INVESTIGATING PATIENTS' KNOWLEDGE AND USE OF THE PATIENT INFORMATION LEAFLET REGARDING THEIR WARFARIN THERAPY

BY: KARMISHTHA HUTHERAM (214582347)

(BTech Pharmaceutical Sciences)

Submitted as the dissertation component in partial fulfillment of the requirements for the degree of Master of Health Sciences, Pharmacovigilance (By Coursework) in the School of Health Sciences, University of KwaZulu-Natal.

Supervised by:

Dr Elizabeth Ojewole (PhD)

Date Submitted: November 2016

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2016

A dissertation submitted to the School of Health Sciences, University of KwaZulu-Natal, in partial fulfillment of the requirements for the degree of Master of Health Sciences - Pharmacovigilance (by coursework).

This is to certify that the contents of this dissertation are the original research work of Mrs. Karmishtha Hutheram.

Signed: _____

Date: 15/11/16

As the student's supervisor, I have approved this dissertation for submission.

Supervisor's Name: Dr Elizabeth Ojewole

Signed: _____

Date: **15/11/2016**

DECLARATION 1-PLAGIARISM

I, **Karmishtha Hutheram** declare that

1. The research reported in this dissertation, except where otherwise indicated, is my original research.
2. This dissertation has not previously been submitted to UKZN or another tertiary institution for purposes of obtaining a degree or any other academic qualification
3. This dissertation does not contain other persons' data, pictures, graphs or other information, unless specifically acknowledged as being sourced from other persons.
4. This dissertation does not contain other persons' writing, unless specifically acknowledged as being sourced from other researchers.

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5. This dissertation does not contain text, graphics or tables copied and pasted from the Internet, unless specifically acknowledged, and the source being detailed in the dissertation and in the references sections.

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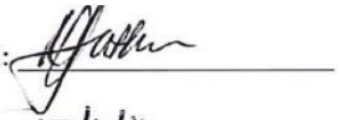
Signed: 

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DECLARATION 2 – MANUSCRIPT FOR PUBLICATION

1. **Hutheram, K., Connolly, C., Ojewole, E. "*Knowledge and use of patient information leaflet regarding Warfarin therapy among patients at private clinics in Gauteng, South Africa"*** for submission to the African Journal of Pharmacy and Pharmacology.

Authors contributions to the manuscript:

Karmishtha Hutheram as the student, performed the research design, performed all literature reviews, collected and captured the data, and performed interpretation of the results. She drafted the manuscript for journal submission. She agreed to the submission of manuscript for journal publication. **Catherine Connolly** performed the statistical data analysis and confirmed the interpretation of the results. She agreed to the submission of manuscript for journal publication. **Dr Elizabeth Ojewole** supervised the research and contributed to the overall research process, including the proposal, the manuscript and dissertation writing. She approved the manuscript submission for journal publication.

DECLARATION 3-ETHICAL APPROVAL

This study titled *"**Investigating patients' knowledge and use of Patient Information Leaflet regarding their Warfarin Therapy"*** was approved by the Humanities and Social Sciences Research Ethics Committee (HSSREC) at the University of Kwa-Zulu Natal (UKZN). The Ethics Approval number for the study is HSS/0667/015M.

A copy of the ethical approval letter can be found in the Appendix, on page 58.

RESEARCH OUTPUT

A. MANUSCRIPT PREPARED FOR PUBLICATION

1. **Hutheram, K., Connolly, C., Ojewole, E. "*Knowledge and use of patient information leaflet regarding Warfarin therapy among patients at private clinics in Gauteng, South Africa"*** for submission to the African Journal of Pharmacy and Pharmacology.

DEDICATION

- ***To GOD for giving me the strength to complete this dissertation***
- ***To my loving husband, family and friends for all the support***
- ***Dr Elizabeth Ojewole my supervisor at the UKZN for her expert's guidance***

ACKNOWLEDGEMENTS

Firstly I would like to acknowledge the assistance and constant guidance of Dr Elizabeth Ojewole who has supervised me throughout this journey. I will be forever grateful for the encouragement and support.

To all the respondents of the study, I would like to take the opportunity to thank you for your participation, without which this study would not have been possible. A special thanks to the management team of the pathology company for allowing me to use the various sites to conduct my study.

To Dr Haines at the University of Maryland USA, thank you for sharing your knowledge by allowing me to use the validated OAK questionnaire as a data generating tool in this study.

Lastly but most importantly, I would like to thank my family and friends for all the support and love during this phase of my life.

LIST OF ABBREVIATIONS

ADRs: Adverse Drug Reactions

CEM : Cohort Event Monitoring

DVT: Deep Vein Thrombosis

EDP: Essential Drug Programme

EMA: European Medicine Agency

GVP: Good Pharmacovigilance Practice

HIV: Human Immuno-deficiency Virus

INR: International Normalized Ratio-Blood test used to monitor patients response to Warfarin dosage.

IT: Information Technology

MCC: Medicines Control Council

MRA: Medicines Regulatory Authority

NSAIDS : Non-Steroidal Anti-Inflammatory Drugs

OTC: Over the Counter

PE: Pulmonary Embolism

PIL: Patient Information Leaflet

PV : Pharmacovigilance

SATI: South Africa Translators Institute

TB: Tuberculosis

TIA: Transient Ischemic Attack

TSR : Targeted Spontaneous Reporting

WARF: Wisconsin Alumni Research Foundation

WHO: World Health Organization

LIST OF DEFINITIONS

Antagonist: A substance that acts against and blocks an action. Antagonist is the opposite of agonist. Antagonists and agonists are key players in the chemistry of the human body and in pharmacology.

Anticoagulant: An agent that is used to prevent the formation of blood clots.

Bioavailability: Refers to the extent and rate at which the active moiety (drug or metabolite) enters systemic circulation, thereby accessing the site of action.

Coagulation Cascade: The series of steps in the activation of the intrinsic, extrinsic and common pathways that results in the formation of a fibrin clot to stop bleeding.

Coronary heart disease: is a common term for the buildup of plaque in the heart's arteries that lead to heart attack.

Kruskal -Wallis equality-of-populations rank test: Test used to test the hypothesis that several samples came from the same population.

Patient information Leaflet (PIL) : The PIL contains information relevant to the drugs usage, directions of use, dosage, side effects, drug-food interactions and drug-drug interactions.

Pulmonary Embolism: Is a sudden blockage in the artery of the lung that can be caused by a blood clot in the leg that travels through the blood stream to the lung.

Pharmacovigilance (PV): Is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.

Prophylaxis: Is a measure taken to maintain health and prevent the spread of disease.

Stroke: Occurs when the blood supply to part of the brain is interrupted or severely reduced, depriving brain tissue of oxygen and nutrients.

Therapeutic Index: Ratio between the therapeutic effect of a drug and toxic effect of a drug.The smaller the therapeutic index of a drug the higher the chance of toxicity or subtherapeutic levels being reached.

Thrombosis: The formation or presence of a blood clot in a blood vessel.

Transient ischemic attack (TIA): Is a brief interruption of blood flow to part of the brain that causes temporary stroke like symptoms.

Warfarin: Is an anticoagulant (blood thinner).Warfarin is used to treat or prevent blood clots in veins or arteries, which can reduce the risk of a stroke, heart attack or other serious conditions.

Wilcoxon rank-sum (Mann-Whitney) test: Tests the hypothesis that 2 independent samples came from populations with the same distribution.

Table of Contents

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

Background: Warfarin is the gold standard drug of choice to manage thrombotic disorders, but may interact with certain foods and drugs, resulting in unwanted adverse effects. The use of patient information leaflet (PIL) as a standardized educational material is essential to ensuring optimal therapy. The aim of the study was to determine patient's knowledge and use of PIL regarding their Warfarin therapy.

Methods: A descriptive cross-sectional survey design required respondents to complete an anonymous questionnaire survey over 18 weeks. Responses were captured and analyzed using STATA version 13.

Results: 34 patients responded in this study, of whom 56% (n=19) were males and 73.5% (n=25) had been on Warfarin treatment for less than 10 years. Only 50% (n=17/34) had knowledge of the PIL, 91% (n=31) knew about the International Normalized Ratio (INR) and 97% (n=33) understood its importance. While 76.5% (n=26) had knowledge of other drugs and foods that interact with Warfarin, and 70.5% (n=24) knew that consuming leafy green vegetables could reduce its effectiveness, only 58.8 % (n=20) understood the effect of alcohol on Warfarin. 91% (n=31) scored above 50% on the Oral Anticoagulant Knowledge (OAK) Test, with a moderate negative correlation between this and the respondent's age (Spearman correlation = -0.27).

Conclusion: INR testing and its importance in Warfarin therapy appeared to be known by most respondents, their lack of knowledge about PIL, as well as drug, alcohol and food interactions with Warfarin highlights the need for education and counseling to reinforce their knowledge and use of PIL.

Keywords: Warfarin therapy, knowledge of PIL, patient information leaflet, patient education, Warfarin-food interactions, Warfarin-drug interactions

CHAPTER 1. INTRODUCTION

1.1 Introduction

Thrombotic disorders are a global problem, and are caused by clots or thrombosis in blood vessels, which can result in death if not treated effectively. Warfarin has become the drug of choice worldwide to prevent or treat thrombotic disorders and has been in use since the 1950s. However, its use remains problematic, with consumers not always adhering to treatment management guidelines, as indicated in the information leaflet that normally accompanies the tablets as an insert. It is generally assumed the patients have access to and read this leaflet, but problems associated with its use suggest that this is not the case, specifically in Gauteng Province in South Africa. This study therefore investigated patients' knowledge and use of the Warfarin patient information leaflet (PIL) to establish whether or not it is being used.

This chapter outlines the background to the study and the knowledge gaps that exists in the South African context. It presents the aim and objectives of this research, as well as the methods used, and concludes with a brief summary of each chapter.

1.2 Background and Rationale for the study

Wardrop and Keeling (2008) reviewed the history of Warfarin in a review titled *"The story of the discovery of heparin and Warfarin",* which traced its origin to 1920s to a field in Canada, where a sweet clover (Melilotus alba and Melilotus officinalis) infected with mould (Penicillium nigricans and Penicillium jensi) resulted in the deathly *"Sweet clover disease".* Having killed off the livestock due to unexplained internal bleeding, this *"Sweet clover disease"* displayed properties of anticoagulation, as discovered by veterinary surgeons Schofield and Roderick (Schofield, 1924; Roderick, 1929, 1931). In 1945, Dicoulmarol was patented by Karl Link as a result of the funding he received from Wisconsin Alumni Research Foundation (WARF). After several variations, the Coumadin derivative was promoted as a pesticide for killing rodents. Warfarin made an honorable appearance on the clinical scene when it was first given to President Dwight Eisenhower for his myocardial infarction in 1955 (Wardrop and Keeling 2008).

"*The principal advantages of Warfarin were its high water solubility and high oral bioavailability"* Wardrop and Keeling (2008).

Having ticked the boxes of high bioavailability and an oral dosage form, Warfarin although being discovered over a century ago, remains the gold standard drug of choice by many physicians requiring the use of a trusted anticoagulant in treating thrombotic events (Wardrop and Keeling 2008).

The Indiana Hemophilia and Thrombosis Centre (2016) describe "Thrombosis" as the formation of a blood clot in a blood vessel that impairs the flow of blood to the affected area. The World Federation of Hemophilia explains that blood clot formation is essential to the healing of the human body as it stops bleeding from the injured site by forming a platelet plug. Platelets or thrombocytes are a component of whole blood that migrate to the injured site and initiates the coagulation cascade which is a series of processes and clotting factors that end in the formation of a fibrin clot to stop bleeding. In some cases despite the absence of an injury this process is triggered and results in abnormal blood clot formation in a vein or artery.

The Indiana Hemophilia and Thrombosis Centre (2016) have divided thrombotic disorders into two categories, namely acquired and inherited causes of thrombotic disorders. Acquired causes are pregnancy, hormone therapy, immobility, post-operative and malignancy to name a few. Inherited causes of thrombosis are increased levels of procoagulants, decreased levels of natural anticoagulants, abnormal fibrinolysis and other inherited causes. These conditions, whether inherited or acquired, can result in the development of a thrombosis (blood clot) anywhere in the vascular system resulting in a lack of oxygen and nutrients to the affected anatomy.

The signs and symptoms of the thrombosis are purely based on the location of the thrombosis in the vascular system. A deep vein thrombosis (DVT) is usually located in a lower limb and may have a clinical presentation of pain, tenderness and swelling of the area and could result in disability or death should the thrombosis travel to the circulation in the lung causing a pulmonary embolism (PE) (CDC 2016).

Warfarin has been the drug of choice worldwide to treat thrombotic disorders since 1954 (Pirmohamed, 2006). Indications for Warfarin therapy as per the COUMADIN (Warfarin Sodium) package insert by Bristol-Myers Squibb Pharmaceuticals would include the following: Trans ischemic attacks (TIA), recurrent deep vein thrombosis, Stroke or Cerebral vascular incidents (CVI), cardiovascular problems, Pulmonary Embolism and Prophylaxis. These conditions are associated with the vascular system of the human body and require

patients to be on it for life. The implications of not keeping these disorders under control can results in death of the patient.

Wendelboe and Raskob (2016) describe thromboembolic disorders as the leading cause of mortality resulting in 1 in 4 deaths globally in 2010. Mortality rates (MRs) of thromboembolic disorders have improved in developed countries but are on the rise in developing countries (Wendelboe and Raskob, 2016). Maredza, Bertram and Tollman, (2015) estimated that stroke is the cause of 25000 deaths annually in South Africa and this indicates why this study is important as Warfarin is the anticoagulant which is used in the treatment and management of stroke as well as other thrombotic disorders.

For Warfarin to reach and maintain optimal therapeutic levels, patients have to adhere to specific guidelines while taking it. These are having a balanced diet with moderate amounts of Vitamin K, reducing alcohol intake and taking their Warfarin as prescribed. On starting Warfarin, patients should receive detailed education from their physician, local pharmacist or nursing staff to ensure that they are aware of the various lifestyle changes they need to maintain to ensure its effectiveness.

Khudair and Hanssens (2010) evaluated patient's knowledge about Warfarin among out-patient clinics in Qatar, and found that there were knowledge gaps in their education regarding the food interactions and drug interactions. Their recommendation was to implement a multidisciplinary programme to educate patients at their hospital in Qatar about anticoagulant therapy in order to reduce the work load on the healthcare staff whose responsibility it was to inform the patients about Warfarin use.

Wang et al. (2014) reported an association between the lack of knowledge and fluctuations in patients' International Normalized Ratio (INR), a blood test used to monitor the effectiveness of Warfarin therapy, and indicated a dependency relationship between INR levels and patient education, or the lack thereof.

Wofford Wells and Singh,(2008) described how the time consuming practice of giving patient education by clinicians and the overwhelming amount of information resulted in proper patient education being neglected. They looked at different strategies with regard to patient education in the hopes of determining which method would prove fruitful. Finding an effective knowledge transfer method in ensuring effective anticoagulant therapy remains an ongoing

challenge, especially with highly sensitive anticoagulants such as Warfarin. Nasser, Mullan, and Bajorek (2012) explored the idea of using information technology to educate patients on Warfarin therapy, and used a survey to obtain healthcare professionals perspectives with regard to this. They found that healthcare professionals agreed with the use of information technology to educate patients on Warfarin therapy, but their concerns were the cost of the IT resources as well as the ability to operate these resources, as these could impair the effective implementation of these resources in educating patients (Nasser, Mullan and Bajorek, 2012).

