tertiary (Grey's Hospital) hospitals in Pietermaritzburg, KwaZulu-Natal (KZN). There are 40 dedicated burns beds across the metropolitan area, and these are managed by two burns surgeons. Ten of these beds are at Grey's Hospital and 30, including 6 high-care beds, are at Edendale Hospital. The PBS provides support to 19 district hospitals in the western third of KZN. The annual patient load consists of ~500 patients exclusively managed as outpatients and a further ~500 - 600 who are managed as inpatients. Patients in western KZN are managed according to the PBS burns protocols, with the aim being that all burns patients are discussed with or seen by one of the two burns surgeons.

The study was conducted in two parts: (*i*) to identify deficits in the knowledge of doctors regarding background analgesia for burn-injured children; and (*ii*) to identify whether patients are being given an inadequate supply of analgesia (a discrepancy between what is prescribed and what is supplied), resulting in their medication running out before their next appointment.

The first part of the study was conducted through an anonymous, voluntary questionnaire completed by medical officers and registrars working in the PBS as well as doctors encountered on outreach visits to the hospitals that refer to the PBS. Completion of the questionnaires occurred over a 6-month period from December 2018 to May 2019. The questionnaire included questions thought to be relevant to testing knowledge of background analgesia for burn-injured children being managed as inpatients. Demographic information, including the level of the hospital where the respondent worked and number of years' experience working as a doctor, was collected. Evaluation of prescribing practices for background analgesia included questions on which drugs were used, as well as dosages and frequency at which the drugs were prescribed for inpatient administration. Data were collected on an Excel spreadsheet, version 16.40 (Microsoft, USA).

The second part of the study was conducted through an audit of the outpatient folders of children attending the burns clinic in the surgical outpatient department for a 2-month period, January and February 2019. Information regarding the dosage and frequency of analgesia, duration of the prescription for analgesia, and volume of the analgesia medication supplied was collected on an Excel spreadsheet. This information was used to calculate the volume of medication that the patient had been prescribed and the difference between the volume prescribed and the volume supplied to the patient.

Statistical analysis was performed by the authors using R Studio version 1.1.463 (R Foundation for Statistical Computing, Austria). A Wilcoxon signed-rank test was conducted to compare the supplied v. prescribed doses for each drug.

The study was granted ethical clearance by the Biomedical Research and Ethics Committee of the University of KwaZulu-Natal (ref. no. BE594/18).

Results

The anonymous questionnaire was completed by 36 doctors working at district, regional and tertiary hospitals across western KZN. Table 1 summarises the results of the questionnaire. While the vast majority of doctors (94%) prescribed background analgesia, just over half of them prescribed paracetamol and less than half prescribed the correct dose. Half of the doctors prescribed tilidine, and again only half of them knew the correct dose. Forty-seven percent of the doctors prescribed both paracetamol and tilidine for background analgesia.

The audit of the outpatient folders of children attending the burns clinic in the surgical outpatient department included 59 visits where

Table 1. Questionnaire results

Respondents	
Responded to questionnaire, *N*	36/36 (100% response rate)
Level of hospital, *n*	
District	18
Regional	9
Tertiary	9
Designation, *n*	
Medical officer	30
Registrar	6
Years qualified, mean (SD)	8.7 (6.2)
Background analgesia, *n*/*N* (%)	
Background analgesia prescribed	35/36 (94)
Paracetamol	
Prescribed	21/36 (58)
Correct dose prescribed	10/21 (48)
Tilidine	
Prescribed	18/36 (50)
Correct dose prescribed	9/18 (50)
Participants who prescribed both paracetamol and tilidine	17/36 (47)
Participants who claimed to prescribe background analgesia and used other drugs	2/36 (6)
Participants who claimed to prescribe background analgesia and did not indicate which drugs or doses	9/36 (25)

SD = standard deviation.

analgesia had been prescribed. The demographics of the children whose files were audited are summarised in Table 2. Further details of the analgesia prescribed and supplied are provided in Table 3.

Paracetamol was prescribed to 53 patients. The duration of the scripts ranged from 7 to 28 days. The mean (standard deviation (SD)) volume of paracetamol syrup prescribed was 471 (383.2) mL, and the mean (SD) volume supplied to the patient was 129 (87.5) mL. A Wilcoxon signed-rank test showed a statistically significant difference between the paracetamol prescribed and the paracetamol supplied by the pharmacy ($p<0.0001$). Fig. 1 depicts the relationship between the paracetamol prescribed and that supplied to the patients.

Ibuprofen was prescribed to 24 patients. All these patients were also prescribed paracetamol. The duration of these prescriptions also ranged from 7 to 28 days. A Wilcoxon signed-rank test showed a statistically significant difference between the ibuprofen volume prescribed and the volume supplied ($p<0.0001$). The mean (SD) ibuprofen volume prescribed was 335.6 (342.7) mL and the mean volume supplied was 110.1 (62.9) mL.

Discussion

The controversy surrounding provision of adequate analgesia is not a new one. An anonymous editorial advocating the formation of analgesia-providing teams was published as long ago as 1972.[11] Despite the availability of effective analgesics, an unacceptable number of patients continue to experience intense pain.[12] The provision of adequate analgesia, not only for burn-injured children but for all patients in pain, is dependent on various factors. In the case of children, poor objective pain assessment, poor communication between the child, the parents and the hospital staff, and inexperience of both those prescribing analgesia and those administering it, are a few of these.[13]

In our setting, factors contributing to inadequate analgesia can be divided into healthcare practitioner-related factors and system-related factors, and in burns, burn-related factors.

Our study, which demonstrated that approximately half the doctors who responded adhered to analgesia protocols and approximately half of those knew the correct drug dosages, is in keeping with other literature regarding healthcare practitioner-related factors that may contribute to inadequate analgesia.[3 14 15] These factors include lack of training with regard to recognition of inadequate analgesia as well as lack of knowledge of the treatment modalities available.[14] Historically, a low educational emphasis has been placed on pain management in both undergraduate and postgraduate medical training.[14] Burns patients are at a further disadvantage, as there is an even greater deficit in burns training in undergraduate and postgraduate training programmes.[3 15] This inadequate education in burns and pain management culminates in healthcare professionals who are managing patients with severe pain lacking the appropriate knowledge, attitudes and skills to manage analgesia requirements effectively.[16]

System-related factors contributing to inadequate analgesia include drug stock-outs and budgetary restraints.[10] A collective probe by four influential non-governmental organisations looking specifically at stock-outs of HIV and tuberculosis drugs identified

Table 2. Demographics of children included in file audit (*N*=59)

Age (years), median (IQR)	5 (1 - 9)
Gender, *n* (%)	
Female	32 (54)
Male	27 (46)
Total body surface area (%), median (IQR)	9 (1 - 35)
Depth, *n* (%)	
Superficial partial	21 (36)
Deep dermal	27 (46)
Full thickness	11 (18)
Mechanism, *n* (%)	
Hot water scald	41 (70)
Flame	9 (15)
Electrical	1 (2)
Hot surface	6 (10)
Hot food	2 (3)

IQR = interquartile range.

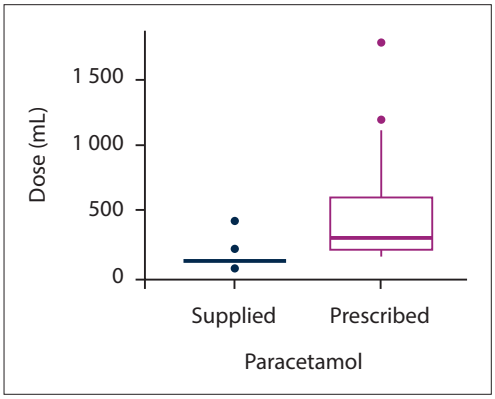

Fig. 1. Box plot of the discrepancy between paracetamol supplied and prescribed.

Table 3. Audit of analgesia supplied and prescribed

Scripts, *N*	59
Paracetamol syrup	
Patients prescribed paracetamol syrup, *n*	53
Difference between what was prescribed and what was supplied (mL), median (IQR)	170 (68.0 - 460.0)
Difference between what was prescribed and what was supplied (mg), median (IQR)	4 080 (960.0 - 11 040.0)
Ibuprofen syrup	
Patients prescribed ibuprofen syrup, *n*	24
Difference between what was prescribed and what was supplied (mL), median (IQR)	97 (47.0 - 327.5)
Difference between what was prescribed and what was supplied (mg), median (IQR)	2 200 (1 150.0 - 6 700.0)

IQR = interquartile range.

that a wide range of other essential medications, including analgesics, are also greatly affected by drug stock-outs in SA.[10] Various factors contribute to these stock-outs, including a shortage of pharmacists, inadequate communication between suppliers, depots and facilities, corruption, and mismanagement within the supply chain.[4] Another systems-related factor that may contribute to inadequate analgesia is the fact that the cost of the most effective analgesics may result in their being omitted from formularies.[17] Our study highlights the issue that patients are given restricted volumes of analgesia regardless of the volume prescribed, resulting in inadequate analgesia owing to medication running out prior to their follow-up appointment.

Low drug stock levels and budgetary constraints are also in part to blame for patients receiving inadequate supplies of medication for analgesia. Pharmacy policies and procedures require pharmacists to confirm proper doses of prescribed medications,[18] However, in resource-limited settings, in the case of drugs that are prescribed often by many disciplines, such as analgesics, the volume supplied is often limited in an attempt to stretch the resources as far as possible and ensure that more patients get some medication at least. This situation results in under-dosing of medication, even if it means that the medication may become depleted before the next visit to the hospital, in an attempt to provide as many patients as possible with at least some analgesia.

Study limitations

One of the limitations of this study is the sample size of doctors completing the questionnaire regarding background analgesia, which was restricted by the number of doctors encountered on outreach visits. Another limitation is the fact that patient compliance was not assessed as a further factor contributing to inadequate analgesia.

Recommendations

The dilemma of providing adequate analgesia to burn-injured patients is not an easy problem to solve. There are multiple barriers that need to be overcome for the situation to improve.

The first barrier that needs to be addressed is lack of education. A more substantial portion of undergraduate training needs to be dedicated to pain management. For surgical specialties, it is imperative that postgraduate trainees receive appropriate training in the management of burn care, including the intricacies of pain management in burn-injured patients. Trainees specialising in these fields should be required to do a clinical rotation through burns. An understanding of the pathophysiology of burns, and in particular burn pain, will allow these doctors to prescribe analgesia more judiciously to achieve better pain control for burn-injured patients. The better understanding of burn pain will also contribute to altering the perception that burns 'are just painful' and will promote the realisation that it is possible to achieve adequate analgesia for burn-injured patients. Practitioners across the board have knowledge gaps related to analgesia, both background and procedural, in paediatric burns patients. Educational efforts need to be aimed at all doctors managing burns.

System-related factors contributing to inadequate analgesia provision are more challenging to tackle. Improved communication between suppliers, depots and facilities would contribute to a more consistent supply of essential drugs. Many of the systems being used by supply chain management in developing countries are paper based, and implementing electronic ordering systems will improve efficiency. There also needs to be an improved understanding of supply and demand and improved management of stock to ensure that orders are placed before stock levels become critically low, in order for new stock to arrive before the existing stock is depleted.

Conclusions

Burn-injured children commonly receive inadequate analgesia. The reasons for this are multifactorial. The correct dose and the correct drugs for burn-related background pain are deficits in the knowledge of doctors who deal with this common problem. Furthermore, even if the correct drug and dose are prescribed, the correct volume of medication is often not issued by the pharmacy. This study highlights barriers to achieving adequate analgesia in children with burns being managed as outpatients, and potential strategies to overcome barriers include improving education with regard to pain management and burns at an undergraduate and postgraduate level, and improved supply chain management.

Declaration. The research for this study was done in partial fulfilment of the requirements for SLW's PhD degree at the University of KwaZulu-Natal.
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Author contributions. SLW, DLC, HN and NLA all contributed to the conception, write-up and approval of the final version of this article.
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Conflicts of interest. None.

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6.6 CONCLUSION

This chapter aims to further demonstrate challenges in the management of burn pain. Patients with inadequate background analgesia are also at risk of secondary hyperalgesia or ‘wind up pain’. (97,98) This inadequately prescribed background analgesia and inadequate supply of analgesia contributes to a higher analgesia requirement for dressings changes. This ties into the study that was presented in chapter 5 regarding patients with inadequate analgesia requiring higher doses of ketamine for subsequent dressings changes. Files for this study were collected over a 2 month period and in that time we collected 59 files. We did not feel the need to collect further files as we repeatedly saw the same pattern of medication supply in the files collected and did not feel futher collection of data would change the outcome of the study.

By tackling the challenges in the provision of background analgesia, achieving adequate procedural analgesia may be easier. Chapter 7 describes the use of methoxyflurane for procedural analgesia. Subjectively our impression was that anxious patients did not have as satisfactory response to methoxyflurane for dressing changes as patients who were less anxious, however this data was not collected. Patients who are in pain are more anxious and by addressing background pain, the efficacy of methoxyflurane for dressing changes may be improved even further.

CHAPTER 7

THE USE OF AN ALTERNATIVE ANALGESIA AGENT IN A REGIONAL BURN SERVICE OUTPATIENT CLINIC

7.1 SUMMARY

Ketamine is the cornerstone of many procedural analgesia protocols, but it is not without its limitations. It requires monitoring of the patient after administration and the child remains sedated for a number of hours after the dressing change has been completed. It is with this in mind that we investigated alternative analgesic options. Methoxyflurane appeared to meet all of these criteria we desired in a procedural analgesic in the out-patient department. A quick onset of action, short recovery time and no monitoring required. With this in mind we opted to investigate the efficacy of methoxyflurane as an alternative procedural analgesia option in our busy outpatient clinic. Other alternatives such as a combination of Fentanyl and Propofol or Fentanyl and Midazolam all have similar limitations to Ketamine in terms of the need for monitoring for safe administration. This study demonstrates that Methoxyflurane is a viable alternative to Ketamine in a busy outpatient department, with its rapid onset of action and a quick recovery time, with little to no monitoring.

