FINAL YEAR STUDENTS’ KNOWLEDGE ON PHARMACOTHERAPY-
INDUCED OTOTOXICITY AMONG MEDICAL, PHARMACY,
AUDIOLOGY AND NURSING STUDENTS ACROSS SOUTH AFRICAN
UNIVERSITIES

A mini-dissertation submitted by

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DECLARATION

I, Omphile Mogole, declare that the mini-dissertation hereby submitted to the Sefako Makgatho Health Sciences University, for the degree of Master of Pharmacy, School of Pharmacy has not previously been submitted by me for a degree at this or any other university; that it is my work in design and execution, and that all material contained herein has been duly acknowledged.

__________________________________  __________________
Mogole, O (Mr)                      Date
DEDICATION

To my mom Josephine Mogole and my sister Omphemetse Mogole, thank you for being my support system throughout my life. To my close friends, you guys have been my motivation from my first year of BPHARM, your support is really appreciated.
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ABBREVIATIONS AND ACRONYMS

AIDS – Acquired Immunodeficiency Syndrome

COX – Cyclooxygenase

DCI – Data collection instrument

DNA – Deoxyribonucleic acid

HAART – Highly Active Antiretroviral

HIV – Human Immunodeficiency Virus

ICU – Intensive Care Unit

IPE – Inter-professional education

MDR-TB – Multi-drug resistant Tuberculosis

mRNA – Messenger ribonucleic acid

NDoH – National department of health

NSAIDs – Non-steroidal anti-inflammatory drugs

rRNA – Ribosomal ribonucleic acid

SMUREC - Sefako Makgatho University Research Ethics Committee

TB – Tuberculosis

WHO – World Health Organisation
ABSTRACT

FINAL YEAR STUDENTS’ KNOWLEDGE ON PHARMACOTHERAPY-INDUCED OTOTOXICITY AMONG MEDICAL, PHARMACY, AUDIOLOGY AND NURSING STUDENTS ACROSS SOUTH AFRICAN UNIVERSITIES

BACKGROUND AND OBJECTIVES: The growing disease burden in South Africa results in detrimental side-effects from the drugs used to treat these conditions. HIV, TB and malaria have a high prevalence in South Africa and some of the drugs used to treat these conditions are ototoxic. It is therefore important that healthcare professionals are able to identify these drugs and their effects to ensure effective care of the patient. The aim of the study was to assess the knowledge of final year pharmacy, medicine, audiology and nursing students across South African universities regarding pharmacotherapy-induced ototoxicity.

METHODS: A descriptive cross-sectional study was conducted where quantitative data was collected prospectively. A structured, self-administered online questionnaire was administered and was structured according to the objectives.

RESULTS: An overall response rate of 41% (n=720) was obtained. Majority of the respondents were female between the ages of 21 – 25. A vast majority of the respondents (95%) understood the general concept of what pharmacotherapy-induced ototoxicity is, with only a few (39%) knowing the general signs and symptoms of ototoxicity. Very few of the could identify ototoxic medication and the type of damage caused by ototoxic medicine

CONCLUSION: There were significant differences between the respondents with regards to undergraduate education on pharmacotherapy-induced ototoxicity. In order minimise pharmacotherapy-induced ototoxicity, a multidisciplinary healthcare team must have sufficient knowledge about ototoxicity. Therefore efforts should be made to extensively introduce concepts of pharmacotherapy-induced ototoxicity into the undergraduate curricula of pharmacy, medicine, nursing and audiology programs.
Chapter 1: Introduction

INTRODUCTION

1.1 INTRODUCTION

This chapter discusses the background and rationale for the study. It includes the aim and the objectives and provides an outline of this dissertation. The importance and significance of the study are also described. The chapter ends with a short overview of the outline of the dissertation. The word drug and medicine will be used interchangeably.

1.2 BACKGROUND AND RATIONALE FOR THE STUDY

The global incidence of Multidrug-Resistant tuberculosis (MDR-TB) by 2015 was 580 000 (World Health Organisation, 2016). In South Africa, this rapid spread in MDR-TB is usually seen amongst Human Immunodeficiency Virus (HIV) infected patients due to the impaired ability of their immune system to contain the MDR-TB bacilli (Umanah, Ncayiyana, Padanilam & Nyasulu, 2015). South Africa has the highest rate of new HIV infections in the world (Khoza-Shangase & Van Rie, 2016) and is one of five countries in the world with the largest incidence of active tuberculosis (TB) (Govender & Paken, 2015; Stoltz, 2015). In developing countries, there is usually a co-infection of tuberculosis (TB) and HIV, which warrants a simultaneous administration of highly active antiretroviral therapy (HAART) and ototoxic TB drugs, thus increasing the potential for ototoxicity (Khoza-Shangase & Stirk, 2016).