South Africa's drug regulating body is the Medicine Controls Council which has set regulations to protect and keep the public safe, by implementing guidelines, such as the patient information leaflet (PIL) for numerous drugs, as per Regulation 10 of the Medicines and Related Substances Control Act 101 of 1975. These leaflets are provided in English to aid the patient by bridging the knowledge gap and providing with information that they can take with them, which serves as a pharmacovigilance tool to ensure drug safety. Information that is included in a standard PIL according to MCC regulation are the indication of the medicine, how to use the the medicine, drug and food interactions,drug- drug interactions, safety precautions, possible side effects as well as storage requirements for medicine.However, patients either do not receive this information or do not understand the contents of the PIL. Herber et al. (2014) conducted a focus group study to explore patient's emotions and behavior towards the PILs of commonly prescribed medicines and they found that information regarding the potential risks of the medicines were in a language that frightened the patients. PILs need to be in a language that is less frightening so that the patients are able to understand the information within the PIL in order to make an informed decision regarding their medicine (Herber et al.2014).

In a study titled *"Development and Evaluation of Patient Information Leaflets (PIL) Usefulness",* Adepu and Swamy (2012) reported that patient education accompanied by a well designed PIL could have a greater impact on patient knowledge and attitude regarding their disease. As discussed by Adepu and Swamy (2012), the PIL improves patient knowledge and attitude with regard to management of their disease.

While information leaflets are provided to patients at most private sector health facilities across South Africa, including the province of Gauteng little is known about the diet and lifestyle one

should lead while taking certain medications. The PIL is a regulated document that contains information on the interactions of drugs with food, alcohol and other drugs.

1.3 Aim and Objectives

The aim of this research was to investigate patient knowledge and use of the Patient Information Leaflet regarding Warfarin therapy at private sector INR clinics in the Gauteng area in South Africa

To accomplish this aim, the study had the following objectives:

1. To determine whether or not the patients know about the Patient Information Leaflet and use it
2. To establish the patients' level of knowledge about Warfarin therapy.
3. To determine the patients' knowledge of the International Normalized Ratio.
4. To determine the patients' knowledge of Warfarin therapy regarding possible interactions with food and other medicines.

1.4 Methodology

The section describes the study site and sample, the data collection tool and process, as well as how the data was analyzed and managed.

1.4.1 Study site and sample

A descriptive cross-sectional study was carried out using a structured questionnaire that was developed and distributed to respondents at 10 private sector INR clinics within the Gauteng Province. The study took place at private pathology laboratory International Normalized Ratio clinics with its patients coming from a range of private practitioners who are referred to them for INR testing. The urban based clinics are located in a mixed race suburbs in the Gauteng area. A convenience sample was drawn from the target population of 100 patients who attended the private pathology INR clinics in the Gauteng area. Patients in the waiting room who met the criteria for participation were requested to complete a questionnaire after granting written consent.

The inclusion criteria to determine eligibility for participation were:

- males and females between the ages of 20 and 90,

- were on Warfarin Therapy,
- resided within the Gauteng province.

Respondents who did not meet these criteria were not invited to participate in the study.

The exclusion criteria for the study were:

- Males and females younger than 20 years or older than 90 years
- People who were not prescribed Warfarin Therapy
- People who did not reside in the Gauteng area

1.4.2 Data Collection Tool

Dr Andy Field stated that a good questionnaire must meet the following requirements: validity, reliability and discrimination. He goes on to describe validity of a questionnaire as *"whether an instrument actually measures what it sets out to measure"* whereas reliability *"is whether an instrument can be interpreted consistently across different situations"* (Field, 2013).

Zeolla et al. (2006) in their paper titled "Development and validation of an instrument to determine patient knowledge: the oral anticoagulation knowledge test" identified the lack of validated knowledge assessment tools in assessing patient knowledge regarding oral anticoagulation therapy. Zeolla et al. developed and validated the Oral Anticoagulation Knowledge (OAK) test, which comprises of a 20 itemed multiple choice questionnaire. The contents of the OAK test includes questions on Warfarin interactions with diet and other drugs as well as how to take Warfarin and possible side effects of Warfarin. (See Appendix V)

The OAK test has been used in numerous studies across the globe to assess patient anticoagulant knowledge as it has proved validity and reliability by Zeolla et al (2006). Matalqah et al. (2013) used the OAK test and translated it into the Malay language to accommodate their Malaysian patient population, and found its use to determine patient knowledge of anticoagulant therapy.

The validated OAK test was used for this study to obtain data that assessed patient's knowledge of their Warfarin therapy. Written permission from Dr Haines at the University of Maryland to use the OAK test was obtained prior to starting the study. The OAK test is already validated and was translated into Afrikaans and Tswana by two translators accredited with

SATI (South African Translations Institute) to accommodate the dominant language groups in the study area.

The OAK questionnaire consists of 1 section, to which three were added to address the study objectives as follows:

Section A :Patient demographic details: age, gender, ID number, area of residence, marital status, highest level of education, occupation, reason for Warfarin use and number of years on Warfarin.

Section B: Knowledge and use of the Patient information Leaflet (Objective 1): Open ended questions addressing patients' knowledge and understanding of the PIL and whether they have received and understood the information contained within the PIL.

Section C: Oral Anticoagulant Knowledge (OAK) questionnaire (Objective 2 and Objective 4): multiple choice questions addressing patient knowledge of Warfarin and interactions.

Section D: Knowledge of the International Normalized ratio (INR) (Objective 3): Opened ended questions addressing patient knowledge and importance of the INR blood test and whether their INR was in range in the last 6 months.(See Appendix V)

A pilot study was conducted on two patients to determine if the translated questionnaires would cater for the diverse South African population. The pilot study was conducted at a Centurion private pathology INR clinic depot that was not part of the study sites for data collection. Afrikaans questionnaires were piloted to ensure validation of the translated OAK test. The pilot study was run for a period of 2 weeks. On completion of the pilot study only two Afrikaans questionnaires. Patients who completed the Afrikaans questionnaires displayed no difficulty in comprehending the questionnaire. The Tswana questionnaire could not be piloted as there were no patients during the 2 week period who requested to complete the questionnaire in Tswana. However if a Tswana patient chose to participate in the study then a nurse translator would have be made available either in person or telephonically. The practical considerations that needed attention included: time limit per patient to complete the questionnaire, which was increased from an anticipated 10 to 20 minutes, and the language that the patient preferred to complete the questionnaire in.

1.4.3 Data collection process

Ethical approval was obtained from the Humanities and Social Sciences Research Ethics Committee (HSSREC) of the University of KwaZulu-Natal (UKZN) (HSS/0667/015M). Following ethical approval, the private pathology company was approached for permission and this was granted to conduct the study at their INR Clinics within the Gauteng Province. Written Informed consent was obtained from participants who met the inclusion and exclusion criteria and who verbalized the voluntary participation in the study.

Karmishtha Hutheram was present at the various sites to assist respondents in completing the questionnaires. Staff of the private pathology INR clinics were shown how to obtain written informed consent from the respondents then hand over the questionnaire to the respondents to complete in my absence. The data collection process took place over the period of 27th of July 2015 till the 27th of November 2015.

1.4.4 Data Analysis

Data were captured, cleaned up and analyzed using Stata statistical software version 13. Descriptive statistics such as the mean, the range, the standard deviation and the median were used to describe the continuous variables (e.g. the respondent's age). Frequencies and percentages were used to describe the categorical variables like, gender, occupation, highest education, reason for Warfarin use; months on Warfarin and OAK test Score.

Kruskal -Wallis equality-of-populations rank test is used to test whether several samples came from the same population. Kruskal -Wallis equality of populations rank test was used on respondent's demographics like age, marital status, highest qualification and occupation. The two-sampled Wilcoxon rank-sum (Mann-Whitney) test is used to test the hypothesis that 2 independent samples came from populations with the same distribution .Wilcoxin rank sum (Mann-Whitney) test was used to test whether the respondent's gender played a role in their OAK score.

1.5 Overview of dissertation

This dissertation consists of the following chapters:

Chapter 1: Introduction: describes the background and rationale for the study, aim and objectives, methodology and overview of the dissertation.

Chapter 2:Literature Review: this chapter provides the literature review of Pharmacovigilance; Practice of Pharmacoviglance; Warfarin Therapy ; the use of the PIL in Warfarin Therapy ; the PIL as a counseling and educational tool ; patient education regarding Warfarin therapy ; challenges of drug and food interactions with Warfarin; INR and its importance in Warfarin therapy, and patients compliance to Warfarin therapy.

Chapter 3: Manuscript for publication: This is a manuscript titled "Knowledge and use of patient information leaflet regarding Warfarin therapy among patients at private clinics in Gauteng, South Africa" and will be submitted for publication in the African Journal of Pharmacy and Pharmacology.

Chapter 4: Conclusion: this chapter describes the conclusion of the significant findings of the study; some limitations were highlighted as well as recommendations for future work provided.

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CHAPTER 2. LITERATURE REVIEW

2.1 Introduction

This chapter will provide a literature review on Pharmacovigilance, practice of pharmacovigilance, Warfarin Therapy, use of the patient information leaflet (PIL) in Warfarin therapy, PIL as a counseling and education tool, patient education on Warfarin therapy, challenges of drug and food interactions with Warfarin, International Normalized Ratio (INR) and its importance in Warfarin therapy, patients' compliance to Warfarin therapy and a conclusion. The purpose of this chapter is to provide the background to the study, outline the importance of Warfarin Education and justify the research.

2.2 Pharmacovigilance

According to the World Health Organization (WHO, 2002), *"Pharmacovigilance (PV) is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem."* This definition embodies the essence of the practice that is set to reduce adverse effects as a result of medicine usage. The European Medicines Agency has identified the objectives of Pharmacovigilance that contribute to the protection of public health, and include *"preventing harm"* to the patient and *"promoting safe and effective use of medicinal products"*. Benefit verse risk ratio is something that has always been evaluated prior to medicines reaching the market, thus ensuring the safety of the patient. As discussed by Jeetu and Anusha (2010), harm can be minimized if medicines are of a good quality, are used rationally and patients are involved in the decision making process of their therapy. Health care professionals have to be adequately trained in pharmacovigilance in order for good practices to be followed to minimize ADRs (Upadhyaya et al.2015).

2.3 Practice of Pharmacovigilance

A national pharmacovigilance workshop was held on the 12th of August 2012 in South Africa to address current pharmacovigilance practices in the country. The findings and recommendations discussed at this workshop were documented by Mehta et al. (2012) in a report titled *"Strengthening Pharmacovigilance in South Africa".* In 1992, South Africa became the first country in Africa to form part of the WHO Programme for International Drug Monitoring to

coordinate international pharmacovigilance activities (Mehta et al.2012). The authors noted that *"The national pharmacovigilance system should contribute to treatment policy decision-making and improved patient care"* (Mehta et al .2012).

While patient safety forms a vital component in holistic patient care, unpleasant experiences with medication tend to linger, making patients fearful, which results in non-compliance to treatment (Baughman , Spurling and Mangoni, 2008). Due to the narrow therapeutic index of Warfarin, the patient would be required to adhere to certain guidelines regarding diet and lifestyle to ensure that the patient does not experience any sub or supra therapeutic effects (Baughman , Spurling and Mangoni2008). To ensure the prevention of adverse events of marketed medicines, several pharmacovigilance tools are used, namely Cohort Event Monitoring (CEM), Targeted Spontaneous Reporting (TSR) and Active Surveillance for existing Cohort Studies (Mehta et al 2014). These pharmacovigilance systems, as discussed by Mehta et al, were in place for Immunization, Human Immuno-deficiency Virus (HIV), Tuberculosis (TB), pediatric HIV and Dermatology programmes. Mehta et al. (2014) noted that pharmacovigilance is a responsibility that is shared between various sectors, namely the Medicines Regulatory Authority (MRA), pharmaceutical industry, Essential Drugs Programme (EDP) and Public Health Programmes. Apart from the respective sectors that share the responsibility, health care professionals also need to be adequately educated on the good practices of Pharmacovigilance. A lack of knowledge on ADRs was identified by Upadhyaya et al. (2015) in postgraduate residents at a hospital in Gujarat, who suggested the need for improving education on pharmacovigilance and ADRs reporting systems.

2.4 Warfarin Therapy

Warfarin has been used for decades worldwide to treat thrombotic disorders, with success being due to it being highly effective. Its high water solubility and oral bioavailability are added advantages for its use as a drug of choice (Wardrop and Keeling 2008). However, for Warfarin to reach optimal therapeutic levels in the blood; patients must adhere to strict guidelines while taking it. These include patients eating a balanced diet with moderate amounts of vitamin K, reducing alcohol intake and taking their Warfarin as prescribed (Akinwunmi, 2011). Wardrop and Keeling (2008) reported on *"The story of the discovery of heparin and Warfarin"* , which traced the origins of Warfarin back to a field in Canada, where a sweet clover (Melilotus alba

and Melilotus officinalis) infected with mould (Penicillium nigricans and Penicillium jensi) resulted in the deadly *"Sweet clover disease".* Having killed off the livestock due to unexplained internal bleeding, this disease displayed properties of anticoagulation (Schofield, 1924; Roderick, 1931). Of all the numerous developments and advancements in drug discovery, as well as the availability of these technologically advanced anticoagulants, Warfarin remains the gold standard drug of choice in South Africa for many thrombotic conditions, such as atrial fibrillation related stroke or trans ischemic attacks (TIA) and peripheral embolism, that require prophylactic use of blood thinning agents (Sonuga et al.2016).

In ensuring the safety and management of patients on Warfarin, pharmacovigilance tools such as regular blood testing and health education are used. Regular monitoring of patients on Warfarin is of the utmost importance to ensure that patients remain within the therapeutic index. International Normalized Ratio (INR) testing monitors the effectiveness of Warfarin therapy, and ensures that the recommended dosage of Warfarin results in an effective therapeutic index (Zeolla et al. 2006)

2.5 The OAK Test

Zeolla et al. (2006) in their paper titled "Development and validation of an instrument to determine patient knowledge: the oral anticoagulation knowledge test" identified the lack of validated knowledge assessment tools in assessing patient knowledge regarding oral anticoagulation therapy. Zeolla et al. developed and validated the Oral Anticoagulation Knowledge (OAK) test, which comprises of a 20 itemed multiple choice questionnaire. The contents of the OAK test includes questions on Warfarin interactions with diet and other drugs as well as how to take Warfarin and possible side effects of Warfarin. (See Appendix V)

The OAK test has been used in numerous studies across the globe to assess patient anticoagulant knowledge as it has proved validity and reliability by Zeolla et al (2006). Matalqah et al. (2013) used the OAK test and translated it into the Malay language to accommodate their Malaysian patient population, and found its use to determine patient knowledge of anticoagulant therapy.

2.6 Use of Patient Information Leaflet in Warfarin Therapy

A study to investigate the association of health literacy with Warfarin knowledge and adherence showed that limited health literacy was associated with knowledge deficits in patients on Warfarin therapy (Fang et al.2006).Suggestions to investigate alternative means of educating patients on the risks of anticoagulant therapy were recommended by Fang et al. (2006).