7.2 PUBLICATION DETAILS

Title	Use of methoxyflurane for paediatric patients in a regional burn service outpatient clinic
Authors	S.L. Wall, D.L. Clarke, M.T.D. Smith, N.L. Allorto
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Pages	21-25
Year	2020
DOI Number	10.36303/SAJAA.2020.26.2.2311

7.3 JOURNAL DETAILS

The Southern African Journal of Anaesthesia and Analgesia is a bi-monthly peer-reviewed journal. The journal publishes open access research papers and review articles. The journal aims to promote the continued professional development of anaesthetists and general practitioners. AJAA is accredited by the Department of Higher Education and Training (DHET) for the measurement of research output of public higher institutions of South Africa (SAPSE accredited). No impact factor was found for this journal.

7.4 PUBLICATION TIMELINE

The first draft of this article was submitted to the Southern African Journal of Anaesthesia and Analgesia (SAJAA) on 10 September 2019. Favourable reviews with the request for minor revisions were received on the 6 November 2019. The response to the queries was resubmitted on 12 November 2019. The manuscript was accepted on 14 August 2020 and publication in the next issue has been confirmed.

7.5 CONTRIBUTION DETAILS

This paper was conceptualised, developed and written by the candidate. Assistance in conceptualisation of the paper was provided by Professor Clarke and Dr Allorto. They also contributed significantly to the editing of the draft manuscript and in addressing queries from the reviewer. The statistical analysis was also done by the candidate.

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REVIEW

Use of methoxyflurane for paediatric patients in a regional burn service outpatient clinic

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Background: Procedural analgesia is essential for burn-injured patients. Ketamine is the cornerstone of many procedural analgesia protocols for children as it is safe and effective. However, it requires monitoring and the child may remain sedated for a number of hours. We sought an alternative analgesic option. Methoxyflurane is an inhalational analgesic with rapid onset of action for short term analgesia. There is little literature on the use of this drug in children in South Africa, particularly in burns patients. This paper describes our introduction of methoxyflurane into our procedural analgesia protocols for pain associated with dressing changes for paediatric burns.
Methods: We performed a retrospective review of data from the burns database for a two-month period after the addition of methoxyflurane to the paediatric burn outpatient procedural analgesia protocol as the first line analgesia option.
Results: Ninety-five children were reviewed in the clinic over the two-month period. Thirty patients did not require analgesia for their dressing changes. Methoxyflurane provided effective analgesia in 49/65 (75%) patients.
Conclusion: This study has shown that methoxyflurane is a viable option for analgesia for burns dressing changes in a busy outpatient setting. It is an effective and safe alternative to ketamine. Further research is required into the use of methoxyflurane in other burns settings to clarify predictors of failure, ease of use and possible side effect profiles.

Keywords: Paediatrics, burns, analgesia, methoxyflurane, pain

Introduction

Procedural analgesia is an essential component of care for burn-injured patients in both inpatient and outpatient settings. Ketamine is regarded as safe and effective for procedural analgesia during burns dressings with minimal side effects.[1-3] While ketamine is the mainstay of our current protocol, it is limited by requirements for monitoring and prolonged recovery in a busy outpatient clinic.[4-6] We sought an alternative analgesic option. The aim of this study was to determine if methoxyflurane was a viable alternative to ketamine in this setting.

Methoxyflurane is an inhalational analgesic with rapid onset of action for short term analgesia. It belongs to the fluorinated hydrocarbon group of anaesthetic agents. The analgesic potency is high in low concentrations compared with other volatile anaesthetic agents and methoxyflurane was previously used as part of general anaesthesia.[7] Pain relief begins after 6-8 breaths and continues for several minutes after inhalation has ceased.[8] Methoxyflurane has been described for the management of acute trauma pain, particularly in the pre-hospital and emergency department setting.[9] It has also been used for short procedures such as dentistry and dressing changes.[8]

Setting

Edendale Hospital is a regional level hospital serving a population of three million. The burn service consists of a dedicated team, six high care beds and 24 beds in the general surgical wards. The outpatient clinic runs once weekly. This clinic consists of four rooms and between 20 and 50 patients are reviewed per clinic. Patients may be referred from the emergency department, local clinics and referral hospitals, or they will have been admitted to our burn facility and are now treated as outpatients. The doctor seeing the patient administers the analgesia, either ketamine or methoxyflurane, and does the dressing in one of the four consulting rooms. No monitoring equipment is available in these rooms. Once the dressing has been done by the doctor, the child is then returned to the caregiver and they proceed to the pharmacy queue to fill their analgesia prescription.

Methods

Data during dressing changes are routinely recorded as part of the burns registry. This has class approval granted by the Biomedical Research and Ethics Committee, University of KwaZulu Natal (BCA106/14), which is renewed annually. Information recorded includes patient demographics, details of the burn injury, wound and medication administered. Pain scores were recorded using the face, legs, activity, cry, consolability (FLACC) scale (Table 1).[7] One of two consultants supervises and records this data. The registry computer is located in a secure area and is password protected.

We reviewed this data retrospectively for a two-month period, January to February 2019, after the addition of methoxyflurane to the paediatric burn outpatient analgesia protocol as the first line analgesic option. All children (age < 12 years) presenting to the burn outpatient clinic were included in the study. The protocol used 1 ml of methoxyflurane (Penthrop®) for all dressing changes, administered with a soft silicone mask (Figure 1). Methoxyflurane was administered without the dilutor hole in the inhaler covered, thus delivering a concentration of

Table 1: Face, legs, activity, cry, consolability (FLACC) scale

Behaviour	**0**	**1**	**2**
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting, back and forth, tense	Arched, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimpers; occasional complaint	Crying steadily, screams, sobs, frequent complaints
Consolability	Content, relaxed	Reassured by touching, hugging or being talked to, distractible	Difficult to console or comfort
Assessment of Score:			
0 =	Relaxed and comfortable		
1-3 =	Mild discomfort		
4-6 =	Moderate pain		
7-10 =	Severe discomfort/pain		

Table 2: Burn characteristics

	Methoxyfluorane Group	**Ketamine Group (Methoxyflurane Failure)**	**No Analgesia Group**	**Total**	**Statistical Significant impact on Methoxyflurane success***
Number in sample	49	16	30	95	
Age					$p = 0.04$
Mean Age in years ± SD (standard deviation)	2.87 ± 2.3	1.90 ± 1.45	4.21 ± 3.05	3.13 ± 2.57	
Gender					
Male	23 (47%)	9 (56%)	15 (50%)	47 (49%)	
Female	26 (53%)	7 (44%)	15 (50%)	48 (52%)	
Day post burn					$p = 0.31$
Minimum days	1	3	7	1	
Maximum days	306	44	97	306	
Mean days ± SD	27.7 ± 46.0	21.7 ± 14.67	27.3 ± 21.79	26.6 ± 35.59	
Burn depth					$p = 0.003$
Superficial partial burn	19 (39%)	2 (13%)	20 (66%)	41 (43%)	
Mid-dermal burn	10 (20%)	5 (31%)	2 (7%)	17 (18%)	
Mixed depth burn	12 (25%)	6 (37%)	2 (7%)	20 (21%)	
Deep burn	8 (16%)	3 (19%)	6 (20%)	17 (18%)	
Mechanism					$p = 0.12$
Hot water scald	34 (69%)	14 (88%)	22 (73%)	69 (73%)	
Flame	6 (12%)	2 (12%)	1 (3%)	9 (9%)	
Other	9 (19%)	0 (0%)	7 (24%)	17 (18%)	
Total body surface area (tbsa) in %					$p = 0.88$
Initial BSA (mean) in % ± SD	5.8 ± 6.4	6.9 ± 8.4	4.8 ± 5.3	5.7 ± 6.4	
Residual TBSA (mean) in % ± SD	2.3 ± 2.6	3.1 ± 3.8	2.1 ± 3.5	2.4 ± 3.1	
Skin grafting	11	2	6	19	$p = 0.05$

* A logistic regression model was run to determine possible impact of specific variables on the success of methoxyflurane. While this study was under powered to predict factors resulting in failure of methoxyflurane, this may guide future research into predictors of failure of methoxyflurane.

0.2–0.4%. After 5 minutes, clinical assessment is made as to the adequacy of the analgesia.

Ketamine was used (5 milligrams per kilogram intramuscularly) if:

1. The child refused the face mask and, therefore, the methoxyflurane was not able to be administered.
2. The methoxyflurane was not achieving adequate analgesia (FLACC scale score of 3 or more).

No monitoring equipment is available in the consulting rooms and as a result no monitoring was conducted for either the methoxyflurane or the ketamine administration.

Figure 1

Statistical analysis was conducted by the authors using R studio version 1.1463.[8] Descriptive statistics were used to describe the variables age, gender, day post burn, burn depth, mechanism of burn and total body surface area of the burn. A binary logistic regression model was run to assess possible impact of certain variables on methoxyflurane success. This model compares the methoxyflurane success group to the methoxyflurane failure group. A *p*-value of < 0.05 was considered significant.

Results

Ninety-five children were reviewed in the clinic over the two-month period and one-hundred and twenty dressing changes were performed. Twenty-five of these children were seen more than once in the burns clinic for dressing changes. In all cases where Methoxyflurane had been successful for the first dressing change, it was successful again at subsequent dressing changes. The children reviewed consisted of 47 males and 48 females. The mean age of the whole sample was 3.13 ± 2.57 years. The methoxyflurane group had a mean age of 2.87 ± 2.3 years and the ketamine group a mean age of 1.9 ± 1.45 years.

On average, the patients were seen on day 27 post-burn with a median of 17 days and a range of 1–306 days. The child who presented at 306 days had completely healed burns but had a contracture that had torn during mobilisation and had re-presented as a result of this. Burn characteristics are summarised in Table 2. A comparison of characteristics between the methoxyflurane group (i.e. success group) and the ketamine group (i.e. the methoxyflurane failure group) are also shown in Table 2.

In terms of distribution of burns, 72% (68/95) of the patients had burn wounds at a single anatomical location. The burns were distributed as follows: 12% had head/facial burns, 25% upper limb burns (not including hands), 9% hand burns, 18% torso burns, 21% lower limb burns (not involving the feet), 12% feet burns and 3% perineal burns.

Forty-nine patients received methoxyflurane alone. Sixteen received intramuscular ketamine: six received ketamine alone as they refused to accept the mask and we were unable to administer the methoxyflurane, and ten received salvage intramuscular ketamine following methoxyflurane. Methoxyflurane provided effective analgesia in 49/65 (75%) patients. Thirty patients did not require any analgesia for their dressing changes.

Discussion

Dressing changes are an essential component of burns care. These dressings can be exceptionally traumatic for children, parents and staff members if done when the child has inadequate pain control.[9,10] Ketamine has been the mainstay of our analgesia protocol. Despite being an excellent analgesic, it has limitations in a busy outpatient department. Although ketamine can be administered orally, in this setting, the analgesic needs to have a rapid onset of action and is therefore administered as an intramuscular injection, which is painful. The safe administration of ketamine requires monitoring and an extended recovery period, which is challenging in a busy outpatient department.[11] This was our motivation for introduction of an alternative analgesic, methoxyflurane, to provide non-invasive analgesia with a rapid onset of action and short duration of action without the need for monitoring.

In South Africa, methoxyflurane is supplied as a 3 ml vial which is poured onto the wick of a hand-held inhaler. Once the wick is saturated with methoxyflurane, the patient then inhales the methoxyflurane via the mouth-piece.[5] It can be administrated at two different concentrations, depending on whether the dilutor hole, which entrails air during inhalation, is occluded or not. When the dilutor hole is covered with a finger, methoxyflurane is delivered at a concentration of 0.5–0.7%. A concentration of 0.2–0.4% is delivered when the dilutor hole is not covered.[5] It costs R400 per vial and hand-held inhaler. It is available in private practice and can be made available in state with motivation. This is particularly pertinent in light of the global/national ketamine shortage where finding alternative solutions for procedural analgesia is necessary. It is simple to use, with no training required, which our experience confirmed.

The prolonged recovery period following ketamine sedation is problematic in a busy outpatient setting. Firstly, adequate monitoring is difficult to achieve. Secondly, caregivers are required to fulfil their pharmacy prescription where there are often long delays. This is not achievable with a sedated child. Methoxyflurane is exceptionally useful in our setting as the child recovers from the methoxyflurane and is able to ambulate within minutes of the dressing change, negating the caregiver having to care for the child.[4,5] We used the lower concentration of 0.2–0.4% given that monitoring facilities are absent. Once further investigation has been done into cases at risk of failure, these patients could potentially receive the higher concentration of 0.5–0.7% in a monitored setting.