According to Schellack, Wium, Ehlert, Van Aswegen, & Gous (2015), pharmacotherapy-induced ototoxicity is a growing problem, especially in developing countries like South Africa. The prevalence of TB, HIV and malaria in South Africa predisposes these patients to hearing loss which is induced by some agents used to treat these conditions (Schellack et al, 2015). Neonates, particularly premature ones, are more prone to infections due to their immunocompromised nature and the antibiotics used to treat these infections are ototoxic, e.g. amikacin (Engler, Schellack, Naude & Gous, 2013).

Further to this, Schellack et al (2015) states that pharmacists play a role in identifying and monitoring ototoxic agents, while audiologists often only get involved after the patients has completed therapy and start experiencing hearing loss. Early identification of hearing loss and balance problems is of paramount importance to prevent or minimize permanent impairment and therefore improve quality of life post treatment (Saindane, 2016).
Chapter 1: Introduction

According to Treadwell & Havenga, interprofessional education (IPE) refers to healthcare students learning from and about one another to improve collaboration and the quality of patient care. IPE is an important approach to develop healthcare students as the trained students are more likely to become collaborative interprofessional team members who show respect and positive attitudes towards each other and work towards improving patient outcomes (Bridges, Davidson, Odegard, Maki and Tomkowiak, 2011). Nursing, medicine, audiology, pharmacy and other allied health professions are required to work together in a clinical environment, which requires effective teamwork and communication skills. Majority of the university-based health professional education currently deliver a discipline specific model of teaching (Lapkin, Levett-Jones & Gilligan, 2011).

A relationship between physicians (as the prescribers) and nurses (as the care takers) needs to be established and supported by education regarding the importance and benefits of monitoring and evaluation of hearing loss which should be discussed with the patients (Konrad-Martin, Wilmington, Gordon, Reavis and Fausti, 2005). According to Vasquez and Mattucci 2003, many physicians do not understand the importance of otolaryngologist and audiologists in pre-treatment counselling and evaluation and the need for follow-up assessments of the patient’s auditory function.

A multidisciplinary team approach is integral in collaborative patient’s education programs with physicians, pharmacist, nurses and audiologists regarding ototoxic medication, considering that most primary care clinicians and clinical pharmacists have seen patients who have suffered from ototoxicity at some point in their careers (Schellack et al, 2015). However literature pertaining to the core curriculum or knowledge and perceptions of these healthcare workers in training is limited.

1.3 RESEARCH QUESTION

The study posed more than one research question:

The primary question posed was:

What knowledge do final year pharmacy, medicine, audiology and nursing students across South African universities have regarding pharmacotherapy-induced ototoxicity?

The secondary research questions were:
Chapter 1: Introduction

- What knowledge do final year pharmacy, audiology and medicine students have regarding **prevention** of pharmacotherapy-induced ototoxicity?
- What knowledge do final year audiology students have regarding **monitoring** of pharmacotherapy-induced ototoxicity?
- What knowledge do final year medicine students have regarding the **prescribing** of ototoxic drugs?

1.4 AIM OF THE STUDY

The aim of the study was to assess the knowledge of final year **pharmacy, medicine, audiology and nursing** students across South African Universities have regarding **pharmacotherapy-induced ototoxicity**.

1.5 OBJECTIVES OF THE STUDY

The objectives of the study were as follows:

- To assess the **general knowledge** of final year pharmacy, audiology, medicine and nursing students across South African universities on pharmacotherapy-induced ototoxicity.

- To assess the knowledge of final year pharmacy, audiology and medicine students across South African universities on the **prevention** of pharmacotherapy-induced **ototoxicity**.

- To assess the knowledge of final year audiology students across South African universities on the **monitoring** of pharmacotherapy-induced **ototoxicity**.

- To assess the knowledge of final year **medicine students** across South African universities on the **prescribing** of ototoxic drugs.

1.6 IMPORTANCE OR SIGNIFICANCE OF THE STUDY

According to Van Aswegen *et al.* (2016), Schellack *et al.* (2015), Engler *et al.* (2013) and Schellack and Naude (2013) there is a need for ototoxicity monitoring. There is also a need in the community for disciplines to work together to serve the need for ototoxic monitoring, with the potential to improve the quality of life for oncology patients (Kocchar, Sharma, Kumar, Sharma and Shubhanshu, 2016).
Chapter 1: Introduction

The aforementioned background provides the importance of the study by stressing the national and global incidence of HIV and MDR-TB as the drugs used to treat these conditions are ototoxic.

The National Department of Health (NDoH) of South Africa established the public health domain which outlines how facilities should work together with local communities and relevant sectors to promote health, prevent illness and reduce further complications and ensure that integrated and quality care is provided for their whole community (National Department of Health, 2011).

The patient safety, clinical governance and clinical care domain provides a guide on how to ensure quality nursing, clinical care and ethical practice; how to reduce unforeseen harm to health care users or patients in identified cases of greater clinical risk; how to prevent or manage problems or adverse events; and support any affected patients or staff (National Department of Health, 2011).