The Patient information leaflet (PIL) is a regulated document that is approved together with the medicines registration process of every drug. The drug approval process is carried out by a specific regulatory authority of every country that requires a strict compilation of a medicines dossier prior to the drug reaching the market. In South Africa, the Medicines Control Council (MCC) provides guidelines for dossier submission that include the design of medicine labels and PILs. Information that is included in a standard PIL according to MCC regulation are the indication of the medicine, how to use the medicine, drug and food interactions, drug- drug interactions, safety precautions, possible side effects as well as storage requirements for medicine. The PIL for Warfarin in South Africa was obtained from Cipla Pharmaceuticals South Africa and adheres to the MCC guidelines (2014). Patient Information Leaflets affect health outcomes and Kenny et al. (1998) have concluded that patients want the PIL and they use the information provided therein to manage their health. During their literature search on Medline, Kenny et al. (1998) identified that patients like to be given written information after a consultation with a Doctor to take home and read or to refresh their knowledge. The content of pamphlets was also discussed, and it was noted that all information contained therein should be correct, balanced, unbiased and independent of commercial interests (Kenny et al.1998).

2.6.1 Patient Information Leaflet as a counseling and educational tool

The PIL provides the written information needed for the patient to refresh their memory after consultation, as studies have proved that patients forget information within five minutes of the consultation session (Kenny et al.1998). The PIL can be the key training aid in providing effective Warfarin counseling, as the healthcare professional can explain the PIL to the patient while reinforcing important aspects of the drug interactions with food and other medication. In a study titled *"Development and Evaluation of Patient Information Leaflets (PIL) Usefulness",* Adepu and Swamy (2012) reported that patient education accompanied by a well designed PIL could have a greater impact on patient knowledge and attitude regarding their disease. As

discussed by Adepu and Swamy (2012), the PIL improves patient knowledge and attitude with regard to management of their disease.

2.7 Patient education regarding Warfarin therapy

A qualitative study was conducted to determine the patient's perspective on taking Warfarin found that patients had a superficial understanding of the risks and benefits of taking Warfarin (Dantas et al. 2004). Safety knowledge on oral anticoagulants were assessed by Chenot et al. (2014) who found that gaps in knowledge may affect the safety and efficacy of oral anti-coagulant therapy.

According to research conducted by Baughman Spurling and Mangoni. (2008), the education provided to patients in hospitals by doctors and nurses regarding the use of Warfarin therapy is insufficient. During the dispensing of Warfarin, the pharmacist will provide the patient with the necessary information on how to take Warfarin therapy, what diet changes are needed for optimal therapeutic effect and supply the patient with the PIL (Akinwunmi, 2011).

Patient education regarding Warfarin therapy is important as insufficient information regarding diet and drug interactions may lead to sub- or supra-therapeutic effects of the drug (Baughman Spurling and Mangoni, 2008). Patients need to be properly informed about the drug interactions with Warfarin prior to commencing therapy. Warfarin is a highly sensitive drug that requires constant monitoring and lifestyle changes to ensure its effectiveness. There are a variety of foods that could affect the bioavailability of Warfarin, either reducing or increasing the effectiveness of the drug (Jank et al.2008).

Khudair and Hanssens (2010) concluded in their study at a hospital in Qatar that a Warfarin Education programme may be able to not only improve patient's knowledge and compliance, but also decrease the workload on healthcare workers by reducing the number of clinic visits they require. They also noted that staff that will be providing the education must be able to communicate to the patient in their mother tongue to ensure that effective learning takes place.

Munir Pirmohamed (2006), from the Department of Pharmacology and Therapeutics, University of Liverpool, in his article titled " Warfarin: almost 60 years old and still causing problems ",

argued that after being on the market for so long, all issues associated with Warfarin and its use should have been addressed. However, this is not the case, with adverse effects and other drug related issues being an ongoing problem, requiring the use of monitoring tools and effective patient education to overcome the resulting problems.

2.8 Challenges of drug and food interactions with Warfarin

In a Nationwide study conducted in Sweden titled "Adherence to Guidelines for Avoiding Drug Interactions Associated with Warfarin", Lindh et al. (2014) demonstrated that physicians avoided prescribing Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) to patients currently on Warfarin mainly due to the risk of NSAIDs causing gastro-intestinal bleeding. However, due to their lack of knowledge regarding other drug-Warfarin interactions, they continued to prescribe substances such as Sulfamethoxazole and Tramadol, which result in hemorrhaging, when used in combination with Warfarin. The study emphasizes the need for continuous medical education on basic pharmacology regarding drug interactions for physicians to ensure compliance to drug prescribing standards. Chua et al. (2015), in their literature review, were able to identify specific areas in which some traditional Chinese medicines were used in conjunction with Warfarin and resulted in near fatal ADRs. Herbs such as Danshen, Gingko, Dongquai, American Ginseng, Safflower, Peach Kernal, Licorice, Lycium, Ginger and Notoginseng were found to cause an increase in INR in various case reports. A study conducted in Germany by Jank et al. (2008) showed knowledge gaps in patients regarding drug-drug and drug-food interactions. Continuous education regarding these interactions with oral anticoagulants will allow these gaps in knowledge to be bridged, thus ensuring safety and efficacy of Warfarin.

2.9 International Normalized Ratio and its importance in Warfarin therapy

The International Normalized Ratio (INR) was developed by the WHO in 1982 to standardize the reporting of prothrombin time globally. It has since been used as an effective tool to manage anticoagulant therapy, with the results having shown considerable efficacy and safety (Poller 2004).

In describing "Practical tips for Warfarin dosing and monitoring", Jaffer and Bragg (2003) mention that patients "walk a tightrope between bleeding and clotting" while taking Warfarin,

once again emphasizing its narrow therapeutic index. Any healthcare professional prescribing Warfarin should have knowledge on the mechanism of action; pharmacodynamics and pharmacokinetics; interactions with diet and other drugs; as well as how to use the INR in monitoring (Jaffer and Bragg, 2003).

Verma and Kole (2014) conducted a study on trauma patients to determine the mortality risk due to hemorrhage using the INR as it has the quickest turnaround time. The findings of the study showed that the INR test has a high level of accuracy in predicting mortality in trauma patients (Verma and Kole, 2014). As noted by Kuruvilla and Turner (2001) " The goal of anticoagulant therapy with Warfarin is to administer the lowest effective dose of the drug to maintain the target INR". They reported that to ensure safety and effectiveness of Warfarin, an INR within the target range is required, this being 2.0-3.0 to avoid any sub- or supra- therapeutic affects that could result in either a bleeding or thrombotic event.

2.10 Patients' compliance to Warfarin Therapy

In an article published in an online journal called Thrombosis Research titled "Knowledge, satisfaction, and concerns regarding Warfarin therapy and their association with Warfarin adherence and anticoagulation control" Wang et al. (2014) were able to demonstrate an association with adherence to Warfarin by the patient and INR control. Another factor that could contribute to the compliance of Warfarin therapy is patient understanding of their anticoagulant therapy. A study conducted in the United Kingdom (UK) by Nadar et al. (2003) determined the perception of anticoagulant therapy of patients from different ethnic groups. The findings from the study showed that there were gaps in the knowledge of patients from ethnic minorities (Nadar et al.2003).

2.11 Conclusion

Based on the literature review, Pharmacovigilance plays a role in protecting the public against adverse drug reactions. The patient information leaflet (PIL) provides information to the patient regarding the management of their drug therapy. Warfarin with its narrow therapeutic index requires strict monitoring and proper patient education. Currently there is no research to date that investigated the patient's knowledge and use of the PIL regarding their Warfarin Therapy.

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CHAPTER 3 MANUSCRIPT FOR PUBLICATION

This chapter is presented in the form of a manuscript for submission to a journal for publication, and provides the methodology, results and discussion. The results are presented in the order of the four objectives, these being:

1. To determine whether or not the patients know about Patient Information Leaflet and use it
2. To establish the patients' level of knowledge about Warfarin therapy.
3. To determine the patients' knowledge of the International Normalized Ratio.
4. To determine the patients' knowledge of Warfarin therapy regarding its possible interactions with food and other medicines.

The manuscript is prepared for submission to the African Journal of Pharmacy and Pharmacology

Title: Knowledge and use of patient information leaflet regarding Warfarin therapy among patients at private clinics in Gauteng, South Africa.

Karmishtha Hutheram[1] Catherine Connolly[1] Elizabeth Ojewole[1]*

[1] College of Health Sciences, University of KwaZulu-Natal, P B X54001, Durban 4000. South Africa.

Details of authors:

Karmishtha Hutheram Discipline of Pharmaceutical Sciences, College of Health Sciences, University of KwaZulu-Natal, P B X54001, Durban 4000. South Africa, Cell: +27783063693, Email: kammy91985@gmail.com

Catherine Connolly School of Public Health and Nursing, College of Health Sciences, University of KwaZulu-Natal, P B X54001, Durban 4000. South Africa., Cell: +27727629684, Email: cconnolly205@gmail.com

Dr Elizabeth Ojewole* Discipline of Pharmaceutical Sciences, College of Health Sciences, University of KwaZulu-Natal, P B X54001, Durban 4000. South Africa. Cell: +27735872149, Email: Ojewolee@ukzn.ac.za

Summary of the manuscript: 6295 words, 21 pages, 2 figures, 5 tables and references

ABSTRACT

Background: Warfarin is the gold standard drug of choice to manage thrombotic disorders, but may interact with certain foods and drugs, resulting in unwanted adverse effects. The use of patient information leaflet (PIL) as a standardized educational material is essential to ensuring optimal therapy. The aim of the study was to determine patient's knowledge and use of PIL regarding their Warfarin therapy.

Methods: A descriptive cross-sectional survey design required respondents to complete an anonymous questionnaire survey over 18 weeks. Responses were captured and analyzed using STATA version 13.

Results: 34 patients responded in this study, of whom 56% (n=19) were males and 73.5% (n=25) had been on Warfarin treatment for less than 10 years. Only 50% (n=17/34) had knowledge of the PIL, 91% (n=31) knew about the International Normalized Ratio (INR) and 97% (n=33) understood its importance. While 76.5% (n=26) had knowledge of other drugs and foods that interact with Warfarin, and 70.5% (n=24) knew that consuming leafy green vegetables could reduce its effectiveness, only 58.8 % (n=20) understood the effect of alcohol on Warfarin. 91% (n=31) scored above 50% on the Oral Anticoagulant Knowledge (OAK) Test, with a moderate negative correlation between this and the respondent's age (Spearman correlation = -0.27).

Conclusion: INR testing and its importance in Warfarin therapy appeared to be known by most respondents, their lack of knowledge about PIL, as well as drug, alcohol and food interactions with Warfarin highlights the need for education and counseling to reinforce their knowledge and use of PIL.

Keywords: Warfarin therapy, knowledge of PIL, patient information leaflet, patient education, Warfarin-food interactions, Warfarin-drug interactions

3.1 INTRODUCTION

In South Africa, the Medicines Control Council (MCC) has stipulated in Regulation 10 of the Medicines and Related Substances Act, (Act 101 of 1965) that "*each package of a medicine shall have a Patient Information Leaflet (PIL) and prescribes the information that must be contained therein."* It furthermore requires that *"a person dispensing or administering a medicine must ensure that a PIL is made available at the point of such dispensing as well as the administration"*. The Act stipulates that patients receiving medicine must obtain the regulated leaflet, thus ensuring that they have access to information regarding their prescribed medicine.

The patient information leaflet (PIL) serves as a pharmacovigilance tool to ensure patients and drug safety. It protects the patient by providing information about the medicines, any precautions and their use, this being important in order to ensure optimal drug therapy and patient safety. The use of PIL as a pharmacovigilance tool is therefore strongly suggested and patients should be educated to understand their content so as to promptly report any untoward effects regarding their medicines (Upadhyaya, 2015).

According to the World Health Organization (WHO,2002), *"Pharmacovigilance (PV) is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem."* In 1992, South Africa became the first country in Africa to join the WHO International Drug Monitoring Programme (Mehta et al. 2014). In ensuring the prevention of adverse events of marketed medicine in countries throughout the world, several pharmacovigilance tools are used. Those used in South Africa are Cohort Event Monitoring (CEM), Targeted Spontaneous Reporting (TSR) and Active Surveillance for existing Cohort Studies (Mehta et al. 2014). These pharmacovigilance systems, as discussed by Mehta et al. (2014), were in place for Immunization, HIV, TB, pediatric HIV and Dermatology programmes. The authors described pharmacovigilance as a responsibility that is shared between various sectors namely: the Medicines Regulatory Authority (MRA), pharmaceutical industry, Essential Drugs Programme (EDP) and Public Health Programmes (Mehta et al. 2014). Pharmacovigilance is an important practice, with the South African Medicines and Related Substances Act (Act 101 of 1965) Guidelines 2.11 stipulating the practices required during clinical trials as well as for unregistered medicines, and Guidelines 2.33 outlining the strategies required post registration.

Pharmacovigilance systems are in place to collect information useful to the surveillance of medicinal products, with specific reference to Adverse Drug Reactions (ADR). The purpose of Pharmacovigilance, as discussed by the WHO are *"to enhance patient care and patient safety in relation to the use of medicines; and to support public health programmes by providing reliable, balanced information for the effective assessment of the risk-benefit profile of medicines."* (WHO, 2002). The practice of Pharmacovigilance is important, as it serves to protect the public from drug related adverse effects and to ensure that the benefits of medicines outweigh the risks (WHO, 2002).

Drugs with a narrow therapeutic index require stricter monitoring, as the sub- and supra-therapeutic indexes are easily reached due to contributing factors, such as diet and drug interactions either increasing or decreasing the effect of the drug. Warfarin, a drug that has been used for decades worldwide as an anticoagulant to treat thrombotic disorders, although displaying characteristics of high oral bioavailability (Wardrop and Keeling, 2008), is one of those drugs that require regular monitoring due to its narrow therapeutic index. Kuruvilla and Gurk-Turner (2001) noted that *"The goal of anticoagulant therapy with Warfarin is to administer the lowest effective dose of the drug to maintain the target international normalized ratio (INR)".* For Warfarin to reach optimal therapeutic levels in the blood, patients must adhere to strict guidelines. These include patients eating a balanced diet with moderate amounts of Vitamin K, reducing the alcohol intake and taking their Warfarin as prescribed (Akinwunmi, 2011). The pharmacovigilance of Warfarin through the Norwegian Spontaneous reporting system assessed drug associated bleeding events due to pharmacokinetic medicine interactions, and the findings showed a higher INR at the time of the bleeding event (Narum et al.2011).