Methoxyflurane is not a new agent. The first report of clinical evaluation of methoxyflurane was published in 1960.[12] The use of methoxyflurane for burns dressings in children dates back to the 1970s.[5,13,14] Various authors found methoxyflurane to be an efficacious analgesic agent in this population.[6,13-16] Despite its analgesic properties, numerous other advantages of methoxyflurane were noted in these studies, including mood-modifying effects, retrograde amnesia, minimal sedation, lack of the need for starvation prior to administration and avoidance of painful intramuscular or intravenous administration.[6,13-16] There was growing concern about potential renal toxicity of methoxyflurane in the mid-1960s.[17] In the late 1970s, methoxyflurane was withdrawn from North American clinical practice and over the subsequent 10 years, as newer volatile agents gained popularity, methoxyflurane gradually fell into disuse.[5] No evidence of methoxyflurane-induced renal toxicity, either clinical or biochemical, was ever found when it was used for procedural analgesia in the short term at low doses.[18-20] Renal tubular dysfunction was observed after high cumulative doses of methoxyflurane from long duration inhalation anaesthesia in a retrospective setting only.[18,21] Numerous studies have shown no adverse effects to multiple exposures of methoxyflurane.[13-16] Firn's study exposed children to methoxyflurane between one and thirteen times with no complications. In fact, they reported that after poor effect at first administration, further uses always yielded improved response.[14]

The use of methoxyflurane is discouraged by the manufacturers in patients with renal impairment to a history of malignant hypothermia. While our patients were not specifically tested for these conditions, none of the patients had a history of either condition. It is also discouraged on consecutive days. Our patients received methoxyflurane at most once a week at their clinic follow-up.

Available literature indicates that methoxyflurane is an efficacious analgesic in the paediatric population, although not for all patients.[12-16] Our findings were consistent with this. In the majority of patients (seventy-five percent) presenting for review or dressing change who required analgesia for their dressing changes, methoxyflurane was an effective analgesic. Despite the fact that life-threatening adverse events with ketamine are exceedingly rare, ketamine is not without side effects.[22] Vomiting, agitation, hypoxia and apnoea are well described side-effects of ketamine.[22] The use of methoxyflurane for burns dressings in the outpatient clinic results in the avoidance of ketamine and the risk of these side effects in sixty percent of these patients.

Burn pain is complex and hyperalgesia, allodynia, neuropathy, anxiety and "windup" are common components of the overall syndrome. This is particularly the case if the child has experienced inadequate analgesia at a previous dressing change.[23] These other components of the pain syndrome may contribute to the failure of methoxyflurane in some patients as it does not address these components of pain. Other possible factors relating to methoxyflurane failure relate to genetically determined metabolism of methoxyflurane. It was our clinical impression that methoxyflurane is not effective in the anxious child. This however is subjective, and data was not collected.

In our study, sixteen patients had failure of methoxyflurane, either due to not accepting the mask resulting in us being unable to administer the methoxyflurane or due to the methoxyflurane not being effective. Literature suggests that burns patients demonstrate an altered pharmacodynamic and pharmacokinetic response to numerous drugs.[24] This may be a possible explanation

for the failure of the methoxyflurane in the patients who required salvage intramuscular ketamine following the administration of methoxyflurane. Our data also suggests that methoxyflurane is less likely to be successful in groups of patients with deep burns and in those who have undergone skin grafting. Unfortunately, our study was underpowered to conclude this definitively and further research into this is required.

Despite the package insert for Penthrop stating that children 1–11 years can be given up to 3 ml of methoxyflurane, only 1 ml was administered. The dose of methoxyflurane is dependant on time and tidal volume of the patient. In adults, 3 ml lasts 25–30 minutes with continuous use and one hour with intermittent use.[20] We felt that a volume of 1 ml should be adequate in children as did not require such a long duration of action.

Recommendation for future research includes investigation into predictors of failure of methoxyflurane which will guide the choice of analgesia in the outpatient setting pragmatically.

The limitations to this study include the small number of patients and the retrospective analysis, especially as it pertains to a lack of data on previous dressing changes and evaluation of anxiety. However, our findings show that the effective use of methoxyflurane can be achieved in resource-limited settings.

Conclusion

Our study suggests that methoxyflurane is a viable analgesic alternative for burns dressing changes in a busy outpatient setting. This is due to its rapid onset of action and short duration of action. Further investigation into the predictors of failure of methoxyflurane and the role of anxiety in its failure is needed, but methoxyflurane should still be considered a useful adjunct in the analgesia armamentarium of the burn doctor.

Conflict of interest

The authors declare no conflict of interest.

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7.6 CONCLUSION

Ketamine has been the cornerstone of our procedural analgesia protocol for many years. However, despite being exceptionally effective, it is not without its challenges. In the busy outpatient setting, one of the requirements for procedural analgesia is rapid onset of action. Ketamine does have a rapid onset of action but only when administered either as an intramuscular injection or intravenously. Both of these require a painful procedure in terms of the injection or insertion of an intravenous line to administer the ketamine which is not ideal for children already traumatized by their injury. Oral ketamine is effective, but it has a slow onset of action, and this is not appropriate for an out-patient setting with a high patient burden. Ketamine also has a long recovery time. Our patients often have to travel long distances to attend their clinic appointments. The children often come with their elderly grandmothers for their clinic appointments. In smaller children the grandmothers can easily carry them home but as the children get slightly bigger carrying these children the long distances while still under the effects of ketamine is exceptionally challenging. Patients require monitoring after ketamine for its safe administration. Methoxyflurane offers a solution to all of these challenges that ketamine presents. It has a rapid onset of action without painful administration. It is self-administered, it is unlikely to result in over sedation, it does not require monitoring for safe administration, and it has a fast recovery time. This fast recovery time allows patients to walk out of the dressing room within minutes of the procedure pain free negating the need for the caregiver to carry these children long distances home.

In this study, some patients had ketamine administered on more than one occasion for dressing changes. We did not find any tachyphylaxis. The same dose of methoxyflurane provided adequate analgesia for subsequent dressing changes. Methoxyflurane is stable at room temperature. The cost of methoxyflurane is R400 per whistle and 3ml vial of methoxyflurane. We used 1ml of the methoxyflurane per dressing change and labelled the whistle with the child's name and used the same whistle with another 1ml of methoxyflurane for the dressing the next week. As a result the single methoxyflurane whistle and 3ml vial were used for 3 dressing changes.

This study was conducted in the outpatient setting only. Future research on methoxyflurane in the inpatient setting is planned as well as a comparative study looking at its efficacy in comparison to ketamine in both the inpatient and outpatient setting.

CHAPTER 8

AN ANALGESIA PROTOCOL TO ACHIEVE ADEQUATE ANALGESIA FOR BURN-INJURED PAEDIATRIC PATIENTS – EXPERT CONSENSUS

8.1 SUMMARY

Despite the exceptional burden of burns in low-middle-income countries (LMIC), and the importance of adequate analgesia in burn care, there is a lack of analgesia protocols developed in resource-scarce settings. This paper presents the findings of a Delphi study aimed at achieving consensus by a panel of experts in the management of burn injuries from low-middle-income settings across Africa. The importance of the analgesia protocol developed after the two-round modified Delphi survey lies in the fact that is it has been developed with specificity to low-middle-income settings, by people who work in resource-limited settings. This protocol will provide a guide to doctors working in resource-limited settings, and through its use the overall pain control for children with burn injuries can possibly be improved.

8.2 PUBLICATION DETAILS

Title	Reaching consensus on an analgesia protocol for paediatric burn patients in a resource-scarce South African community
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8.3 JOURNAL DETAILS

South African Family Practice (SAFP) is a peer-reviewed scientific open access journal. SAFP is internationally indexed and is accredited by SCOPUS. The journal focuses on the disciplines of family medicine, primary health care, rural medicine and district health. The

journal is aimed at doctors working in South Africa within the primary health care settings, both rural and urban. The scope of the journal includes original research, clinical reviews and commentaries.

8.4 PUBLICATION TIMELINE

The first draft of this article was submitted to SAFP on 14 July 2020. On 14 August, the reviewers decision was received requesting minor changes to the manuscript. These were made and submitted on the 13 September 2020. Further revisions were requested on the 29 October 2020. These revisions were submitted on the 4 November 2021. The paper was then accepted for publication on 11 November and was published on the 23 February 2021.

8.5 CONTRIBUTION DETAIL

The candidate conceptualised the paper with the help of Dr Verusia Chetty. The candidate developed and wrote the paper. Dr Chetty and Dr Allorto contributed significantly to the editing of the drafting of the draft manuscript. The statistical analysis for the paper was done by Dr Gill Hendry.

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Reaching consensus on an analgesia protocol for paediatric burn patients in a resource-scarce South African community

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Background: Despite the exceptional burden of burns in low- and middle-income countries (LMIC) and the importance of adequate analgesia in burn care, there is a lack of analgesia protocol developed in resource-scarce settings. This necessitates the development of an analgesia protocol applicable to the resource-scarce setting. This study presents the findings of a modified Delphi study aimed at achieving consensus by a panel of experts in the management of burn injuries from low- and middle-income settings across Africa.

Methods: A two-round Delphi survey was conducted to achieve consensus on an analgesia protocol for paediatric burn patients for a resource-limited setting. The Delphi panel consisted of nine experts with experience in management of burn injuries in low-income settings.

Results: Consensus was determined by an a priori threshold of 80% of agreement for a drug to be included in the analgesia protocol. There was a largely overarching agreement with regard to the background analgesia protocol and strong agreement regarding the use of an initial dose of ketamine and midazolam for procedural sedation.

Conclusion: A modified Delphi method was used to obtain expert consensus for a recently adopted analgesia protocol for burn-injured children in a resource-limited setting, with experts in the management of burn injuries in low- and middle-income settings. The expert consensus leads to the rigour and robustness of the protocol. Delphi methods are exceptionally valuable in healthcare research and the aim of such studies is to find converging expert opinions.

Keywords: analgesia protocol; low- and middle-income countries; LMIC's; burns; paediatrics; resource-limited.

Introduction

The burden of burn injuries on sub-Saharan countries, especially amongst children, is huge. Of all the children in the under – five age group in this region, it is estimated that between 300 000 and 17.5 million children sustain burn injuries annually.[1,2] In the medical approach to care, it has long been recognised that inadequate pain control can have adverse physiological and emotional sequelae. Despite this, pain control remains inadequate, not only in the sub-Saharan region but across the globe.[2,3,4,5] Adequate analgesia in burns is essential, but it is often difficult to achieve. Additionally, burn pain is dynamic and needs constant reassessment by medical practitioners.

There is a lack of analgesia protocols which have developed in resource-scarce settings despite the exceptional burden of burns in low- and middle-income countries (LMIC) and the importance of adequate analgesia in burn care. Whilst analgesia protocols have been published, these are predominantly developed in high-income countries (HICs) and may not be applicable in LMICs with their limited availability of medication and monitoring equipment. Worldwide, there is uneven distribution of resources for the administration of adequate analgesia to children for painful procedures.[6] In many regions, such as sub-Saharan Africa, these resources are exceptionally scarce.[6] This necessitates the development of an analgesia protocol which is applicable to the resource-scarce setting.

Previous studies show lack of knowledge and poor clinical practice in the area of analgesia and burns in our setting.[7,8] There is an abundance of knowledge and practices published on this topic but tend to be very generalised.[9,10,11] Burns in our setting are managed by interns to senior medical officers both in our institution and those that refer to us. They have varying experience

with pain management and it is most commonly lies beyond their area of expertise. Protocols can be a practical starting point for doctors with only general skills. Not providing a protocol leads to varying degrees of care that is at risk of falling below an acceptable standard.[12] The protocol was thus developed by surgeons and anaesthetists with experience in burn and pain management to offer assistance to those with less expertise. It is highly unlikely that this problem is unique to us.

This study presents an expert consensus on an analgesia protocol that has recently been adopted by our service. The analgesia protocol presented for consensus, aims to provide safe analgesia strategies to improve pain control for paediatric burn patients for use at district, regional and tertiary hospitals across KwaZulu-Natal (KZN). This study presents the findings of a modified Delphi study aimed at achieving consensus by a panel of experts on pain management for burn injuries from low- and middle-income settings which could be adapted for application in other LMIC's across Africa. Expert opinions were explored to strengthen the proposed analgesia protocol for paediatric burn patients in KZN.

The basis of the initial questionnaire for this Delphi study was the work previously done in analgesia in paediatric burn patients conducted in the same setting.[7,13,14] These previous studies highlighted the lack of knowledge of doctors with regard to analgesia options and doses for children with burn injuries. Although there are challenges with the implementation of protocols, analgesia protocols remain invaluable to aid healthcare professionals with little experience in the management of burn-injured children.[7] They also emphasised the complications of inadequate analgesia, reiterating how imperative adequate analgesia is from the outset in the management of these patients.[13] The provision of analgesia to burn-injured children can be divided into background analgesia and procedural analgesia. Sections dedicated to each of these were included in the protocol and included in the Delphi survey.[15]

Setting

The Pietermaritzburg Burn Service (PBS) is managed by two burns surgeons and operates across the regional (Edendale Hospital) and tertiary (Greys Hospital) hospitals in Pietermaritzburg. The two burns surgeons manage the patients admitted to the 40 dedicated burns beds across the metropolitan but also offer support to all the regional hospitals who refer to the PBS. The PBS provides support to 19 district hospitals in the western third of KZN Province. The doctors in these hospitals who refer to the PBS have access to the burns surgeon on call 24-h a day for advice on the management of all burn-injured patients. Patients in western KZN are managed according to 'The PMB Way Burns Protocols' and the aim is that all burns patients are discussed with or seen by one of the two burns surgeons.

Methods

A modified Delphi technique was used to engage an expert panel of doctors managing burn injuries in low- and middle-income settings, in order to gain consensus on an analgesia protocol for paediatric burn patients applicable for KZN. This was conducted between October 2019 and April 2020.