In ensuring the safety and management of patients on Warfarin, pharmacovigilance tools, such as regular blood testing and health education, have been used. The regular monitoring of patients on Warfarin is essential to ensure that patients remain within therapeutic index (Jaffer and Bragg, 2003). The International Normalized Ratio (INR) test monitors the effectiveness of Warfarin therapy and ensures that the recommended dosage results in an effective therapeutic index. The therapeutic index of Warfarin is usually an INR of between 2.0 -3.0, with a value of below 2.0 possibly resulting in a thrombotic event, while above 3.0 it could result in a bleeding episode. (Kuruvilla and Turner, 2001). Akinwunmi (2011) discussed common concerns regarding patients on Warfarin therapy that included side effects, drug interactions, missed

dosages, diet and alcohol consumption. Akinwunmi (2011) suggested that these aspects are to be discussed with the patients by community pharmacists. In accordance with MCC's regulations, patients should receive detailed education from their physician, pharmacist and or nurse on starting Warfarin therapy so that patients are aware of any lifestyle changes they may have to maintain to ensure the drugs' effectiveness (Wofford, Wells and Singh, 2008). It is therefore important that patients understand the Warfarin information provided to them in order to ensure their safety and its optimal therapy. However, the lack of proper patient education regarding the use of anti-coagulation therapy has become a global problem (Khudair and Hanssens 2010). Wang et al. (2014) reported an association between the lack of knowledge and fluctuations in patients INR, which influenced their anticoagulant control.

The time consuming nature of providing patient education by clinicians, as well as the large amount of information required by patients on Warfarin therapy, have led to proper patient education being neglected (Wofford, Wells and Singh, 2008). It was therefore shown that the standardization of educational material and efficient delivery of education is necessary to improve the quality of Warfarin Therapy. Various methods, such as using information technology (IT), have been explored by Nasser, Mullan and Bajorek (2012). They concluded that there is a need to improve the use of and access to IT based Warfarin education resources, particularly by health care professionals. Effective methods for improving Warfarin education to patients are still being explored and various avenues, such as the one discussed by Nasser, Mullan, and Bajorek (2012) are being used to help bridge this knowledge gap.

Finding an effective knowledge transfer method to ensure effective anticoagulant therapy is thus an on-going challenge, specifically regarding highly sensitive anticoagulants such as Warfarin. The aim of the study was to determine patient's knowledge and use of PIL regarding their Warfarin therapy. The aim of this research was to investigate patient knowledge and use of the Patient Information Leaflet regarding Warfarin therapy at private sector INR clinics in the Gauteng area in South Africa

3.2 MATERIALS AND METHODS

A descriptive, cross-sectional questionnaire survey design was used at 10 INR clinics of a private pathology company in Gauteng Province of South Africa. A convenience sampling technique was used and patients who used Warfarin and resided in Gauteng Province between the ages of 20 and 90 were invited to participate in the study. Possible respondents were approached on arrival to the clinics between 27th July 2015 and 27th November 2015, prior to their blood being drawn for INR testing. Those who agreed to participate were provided with information about the research, asked to sign written consent and then completed the questionnaire. Only 34 patients were eligible and completed the structured, self-administered questionnaire.

The questionnaire consisted of four sections; A. respondent's demographics, B. knowledge and use of the patient information leaflet, C. content and section D. knowledge of INR. The questions for Section C were adapted from the developed and validated OAK Test by Zeolla et al. (2006). The questionnaire also contained questions that were based on the standard Warfarin PIL that was developed by Bristol-Myers Squibb International, as well as that from Cipla Pharmaceuticals that contained information that guides the patient on how to manage their diet and lifestyle while on Warfarin in South Africa. The questionnaire was translated into Afrikaans and Tswana by two language translators licensed by South African Translators Institute (SATI). A pilot study was conducted prior to the data collection. Two patients completed the Afrikaans questionnaires and their feedback was used to modify the questionnaire for the final survey. The respondents requested an extension of time to complete the Afrikaans questionnaires to enable them to provide detailed responses. The time required to complete the questionnaire was amended from 10 to 20 minutes, and no respondents wanted to complete the questionnaire in the Tswana language.

Data were captured, cleaned up and analyzed using Stata statistical software version 13. Descriptive statistics, such as the mean, the range, the standard deviation and the median, were used to describe the continuous variables (e.g. age). Frequencies and percentages were used to describe the categorical variables, such as gender, occupation, highest education, reason for Warfarin use; months on Warfarin and OAK test Score.

Kruskal -Wallis equality-of-populations rank test was used to test whether several samples came from the same population in Gauteng. Kruskal -Wallis equality of populations rank test was used to analyze the respondent's demographics, such as age, marital status, highest qualification and occupation. The two-sampled Wilcoxon rank-sum (Mann-Whitney) test was used to test whether 2 independent samples came from populations with the same distribution in Gauteng. The Wilcoxin rank sum (Mann-Whitney) test was used to test whether the respondent's gender played a role in their OAK score.

Ethical approval was obtained from the Humanities and Social Sciences Research Ethics Committee (HSSREC) of the University of KwaZulu-Natal (UKZN) (HSS/0667/015M). Following ethical approval, the private pathology company was approached for permission and this was granted to conduct the study at their INR Clinics within the Gauteng Province.

3.3 RESULTS

Thirty-four patients agreed to participate in the survey from a target population of 100 patients in the Gauteng area. The initial sample size was 80 using a confidence level of 95%, margin of error of 5% and a response distribution of 50%. The response rate of the study was 42.5%. These consisted of 56% (n=19) males and 44% (n=15) females, with their age ranges being 20-90 years, with a mean age of 68 years and a standard deviation of 12 years. Regarding their time on Warfarin, more than half (73.5%, n=25) had taken Warfarin for less than 10 years. Fifty-six percent (n=19) of the respondents were from the Centurion area and 44% (n=15) were from the Vereeniging area. As indicated in Table 1, 71% (n=24) of respondents were married, 24% (n=8) were widowed and 6% (n=2) were single. Regarding the educational levels, 53% (n=18) had tertiary education, and the rest were in the categories of grade 12 and lower. Twenty-nine percent (n=10) were employed while 59% (n=20) reported that they were retired.

The majority of the respondents 91% (n=31) scored above 50% on the OAK test. The conditions for which they used Warfarin were 41% (n=14) for heart related problems, 38% (n=13) for deep vein thrombosis (DVT), 9% (n=3) for embolism and the 9% (n=3) for stroke, clotting disorder and post-operative prophylaxis. The demographics of the respondents were tested for associations using the Kruskal-Wallis equality of populations rank test and the Wilcoxin rank

sum (Mann-Whitney).Table 1 shows the demographics that were tested as well as the statistical tests carried out on the variables. A *p-value* of less than 0.05 was used to describe statistical significance, with no statistical significance being found between these variables (p values > 0.05).

Table 1: Analysis of the respondents' demographic characteristics

Variables	n (%)	Median	p values	SD	SEM
Age					
<60	8 (24)	15	0.3	12.15	2.08
60-69	8 (24)	14			
70-79	13 (38)	14			
>-80	5 (15)	12			
Total	34 (100)	14			
Gender					
Male	19 (56)	14	0.9	0.50	0.08
Female	15 (44)	14			
Marital Status					
Married	24 (71)	14	0.7	0.86	0.14
Unmarried/Single	2 (6)	13.5			
Widow	8 (24)	12.5			
Highest Qualification					
Matric	11 (32)	14	0.3	0.91	0.15
Below Matric	5 (15)	16			
Tertiary	18 (53)	14			
Occupation					
Working	10 (29)	14.5	0.2	0.81	0.14
Pensioner/Retire	20 (59)	14			
Homemaker	3 (9)	15			

There was a moderate negative correlation between the age of the respondents and their OAK score (Spearman correlation = -0.27), with age increasing as the knowledge score decreased (Figure 1).

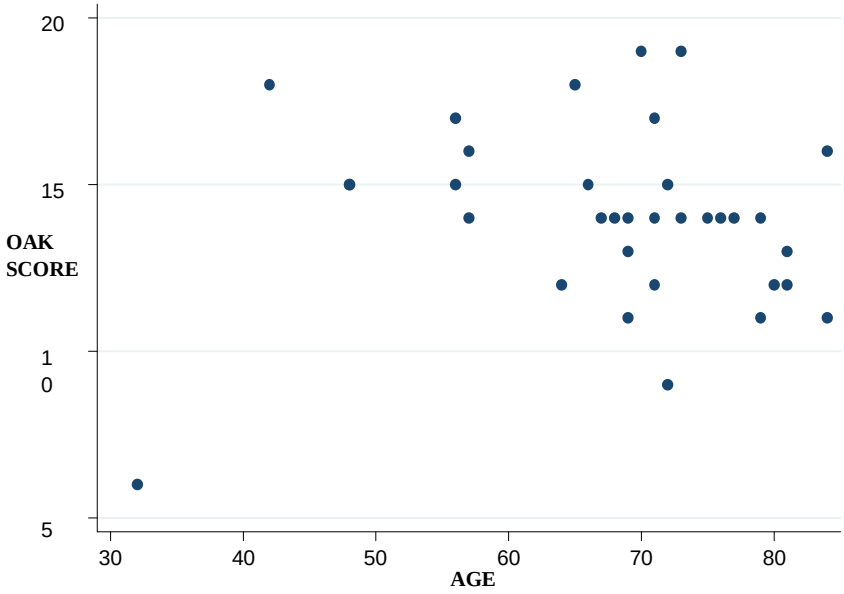

Figure 1: Age versus OAK score

3.3.1 Respondent's knowledge of PIL and use regarding Warfarin Therapy

Objective 1 of the study was to determine whether patients knew what the PIL was and if they had used it before to manage their therapy. Fifty-percent (n=17) indicated that the PIL was a source of information about the drug, while the 26% (n=9) who said they did not know what the PIL was, they reported receiving information from the pathology INR clinic. Of the remaining 24%, 21% (n=7) indicated 'Not applicable' to this question and 3% (n=1) said they were 'Unsure'. When asked if they ever collected and read the PIL when they received their Warfarin, 56 % (n=19) received and read the PIL, and 44% (n=15) did not. Of the 56% (n=19) who said that they received and read the PIL, only 50% (n=17) understood the information contained within it (Table 2).

The respondents who did not receive the PIL had scored higher on the OAK test compared to those who said they received it (14.7(43%) (SD±2.6 vs. 13.3(39%) (SD±2.8)), however, the difference was not statistically significant (p=0.2). The respondents who did not read the PIL also scored significantly higher on the OAK test compared to those who read the PIL (15.6(46%)

(SD±2.5) vs. 13.3(39%) (SD±2.7), p=0.03. Despite not having knowledge of the PIL or the contents, the respondents scored high on the OAK test.

Table 2: Relationship between use of PIL and OAK Score

Questions	n (%)	mean	SD	p value
Do you know about PIL?				
No	10 (29)	15.6	2.72	0.035
Yes	17(50)	13.7	1.84	
Do you receive a PIL with your Warfarin tablets?				
No	16(47)	14.7	2.57	0.19
Yes	18(53)	13.4	2.81	
Have you read the PIL on Warfarin?				
No	11(32)	15.6	2.5	0.03
Yes	21(62)	13.3	2.69	
Did you understand the contents of the PIL?				
No	7(21)	15.0	2.58	0.18
Yes	21(62)	13.4	2.71	

3.3.2 Respondent's knowledge of the use of INR

Regarding objective 2, the respondents answered questions about their understanding of INR testing and its importance. Of the 34 respondents, 91% (n=31) reported that INR testing is used in monitoring the viscosity of the blood. Ninety-four percent (n=32) of participants knew about the importance of INR testing and reported that it monitors Warfarin therapy. About 62% (n=21) said that their INR was in range in the last six months, compared to 26.4% (n=9) who noted that their INR was not. As shown in Table 3, 97% (n=33) knew that the INR test is used to monitor their Warfarin, 94% (n=32) were aware that they should have it tested once a month after they had stabilized on the dose, and 79% (n=27) knew that an INR above the goal range will increase their risk of bleeding. Of the 97% (n=33) who knew the importance of INR, only 35% (n= 12) had an INR that was within the given range, while 65% (n=22) did not.

Table 3: Respondent's knowledge of INR (n=34)

Questions	Correct n (%)	Incorrect n (%)
A patient on Warfarin should contact the physician or healthcare provider who monitors it when: (Answer: Another physician adds a new medication or stops or changes the dosage of current medication)	28 (82.3)	6 (17.6)
A person on Warfarin should seek immediate medical attention: (Answer: If they notice blood in their stool when going to the bathroom.)	10 (29.4)	24 (70.5)
It is important for a patient on Warfarin to monitor for signs of bleeding: (Answer: At all times)	32 (94.1)	2 (5.8)
Each time you get your INR checked, you should: (Answer: Let your Dr know if you missed any doses of Warfarin)	27 (79.4)	7 (20.5)
The INR test is: (Answer: a blood test used to monitor your Warfarin therapy)	33 (97.0)	1 (2.94)
Once you have been stabilized on the correct dose of Warfarin, about how often should your INR value be tested? (Answer: Once a month)	32 (94.1)	2 (5.8)
A patient with an INR value above the goal range: (Answer: Is at an increased risk of bleeding)	27 (79.4)	7 (20.5)

3.3.3 Knowledge of INR versus OAK score

Objective 3 of the study was to determine the patients' knowledge of the International Normalized Ratio. A two sampled t-test with equal variance showed no significance (*p* value=0.3) in OAK score between respondents with and without knowledge of the ideal INR range, with no knowledge 13.2 (SD±3.5) vs. knowledge 14.3 (SD±2.3), as shown in Table 4, indicating that knowledge of the ideal range was not associated with a high OAK score.

Table 4: Knowledge of INR versus OAK score

Questions	n (%)	mean	SD	p value
What is your understanding of the INR test				
I do not know what an INR test is	1 (3)	15	.	n/a
I know that INR testing is used to monitor Warfarin Therapy	31 (91)	13.9	2.81	
Why is INR important?				
To monitor Blood sugar	1 (3)	18.0	.	n/a
To monitor Warfarin Therapy	32 (94)	13.8	2.67	
The INR should ideally be in the range of 2.0-3.0 Has your INR been in range in the last 6 months?				
No	11 (32)	13.2	3.54	0.3
Yes	21 (62)	14.3	2.26	

* Patients who responded N/A were omitted

3.3.4 Respondents' knowledge of Warfarin therapy regarding interactions with food and other medicines

Objective 4 explored the knowledge of Warfarin therapy regarding possible interactions with food and other medicines among the respondents (Table 5)**.** The knowledge of Warfarin and food interactions among the respondents indicated that 70.5% (n=24) were aware that occasional consumption of large amounts of green leafy vegetables can reduce its effectiveness. However, only 23.5 % (n=8) could identify that people need to be consistent and eat a diet that includes all types of food. When asked about consuming alcohol while on Warfarin, 58.8% (n=20) said that alcohol would affect the INR. The knowledge of the interaction of Warfarin with other medicines indicated that only 38.2% (n=13) identified correctly that herbal, dietary and OTC supplement interacts with Warfarin. Non-steroidal anti-inflammatory medication (NSAIDS) increase a person's risk of bleeding when taken with Warfarin and questions about which 70.5% (n=24) responded correctly.