In accordance with the tenets of the Delphi approach, methodological rigour was maintained through the consensus of expert opinion from medical practitioners who are experienced in the management of burn-injured children in low-resource settings, albeit dispersed geographically across the African continent. This is founded on the belief that the collective views of a group of experts are preferable to those of an individual.[16] Anonymity, iteration, controlled feedback and group response further enhanced rigour.[16,17] Additionally, researchers used purposive sampling, an emergent design and structured communication to satisfy the underpinnings of a consensus survey.[16]

The lead researcher distributed invitations, which included the study information letter and the ethical approval, as well as the first-round questionnaire, in person to the experts at a burns congress where all the experts had converged. The first-round questionnaires were returned and a research assistant de-identified the questionnaires to ensure anonymity. The second-round questionnaire was conducted using a Google form. A link to the Google form was e-mailed to the panellists. The form was anonymised prior to analysis. Through iteration and by communicating results from the previous round to the expert panellists, stability of the feedback was established.[18]

Panel recruitment

There is a great shortage of experts in the management of burn-injured patients in Africa, and South Africa is no exception to this problem.[19,20] Because of a lack of experts in certain healthcare fields in LMICs, studies in these healthcare contexts lend themselves to the recruitment of a smaller number of panellists.[16] In keeping with the Delphi healthcare research approaches, 10 experts were identified and invited to participate.[17]

A panel of experts in the management of burn injuries in low-income settings was selected. Ten experts were identified through burn organisations known to work in low- and middle-income settings. The potential participants included general surgeons, plastic surgeons, paediatric surgeons and anaesthetists. The criteria for being included in the expert panel were medical doctors, having 10 or more years' experience in the management of burn-injured patients in a resource-limited setting, and/or with published research in the field of paediatric burn injuries. One of the identified experts, after agreeing to participate in the study, did not return the first-round questionnaire, and on completing the first-round questionnaire, another expert did not respond to further e-mails regarding round two. Round one, therefore, consisted of nine experts and round two consisted of eight

experts. Unfortunately because of the limited number of specialists who manage burns on a regular basis in Africa, there are a very limited number of people who meet the criteria as an expert in the field. The majority of burns are managed at the primary healthcare or district healthcare level by generalists, who only occasionally manage burns patients, often with limited training in the management of such patients.[20,21] As a result, we were not able to replace the panellist who accepted the questionnaire but did not return it.

Overview of the Delphi process

Consensus was achieved following a two-round modified Delphi survey. An overview of the Delphi process used for this study is depicted in Figure 1.

Step 1 involved an analgesia protocol that we had recently adopted and was framed in a q uestionnaire which included a four-point ordinal scale to rate the specific drug of the protocol as: (1) *Essential:* the drug must definitely be included in the protocol; (2) *Useful:* the drug can be included in the protocol; (3) *Unnecessary*: the drug must definitely be excluded from the protocol and (4) *Unsure:* unsure about this drug.[22,23,24] The protocol, and therefore the questionnaire, was divided into two sections: 'Background analgesia and sedation' and 'Procedural analgesia and sedation'.[24] All drugs are shown in Table 1. The first-round questionnaires were then distributed to the panellists, together with the study information letter and informed consent. The data from the first round were then analysed and used for the generation of the second-round questionnaire. The data from round one was collated and analysed using Excel version 16.35. An a priori threshold of 80% agreement determined consensus, using frequency distributions on *essential* and *useful* responses collaboratively on the four-point scale.[24]

Step 2 involved the development of the second-round questionnaire using only the questions where consensus was not obtained in the first round. A similar ordinal scale was used; however, this was reduced to a three-point ordinal scale: (1) *Essential;* (2) *Useful and* (3) *Unnecessary*.[25,26] This questionnaire was distributed to the panellists via an e-mail link to a Google form which the panellists completed online. Round-two questionnaires were returned over 4 weeks. Unfortunately, only eight of the panellists replied and despite numerous e-mails, the last panellist did not respond. There was a high level of consensus in round two, which is shown in Table 1. The Delphi study was concluded once the objective of the study had been met and consensus had been achieved with regard to the content of the analgesia protocol.

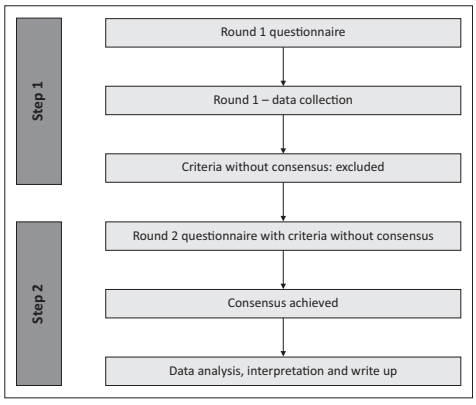

FIGURE 1: Overview of the Delphi process.

Ethical consideration

This study was granted ethical clearance by the Biomedical Research and Ethics Committee of the University of KwaZulu-Natal with clearance number: BE594/18. The participants signed an informed consent letter after reading a study information document. Anonymity was maintained throughout the study, as described above. No incentives were offered for participation. This article followed all ethical standards for research without direct contact with human or animal subjects.

Results

The modified Delphi survey was conducted in two rounds. The first round included nine panellists. In the second round, one of the initial nine panellists opted out of the study. The demographics of the panellists are summarized in Table 2.

The first round of questionnaires yielded agreement on the majority of the drugs in the protocol. There was a high level of consensus (more than 87% of the panellists) for nine of the 18 questions. We will discuss the findings in terms of 'Background analgesia and sedation' and 'Procedural analgesia and sedation'. The consensus for each of the drug items across the two rounds is presented in Table 1.

Background analgesia and sedation

There was overarching agreement with regards to the use of paracetamol, ibuprofen, morphine and clonidine in a stepwise manner in the analgesia protocol. Half of the panellists were in agreement with regards to tilidine (Valeron®) and the other half had no experience with it as it was not available in their settings, as was indicated in their additional comments. In the second round of the Delphi survey, there was 75% agreement, but consensus was still not achieved. The majority of the panel (87.5%) agreed that Allergex® (chlorpheniramine) should be included in the protocol for the treatment of itch.

Procedural analgesia

There was strong agreement regarding the use of an initial dose of ketamine and midazolam for procedural sedation, with all of the panellists believing this was essential. The majority (at least 87.5%) also felt that additional doses of ketamine were required should adequate analgesia not have been achieved with the initial doses.

TABLE 1: A summary of the consensus for each of the drug items across the two rounds.

Variable	Round 1 (*n* 9)				Round 2 (*n* 8)			
	Essential/useful (of those who responded)		Unnecessary/unsure (of those who responded)		Essential/useful		Unnecessary	
	n	%	*n*	%	*n*	%	*n*	%
Background analgesia and sedation								
Mandatory								
Paracetamol 15 mg/kg 6-hourly	9/9	100.0	-	0.0	-	-	-	-
Mandatory								
Tilidine 1 mg/kg 6-hourly	4/8	50.0	4/8	50.0	6/8	75.0	2/8	25.0
Add if pain not controlled and for donor site pain								
Ibuprofen 10 mg/kg 8-hourly	8/8	100.0	-	0.0	-	-	-	-
Consider contraindications of Ibuprofen Curling's ulcer, acute kidney injury and comorbidities	4/4	100.0	-	0.0	9/9	100.0	-	0.0
Consider if > 15% TBSA								
Morphine syrup Start at 0.2 mg/kg 6-hourly. Increase frequency up to 2-hourly then increase dose by 25%. Consider an infusion.	9/9	100.0	-	0.0	-	-	-	-
Add if pain not controlled or neuropathic pain								
Clonidine 25 mcg 8- hourly. Increase to maximum 50 mcg 8-hourly	8/9	88.9	1/9	11.1	-	-	-	-
For neuropathic pain and or severe itch								
Pregabalin start at 25 mg 12-hourly. Increase in 25 mg increments to max 75 mg 12-hourly	6/6	100.0	-	0.0	8/8	100.0	-	0.0
Gabapentin 10 mg/kg 8-hourly. Increase in increments of 100 mg/dose up to 600 mg 8-hourly	6/6	100.0	-	0.0	8/8	100.0	-	0.0
If itch and no Pregaba/Gabapentin								
Allergex 0.1 mg/kg. Start 12-hourly, can be increased to 8-hourly	7/8	87.5	1/8	12.5	7/8	87.5	1/8	12.5
For ICU patients/large TBSA burns (MORPHINE mixed as 1 mg/ml solution, i.e. 10 mg in 10 mL or 50 mg in 50 mL)								
Morphine IVI 0.1 mg/kg loading dose, then 0.1 mg/kg/h infusion Increase to effect, reload and increase rate by 0.05 mg/kg	8/8	100.0	-	0.0	-	-	-	-
For PTSD or anxiety or opioid withdrawal								
Valium 2.5 mg nocte, titrate to effect. Can be increased to 8-hourly	5/7	71.4	2/7	28.6	7/8	87.5	1/8	12.5
Procedural medication								
IV access/ICU/high care								
Ketamine 1 mg/kg IVI titrations. Quick onset, quick offset	9/9	100.0	-	0.0	-	-	-	-
Ward dose 1								
Ketamine 5 mg/kg per os Midazolam 0.25 mg/kg per os mixed together. 20–30 mins to work	9/9	100.0	-	0.0	-	-	-	-
Ward dose 2 (for pain score > 3)								
Ketamine. Half the previous ketamine dose given IMI. 5–10 mins onset. NO midazolam	6/9	66.7	3/9	33.3	7/8	87.5	1/8	12.5
Ward dose 3 (for pain score > 3)								
Ketamine half the previous ketamine dose IMI	6/8	75.0	2/8	25.0	8/8	100.0	-	0.0
The final total dose of ketamine given at the procedure must be written as the script for the following dressing change. Do not leave the inadequate dose as the prescription	1/1	100.0	-	0.0	8/8	100.0	-	0.0
Clinic								
Ketamine 5 mg/kg IMI OR Methoxyflurane 0.5 mL inhaled	6/7	85.7	1/7	14.3	7/8	87.5	1/8	12.5
Emergency department								
Ketamine 5 mg/kg IMI	9/9	100.0	-	0.0	-	-	-	-

TBSA, total body surface area; PTSD, post-traumatic stress disorder; IMI, intra-muscular injection; per os, per mouth.

Discussion

Burn injuries, and the management thereof, are fraught with not only the pain associated with the burn wound, but also with painful procedures required to ensure recovery. All children with a burn injury will experience pain during their treatment and recovery.[27] All over the world, the management of burn pain remains inadequate, despite extensive evidence of the negative physiological and psychological impact of pain on children.[27,28] Poor pain control may result in delayed wound healing and long-term sensory problems, as well as debilitating long-term psychological conditions and chronic regional pain syndromes.[27,29,30]

The management of pain is essential in burn-injured children. Worldwide, resources for the delivery of services, such as analgesia and anaesthesia during surgery and painful procedures for both children and adults, are unevenly distributed; in sub-Saharan Africa, these resources are exceptionally scarce.[6] Due to the fact that health-provider training in paediatric anaesthesia and analgesia is especially uncommon in many low-income countries, the lack of healthcare providers to deliver anaesthesia and analgesia to children is even more significant than for adult patients.[31,32,33] Whilst there are analgesia protocols available for the management of burn-injured children, the majority of these

TABLE 2: Demographics.

Variable	Round 1 (*n* 9)	Round 2 (*n* 8)
Gender		
Male	100.0%	100.0%
Age in years		
31–40	11.1%	12.50%
41–50	22.2%	12.50%
51–60	44.4%	50%
> 60	22.2%	25%
Profession		
Plastic surgeon	44.4%	37.50%
General surgeon	33.3%	37.50%
Anaesthetist	11.1%	12.50%
Paediatric surgeon	11.1%	12.50%
Years' experience in the health profession		
11–15	11.1%	12.50%
16–20	11.1%	12.50%
> 20	77.8%	75%
Years' experience in burns		
6–10	11.1%	12.50%
11–15	11.1%	12.50%
16–20	22.2%	12.50%
> 20	55.6%	62.50%

are either for HICs or are developed for LMICs by HICs. These protocols often do not take cognisance of the lack of monitoring or drug restrictions in a resource-limited environment.

Published protocols remain vague which still poses a problem for healthcare providers who are unsure how to manage pain for burn-injured patients. We aimed to provide a protocol with specific recommendations in terms of doses, when and how to titrate. With this in mind, the researchers purposed to develop an analgesia protocol which was a collaborative effort by a team of surgeons and anaesthetists with both clinical experience with burn dressings and extensive knowledge regarding monitoring capabilities, and the lack thereof, in resource-limited settings, as well as drug availability. Using a Delphi survey, the researchers sought expert consensus from doctors from resource-limited settings to develop an analgesia protocol for burn-injured children in resource-limited settings.

The expert panel agreed that provision needed to be made for both background analgesia and procedural analgesia. Whilst this may seem intuitive, another factor dividing the developed and the developing world is analgesia, especially in the paediatric population.[34] In the face of limited resources, the provision of pain relief for burns is a challenge because of a limited spectrum of analgesics, inadequately trained staff and a lack of monitoring equipment.[34] In round 1 of the modified Delphi survey, there were numerous drug items with no responses. The researchers deduced that insufficient access to certain drugs resulted in failure to answer questions about those drugs but there is no evidence to support this deduction.

In terms of background analgesia, there was consensus amongst the expert panellists regarding the inclusion of paracetamol and morphine in the analgesia protocol for a resource-limited setting. There was no consensus on the use of tilidine (Valeron®). The reason for this lack of consensus was its unavailability in many resource-limited settings, and therefore the researchers have removed it from the analgesia protocol. However, when tilidine is available, researchers would still advocate its use. The use of ibuprofen for background pain was unanimously agreed on.