Table 5: Knowledge of Warfarin interactions with food and other medicines (n=34)

Questions	Correct n (%)	Incorrect n (%)
Occasionally eating a large amount of leafy green vegetables while taking Warfarin can: (Answer: Reduce the effectiveness of Warfarin)	24 (70.5)	10 (29.4)
Drinking alcohol while on Warfarin: May affect your INR	20 (58.8)	14 (41.1)
When it comes to diet, people taking Warfarin should: (Answer: Be consistent and eat a diet that includes all types of food)	8 (23.5)	26 (76.5)
Which of the following vitamins interacts with Warfarin? (Answer: Vitamin K)	29 (85.2)	5(14.7)
When is it safe to take medication that interacts with Warfarin? (Answer: If your healthcare provider is aware of the interaction and checks your INR.)	8 (23.5)	26 (76.5)
Taking a medication containing aspirin or other non-steroidal anti-inflammatory medications such as ibuprofen while on Warfarin will:(Answer: Increases your risk of bleeding from the Warfarin)	24 (70.5)	10 (29.4)
Which of the following over-the-counter products is most likely to interact with Warfarin?(Answer: Herbal/Dietary supplements)	13 (38.2)	21 (61.7)

Figure 2 indicates the number of respondents who answered questions addressing their knowledge of Warfarin correctly. Ninety-one percent (n=31) of patients were aware that Warfarin is primarily used in the treatment of blood clots. Seventy-four percent (n=25) of respondents responded with the correct answer that missing one dose of Warfarin alters the effectiveness of the drug and 97% (n=33) of respondents were able to do damage control if they missed a dose that they would take the next scheduled dose and inform their Doctor. Sixty-one percent (n=21) of respondents knew that skipping one dose of Warfarin would cause their INR to fall below the goal range. Seventy-six percent (n=26) of respondents could distinguish between the different strengths of Warfarin (1mg, 3mg and 5mg).

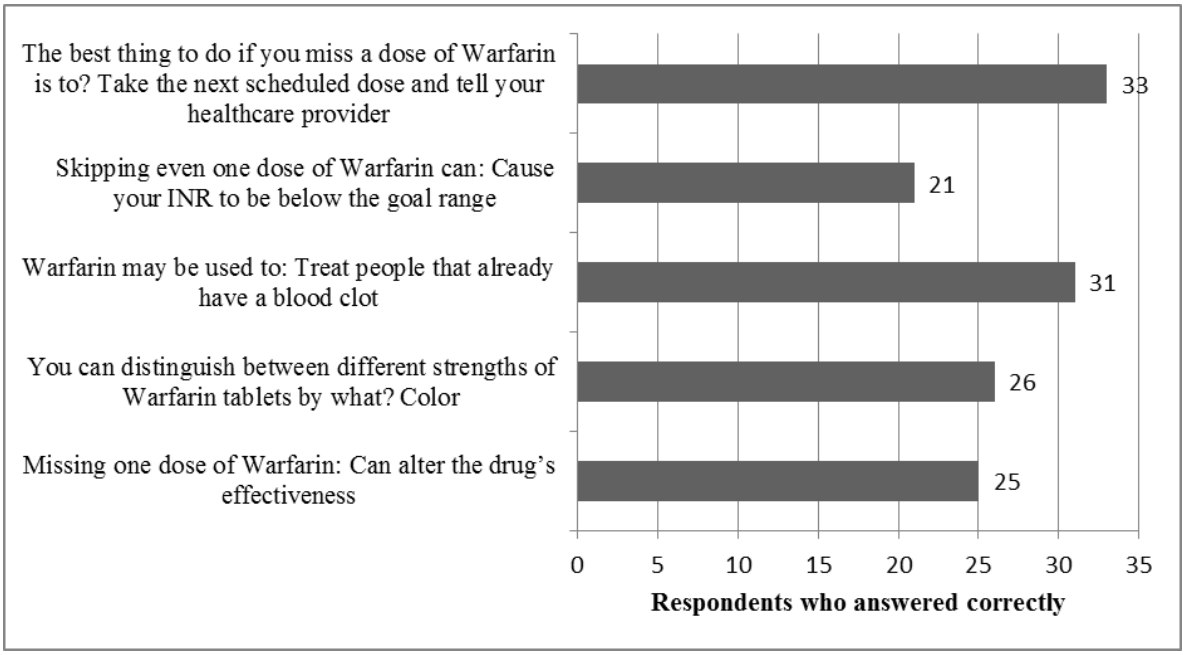

Figure 2: Number of Respondents who had correct knowledge regarding Warfarin (n =34)

3.4 DISCUSSION

The aim of the study was to investigate patient's knowledge and use of the Patient Information Leaflet (PIL) regarding their Warfarin therapy. The knowledge of INR and Warfarin interactions with food and other medicines was also assessed.

With respect to whether or not the respondents know about the Patient Information Leaflet (PIL) and used it, results from the study showed that respondents who did not receive the PIL scored higher on the OAK test compared to respondents who received the PIL. Respondents who did not read the PIL also scored significantly higher on the OAK test than those who read it. This suggests that despite not receiving the PIL or reading it, 91% (n=31) of the respondents scored moderately high on the OAK test (OAK $\geq$50%) (Matalqah et al. 2013). Knowledge and usage of the PIL has no effect on OAK score, according to the results of this study. Leemans et al. (2011) concluded that only one in four people read the PIL.

With regard to respondents level of knowledge about Warfarin therapy 91% (n=31) of patients were aware that Warfarin is primarily used in the treatment of blood clots. Seventy-four percent (n=25) of respondents responded with the correct answer that missing one dose of Warfarin

alters the effectiveness of the drug and 97% (n=33) of respondents were able to do damage control if they missed a dose that they would take the next scheduled dose and inform their Doctor. 61% (n=21) of respondents knew that skipping one dose of Warfarin would cause their INR to fall below the goal range. Seventy-six percent (n=26) of respondents could distinguish between the different strengths of Warfarin (1mg, 3mg and 5mg). In this study respondents scored high with the OAK test when assessed on dosing indications and color. This study is similar to the study by Matalqah et al. (2013) were participants scored moderately high on the OAK score of more than 50%.

When respondent's knowledge of the International Normalized Ratio (INR) was determined all but 3% (n=1) respondents knew why INR testing was important, of whom only 35% (n=12) had an INR that was within the given range and 65% (n=22) did not. This indicates that having knowledge on the importance of INR does not really imply whether respondents would have an INR in range or not. The results from this study showed no significance in OAK score between respondents with and without knowledge on the ideal INR range .Therefore knowledge of the ideal range was not associated with OAK score. Using the validated OAK test Rahmani et al. (2016) found that although younger educated patients may pass the OAK test, the OAK test results could not be used as tool to predict INR as well as the possibility of bleeding or thrombotic episodes. Findings by Rahmani et al. (2016) are in keeping with the results of this study that showed no significance in OAK score in respondents with and without knowledge of the ideal INR range.

Adhering to the recommended lifestyle changes in order to have an INR in range would require the respondents to have adequate knowledge of the interactions of food and other drugs with Warfarin. With regard to determining respondent's knowledge of Warfarin therapy regarding possible interactions with food and other medicines the data from this study showed that only 38.2% (n=13) of respondents identified correctly that herbal, dietary and OTC supplements interact with Warfarin. With regard to food interactions with Warfarin only 23.5 % (n=8) could identify that people need to be consistent and eat a diet that includes all types of food and not make drastic changes to their diet.

To obtain optimum effectiveness of Warfarin according to their therapeutic indications, patients require adequate education with regard to food and other drugs that could interact with Warfarin

resulting in increased bleeding or thrombotic events. In this study, 58.8% (n=20) of respondents were aware that alcohol would affect the INR. Havrda et al. (2005) identified that low dose beer consumption increases the effect of Warfarin resulting in a higher INR. The findings as discussed by Havrda et al. (2005) suggest that even low dose beer consumption increases the INR, which could result in a bleeding episode. Respondents need to be made aware of this as 41.1%(n=14) are still under the impression that either alcohol consumption is safe as long as you are on a low dose of Warfarin or it does not even affect your INR.

In addition to medicines known to alter the effectiveness of Warfarin and in turn impact the expected levels (or range) of INR, foods can also impact on the effectiveness of Warfarin. Bushra et al. (2011) reported that consuming large amounts of green vegetables like broccoli, brussel sprouts, kale, parsley and spinach may alter the effectiveness of Warfarin and that this was also true should the consumed amounts of these vegetables changed suddenly.

In this study, 71% (n=24) of respondents knew that large amounts of leafy green vegetables will reduce the effectiveness of Warfarin. According to the National Institutes of Health (NIH), Phylloquinone known as Vitamin K 1 is available for dietary consumption in most green leafy vegetables and Warfarin being a Vitamin K antagonist enables it to interfere with Vitamin K dependent clotting factors in the Liver altering the coagulation process (Bhonoah, 2003). .Results from this study show that, 85.2% (n=29) of respondents identified that Vitamin K would interact with Warfarin and this is in keeping with Greenblaat et al (2005) who discussed that fluctuations in dietary Vitamin K intake is a cause of inconsistency in the response of Warfarin and that consistence in the Vitamin K intake of Warfarin treated patients is important . The respondents from this study could identify that Vitamin K would interact with their Warfarin therapy which is in keeping with Franco et al. (2003) who concluded that Vitamin K is an important independent variable that interferes with therapeutic stability of Warfarin.

Choi et al. (2010) have identified risk factors for increase in the INR after administration of non-steroidal anti-inflammatory drugs (NSAIDS) together with Warfarin. NSAIDS alter the effectiveness of Warfarin and increase the chances of bleeding. Warfarin-herb interactions have been investigated by Gohil and Patel (2007), and they concluded that the number of herbs that interact with Warfarin continue to grow (Gohil and Patel 2007). Patients were advised to avoid

taking these herbal medicines, and it was suggested that their INR be tested within two weeks of commencing herbal medicines.

Knowledge of medication interactions with Warfarin where investigated, and the results showed that 24% (n=8) of respondents were aware that it is safe to only take medications that interact with Warfarin if their physicians are aware and regularly check the INR. Knowledge on the Warfarin interaction with Aspirin or NSAIDS was present in 70.5% (n=24) of respondents however only 38.2% (n=13) of respondents were aware that OTC herbal products would interact with Warfarin (Table 5). Knowledge of the interactions between drug and herbal products are very important when taking Warfarin due to its narrow therapeutic index. Teklay et al (2014) conducted a study to determine the risk of bleeding from drug-drug interactions with Warfarin and concluded that bleeding complications as a result of the interaction was high. Of the 133 patients enrolled in their study 22 (16.5%) developed bleeding complications and 65 (48.8%) had one major drug-drug interaction (Teklay et al 2014). Results from the study conducted by Teklay et al. (2014) showed bleeding complications as a results of drug-drug interactions.

Shuaib et al. (2014) conducted an online survey to determine patient knowledge of Warfarin . Of the 200 patients that participated in the survey 88% were compliant to treatment but 56% were unaware of the potential drug-drug interaction with Warfarin (Shuaib et al. 2014). According to the findings by Shuaib et al. (2014), effective health education regarding drug-drug interactions of Warfarin therapy should be thoroughly addressed by healthcare professionals to avoid patients experiencing any adverse effects as a result of the narrow therapeutic index of Warfarin.

Demographic associations were investigated and the results showed that as Age increases; knowledge scores on the OAK test decreased. Spearman correlation = -0.27 showed a moderate negative correlation between Age and OAK score. The findings from this study are consistent with Nasser et al. (2011) who concluded in a population of older than 65 years of age that Warfarin knowledge was suboptimal which could impact on therapeutic outcomes of anticoagulant therapy.

The findings of the study are only applicable the private sector INR clinics in Gauteng. This study was not conducted at public sector INR clinics in Gauteng as well as other provinces in

South Africa. Therefore the generalization of the study findings to the whole of South Africa will be limited.

3.5 CONCLUSION AND RECOMMENDATION

This study showed that the respondents have adequate knowledge of PIL regarding their Warfarin therapy, and that knowledge decreased with age and no association was identified between PIL usage and Warfarin knowledge based on the OAK score results. However the knowledge acquired by patients is still insufficient in ensuring safety on Warfarin. Possible implementation of Warfarin counseling sessions on a six monthly basis may assist in reinforcing knowledge.

3.6 ACKNOWLEDGEMENTS

The authors are grateful to all the respondents for their voluntary participation in the study as well as the private pathology company for permission. A sincere thanks to Zeolla and colleagues as well as Dr Haines for granting permission to use the OAK questionnaire.

3.7 CONFLICT OF INTEREST

None declared

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CHAPTER 4. CONCLUSION

4.1 Introduction

Warfarin has been used in the treatment of thrombotic disorders since 1954 (Pirmohamed, 2006). However despite its convenience of oral dosage form and high bioavailability, Warfarin has a narrow therapeutic index and requires strict adherence to its usage guidelines in order to maintain effectiveness. In South Africa Warfarin still remains the drug of choice in the treatment of thrombosis (Sonuga et al.2016). South Africa's drug regulating body is the Medicine Controls Council, which has set regulations to protect and keep the public safe, and by implementing guidelines, such as the patient information leaflet (PIL) for numerous drugs, as per Regulation 10 of the Medicines and Related Substances Control Act 101 of 1975. The Royal Pharmaceutical Society advises that risk minimization tools like the PIL and a summary of product characteristics will serve to minimize severity of the risk or reduce its frequency. The PIL is therefore an effective Pharmacovigilance tool in providing education to patients regarding their medicines. This study investigated patient knowledge and use of the Patient Information Leaflet (PIL) regarding their Warfarin therapy at private sector INR clinics in the Gauteng area in South Africa. This chapter presents the conclusions drawn from the study findings and highlights the significance of the study. It also identifies the possible limitations of the study, and highlights recommendations for future work.

4.2 Conclusions from the study findings

This study was conducted in South Africa to investigate patient's knowledge and use of the Patient Information Leaflet (PIL) regarding Warfarin Therapy at private sector INR clinics in the Gauteng area. In conclusion the results from the study identified that despite not receiving the PIL or reading it, the respondents scored moderately high on the OAK test knowledge and usage of the PIL has no effect on OAK score, according to the results of this study. The results from this study also identified no significance in OAK score between respondents with and without knowledge on the ideal INR range. The findings from this study showed that only 38.2% (n=13) respondents identified correctly that herbal, dietary and OTC supplements interact with Warfarin. With regard to food interactions with Warfarin only 23.5 % (n=8) could identify that people need to be consistent and eat a diet that includes all types of food and not make drastic

changes to their diet. To obtain optimum effectiveness of Warfarin according to therapeutic indications, patients require adequate education with regards to food and other drugs that could interact with Warfarin and resulting in increased bleeding or thrombotic events. Provision for effective health education as well as PIL regarding Warfarin therapy should therefore be emphasized for healthcare professionals in order to stop patients from experiencing any adverse effects due to food and drug-interactions with Warfarin therapy.

4.2.1 Implications of study findings

Drawing from the conclusions as discussed above there are implications regarding patient care that all health care professionals need to consider when treating patients on Warfarin. Health care professionals need to make a conscious effort in educating patients on Warfarin on a continuous basis to ensure knowledge is reinforced and patients are reminded of the narrow therapeutic index of Warfarin. This will not only ensure patient safety against adverse drug reactions but will also ensure patient compliance to treatment and consumption guidelines as set out in the PIL.