Burn pain is dynamic in nature and this is, in part, related to the fact that the hypermetabolic response to burn injuries result in the altered metabolism of analgesic drugs.[35] In burn-injured patients, there is an inevitable complex interaction between pain and anxiety, and this also contributes to the dynamic nature of burn pain. [36] The dynamics of burn pain necessitates constant reassessment of the analgesia plan for these patients. If the first three tiers of analgesia, namely paracetamol, ibuprofen and morphine are ineffective to achieve adequate analgesia, clonidine is another useful drug in the armamentarium against pain. There was consensus amongst the experts that clonidine is an essential part of the analgesia protocol. Clonidine has opioid-sparing effects which are useful in addressing tachyphylaxis that burns patients experience.[27] It has been demonstrated in the literature that the benefits of clonidine are not limited to improved analgesia and the morphine-sparing effects, but clonidine also reduces sympathetic overactivity associated with burns.[37]

There was consensus regarding the inclusion of pregabalin and gabapentin for burn pruritus. Post-burn itch is a distressing syndrome, the severity of which is variable.[38] The severity of burn pruritus is usually most severe immediately after wound closure.[39] In paediatric burn-injured patients, post-burn pruritus is highly prevalent.[40] Whilst burn itch was historically managed by emollient massage and antihistamines, both gabapentin and pregabalin have been shown to be very effective to treat it. The expert panellists acknowledge these drugs as being essential for the analgesia protocol.

Dressing changes are an unavoidable part of burn care. There is a limit on theatre time in LMICs. As a result, it is not possible for burn-injured children to have their dressing changes exclusively under anaesthesia in the theatre. This makes procedural sedation and analgesia invaluable. Ketamine has been proven to be safe and effective, and is relatively cheap.[41,42] For these reasons, anaesthesia and conscious sedation for painful procedures in resource-limited settings, particularly for children, remains largely ketamine-based.[33] The expert panel agreed that ketamine is essential as the cornerstone of procedural analgesia for the analgesia protocol. There was also consensus regarding top-up doses to overcome tachyphylaxis.

Limitations

A selection of specialists is required for the participant panel for the Delphi technique, by virtue of the design and method.

The number of doctors with the required expertise to participate was low. Although 10 healthcare professionals were identified to participate, only nine agreed to participate in round one and all nine panellists were not retained in round two. The small number of panellists renders the results not generalisable. All of the panellists included were males. There are very few female surgeons managing burns in Africa. As a result, there were no females in our panel. Whilst we do not feel this would have influenced our results, it would have been beneficial to have included female panellists.

Conclusion

A modified Delphi method was used to obtain expert consensus for a recently adopted analgesia protocol for burn-injured children in a resource-limited setting, with experts in the management of burn injuries in low and middle-income settings. The expert consensus leads to the rigour and robustness of the protocol. Delphi methods are exceptionally valuable in healthcare research and the aim of such studies is to find converging expert opinions.

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Competing interests

The authors have declared that no competing interests exist.

Authors' contributions

All authors contributed equally to this work.

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Data availability statement

Data will be made available by the authors upon reasonable request.

Disclaimer

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency of the authors.

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8.6 CONCLUSION

Burn care in LMICs is vastly different than in HICs. Dressing changes are also vastly different. There is often a limitation in drug choice and limited monitoring equipment available. Due to lack of theatre time, in-patients are frequently dressed in their beds in the wards and less often in dressing rooms adjacent to the ward. In the outpatient setting, some of the requirements for procedural analgesia include rapid onset of action, rapid recovery and safe administration with little to no monitoring equipment.

This paper presents an analgesia protocol which has been subjected to expert consensus by doctors with experience in burn care in LMICS. The protocol was developed for resource-limited settings in KwaZulu Natal, by doctors working in resource limited settings. It takes the limited montiroing equipment and the drug availability into account to ensure that the analgesia protocol is locally applicable. It centres around drugs which have been proven to be safe in attempt to present a protocol that is safe, even in inexperienced hands.

Key differences in the protocol presented in this paper is the addition of methoxyflurane. This was done as a result of the studies preceding this paper looking for a solution to ketamine shortages and the need for monitoring. We wished to establish if the experts agreed with the addition of methoxyflurane to the protocol. Alternatives, such as the combination of fentanyl and propofol or fentanyl and midazolam, have limitations equal to or exceeding those of ketamine. They also require monitoring and have a higher risk of apnoea and hypotension than ketamine. We are proposing an alternative procedural sedation drug that requires no monitoring and the patients are ambulant soon afterwards, and can be self-administered of used by caregiver.

CHAPTER 9

CONCLUSION AND FUTURE RECOMMENDATIONS

9.1. INTRODUCTION

This final chapter will provide an overall summary of the work contained in this thesis. Specific reference will be made to the aims and objectives laid out in the introductory chapter. The significance of the findings of this study will be discussed. Limitations of this study and recommendations for the future are also presented in this concluding chapter.

9.2. ALIGNMENT OF PHD THESIS WITH STUDY AIM AND OBJECTIVES

The overall aim of this study was to provide an alternative approach to pain management to improve pain control for burn-injured children in KwaZulu-Natal (KZN). The objectives for this study were as follows:

- Objective 1: *to identify deficits in the knowledge of doctors in terms of prescribing procedural sedation for children with burn*. This was achieved through an anonymous questionnaire for doctors working in both the Pietermaritzburg Hospital Complex Department of Surgery and the doctors working in the hospitals which refer to the Pietermaritzburg Burn Service. The results are presented in Chapter 3.

- Objective 2: *to compare the analgesic requirements of children presenting with acute burns, versus those with a delayed referral*. This was achieved through a retrospective review of data from the burns database regarding total Ketamine requirements during admission, taking patient weight, total body surface area of the burn and days admitted into account. Chapter 5 summarises these results. Study

- Objective 3: *to investigate obstacles to adequate analgesia in paediatric burns*. This was achieved in two parts: firstly, by means of an anonymous questionnaire completed by doctors working at hospitals who refer to the Pietermaritzburg Burn Service to demonstrate their lack of knowledge regarding background analgesia for paediatric burns patients; secondly, by means of a retrospective audit of the files of children attending the burns outpatient clinic to

demonstrate that, even when the correct dosage of drugs is prescribed, the patients are receiving inadequate volumes of the drugs from the pharmacy. These results are presented in full in Chapter 6. Chapter 4 provides some insight into one of the other barriers to adequate analgesia for dressing changes, the shortage of Ketamine, which is currently the cornerstone of most procedural analgesia protocols.

- Objective 4: *to evaluate the use of an alternative analgesic agent, Methoxyflurane, for pain management during dressing changes in both outpatient setting.* Chapter 7 presents the results for these objectives. Chapter 7 provides some insight into one of the other barriers to adequate analgesia for dressing changes, the shortage of Ketamine, which is currently the cornerstone of most procedural analgesia protocols.

- Objective 5: *to gain expert consensus on a feasible analgesia protocol for burn-injured children through a modified Delphi survey.* Chapter 8 presents an expert consensus study of an alternative analgesia protocol for achieving adequate analgesia for burn-injured children. The protocol was submitted to an expert panel to validate the protocol as being safe, reliable and relevant to a resource-limited setting. The results of a modified Delphi method of establishing consensus are presented in this chapter.

9.3. SIGNIFICANCE

Burn injuries are a major global public health problem, the burden of which is carried predominantly by LMIC's. (99) The burden of burn injuries in sub-Saharan Africa is particularly heavy. A substantial number of burns in the region occur in children under five years of age. In this region, it is estimated that between 300 000 and 17.5 million children in this age group sustain burns annually.(10) Burn injuries and pain are virtually synonymous. Regardless of the cause, size or depth of burn injuries, all children with burns will experience pain. (15) Pain is poorly managed world-over, despite long-standing acknowledgement of the detrimental effects of inadequately managed pain. (15,16) This PhD centres on achieving adequate analgesia in paediatric burn-injured patients in KwaZulu-Natal, South Africa.

There are numerous analgesia protocols for paediatric burns patients published in the literature. However, these have predominantly been developed in high-income countries. There is a lack of analgesia protocols which have been developed in resource-scarce settings, despite the huge burden of burns in LMICs and the importance of adequate analgesia in burn care. Analgesia protocols developed in high-income settings may provide guidance for healthcare workers working in resource-scarce environments. However, these protocols may not take into account the limited availability of medications and the lack of monitoring equipment, rendering them impractical in a low-resource setting. The fact that the majority of analgesia protocols, even protocols developed for low-income settings, are developed in high-income countries, emphasises the great discrepancy in health research capacity in the world. *The Lancet Global Health* recently established that, while 92% of articles address interventions in LMICs, only 35% of the authors are from, or work, in LMICs.(100) This highlights the importance of an analgesia protocol developed for a resource-limited setting by doctors working in a resource-limited setting, and emphasises the value of this PhD project.

A recent survey by the American Burn Association showed that the majority of doctors followed protocols when prescribing procedural analgesia/sedation for dressing changes for paediatric burns patients in the high income setting in the United States. (101) All of the protocols for inpatients included used an opioids and the vast majority of these protocols (92%) included a benzodiazepine for procedural analgesia/sedation with the most commonly used combination being fentanyl and midazolam. (101) While this combination is exceptionally effective and is safe in a setting resource-rich setting, in a setting with limited monitoring equipment to detect complications such a hypotension and desaturation this is not a safe option. For the outpatient setting, the majority of the dressings were done under oral ketamine and midazolam. The same concern regarding the lack of monitoring exists, although, in many low resource settings, ketamine is given without monitoring, this is not best practice. (44,87) The second challenge with oral ketamine is that fact that the onset of action is slow and , which is not practical in a busy outpatient department. (44) The difference with the protocol that we have presented and more specifically, the use of methoxyflurane is that is has a rapid onset of action and a rapid recovery time.(87) Due to the

fact that it is largely self-administered, the risk of over sedation is virtually non-existent and no monitoring is required for the safe administration of methoxyflurane.(87)

The analgesia protocol presented in this PhD offers a practical, easy to use, locally applicable analgesia protocol which can be used in district, regional and tertiary hospitals alike. It is novel in the fact that, not only was it developed for a resource-limited setting by doctors working in resource-limited settings, but it was then subjected to a consensus study; again, by a group of experts working in resource-limited settings. This protocol was developed with the local setting, available medications and monitoring equipment in mind. It was specifically designed to be easy to use, and safe in inexperienced hands. This protocol includes the addition of Methoxyflurane for burns dressings. While Methoxyflurane is used for procedural analgesia in other parts of the world, it is not widely used in South Africa and it is not currently being used for burns dressings in other analgesia protocols in our setting.

The LMIC setting has unique challenges not experienced in HIC where methoxyflurane has previously been used. LMIC's have a much higher burden of burns and as a result a higher number of burns patients. Patients are managed at vastly different levels of care ranging from primary health care nurse management in a primary health care clinic to specialist management in tertiary centres. Many patients who should meet the traditional critera for being managed in a burn centre never reach a burn unit due to an overburdened system. While this protocol is currently aimed at doctors managing patients at hospital at district, regional and teritary level, however, the long term goal is to develop an analgesia protocol which can be administered by nurses in the primary health care setting. While ketamine is beyond their scope of practice due to the risk of side effects and is unsafe in the primary health care setting, methoxyflurane may be the solution to analgesia in the primary health setting. This will be addressed in future research.

9.4. LIMITATIONS

Certain limitations were exhibited at each stage of this PhD. This study was conducted in a single region in KwaZulu-Natal and caution should be taken when attempting to generalise

the results of this study to other parts of South Africa. The study into challenges in the implementation of protocols and doctors' knowledge regarding analgesia was limited by the small sample size. This sample size was dictated by the number of doctors working in the Pietermaritzburg Metropolitan Department of Surgery.

Management of background pain, neuropathic pain and anxiety all influence the amount of procedural analgesia required. This data is challenging to collect and was not collected in the study comparing procedural analgesia between acute and delayed referrals. In order to fully interrogate the impact of anxiety on the experience of pain, a mixed methods study would likely have provided more clarity. Pain in anxiety in children is an even more complex dynamic than in adults. Another consideration is separation anxiety which is common in children. Often, children are accompanied to the hospital by family members not by their parents or primary caregivers. It is not uncommon for parents to have to care for other children at home or for them to have to work resulting in them being unable to spend . This in itself can result in significant anxiety apart from the anxiety from the burn-injury itself and the anxiety from being in a strange environment. Patients who heal within 21 days, by definition, have superficial partial burns and those who heal after 21 days are not superficial burns. As a result, we expect their pain experiences to be different, so a comparison between these two groups may result in bias. Due to tachyphylaxis we expect patients who have been admitted for longer to require more analgesia. What would have potentially been a more appropriate comparison was looking at that the group of patients who are admitted acutely to the PBS but have a length of stay of more than 21 days and compare that group alone to the patients with delayed referral rather than all the patients admitted to the PBS acutely.

In terms of the paper on barriers to adequate analgesia in paediatric burns, again, the sample size was small and was limited by the number of doctors encountered on outreach visits. Another limitation to this study was the fact that patient compliance was not assessed and may be an important factor in inadequate analgesia.

The investigation into Methoxyflurane as an alternative analgesic option was limited by the retrospective nature of the study and the fact that little data exists on dressing changes and the

evaluation of anxiety. A prospective study comparing methoxyflurane to ketamine would be valuable. The statistical power of this study limited some of the analysis that would have strengthened this study. One of the things that we were not able to assess was the predictors of failure of methoxyflurane. With a higher number of patients in the cohort, we could have potentially identified predictors of failure of methoxyflurane.

The limitations of the modified Delphi study stem from the small group of panellists. This is, unfortunately, due to the small number of experts in the field of burn care in resource-limited settings. While, in healthcare contexts, it is not uncommon for there to be fewer people with knowledge and experience in an area being investigated, and it is acceptable to use smaller numbers of experts, this may still influence the results. Due to the small number of experts, the loss of one of the panellist after the first round could have impacted the results for the second round of the modified Delphi study.

9.5. RECOMMENDATIONS

In order for this study to have a meaningful impact on pain management for burn-injured children in KwaZulu-Natal, the analgesia protocol offered by this PhD needs to be presented to healthcare facilities which refer to the Pietermaritzburg Burn Service. To ensure maximum uptake and implementation of the protocol, the protocol needs to be easily accessible to healthcare workers. The Pietermaritzburg Burn Service is in the process of developing a website where 'The PMB Way Burns Protocols' will be freely accessible to anyone who wishes to use them. Outreach visits to the referral hospitals need to be organized where the burns workshops are conducted to upskill doctors in terms of the general management of burns and then additionally the analgesia protocol must be specifically focused on. Once the analgesia protocol has been implemented in these facilities, further studies can be done into the efficacy of the analgesia protocols. The protocol could be instituted in half of the hospitals and a comparative study could be performed to assess if there has been an improvement in both procedural analgesia and prescribing background analgesia following the implementation of the analgesia protocol. A study comparing procedural analgesia requirements in acutely presenting patients and those with a delayed referral could be

repeated to demonstrate no difference in the analgesia requirements if the patients are receiving adequate analgesia at the referral hospital from presentation of the burn.

In the out-patient setting, a prospective cross-over study comparing the efficacy of ketamine and methoxyflurane for dressing changes is needed. A concurrent parallel design could potentially be used to collect quantitative and qualitative data simultaneously with independent analysis of the data types.(102) The experience of the healthcare worker administering the analgesia and the experience of the patient would be useful to ascertain and compare the experiences with ketamine and methoxyflurane.

It is our opinion that the new analgesia protocol is practical and easy to use. This could be assessed whether this assumption is correct as a prospective case-control study by documenting the experience of the healthcare workers using the protocol. Feedback from such a study could be used to further improve on the current protocol.

Repeatedly during this study, the complex relationship between anxiety and pain was raised. The impact of anxiety on pain and pain management was not taken into account in this PhD study. However, it definitely warrants further investigation. Such a study would need to be conducted using a qualitative methodology to fully interrogate the patient's experience of the injury, the hospitalisation, and the painful procedures which are an unavoidable part of burn care; and the anxiety experienced by the patient. The complex interaction between anxiety and pain was beyond the scope of this PhD, but it lends itself to further investigation as a post-doctoral study. A qualitative research design using hermanuetic phenomenology conducted with qualitative open-ended interviews would potentially aid in our understanding of this complex interaction of pain and anxiety.

9.6. CONCLUSION

This PhD thesis centres on improving the care offered to paediatric burns patients by providing an alternative analgesia protocol. Evidence is presented to demonstrate the challenges with the implementation of analgesia protocols, the lack of knowledge on the part

of the doctors managing burn-injured patients' pain, and the sequelae of inadequate analgesia. Methoxyflurane was then investigated as an alternative analgesia option for procedural analgesia for burns dressings. The alternative analgesia protocol for paediatric burn patients, which was developed following an expert consensus study, is the culmination of this PhD research. Pain is an inescapable part of burn injuries, but it can be managed effectively with a systematic approach to prescribing analgesia and a constant re-evaluation of the adequacy of analgesia being provided. This PhD study provides an analgesia protocol to guide healthcare workers managing burn-injured children to better manage the pain associated with burns.

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APPENDICES

GUIDELINES FOR PRESENTATION OF MASTERS AND PHD DISSERTATIONS/THESES BY RESEARCH

1. Purpose

The purpose of this document is to provide guidance to students and supervisors on how to prepare a dissertation/thesis for Masters by Research and PhD degrees using the manuscript or publication format..

2. Introduction

These guidelines must be read together with the College of Health Sciences (CHS) Handbook as well as the Jacobs documents on examination policies and procedures for PhD degrees. The rules on thesis format are based on modification of point 1 of the definition of terms section in the Jacobs document. In this section a thesis is defined as *"the supervised research component of all PhD degrees, whether by supervised research only, or coursework and research, or by papers that are either published or in manuscript form (the supervised research component of the PhD degree by paper(s) comprises the introduction, literature review, account of the methodology, selection of manuscripts, and conclusion)."* A dissertation is defined as "*the supervised research component of all Masters degrees, whether by supervised research only, or coursework and research, or by papers that are either published or in manuscript form (the supervised research component of the Masters degree by paper(s) comprises the introduction, literature review, account of the methodology, selection of manuscripts, and conclusion*)."

2.1 PhD thesis

In the CHS Handbook the rules for a PhD thesis are not in one place; they are stated in DR8 a i & ii, DR9 c and CHS 16. DR8 a i & ii and direct that a thesis be presented in the standard format together with one published paper or an unpublished manuscript that has been submitted to an accredited journal, arising from the doctoral research. CHS16 (thesis by publications states that the thesis may comprise of at least three published papers or in press in accredited journals; such papers must have the student as the prime author. The same CHS16 provides for a thesis by manuscripts that may have at least 3 papers with the student as the prime author that have not yet been published but are in the form of manuscripts; at least two of such papers must constitute original research. In both cases (thesis by publications and manuscripts), there must be introductory and concluding integrative material sections.

The standard type thesis is being phased out in many African countries in favour of the other options that originate from the Scandinavian countries. While this format ensures that all details of the work done for the doctoral degree are captured and thoroughly interrogated, they often remain as grey literature which is mainly useful to other students, usually within the same university, although with digitization of theses, such work may become more accessible beyond the source university. Apart from the risk of losing good work because of it not being on the public domain, as students rarely publish such work after graduating, this approach denies the college additional productivity units (PUs) emanating from publications.

The thesis by publication encourages students to publish key aspects of their doctoral research as they will not graduate if the papers are not published or in press. This approach ensures that the work of the student enters the public domain before the thesis is examined, providing the examiner with some assurance of prior peer review. The thesis must constitute a full study of the magnitude expected of a PhD with the papers providing a sound thread or storyline. Furthermore, the college maximizes the students' work as PUs are awarded for the papers as well as for graduating. However, this approach may negatively affect throughput and frustrate students as

they cannot graduate unless all the papers are published or in press, in addition to the synthesis chapter demonstrating the story line of the thesis.

The option of a thesis by manuscripts ensures that students make efforts to start publishing. The risk of not passing because of failure to publish all papers (as in the thesis by publication) does not exist under this option. However, the PUs emanating from publications from the doctoral work are not guaranteed as the submitted papers may eventually be rejected. Thus there is a possibility of the doctoral work remaining on the university library shelves as is the case for the standard thesis format. The standard thesis does have the advantage that more details of the doctoral work are usually included.

In view of the above, the best option for the college is that of a thesis by publication. However, in the interim, the attractive option is that of thesis by manuscripts, as it provides the possibility of publication without putting the student at risk of delayed graduation when some of the manuscripts are not published/accepted, which also disadvantages the college in terms of PU earnings. The standard thesis option should ultimately be phased out for the stated reasons and students are not encouraged to present their theses in that format. Consequently this document does not describe the standard thesis.

2.2 MSc dissertation

The rules on presentation of MSc dissertations are presented in CR13 (course work), CHS 14 (course work) and MR9 (research) in the CHS Handbook. CR13 c and MR9 c direct that a dissertation "may comprise one or more papers of which the student is the prime author, published or in press in peer-reviewed journals approved by the relevant college academic affairs board or in manuscripts written in a paper format, accompanied by introductory and concluding integrative material." Such a dissertation should include a detailed description of the student's own distinct contribution to the papers. Both CHS14 and CR13 specify that reviews and other types of papers in addition to original research paper/s may be included, provided they are on the same topic.

3 ***Length of thesis and dissertation by word count***

Table 1 provides a guide of the length of a thesis or dissertation by word count excluding preliminary pages and annexes.

Table 1: Thesis length by word count

Sections				
	Minimum	Maximum	Minimum	Maximum
Introduction	2700	2700	2000	2000
Chapters	10000	25000	6000	11000
synthesis	2000	2000	1700	1700
bridging	300	300	300	300
Total	15000	30000	10000	15000

4. *Intention to submit*

A written intention to submit a thesis or dissertation should be submitted to the appropriate postgraduate office with endorsement of the supervisor at least three months before the actual date of submission which should be before November if the student intends to graduate in the following year. The actual submission will under normal circumstances require approval of the supervisor.

5. Format for theses/dissertation

There is little variation in the actual format of the PhD thesis and Masters dissertation for the various types described above. The box below summarise the outline of a thesis/dissertation for the thesis by manuscripts and thesis by publications.

Box 1: Outline of thesis

Preliminary pages

i. Title page
ii. Preface and Declaration
iii. Dedication
iv. Acknowledgements
v. Table of contents
vi. List of figures, tables and acronyms (separately presented)
vii. Abstract

Main Text

1. Chapter 1: Introduction
   Introduction including literature review
   Research questions and/or objectives
   Brief overview of general methodology including study design
2. Chapter 2
   First manuscript/publication
3. Chapter 3
   Second manuscript/publication
4. Chapter n
   Final manuscript/publication
5. Chapter n+1: Synthesis
   Synthesis
   Conclusions
   Recommendations
6. References Appendices

NB. Between the manuscripts or publications there must be a 1 page (maximum) bridging text to demonstrate the link between them

6. Details for thesis/dissertation subheadings

This section summarizes what is expected under each subheading shown in Boxes 1 and indicates where there might be variations between a Masters Dissertation and PhD Thesis.

6.1 Title Page

The officially approved title that is concise (Fewest words that adequately describe the contents of the thesis/dissertation – usually 15 or fewer words) is presented at the top. This should be followed by the candidate's name in a new line. At the bottom the thesis statement should be presented. The thesis statement may be stated as "*Submitted in fulfillment of the requirements for the degree of ____ in the School of _____, University of KwaZulu-Natal"* for a PhD/Masters by Research thesis. In the case of a Masters Dissertation it should be stated as "Submitted as the dissertation component in partial fulfilment (% stated) for the degree of _____ in the School of _____, University of KwaZulu-Natal". For both Masters and PhD the date of submission must be stated.

6.2 Preface (Optional)

The preface merely states the reason (motivating factors) why the study was conducted without getting into details of what was investigated.

6.3 Declaration

This must be structured as follows:

I, Dr/Mr _____, declare as follows:

1. That the work described in this thesis has not been submitted to UKZN or other tertiary institution for purposes of obtaining an academic qualification, whether by myself or any other party.

   Where a colleague has indeed prepared a thesis based on related work essentially derived from the same project, this must be stated here, accompanied by the name, the degree for which submitted, the University, the year submitted (or in preparation) and a concise description of the work covered by that thesis such that the examiner can be assured that a single body of work is not being used to justify more than one degree.

2. That my contribution to the project was as follows:
   This is followed by a concise description of the candidate's personal involvement in and contribution to the project, in sufficient detail that the examiner is in no doubt as to the extent of their contribution.

3. That the contributions of others to the project were as follows:
   This is followed by a list of all others who contributed intellectually to the project, each accompanied by a concise description of their contribution. This does not include people who ordinarily would be "acknowledged" as opposed to considered for authorship.

4. Signed _____ Date_____

6.4 Dedication

This is an optional section. Should it be included it must be very brief merely indicating to whom the work is dedicated. Avoid anything too flowery

6.5 Acknowledgements

This section acknowledges all individuals, groups of people or institutions that the candidate feels indebted to for the support they rendered. The funding source for the work should also be acknowledged.

6.6 Table of contents

Table of contents must be inserted after the preliminary sections and must capture all major sections of the thesis at the various levels (primary, secondary, tertiary subheadings). It should be electronically generated and should be able to take the reader to specific headings in the thesis.

6.7 Lists of figures, tables and acronyms

These lists must be presented separately. All titles of figures presented in the thesis/dissertation must be listed indicating on what page they appear. Similarly for tables the titles must be presented indicating on what page they appear. In the case of acronyms, the acronym is stated and all the words describing the acronym are presented. Only key acronyms should be stated. In some cases they may not be listed as long as full text is presented whenever the acronym is used for the first time.

6.8 Abstract

The abstract should summarize the thesis mainly stating the purpose of the study, highlights of chapters and the new knowledge contributed by the thesis. The abstract must be approved by the supervisor of the thesis and should not be more than 350 words in length.

6.9 Introduction

The introductory chapter for both types of thesis is similar. The section should include literature review and have the following information. Headings are used as appropriate and need not correspond exactly to the following.

i. Background and the context of the study
ii. Description of the core research problem and its significance
iii. A comprehensive, critical, coherent overview of the relevant literature leading to clearly defined knowledge gaps
iv. A coherent problem statement highlighting the nature and magnitude of the problem, the discrepancy, knowledge gaps therein and possible factors influencing the problem.
v. Clear and SMART research questions, objectives and hypothesis and/or theoretical framework
vi. A conceptual framework (optional)
vii. Description of the study area and general methodology *(in a standard thesis this should be a stand-alone section)*
viii. Layout of the thesis (thesis structure) indicating what chapters are presented in the thesis and how they address the objectives.

6.10 Literature review

This section is subsumed in the introduction within the stipulated word count for a thesis or dissertation.

6.11 Methodology

A standalone section is not needed as the methods are adequately described in each manuscript/publication.

6.12 Data chapters/manuscripts/publications

The full published paper or manuscript submitted for publication should be presented as published or submitted to the journal. The actual published paper should be scanned and inserted

in the chapter. There should be a separator page between chapters that has text linking the previous chapter to the next and providing details of the next manuscript/publication indicating publication status.