4.3 Significance of the study

- The study provided information regarding patient understanding of the PIL and if they utilize the PIL as a tool for their Warfarin Therapy.
- This study also heightened the awareness for adequate patient education in South Africa and may form a baseline status of patient knowledge regarding Warfarin.
- The findings of the study showed that despite the absence of the PIL, patients still received adequate health education on Warfarin and applied the recommended lifestyle changes to ensure a stable INR.
- Service delivery at the private sector INR clinics was good in promoting health by educating patients on the management of their Warfarin in the absence of a PIL.
- Planning and implementation of a Warfarin counseling programme may promote health and impart new knowledge to patients regarding Warfarin.
- The PIL may prove to be an effective tool in educating patients on the management of their Warfarin therapy if given to patient on the dispensing of their Warfarin.

4.4 Limitations of the study

- Limitations of the study could be patient's refusal to participate in the study as they were private patients who could have had prior commitments while others could have been rushing back to work.
- The findings of the study are only applicable the private sector INR clinics in Gauteng. This study was not conducted at public sector INR clinics in Gauteng as well as other provinces in South Africa. Therefore the generalization of the study findings to the whole of South Africa will be limited.
- The responses to the questionnaire could have limited the reliability of the results as respondents were self-reporting.

4.5 Recommendations

- Chang et al. (2014) have devised a practical approach in minimizing Warfarin and Vitamin K interactions. They developed a score sheet for Vitamin K rich foods for which patients were scored against on a weekly basis. I would recommend the use of the score sheet for Vitamin K rich foods created by Chang et al. (2014) to be implemented at the INR clinics and Dr's rooms. This score sheet can be effective and beneficial to health care professionals in stabilizing the anticoagulation therapy of patients on Warfarin.
- The implementation of a standardized Warfarin counseling at both public and private sector clinics will ensure patients are educated on the management of Warfarin thus ensuring compliance to consumption guidelines.
- Health care professionals need to create an awareness of the importance of receiving and reading the PIL in order for the patients to effectively manage their Warfarin. Health care professionals need to go through the PIL with the patient in order to clear any misunderstanding and improve the patient's attitude towards the PIL.
- Further research needs to be done by extending study to public hospitals and all INR clinics in South Africa as this would provide sufficient data regarding the use of the PIL regarding Warfarin therapy.

4.6 Conclusion

The findings of this study suggest that despite little or no knowledge of the PIL and having not seen or received the PIL, respondents still scored high on the OAK test. There is therefore a need for improving patient education with respect to use of the PIL regarding Warfarin therapy. Until a time when health care practitioners are able to trust newer anticoagulants to effectively manage thrombotic disorders as Warfarin has done for the last 50 years, educational strategies must take priority when prescribing Warfarin in ensuring patients' adherence to thrombotic management guidelines including the use of the PIL.

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APPENDICES

I: Ethics approval

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

8 July 2015

Mrs Kamishtha Hutheram 214582347
School of Health Scinces: Pharmacy
Westville Campus

Dear Mrs Hutheram

Protocol reference number: HSS/0667/015M
Project title: Investigating patients' kowledge and use of patient information leaflet regarding their Warfarin therapy

Full Approval – Expedited Application

In response to your application received on 4 June 2015, the Humanities & Social Sciences Research Ethics Committee has considered the abovementioned application and the protocol have been granted **FULL APPROVAL.**

Any alteration/s to the approved research protocol i.e. Questionnaire/Interview Schedule, Informed Consent Form, Title of the Project, Location of the Study, Research Approach and Methods must be reviewed and approved through the amendment/modification prior to its implementation. In case you have further queries, please quote the above reference number.

PLEASE NOTE: Research data should be securely stored in the discipline/department for a period of 5 years.

The ethical clearance certificate is only valid for a period of 3 years from the date of issue. Thereafter Recertification must be applied for on an annual basis.

I take this opportunity of wishing you everything of the best with your study.

Yours faithfully

.....

Dr Shenuka Singh (Chair)
Humanities & Social Sciences Research Ethics Committee

/pm

Cc Supervisor: Dr Elizabeth Ojewole
Cc Academic Leader Research: Professor J van Heerden
Cc School Administrator: Ms P Nene

Humanities & Social Sciences Research Ethics Committee
Dr Shenuka Singh (Chair)
Westville Campus, Govan Mbeki Building
Postal Address: Private Bag X54001, Durban 4000
Telephone: +27 (0) 31 260 3587/8350/4557 **Facsimile:** +27 (0) 31 260 4609 **Email:** xmbap@ukzn.ac.za / anymanm@ukzn.ac.za / mohunp@ukzn.ac.za
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II: Gatekeeper permission approval letter

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166 Witch-Hazel Avenue, Highveld Technopark,
Centurion, 0157
Private Bag X9, Highveld, 0169
Tel: (012) 678-1000
Fax: (012) 678-1815

15 May 2015

The Chairperson
Higher Degrees and Ethics Committee
School of Health Sciences, College of Health Sciences
University of KwaZulu-Natal
Durban, 4000

Dear Sir/Madam

CONFIRMATION OF APPROVAL OF RESEARCH: Kammy Hutheram

This letter serves to confirm that the Management of Ampath has considered the above-mentioned staff member's request to conduct research within our organisation, using our INR facility at the Zuid-Afrikaans Hospital. The research topic is: "Investigating patients' knowledge and use of patient information leaflet regarding their Warfarin therapy".

Kindly be advised that the Management of Ampath Trust supports this study as we deem it of great relevance and value not only for us as an organisation, but also our patients.

We wish Kammy every success with her intended research and look forward to receiving the results of her research work.

Kindly contact my office directly should you have any queries regarding this communication and/or require additional information.

Yours sincerely

Dr. L. BOSMAN
Senior Human Resources Manager

III: Gatekeeper permission support letter

PATHOLOGY LABORATORY SUPPORT SERVICES
AMPATH TRUST
AMPATH

166 Witch-Hazel Avenue, Highveld Technopark,
Centurion, 0157
Private Bag X9, Highveld, 0169
Tel: (012) 678-1000

Registration No.: IT190/92
SERVICING DRS DU BUISSON, KRAMER, SWART, BOUWER Inc./Ing.

08 August 2015

Dear Sir/Maam

REQUEST FOR PARTICIPATION IN RESEARCH: Kammy Hutheram (Phlebotomy Training Centre)

This letter serves to confirm that the Management of Ampath has considered the above - mentioned staff member's request to conduct research within our organisation, using our INR facility in the Gauteng area. The research topic is "Investigating patients' knowledge and use of the patient information leaflet regarding their Warfarin therapy."

Kindly be advised that the Management of Ampath Trust supports this study as we deem it of great relevance and value not only for us as an organisation, but also our patients.

You are therefore kindly requested to participate in this research by completing the questionnaire anonymously.

Should you have any queries regarding this communication, kindly contact my office directly at Tel.(012)678-1250 or email: bosmanl@ampath.co.za.

Thanking you in advance for your participation in this research.

Kind regards

Dr. Leon Bosman
Senior Human Resources Manager

IV: Authors' Guidelines African Journal of Pharmacy and Pharmacology

(http://www.academicjournals.org/journal/AJPP/authors)

AJPP - Instructions for Authors

Introduction

Authors should read the editorial policy and publication ethics before submitting their manuscripts. Authors should also use the appropriate reporting guidelines in preparing their manuscripts.

Research Ethics

Studies involving human subjects should be conducted according to the World Medical Association (WMA) Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects. Studies involving non human animals should follow appropriate ethical guidelines such as the Animal Welfare Act, The Animals (Scientific Procedures) Act (Amendment) Order 1993, The EU parliament directive on the protection of animals used for scientific purposes, ARRP policies and guidelines, etc.

Reporting guideline: Responsible reporting of research studies, which includes a complete, transparent, accurate and timely account of what was done and what was found during a research study, is an integral part of good research and publication practice and not an optional extra.

See additional guidelines for reporting of health research.

Preparing your manuscript

The type of article should determine the manuscript structure. However, the general structure for articles should follow the IMRAD structure.

Title

The title phrase should be brief.

List authors' full names (first-name, middle-name, and last-name).

Affiliations of authors (department and institution).

Emails and phone numbers

Abstract

The abstract should be less than 300 words. Abstract may be presented either in unstructured or structured format. The keywords should be less than 10.

Abbreviations

Abbreviation should be used only for non standard and very long terms.

The Introduction

The statement of the problem should be stated in the introduction in a clear and concise manner.

Materials and methods

Materials and methods should be clearly presented to allow the reproduction of the experiments.

Results and discussion

Results and discussion maybe combined into a single section. Results and discussion may also be presented separately if necessary.

Disclosure of conflict of interest

Authors should disclose all financial/relevant interest that may have influenced the study.

Acknowledgments

Acknowledgement of people, funds etc should be brief.

Tables and figures

Tables should be kept to a minimum.
Tables should have a short descriptive title.
The unit of measurement used in a table should be stated.
Tables should be numbered consecutively.
Tables should be organized in Microsoft Word or Excel spreadsheet.
Figures/Graphics should be prepared in GIF, TIFF, JPEG or PowerPoint.
Tables and Figures should be appropriately cited in the manuscript.

References

References should be listed in an alphabetical order at the end of the paper. DOIs, PubMed IDs and links to referenced articles should be stated wherever available.
Examples:

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http://dx.doi.org/10.3102/0002831209345157

Christopoulous DK, Tsionas EG (2004). "Finacial Development and Economic Growth: Evidence from Panel Unit Root and Cointegration Tests" J. Dev.Econ. Pp.55-74
http://dx.doi.org/10.1016/j.jdeveco.2003.03.002

Goren A, Laufer J, Yativ N, Kuint J, Ben Ackon M, Rubinshtein M, Paret G, Augarten A (2001). Transillumination of the palm for venipuncture in infants. Pediatric. Emerg. Care 17:130-131.
http://dx.doi.org/10.1097/00006565-200104000-00013 PMid:11334094

Mishra A, Mishra SC (2001). Cost-effective diagnostic nasal endoscopy with modified otoscope. J. Laryngol. Otol. 115:648-649.
http://dx.doi.org/10.1258/0022215011908739 PMid:11535147

Acceptance Certificate

Authors are issued an Acceptance Certificate for manuscripts that have been reviewed and accepted for publication by an editor.

Payment of manuscript handling fee

Once a manuscript has been accepted, the corresponding author will be contacted to make the necessary payment of the manuscript handling fee. Kindly note that on the manuscript management system, the payment option is only enabled for manuscripts that have been accepted for publication.

Proofs

Prior to publication, a proof is sent to the corresponding author. Authors are advised to read the proof and correct minor typographical or grammatical errors. Authors should promptly return proofs to the editorial office.

Publication

Once proofs are received at the editorial office, the manuscripts are usually included in the next issue of the journal. The article will thereafter be published on the journal's website

Publication Notification

After the article is made available on the journal's website, a publication notice is sent to the corresponding author with links to the issue and article.

V: Data Collection Tools

School of Health Sciences

Discipline of Pharmaceutical Sciences

PATIENT QUESTIONNAIRE/SURVEY

Section A: Patient Demographics

Age:	
Gender:	
Area of Residence:	
Marital Status:	
Highest level of Education:	
Occupation:	
Reason for Warfarin Use:	
Number of years on Warfarin:	

Section B: Knowledge and use of the Patient information leaflet (PIL)

PIL : Patient Information leaflet

****Please answer the following questions as honestly as possible.***

1. ***What do you know about Patient information leaflet?***

   _____

   _____

   _____

_____
_____

2. ***Have you ever collected Patient information leaflet when you received your Warfarin? NB: Please see attached a copy of the PIL from Bristol Meyers Squibb Pharmaceutical Company.***

   _____
   _____
   _____
   _____
   _____

3. ***Have you ever read the PIL when you collected a copy?***

   _____
   _____

4. ***Have you ever understood the information provided in the PIL with regards to your warfarin? Please explain.***

   _____
   _____

<u>Section C: Knowledge and use of Warfarin</u>

<u>PT/INR test: Prothrombin time (Protime) test is used to determine whether the medicine to prevent blood clot is actually working as prescribed.</u>

Instructions: For each question, place an X in the box next to the answer you think is correct or best completes the sentence correctly. Please answer all questions.

1. Missing one dose of Coumadin (warfarin):

□ ***a. has no effect***

□ ***b. can alter the drug's effectiveness***

□ ***c. is permissible as long as you take a double dose the next time***

□ ***d. is permissible as long as you watch which foods you eat***

2. You can distinguish between different strengths of Coumadin (warfarin) tablets by what?

□ ***a. color***

□ ***b. shape***

□ ***c. size***

□ ***d. weight***

3. A patient on Coumadin (warfarin) therapy should contact the physician or healthcare provider who monitors it when:

□ ***a. another physician adds a new medication***

□ ***b. another physician stops a current medication***

□ ***c. another physician changes a dose of a current medication***

□ ***d. all of the above***

4. Occasionally eating a large amount of leafy greens vegetables while taking Coumadin (warfarin) can:

□ ***a. increase your risk of bleeding from Coumadin (warfarin)***

□ ***b. reduce the effectiveness of the Coumadin(warfarin)***

□ ***c. cause upset stomach and vomiting***

□ ***d. reduce your risk of having a blood clot***

5. Which of the following vitamins interacts with Coumadin (warfarin)?

□ ***a. vitamin B12***

□ ***b. vitamin A***

□ ***c. vitamin B6***

□ ***d. vitamin K***

6. When is it safe to take a medication that interacts with Coumadin (warfarin)?

□ ***a. if you take the Coumadin (warfarin) in the morning and the interacting medication at night***

□ ***b. if your healthcare provide is aware of the interaction and checks your PT/INR ("Protime") regularly***

□ ***c. if you take your Coumadin (warfarin) every other day***

□ ***d. it is never safe to take a medication that interacts with Coumadin (warfarin)***

7. The PT/INR ("Protime") test is:

□ ***a. a blood test used to monitor your Coumadin (warfarin) therapy***

□ ***b. a blood test that is rarely done while on Coumadin (warfarin)***

□ ***c. a blood test that checks the amount of vitamin K in your diet***

□ ***d. a blood test that can determine if you need to be on Coumadin (warfarin)***

8. Coumadin (warfarin) may be used to:

□ ***a. treat people that already have a blood clot***

□ ***b. treat people that have high blood sugar levels***

□ ***c. treat people with high blood pressure***

□ ***d. treat people with severe wounds***

9. A patient with a PT/INR ("Protime") value below their "goal range":

□ ***a. is at an increase the risk of bleeding***

□ ***b. is at an increase the risk of having a clot***

□ ***c. is more likely to have a skin rash from the Coumadin (warfarin)***

□ ***d. is more likely to experience side effects from Coumadin (warfarin)***

10. Taking a medication containing aspirin or other non-steroidal anti-inflammatory medications such as ibuprofen (Motrin® / Advil®) while on Coumadin (warfarin) will:

□ ***a. reduce the effectiveness of the Coumadin (warfarin)***

□ ***b. increase your risk of bleeding from the Coumadin (warfarin)***

□ ***c. cause a blood clot to form***

□ ***d. require you to increase your dose of Coumadin (warfarin)***

11. A person on Coumadin (warfarin) should seek immediate medical attention:

□ ***a. if they skip more than two doses of Coumadin (warfarin) in a row***

□ ***b. if they notice blood in their stool when going to the bathroom***

□ ***c. if they experience a minor nosebleed***

□ ***d. if they develop bruises on their arms or legs***

12. Skipping even one dose of your Coumadin (warfarin) can:

□ ***a. cause your PT/INR ("Protime") to be above the "goal range"***

□ ***b. increase your risk of bleeding***

□ *c. cause your PT/INR("Protime") to be below the "goal range"*

□ *d. decrease your risk of having a clot*

13. Drinking alcohol while taking Coumadin (warfarin):

□ *a. is safe as long as you separate your dose of Coumadin (warfarin) and the alcohol consumption*

□ *b. may affect your PT/INR ("Protime")*

□ *c. does not affect your PT/INR ("Protime")*

□ *d. is safe as long as you are on a low dose*

14. Once you have been stabilized on the correct dose of Coumadin (warfarin), about how often should your PT/INR ("Protime") value be tested?