6.13 General discussion/Synthesis chapter

This is a general discussion that demonstrates the logical thread that runs across the various manuscripts/publications (synthesis). There should be no doubt that the manuscripts/publications complement each other and address the original objectives stated in the general introduction of the thesis. The general discussion/synthesis chapter should end with a conclusion and recommendations where necessary.

6.14 References

Only references cited in the introduction and synthesis chapters should be listed as all other references should be within the manuscripts presented under data chapters.

6.15 Annexes

All information (questionnaires, diagrams, ethics certificates, etc) considered important but not essential for inclusion in the actual thesis is put in this section as reference material. In addition papers that emanated from the work but not directly contributing to the thesis may be included.

7. Thesis formatting

For standardisation of thesis the following formatting specifications should be followed.

7.1 Font

Times New Roman 11pt should be used throughout the thesis. However, major headings may be made bigger (12pt) but using the same font type

7.2 Paper size and margins

A4 (297 x 210 mm) should be used and in the final thesis both sides of the paper should be used. However, the loose bound copy submitted for examination should be printed on only one side. The recommended margins are 30mm for all the left, right, top and bottom margins.

7.3 Line spacing

The copy submitted for examination should have 1.5 line spacing but the final copy should have single line spacing. Paragraphs should be separated by a blank line. Published or submitted manuscripts should remain in their original format in all aspects as they are inserted in their published format in appropriate places.

7.4 Headings

A consistent numbering system and captions should be maintained with first level being in CAPS and centred, second level being **normal bold** font and third level being ***italics bold***. If there is need for 4th level it should be *normal italics*.

7.7 Pagination

Page numbers should be centred at the bottom of the page. All preliminary pages should be numbered in lower case Roman numerals and subsequent pages should be numbered as indicated in the Box The title page should not be numbered.

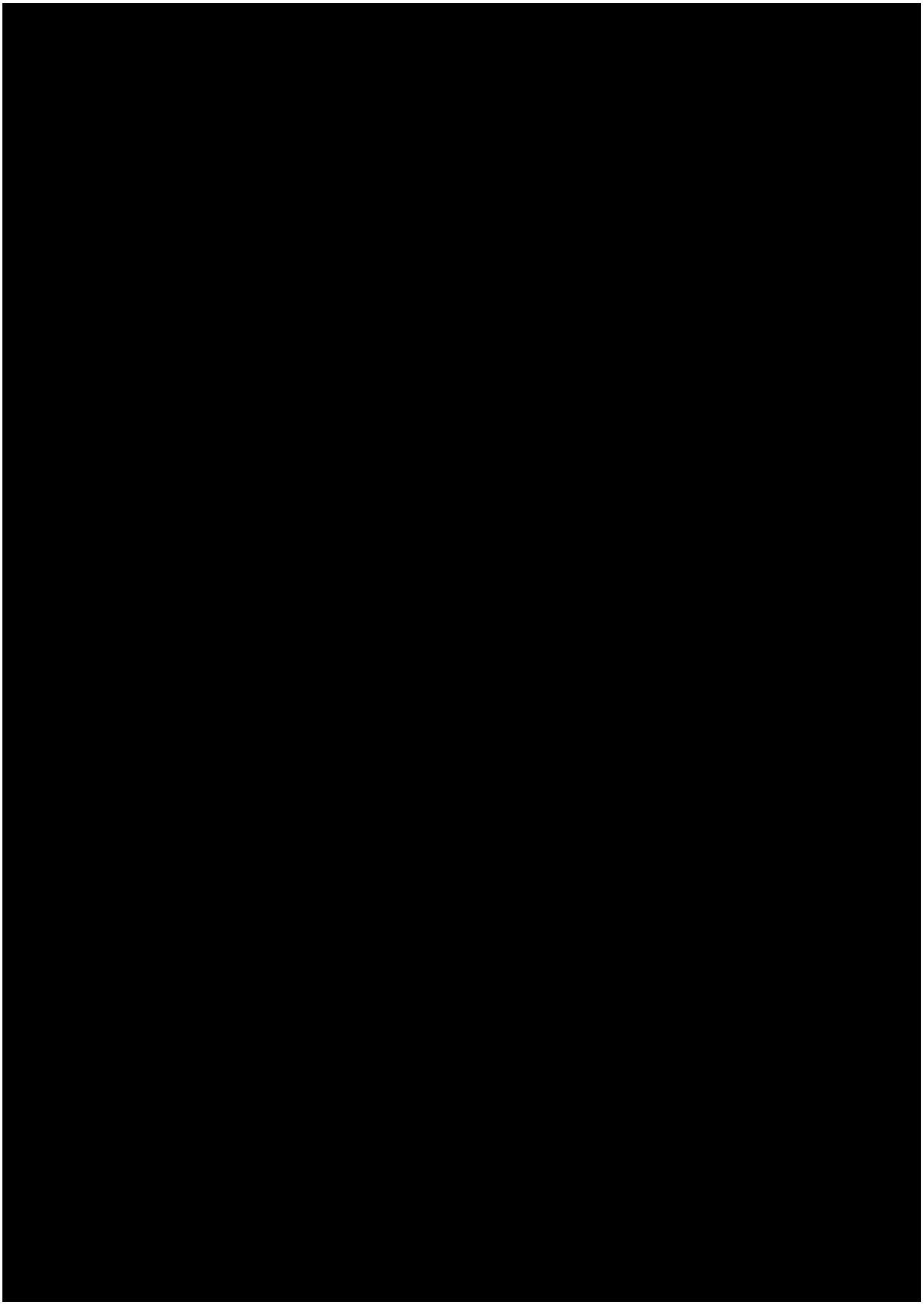
The body of the thesis (chapter 1 onwards) should be numbered consecutively with Arabic numerals. The numbers should continue consecutively from the introduction through the through the publications or submitted manuscripts and subsequent sections. The published papers will therefore bear two numbers: a set specific to the manuscript (it is recommended to place these in the upper right hand corner) or published paper, as well as the consecutive numbers belonging to the thesis as a whole. Care must be taken to distinguish these in terms of position and font.

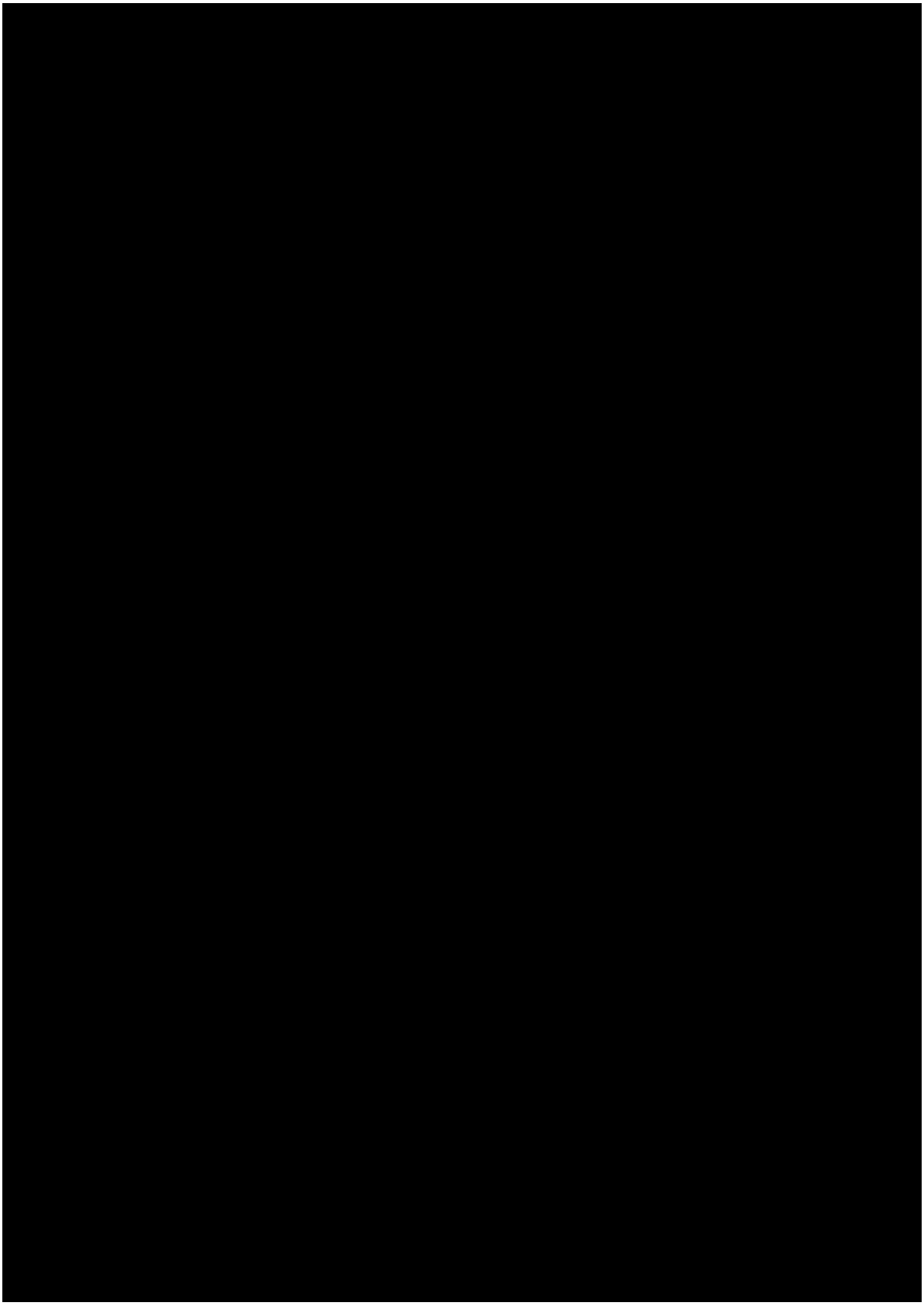
7.8 Referencing

Supervisors have the freedom to decide the type of citation of references but there must be consistency. This is mainly applicable to the standard type of thesis. In the case of thesis by manuscripts or publications, individual papers will maintain the reference system of the journal but the supervisor can decide on the type of referencing for the introductory and synthesis chapters.

8. Final thesis submission

The thesis should be submitted for examination in a loose bound form accompanied by a PDF copy. After the examination process the final version PDF copy of the thesis must be submitted to PG office for onward submission to the library. It is not a requirement to submit a copy fully bound in leather cloth or similar material.





UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

02 October 2020

Dr S Wall (211560758)
School of Clinical Medicine
College of Health Sciences
Shelley_wall@hotmail.com

Dear Dr Wall

Protocol: Obstacles to adequate analgesia in Paediatrics burns patients.
Degree: PhD
BREC REF: BE594/18
NEW TITLE: "Adequate analgesia in caring for paediatric burns patients in a peri-urban setting in KZN"

We wish to advise you that your application for amendments received on 28 September 2020 to change the title to the above new title for the above study has been **noted and approved** by a subcommittee of the Biomedical Research Ethics Committee.

The committee will be advised of the above at its next meeting to be held on 10 November 2020.

Yours sincerely

[redacted]

Ms A Marimuthu
(for) Prof D Wassenaar
Chair: Biomedical Research Ethics Committee

Paediatric Burns: Analgesia Questionaire

Mark your answer with an X

1. Level of Hospital:

Clinic	District	Regional	Tertiary

2. Designation:

Intern	Comm Serve	Medical Officer	Registrar	Consultant

3. How many years have you been qualified as a doctor:

4. Do you give procedural analgesia/sedation for dressing changes in your burns children in the ward?

Yes	No

5. If yes, what drug(s) do you use?

Drug 1:			
Dose:		Route:	
Drug 2:			
Dose:		Route:	
Drug 3:			
Dose:		Route:	

6. How do you assess if the child is adequately analgesed?

Child screaming	Universal Pain score (Faces)	FLACC Score	Clinical Impression	No Assessment

7. Do you give a single dose of procedural analgesia/sedation calculated on weight or do you give an initial dose base on weight and then a top up if necessary?

Single dose	Initial dose then top up

8. How often do you prescribe Ketamine:

Daily	Weekly	Monthly	Very seldom	Never

9. What is the dose of Ketamine:

Per Os:	
Intramuscular:	
Intravenous:	

10. What is the maximum dose of Ketamine:

Per Os:	
Intramuscular:	
Intravenous:	

11. Do you give background analgesia for burns children?

Yes	No

12. If yes, what do you prescribe?

Drug 1:		Frequency:	
Dose:		Route:	
Drug 2:		Frequency:	
Dose:		Route:	
Drug 3:		Frequency:	
Dose:		Route:	

13. Do you use analgesia/sedation when doing dressing changes in burns children in the OPD?

Yes	No

14. If yes, what drug(s) do you use?

Drug 1:			
Dose:		Route:	
Drug 2:			
Dose:		Route:	

15. Do you feel comfortable managing pain for a burns patient?

Yes, Very	Yes, Somewhat	No, not really	No, Not at all

16. Where did you learn about analgesia for burns?

Senior guidance	Own internet research	Burndr Hotline	PMB Burn Service Protocols

UNIVERSITY OF KWAZULU NATAL

Research Topic:

DEVELOPMENT OF AN ANALGESIA PROTOCOL FOR BURN-INJURED CHILDREN IN A RESOURCE LIMITED SETTING IN KWA-ZULU NATAL, SOUTH AFRICA

Dear Participant,

Burn injured children place a huge burden on the health care system. Dressing changes are unavoidable in burns. When these dressings are done in children with inadequate analgesia and sedation, a significant stress is placed on the child, the parents, the nursing staff and the doctors alike. These children develop significant anxiety and complex pain syndromes. Patients who have received inadequate analgesia require ever increasing amounts of analgesia to gain control over their pain. Adequate analgesia is a basic right of every patient we treat. A child should receive adequate analgesia from the outset, with both sufficient background analgesia and procedural analgesia. Pain-free patients are more likely to mobilize better, reducing the risk of pneumonia, bedsores and innumerable other complications associated with bed bound patients and this can reduce hospital stay. The risk of contractures and long-term disabilities is also increased in patients who have pain and are not willing participants in their rehab.

In order to address issues of pain, we have developed an analgesia protocol which forms part of “The PMB Way Burns Protocols”. It was a collaboration between surgeons and anaesthetists to develop a protocol which is safe, effective, easy to use and locally applicable in settings with limited resources and limited monitoring equipment. The aim of this study is to gain expert consensus regarding the protocol we have developed. A modified delphi technique will be used to obtain consensus.

Please consider completing this questionnaire to contribute to the expert opinion regarding the protocol.

Kind Regards

[redacted]

Dr Shelley Wall

Cell no: 082 422 8414

e-mail: shelley_wall@hotmail.com

[redacted]

Supervisor: Dr Nikki Allorto

Cell no: 083 655 7660

e-mail: nikkiallorto@gmail.com

Date: 12 September 2019

QUESTIONNAIRE FOR DELPHI PANEL ROUND ONE

PART A: DEMOGRAPHIC INFORMATION

Please tick (√) the appropriate answer

A1. How old are you?	
1. 20 - 30 years	
2. 31 - 40 years	
3. 41 - 50 years	
4. 51 - 60 years	
5. > 60 years	

A2. Gender	
1. Male	
2. Female	

A3. What is your profession?	
1. Plastic Surgeon	
2. General Surgeon	
3. Anaesthetist	
4. Other:	
If other, please spec fy:	

A4. Number of years experience as a healthcare professional:	
1. < 5 years	
2. 6 -10 years	
3. 11 - 15 years	
4. 16 - 20 years	

5. > 20 years	

A5. Number of years experience working in Burns:	
1. < 5 years	
2. 6 -10 years	
3. 11 - 15 years	
4. 16 - 20 years	
5. > 20 years	

PART B: DELPHI QUESTIONNAIRE

Please answer the following questions with a tick (√) in the appropriate box and add any comments in the space provided.

SCALE	
Essential	This must **DEFINITELY BE INCLUDED** in the analgesia protocol
Useful	**This CAN BE INCLUDED** in the analgesia protocol
Unnecessary	This should be **DEFINITELY BE EXCLUDED** from the analgesia protocol
Unsure	Unsure about this criterion
PLEASE MARK ONLY **ONE** OF THE FOUR CHOICES (ESSENTIAL, USEFUL, UNNECESSARY, UNSURE)	

Background Analgesia and Sedation (these are oral doses unless otherwise stated)					Essential	Useful	Unnecessary	Unsure	Comments
		Drug	**Paediatric**	**Adult**					
1	**Mandatory**	Paracetamol (syrup = 120mg/5ml)	15 mg/kg 6hrly	1g 6 hrly					
2	**Mandatory**	Tilidine (1 drop = 2.5 mg)	1 mg/kg 6 hrly	-					
3	**Mandatory**	Tramadol	-	50 - 100mg 6hrly					
4	**Add if pain not controlled and for donor site pain**	Ibuprofen (100mg/5mls)	10mg/kg 8 hrly	400mg 8hrly					
5		Consider contraindications: Curling's ulcer acute kidney injury comorbidities							

Background Analgesia and Sedation (these are oral doses unless otherwise stated)					Essential	Useful	Unnecessary	Unsure	Comments
		Drug	**Paediatric**	**Adult**					
6	**Consider if > 15%TBSA/ pain still uncontrolled**	Morphine syrup 1mg/ml	Start at 0.2 mg/kg 6 hrly Increase frequency up to 2 hrly then increase dose by 25% consider infusion	0.2 mg/kg 6 hrly Increase frequency up to 2 hrly then increase dose by 25% consider infusion					
7	**Add if pain not controlled OR neuropathic pain**	*Clonidine (25mcg tablets that cannot be broken)*	*25mcg 8 hrly increase to maximum 50mcg 8 hrly*	*75mcg 8hrly increase in increments of 25mcg per dose up to 150mcg 8hrly*					

Background Analgesia and Sedation (these are oral doses unless otherwise stated)					Essential	Useful	Unnecessary	Unsure	Comments
		Drug	**Paediatric**	**Adult**					
8	**Add if pain at night/ difficulty sleeping**	Amitryptiline	-	25mg nocte can be increased to 50 and then 75mg nocte					
9	**For neuropathic pain and or severe itch**	Pregabalin 75 or 150mg tabs mixed into suspension for paeds	start at 25mg 12hrly increase in 25mg increments to max 75mg 12 hrly	start at 75mg 12 hrly increase to max 150mg 12hrly					
10		Gabapentin 100 mg or 300 mg tablet	10mg/kg 8hrly increments of 100mg/dose up to 600mg 8 hrly	300mg 8 hrly increase up to 600mg 8 hrly					

Background Analgesia and Sedation (these are oral doses unless otherwise stated)					Essential	Useful	Unnecessary	Unsure	Comments
		Drug	**Paediatric**	**Adult**					
11	Add if neuropathic pain and no gabapentin/pregablin	Tegretol 200mg tabs	-	200mg 12 hrly increase to max 1200mg/day (400mg 8 hrly)					
12	If itch and no pregaba/gabapentin	Allergex	0.1mg/kg start 12hrly can be increased to 8 hrly	4mg 8 hrly					
13		Pyridoxine	-	25mg daily					

Background Analgesia and Sedation (these are oral doses unless otherwise stated)					Essential	Useful	Unnecessary	Unsure	Comments
		Drug	**Paediatric**	**Adult**					
14	**For ICU patients/large TBSA burns** **(MORPHINE mixed as a 1mg/ml solution ie. 10 mg in 10 mls or 50mg in 50 mls)**	Morphine **IVI** Remember this needs to be weaned and not stopped suddenly! (wean the infusion rate then move to bolus dosing and increase the dose interval over time)	0.1mg/kg loading dose then 0.1mg/kg/hour infusion increase to effect reload and increase rate by 0.05mg/kg	0.1mg/kg loading dose then 0.1mg/kg/hour infusion increase to effect reload and increase rate by 0.05mg/kg					
15	**For PTSD OR anxiety OR opioid withdrawal**	Valium	2.5 mg nocte titrate to effect can be increased to 8 hrly	5 mg nocte titrate to effect can be increased up to 5-10mg 4hrly					
16	**For Delirium**	Haloperidol	-	2.5 - 5mg 8hrly					

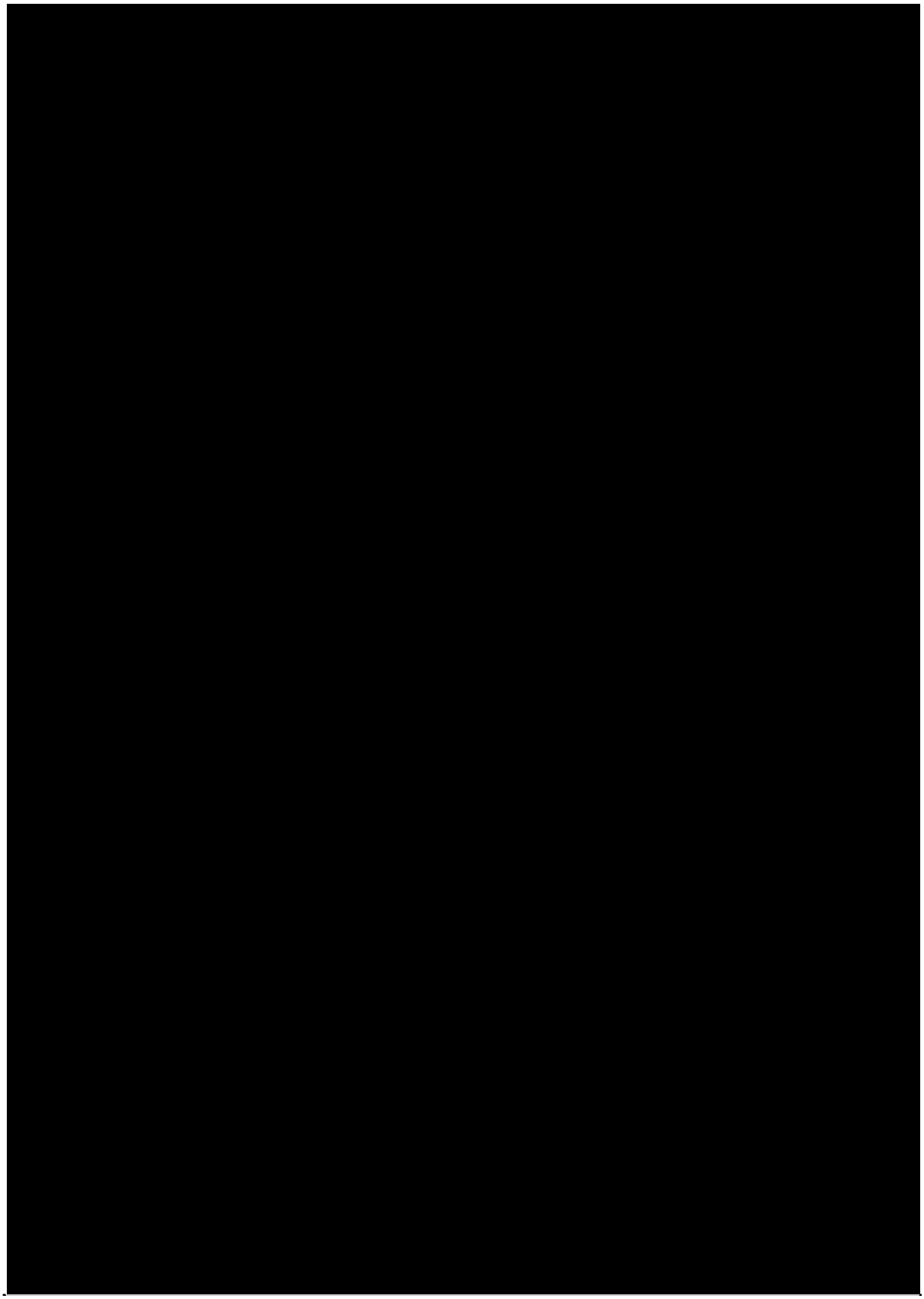
Procedural Medication					Essential	Useful	Unnecessary	Unsure	Comments
		Drug	Paediatric	Adult					
17	IV access / ICU/high care	Ketamine	1mg/kg IVI titrations quick onset quick offset	1mg/kg IVI titrations quick onset quick offset					
18	Ward Dose 1	Ketamine Midazolam	5mg/kg/per os 0.25mg/kg per os mixed together 20-30 mins to work	5mg/kg/per os 2.5 - 5 mg per os mixed together 20-30 mins to work					

Procedural Medication					Essential	Useful	Unnecessary	Unsure	Comments
		Drug	Paediatric	Adult					
19	**Ward** **Dose 2 (for pain score > 3)**	Ketamine NO Midazolam	half the previous dose ketamine IMI 5-10 mins onset	100mg ketamine IMI 5-10 mins onset					
20	**Ward** **Dose 3 (for pain score > 3)**	Ketamine NO Midazolam	half the previous dose ketamine IMI	100mg ketamine IMI					
21		**The final total dose of Ketamine given at the procedure must be written as the script for the following dressing change, do not leave the inadequate dose as the prescription**							

Procedural Medication					Essential	Useful	Unnecessary	Unsure	Comments
		Drug	Paediatric	Adult					
22	Clinic	Ketamine OR Methoxyflurane OR Morphine	5mg/kg IMI 0.5 mls inhaled -	5mg/kg IMI 1-2mls inhaled 10-15mg IMI					
23	Emergency Department	Ketamine Morphine Fentanyl	5mg/kg IMI - -	5mg/kg IMI 0.05mg/kg IVI 50 - 100mcg IVI					

COMMENTS OR SUGGESTIONS ON IMPROVING THIS ANALGESIA PROTOCOL

THANK YOU FOR YOUR PARTICIPATION IN THIS RESEARCH PROJECT



"The PMB Way Analgesia Protocols"			
Procedural Medication			
	Drug	**Paediatric**	**Adult**
IV access/ ICU/high care	Ketamine	1mg/kg IVI titrations quick onset quick offset	1mg/kg IVI titrations quick onset quick offset
Ward Dose 1	Ketamine Midazolam	5mg/kg/per os 0.25mg/kg per os mixed together 20-30 mins to work	5mg/kg/per os 2.5 - 5 mg per os mixed together 20-30 mins to work
Ward Dose 2 (for pain score > 3)	Ketamine NO Midazolam	half the previous dose ketamine IMI 5-10 mins onset	100mg ketamine IMI 5-10 mins onset
Ward Dose 3 (for pain score > 3)	Ketamine NO Midazolam	half the previous dose ketamine IMI	100mg ketamine IMI
	The final total dose of Ketamine given at the procedure must be written as the script for the following dressing change, do not leave the inadequate dose as the prescription		
Clinic	Ketamine OR Methoxyfluorane OR Morphine	5mg/kg IMI 0.5 mls inhaled -	5mg/kg IMI 1-2mls inhaled 10-15mg IMI
Emergency Department	Ketamine Morphine Fentanyl	5mg/kg IMI - -	5mg/kg IMI 0.05mg/kg IVI 50 - 100mcg IVI