□ *a. once a week*

□ *b. once a month*

□ *c. once every other month*

□ *d. once every 3 months*

15. It is important for a patient on Coumadin (warfarin) to monitor for signs of bleeding:

□ *a. only when their PT/INR ("Protime") is above the goal range*

□ *b. at all times*

□ *c. only when their PT/INR ("Protime") is below the goal range*

□ *d. only when you miss a dose*

16. The best thing to do if you miss a dose of Coumadin (warfarin) is to?

□ *a. double up the next day*

□ *b. take the next scheduled dose and tell your healthcare provider*

□ ***c. call your healthcare provider immediately***

□ ***d. discontinue Coumadin (warfarin) altogether***

17. When it comes to diet, people taking Coumadin (warfarin) should:

□ ***a. never eat foods that contain large amounts of vitamin K***

□ ***b. keep a diary of all of the foods they eat***

□ ***c. be consistent and eat a diet that includes all types of food***

□ ***d. increase the amount of vegetables they eat***

18. Each time you get your PT/INR ("Protime") checked, you should:

□ ***a. skip your dose of Coumadin (warfarin) on the day of the test***

□ ***b. avoid eating high fat meals on the day of the test***

□ ***c. avoid foods high in vitamin K on the day of the test***

□ ***d. let your doctor know if you missed any doses of Coumadin (warfarin)***

19. Which of the following over-the-counter products is most likely to interact with Coumadin (Warfarin)?

□ ***a. nicotine replacement therapies***

□ ***b. herbal / dietary supplements***

□ ***c. allergy medications***

□ ***d. calcium supplements***

20. A patient with a PT/INR("Protime") value above the "goal range":

□ ***a. is at an increased risk of having a clot***

□ ***b. is more likely to have drowsiness and fatigue from Coumadin (warfarin)***

□ ***c. is at an increased risk of bleeding***

□ ***d. is less likely to experience side effects from Coumadin (warfarin)***

<u>Section D: KnowledgeofInternational Normalized Ratio (INR)</u>

INR: International Normalized Ratio

INR is a test used to measure the clotting process of the blood. Warfarin works in a way that it affects this clotting process so as to prevent clots from circulating in the blood stream. If these clots travel in the blood stream it could result in deep vein thrombosis, stroke or heart attack. INR is regularly measured to determine if the required dosage of Warfarin is working to hinder the clotting process. From the assessment of INR reading, your Warfarin dosage may be adjusted if required. Certain factors including diet changes, other drugs, etc., could affect the effectiveness of the Warfarin, either by increasing or decreasing its effect. This in turn may affectyour INR.

1. ***What is your understanding of the INR Blood test?***

_____
_____
_____
_____
_____
_____

2. ***Why is INR testing important?***

_____
_____
_____

3. ***The INR should ideally be in the range of 2.0-3.0.***

Do you think your INR has been in the range mentioned above, in the last 6 months? Please explain.

_____
_____
_____
_____
_____

_____

"The OAK test" was compiled by Zeolla MM, Brodeur MR, Dominelli A, Haines Stand Allie N 2006.

Thank you so much for your time ☺

****NB: If you have any queries, please don't hesitate to contact the researcher:***

Karmishtha Hutheram (Kammy)

Cell:0783063693

Email:kammy91985@gmail.com

UKZN-Humanities and Social Sciences Research Ethics Committee (HSSREC)

PremMohun - SAO:HSSREC
Tel: *(031) 260 4557*
Fax: *(031) 260 4609*

Research Office, Westville Campus

Govan Mbeki Building
Private Bag X 54001
Durban
4000

KwaZulu-Natal, SOUTH AFRICA

Skool van Gesondheidswetenskappe

Farmaseutiese Wetenskappe Dissipline

Universiteit van KwaZulu Natal

PASIËNTVRAELYS/-OPNAME

Afdeling A:Pasiëntdemografie

Ouderdom:	
Geslag:	
ID-nommer:	
Woongebied:	
Huwelikstatus:	
Hoogste Kwalifikasie:	
Beroep:	
Rede vir Gebruik van Warfarien:	
Aantal jaar op Warfarien:	

Afdeling B:Kennis en gebruik van die PIB

PIB : Pasiëntinligtingsbiljet

****Beantwoord asseblief die volgende vrae so eerlik moontlik.***

5. ***Hoe verstaan u die Pasiëntinligtingsbiljet?***

_____
_____
_____
_____
_____

6. ***Het u al ooit 'nPasiëntinligtingsbiljet (PIB) saam met u Warfarien ontvang?***
   NB: Hierby aangeheg is 'n afskrif van die PIB van die farmaseutiese maatskappy Bristol Meyers Squibb.

_____
_____
_____
_____
_____

7. ***Het u al ooit die inligting in die PIB gelees wanneer u 'n kopie gekry het?***

_____
_____
_____***4. Het u ooit die inligting wat in die pasiëntinligtingsbiljet verskaf is met betrekking tot u Warfarien verstaan? Verduidelik asseblief.***

_____
_____

<u>Afdeling C:Kennis en gebruik van Warfarien</u>

<u>PI/INR toets: Protrombientyd (Protyd) toets word gebruik om te bepaal of die medisyne om die bloedklont te voorkom, werklik soos voorgeskryf, werk.</u>

Instruksies:By elke vraag, plaas 'n X in die blokkie langs die antwoord wat u dink korrek is of die sin die korrekste voltooi.Antwoord asseblief al die vrae.

1. Om een dosis Koumadien (warfarien) oor te slaan:

□ ***a. het geen uitwerking nie***

□ ***b. kan die medikasie se doeltreffendheid verander***

□ ***c. is toelaatbaar mitsu die volgende keer 'n dubbeldosis neem***

□ ***d. is toelaatbaar mits u bedag is op die kosse watu inneem***

2. U kan tussen die verskillende sterktes Koumadientablette (warfarientablette) onderskei deur hul:

□ ***a. kleur***

□ ***b. vorm***

□ ***c. grootte***

□ ***d. gewig***

3. 'n Pasiënt op Koumadienterapie (warfarienterapie) moet die geneesheer of gesondheidsorgverskaffer wat hom/haar monitor kontak:

□ ***a. wanneer'n ander geneesheer 'n nuwe medikasie byvoeg***

□ ***b. wanneer'n ander geneesheer 'n huidige medikasie staak***

□ ***c. wanneer'n ander geneesheer die dosis van 'n huidige medikasie aanpas***

□ ***d. in al die bogenoemde gevalle***

4. Indien u van tyd tot tyd baie groen blaargroente eet terwyl Koumadien (warfarien) geneem word, kan dit:

□ ***a. u risiko van bloeding weens Koumadien (warfarien) verhoog***

□ ***b. die doeltreffendheid van die Koumadien (warfarien) inperk***

□ ***c. maagongesteldheid en braking tot gevolg hê***

□ ***d. u risiko om 'n bloedklont te kry, verminder***

5. Watter van die volgende vitamiene werk in op Koumadien (warfarien)?

□ ***a. vitamien B12***

□ ***b. vitamien A***

□ ***c. vitamien B6***

□ ***d. vitamien K***

6. Wanneer is dit veilig om medikasie te neem wat op Koumadien (warfarien) inwerk?

□ ***a. indien u die Koumadien (warfarien) in die oggend neem en die medikasie wat inwerk in die aand***

□ ***b. indien u gesondheidsorgverskafferkennis dra van die interaksie en u PT/INR ("Protyd") gereeld nagaan***

□ ***c. indien u uKoumadien (warfarien) elke tweede dag neem***

□ ***d. dit is nooit veilig om medikasie te neem wat op Koumadien (warfarien) inwerk nie***

7. Die PT/INR ("Protrombientyd") toets is:

□ ***a. 'n bloedtoets wat gebruik word om u Koumadienterapie (warfarienterapie)te monitor***

□ ***b. 'n bloedtoets wat selde gedoen word terwyl Koumadien (warfarien) geneem word***

□ ***c. 'n bloedtoets wat die hoeveelheid vitamien K in u dieet nagaan***

□ ***d. 'n bloedtoets wat kan bepaal of u op Koumadien (warfarien) behoort te wees***

8. Koumadien (warfarien) kan gebruik word om:

□ ***a. iemand te behandel wat reeds 'n bloedklont het***

□ ***b. iemand te behandel wat hoë bloedsuikervlakke het***

□ ***c. iemand te behandel wat hoë bloeddruk het***

□ ***d. iemand te behandel wat erge wonde het***

9. 'n Pasiënt met 'n PT/INR-waarde ("Protyd") onder sy/haar "doelwitreeks":

□ ***a. loop 'n groter risiko vir bloeding***

□ ***b. loop 'n groter risiko om 'n bloedklont te kry***

□ ***c. sal meer waarskynlik 'n veluitslag weens die Koumadien (warfarien) kry***

□ ***d. sal meer waarskynlik newe-effekte van Koumadien (warfarien) ervaar***

10. Om medikasie te neem wat aspirien of ander nie-steroïedale anti-inflammatoriese medikasie soos ibuprofeen (Motrin® / Advil®) te neem terwyl Koumadien (warfarien) geneem word, sal:

□ ***a. die doeltreffendheid van die Koumadien (warfarien) inperk***

□ ***b. die risiko van bloeding weens die Koumadien (warfarien) verhoog***

□ ***c. veroorsaak dat 'n bloedklont vorm***

□ ***d. vereis dat uu dosis Koumadien (warfarien) moet verhoog***

11. Iemand op Koumadien (warfarien) moet onverwyld mediese sorg kry wanneer:

□ ***a. hy/sy meer as twee dosisse Koumadien (warfarien) na mekaar oorslaan***

□ ***b. hy/sy bloed in die stoelgang opmerk wanneer hy/sy badkamer toe gaan***

□ ***c. sy/haar neus effens bloei***

□ ***d. hy/sy kneusplekke op die arms of bene ontwikkel***

12. Om selfs een dosis van u Koumadien (warfarien) oor te slaan, kan:

□ ***a. veroorsaak dat u PT/INR ("Protyd") bo die "doelwitreeks" styg***

□ ***b. u risiko van bloeding verhoog***

□ ***c. veroorsaak dat u PT/INR ("Protyd") onder die "doelwitreeks" val***

□ ***d. u risiko vir 'n bloedklont verlaag***

13. Om alkohol te drink terwyl Koumadien (warfarien) geneem word:

□ ***a. is veilig mits u nie u dosis Koumadien (warfarien) en die alkohol op dieselfde tyd inneem nie***

□ ***b. kan u PT/INR ("Protyd") affekteer***

□ ***c. affekteer nie u PT/INR ("Protyd") nie***

□ ***d. is veilig mits u op 'n lae dosis is***

14. Sodra u op die korrekte dosis Koumadien (warfarien) gestabiliseer het, min of meer hoe gereeld moet die waarde van u PT/INR("Protyd") getoets word?

□ ***a. eenkeer per week***

□ ***b. eenkeer per maand***

□ ***c. eenkeer elke twee maande***

□ ***d. eenkeer elke drie maande***

15. Dit is belangrik dat 'n pasiënt op Koumadien (warfarien) vir tekens van bloeding monitor:

□ ***a. slegs wanneer sy/haar PT/INR ("Protyd") bo die doelwitreeks is***

□ ***b. te alle tye***

□ *c. slegs wanneer sy/haar PT/INR ("Protyd") onder die doelwitreeks is*

□ *d. slegs wanneer hy/sy 'n dosis oorgeslaan het*

16. Die beste ding om te doen wanneer u 'n dosis Koumadien (warfarien) oorgeslaan het, is om:

□ *a. die volgende dag 'n dubbeldosis te neem*

□ *b. die volgende geskeduleerde dosis te neem en u gesondheidsorgverskafferte verwittig*

□ *c. u gesondheidsorgverskaffer onverwyld te skakel*

□ *d. heeltemal op te hou om Koumadien (warfarien) te neem*

17. Wanneer dit by dieet kom, moet mense wat Koumadien (warfarien) neem:

□ *a. nooit kosse eet wat groot hoeveelhede vitamien K bevat nie*

□ *b. 'n dagboek hou van al die kosse wat hulle eet*

□ *c. konsekwent wees en 'n dieet inneem wat alle voedselsoorte bevat*

□ *d. die hoeveelheid groente wat hulle eet, verhoog*

18. Elke keer wat u PT/INR ("Protyd") nagegaan word, moet u:

□ *a. u dosis Koumadien (warfarien) vir die dag van die toets oorslaan*

□ *b. nie op die dag van die toets maaltye met 'n hoë vetinhoud eet nie*

□ *c. op die dag van die toets kosse vermy wat baie vitamien K bevat*

□ *d. u dokter inlig indien u enige dosisse Koumadien (warfarien) oorgeslaan het*

19. Watter van die volgende oor-die-toonbankprodukte sal die mees waarskynlikste op Koumadien(warfarien) inwerk?

□ *a. nikotienvervangingsterapieë*

□ *b. kruie-/dieetaanvullings*

□ ***c. allergiemedikasie***

□ ***d. kalsiumaanvullings***

20. 'n Pasiënt met 'n PT/INR-waarde ("Protydwaarde") bo hul "doelwitreeks":

□ ***a. het 'n groter risiko om 'n bloedklont te kry***

□ ***b. is meer geneig om lomerigheid en moegheid weens Koumadien (warfarien) te ervaar***

□ ***c. het 'n groter risiko vir bloeding***

□ ***d. sal minder waarskynlik newe-effekte van Koumadien (warfarien) ervaar***

<u>Afdeling D: Kennis van Internasionale Genormaliseerde Verhouding (InternationalNormalised Ratio)(INR)</u>

INR is 'n bloedtoets wat gebruik word om die stollingsproses van bloed te meet.Warfarien werk op so 'n wyse dat dit hierdie stollingsproses affekteer sodat dit voorkom dat klonte in die bloedstroom sirkuleer.Indien hierdie klonte in die bloedstroom sirkuleer, kan dit lei tot diep veneuse trombose, beroerte of 'n hartaanval. Die INR word gereeld getoets om vas te stel of die verlangde dosering van Warfarien werk om die stollingsproses te verhinder. U dosis Warfarien sal volgens hierdie lesing aangepas word. Faktore soos veranderinge in dieet, ander middels, ens. kan die doeltreffendheid van die Warfarien beïnvloed en die uitwerking daarvan hetsy verhoog of verlaag.Dit sal gevolglik meebring dat u INR-vlakke sal wissel.

1. ***Hoe verstaan u die INR-bloedtoets?***

_____
_____
_____
_____
_____
_____

2. ***Waarom is INR toetsing belangrik?***

_____--

_____

_____

3. ***Die INR moet ideaal tussen 2.0 en 3.0 wees.***

Dink u dat u INR in die bogenoemde reikwydte was in die afgelope 6 maande? Verduidelik asseblief.

_____
_____
_____
_____
_____
_____
_____

"Die OAK toets" is opgestel deur ZeollaMM,BrodeurMR,DominelliA,HainesSTand Allie N 2006.

Baie dankie vir u tyd☺

****NB: Indien u enige navrae het, moet asseblief nie huiwer om die navorser te kontak nie:***

Karmishtha Hutheram(Kammy)

Sel:0783063693

E-pos:kammy91985@gmail.com

UKZN-Humanities and Social Sciences Research Ethics Committee (HSSREC)

PremMohun - SAO:HSSREC
Tel: *(031) 260 4557*

Faks: *(031) 260 4609*

Navorsingskantoor, Westville Kampus

Govan Mbeki Gebou
Privaatsak X 54001
Durban
4000

KwaZulu-Natal, SUID AFRIKA

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

PAMPIRI YA LENAANE LA DIPOTSO YA MOLWETSE/PATLISISO

Compiled by: Peter Mekgwe SATI:1000281

Karolo ya A: Dintlha tsa Molwetse

Dingwaga tsa bogodi:	
Bong:	
Lefelo la Bonno:	
Boemo Jwa Lenyalo:	
Maemo a o feletseng ka one a Thuto:	
Tiro:	
Lebaka la go Dirisa Warfarin:	
Dingwaga tse o di feditseng o dirisa Warfarin:	

Karolo ya B: Kitso le go dirisa pampitshana ya tshedimosetso ya molwetse kgotsa Patient information leaflet (PIL)

PIL : =Pampitshana ya Tshedimosetso ya Molwetse

****Tsweetswee araba dipotso tse di latelang ka boikanyegi ka moo o ka kgonang ka gone.***

8. O tlhaloganya eng ka pampitshana ya tshedimosetso ya Molwetse?

_____
_____
_____
_____
_____
_____

9. A o kile wa ya go tsaya pampitshana ya tshedimosetso ya Molwetse fa o ne o newa Warfarin ya gago?
Ela tlhoko: Tsweetswee leba khopi ya PIL e e mametleletsweng fano go tswa kwa

Bristol Meyers Squibb Pharmaceutical Company.

_____
_____
_____
_____
_____
_____

10. A o kile wa buisa PIL fa o ne o ya go tsaya khopi?

_____
_____
_

4. A o kile wa tlhaloganya tshedimosetso mo PIL malebana le warfarin ya gago? Tsweetswee tlhalosa.

_____
_____
_____
__

<u>Karolo ya C: Kitso ka Warfarin le go e dirisa</u>

<u>Teko ya PT/INR: Nako ya Prothrombin (Protime) e e diretsweg go bona gore a molemo wa kalafi wa go thibela go rema ga madi o dira ka tsela e go ikaeletsweng ka yone.</u>

Ditaelo: Mo potsong nngwe le nngwe, tsenya X mo lebokosong fa thoko ga karabo e o akanyang gore ke yone kgotsa e e feleletsang polelo sentle go di gaisa tsotlhe. Tsweetswee araba dipotso tsotlhe.

1. Go tlodisa tekanyetso-molemo e le nngwe ya Coumadin (warfarin):
□ a. ga go nne le diphelelo dipe
□ b. go ka fetola go dira sentle ga seokobatsi
□ c. go a letlelesega fa fela o nwa tekanyetso-molemo e e menaganeng sebedi mo nakong e e latelang
□ d. go a letlelesega fa fela o nna kelotlhoko gore o ja dijo dife

2. O ka kgona go dira pharologano fa gare ga dinonofo tse di sa tshwaneng tsa dipilisi tsa Coumadin (warfarin) ka eng?
□ a. mmala
□ b. popego
□ c. bogolo
□ d. boima

3. Molwetse yo o dirisang kalafi ya Coumadin (warfarin) o tshwanetse go ikgolaganya le ngaka kgotsa modiredi wa tlhokomelo ya pholo fa:
□ a. ngaka e nngwe e oketsa ka molemo wa kalafi o moša

□ *b. ngaka e nngwe e emisa molemo wa kalafi wa ga jaanong*
□ *c. ngaka e nngwe e fetola tekanyetso-molemo ya molemo wa kalafi wa ga jaanong*
□ *d. tsotlhe tse di fa godimo*

4. Go ja merogo e mentsi e metala e e nang le matlhare ka dinako tse dingwe fa o ntse o nwa Coumadin (warfarin) go ka:
□ *a. oketsa kotsi ya go dutla madi ka ntlha ya Coumadin (warfarin)*
□ *b. fokotsa go dira sentle ga Coumadin(warfarin)*
□ *c. go berekisa mala le go go tlhatsisa*
□ *d. fokotsa kotsi ya gore madi a gago a itire dikgoto*

5. Ke efe ya dibitamine tse di latelang e e tswakanang le Coumadin (warfarin)?
□ *a. bitamine B12*
□ *b. bitamine A*
□ *c. bitamine B6*
□ *d. bitamine K*

6. Go sireletsegile leng go nwa molemo wa kalafi o o o tswakanang le Coumadin (warfarin)?
□ *a. fa o nwa Coumadin (warfarin) mo mosong le molemo wa kalafi o o o tswakanang le yone bosigo*
□ *b. fa modiredi wa gago wa tlhokomelo ya pholo a itse ka go tswakana ga yone a bo a tlhola PT/INR ya gago ("Protime") ka metlha*
□ *c. fa o nwa Coumadin (warfarin) ya gago gangwe mo malatsing a le mabedi*
□ *d. ga go a sireletsega le ka motlha go nwa molemo wa kalafi o o tswakanang le Coumadin (warfarin)?*

7. Teko ya PT/INR ("Protime") ke:
□ *a. teko ya madi e e dirisediwang go baya leitlho kalafi ya gago ya Coumadin (warfarin)*
□ *b. teko ya madi e e dirwang sewelo fela fa o ntse o nwa Coumadin (warfarin)*
□ *c. teko ya madi ya go tlhola selekanyo sa bitamine K mo dijong tsa gago*
□ *d. teko ya madi e e ka kgonang go tlhotlhomisa gore a o tlhoka go nwa Coumadin (warfarin)*

8. Coumadin (warfarin) e ka dirisediwa go:
□ *a. alafa batho bao madi a bone a setseng a itirile dikgoto*
□ *b. alafa batho ba ba nang le dilekanyo tse di kwa godimo tsa sukiri mo mading*
□ *c. go alafa batho ba ba nang le kgatelelo e e kwa godimo ya madi*
□ *d. go alafa batho ba ba nang le dintho tse di masisi*

9. Molwetse yo palo ya PT/INR ("Protime") ya gagwe e leng kwa tlase ga "selekanyo se se batlegang":
□ *a. o mo kotsing e e golang ya go dutla madi*
□ *b. o mo kotsing e e golang ya go itira dikgoto ga madi a gagwe*

□ c. go ka direga fela thata gore a swatoge letlalo ka ntlha ya Coumadin (warfarin)
□ d. go ka direga fela thata gore a nne le ditlamorago tse di sa itumediseng tsa Coumadin (warfarin)

10. Go nwa molemo o o nang le aspirin kgotsa melemo e mengwe ya kalafi ya dithibela-thurugo e e senang di steroid e e jaaka ibuprofen (Motrin® / Advil®) fa o nwa Coumadin (warfarin) go tla:
□ a. fokotsa go dira sentle ga Coumadin(warfarin)
□ b. oketsa kotsi ya go dutla madi ka ntlha ya Coumadin (warfarin)
□ c. baka gore madi a itire dikgoto
□ d. batla gore o oketse tekanyetso-molemo ya Coumadin (warfarin)

11. Motho yo o nwang Coumadin (warfarin) o tshwanetse go batla thuso ya kalafi ka bonako:
□ a. fa a tlodisa ditekanyetso-molemo tse di fetang tse pedi tsa Coumadin (warfarin) ka go latelana
□ b. fa a lemoga madi mo mantleng a gagwe fa a ile ntlwaneng
□ c. fa a dutla madi ka nko go sekae
□ d. fa a tswa matsadi mo mabogong kgotsa mo maotong

12. Go tlodisa tekanyetso-molemo le fa e le nngwe fela ya gago ya Coumadin (warfarin) go ka:
□ a. baka gore PT/INR ("Protime") ya gago e nne kwa godimo ga "selekanyo se se batelang"
□ b. oketsa kotsi ya go dutla madi
□ c. baka gore PT/INR ("Protime") ya gago e nne kwa tlase ga "selekanyo se se batlegang"
□ d. fokotsa kotsi ya go itira dikgoto ga madi a gago

13. Go nwa bojalwa fa o nwa Coumadin (warfarin):
□ a. go sireletsegile fa fela o sa nwe tekanyetso-molemo ya gago ya Coumadin (warfarin) ka nako e le nngwe le bojalwa
□ b. go ka ama PT/INR ("Protime") ya gago
□ c. ga go ame PT/INR ("Protime") ya gago
□ d. go sireletsegile fa fela o nwa tekanyetso-molemo e e kwa tlase

14. Fa o tlhometswe tekanyetso-molemo e e siameng ya Coumadin (warfarin), palo ya PT/INR("Protime") ya gago e tshwanetse go tlhatlhobiwa mo e ka nnang ga kae?
□ a. gangwe ke beke
□ b. gabedi ka kgwedi
□ c. gangwe morago ga dikgwedi di le pedi
□ d. gangwe morago ga dikgwedi di le 3

15. Go botlhokwa gore molwetse yo o nwang Coumadin (warfarin) a ele tlhoko gore a ga

a na matshwao a go dutla madi:
□ a. fa fela PT/INR ("Protime") ya gagwe e le kwa godimo ga selekanyo se se batlegang
□ b. ka dinako tsotlhe
□ a. fa fela PT/INR ("Protime") ya gagwe e le kwa tlase ga selekanyo se se batlegang
□ d. fa fela o tlodisa tekanyetso-molemo

16. Selo se se siameng go di gaisa tsotlhe go se dira fa o tlodisa tekanyetso-molemo ya Coumadin (warfarin) ke go?
□ a. menaganya tekanyetso-molemo sebedi mo letsatsing le le latelang
□ b. go nwa tekanyetso-molemo e e latelang o bo o bolelela modiredi wa tlhokomelo ya pholo
□ c. go leletsa modiredi wa tlhokomelo ya pholo mogala ka bonako
□ d. go tlogela gotlhelele go dirisa Coumadin (warfarin)

17. Fa go tliwa mo kgannyeng ya dijo, batho ba ba nwang Coumadin (warfarin) ba tshwanetse go:
□ a. se tlhole ba ja dijo tse di nang le bitamine K e ntsi
□ b. boloka buka-tsatsi ya dijo tsotlhe tse ba di jang
□ c. se fetole mokgwa o ba ntseng ba dira ka one mme ba je dijo tse di akaretsang tse dingwe tsotlhe
□ d. oketsa selekanyo sa merogo e ba e jang

18. Nako le nako fa go tlholwa PT/INR ("Protime") ya gago, o tshwanetse go:
□ a. tlodisa tekanyetso-molemo ya gago ya Coumadin (warfarin) ka letsatsi le o dirwang teko ka lone
□ b. tila go ja dijo tse di nang le mafura a mantsi mo letsatsing le o dirwang teko ka lone
□ c. tila go ja dijo tse di nang le bitamine K e ntsi mo letsatsing le o dirwang teko ka lone
□ d. itsise ngaka ya gago fa o tlodisitse ditekanyetse-molemo dipe tsa Coumadin (warfarin)

19. Ke dikumo dife mo go tse di latelang tse di rekwang mo khaontareng tse go ka diregang fela thata gore di tswakanngwe le Coumadin (Warfarin)?
□ a. go tsenngwa petshe ya bokgakga
□ b. mere / ditlaleletsi tse di nang le dijo tsa dikotla
□ c. melemo ya kalafi ya dialeji
□ d. ditlaleletsi tsa khalesiamo

20. Molwetse yo palo ya PT/INR ("Protime") ya gagwe e leng kwa godimo ga "selekanyo se se batlegang":
□ a. o mo kotsing e e golang ya gore madi a gagwe a itire dikgoto
□ b. go ka direga fela thata gore a otsele kgotsa a tsenwe ke letsapa ka ntlha ya Coumadin (warfarin)
□ c. o mo kotsing e e golang ya go dutla madi
□ d. go ka se direge go le kalo gore a nne le ditlamorago tse di sa itumediseng tsa

Coumadin (warfarin)

<u>Karolo D: Kitso ka Rešio</u> e e Buseditsweng kwa Boemong jwa Yone jwa ka Gale <u>ya Dinaga di Sele kgotsa International Normalized Ratio (INR)</u>

INR: Rešio ya Dinaga di Sele

INR ke teko e e dirisediwang go lekanya thulaganyo ya go itira dikgoto ga madi. Warfarin e dira ka tsela e e amang thulaganyo eno ya go itira dikgoto ga madi gore dikgoto tseno di se ka tsa elela le madi. Fa dikgoto tseno di ka elela le madi seno se ka felela ka go rema ga madi mo ditshikeng, go swa mohama kgotsa go ema pelo. INR e lekanngwa ka metlha go tlhotlhomisa gore a tekanyetso-molemo e e batlegang ya Warfarin e thibela go itira dikgoto ga madi. Morago ga go lekola dipalo tsa INR, tekanyetso-molemo ya gago ya Warfarin e ka fetolwa fa go tlhokega. Dilo tse dingwe tse di akaretsang go fetola mofuta wa dijo, diokobatsi tse dingwe, jj., di ka ama tsela ya go dira sentle ya Warfarin, ka go oketsa kgotsa go fokotsa go dira sentle ga yone. Gape seno se ka ama INR ya gago.

4. ***O tlhaloganya eng ka teko ya madi ya INR?***

_____
_____
_____
_____
_____
_____
_____

5. ***Goreng teko ya INR e le botlhokwa?***

_____
_____
_____
_____

6. ***Go eletswa gore INR e nne ya selekanyo sa 2.0-3.0.***

A o akanya gore INR ya gago e ntse e le ya selekanyo se se umakilweng fa godimo mo dikgweding di le 6 tse di fetileng? Tsweetswee tlhalosa

_____
_____
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"Teko ya OAK" was e ne ya dira ke ZeollaMM,BrodeurMR,DominelliA,HainesSTand Allie N 2006.

Re lebogela nako ya gago thata ☺

****ELA TLHOKO: Fa o na le dipotso dipe, tsweetswee o se ka wa okaoka go ikgolaganya le mmatlisisi:***

Karmishtha Hutheram(Kammy)
Sele:0783063693
Email:kammy91985@gmail.com

UKZN-Komiti ya Maitshwaro ya Patlisiso ya Disaense tsa Loago le Mekgwa ya Batho (Humanities and Social Sciences Research Ethics Committee [HSSREC])

PremMohun - SAO:HSSREC
Moga: *(031) 260 4557*
Fekese: *(031) 260 4609*
Ofisi ya Patlisiso, Westville Campus
Kago ya Govan Mbeki
Private Bag X 54001
Durban
4000
KwaZulu-Natal, AFORIKA BORWA