Early identification of the causative agents plays an important role in the monitoring process to prevent the progression of hearing loss. A successful ototoxicity monitoring programme should include a multidisciplinary team consisting of a doctor, pharmacist, nurse and an audiologist.

It is therefore important for the multidisciplinary team to have sufficient knowledge regarding pharmacotherapy-induced ototoxicity. Data in the South African healthcare setting is limited, hence the importance of this study.

1.6 CONCLUSION

The rise of new TB and HIV infections in South Africa increases the risk of pharmacotherapy-induced ototoxicity due to the drugs used to treat these conditions. However, data on pharmacotherapy-induced ototoxicity in South Africa is very limited, including its teaching in undergraduate health sciences curriculum.

This study aimed to assess whether final year medicine, pharmacy, nursing and audiology students had sufficient knowledge regarding pharmacotherapy-induced ototoxicity, including the drugs that cause ototoxicity and the type of damage caused by the drugs.

A study of this kind has not been done before in South Africa and therefore this study also aims to give an understanding of where we stand regarding pharmacotherapy-induced
ototoxicity at an undergraduate level in South Africa. This will also give an idea as to whether the students are equipped with enough knowledge to carry out audiologic screening and monitoring services in practice.

Chapter 1 discussed the background and rationale for this study, which allowed for the identification of the two separate research questions. The aim and objectives followed which led to the discussion of the significance and a brief outline of this study. Finally an all-encompassing conclusion was provided. In the next chapter, the emphasis will be on a literature review pertaining to the study.

1.7 OUTLINE OF THE DISSERTATION

Chapter 1 introduces the reader to the study and highlights the rationale thereof. The research questions with subsequent aim and objectives are provided. Chapter 2 describes the literature review on the study topic and outlines previous research conducted in pharmacotherapy-induced ototoxicity, including the implementation of interprofessional education. Chapter 3 provides a detailed description of the methodology of the study. Chapter 4 presents the results of the study with a relevant discussion of the findings. Chapter 5 provides a summary of the results, overall conclusions, and recommendations made, based on the results of the study and the limitations of the study. Figure 1.1 provides a short illustration of the outline of this dissertation.

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**Figure 1.1:** Outline of the dissertation
Chapter 2: Literature Review

CHAPTER 2
LITERATURE REVIEW

2.1 INTRODUCTION

This chapter will give an overview of published literature on ototoxicity. The chapter will begin with defining what ototoxicity is, followed by a discussion on pharmacotherapy-induced ototoxicity. Thereafter, the chapter ends with a discussion of literature regarding the implementation of pharmacotherapy-induced ototoxicity education in the undergraduate curriculum.

2.2 DEFINING OTOTOXICITY

A very recent definition of ototoxicity, according to Paken, Govender, Pillay & Sewram (2016), is a hearing disorder that results from temporary or permanent inner ear dysfunction after treatment with an ototoxic drug. However an earlier definition by Rybak and Ramkumar (2007) included in this definition that ototoxicity as the functional impairment and cellular degeneration of the tissues of the inner ear caused by therapeutic agents, which results in loss of hearing and/or vestibular function. Ototoxicity occurs due to toxic agents destroying the outer hair cells in the basal part of the cochlea which results in high frequency sensorineural hearing loss (Khoza-Shangase and Jina, 2013). Although ototoxicity can results from occupational and/or environmental exposure to ototoxins, majority of the cases result from drug therapy. A drug is considered ototoxic when it causes toxic reactions to the structures of the inner ear which include the cochlea, vestibule, semicircular canals and otoliths (Musleh et al, 2016).

2.3 PHARMACOTHERAPY-INDUCED OTOTOXICITY

Therapeutic drugs are regarded as ototoxic when they have an effect on the inner ear as one of their side effects, and can further be classified as either cochleotoxic or vestibulotoxic (Schacht, Talaska and Rybak, 2012), while some can also be both (Schellack et al, 2012).

2.3.1 Cochleotoxicity

Cochleotoxicity is caused by damage to the auditory system which may present as sensorineural hearing loss which may be permanent, tinnitus, hyperacusis (increased
sensitivity to sounds) and difficulty with speech discrimination (Schellack et al, 2012; Lanvers-Kaminsky, am Zehnhoff-Dinnesen, Parfitt, Ciarimboli, 2016).

2.3.2 Vestibulotoxicity

Vestibulotoxicity is caused by damage or injury to the vestibular system presents as dizziness, disequilibrium, unsteadiness when walking or ataxic gait, oscillopsia, nystagmus and/or vertigo (Schellack et al, 2012; Lanvers-Kaminsky et al, 2016). Available literature suggests that patients with HIV/AIDS often present with auditory and vestibular disorders and the effects can either be due the HIV virus itself or some of the ARV medication prescribed to the patient (Khoza-Shangase & Van Rie, 2016).

2.4 OTOTOXIC DRUGS

The most commonly used ototoxic drug include aminoglycosides (e.g. gentamycin, amikacin), platinum based chemotherapy drugs (e.g. cisplatin), loop diuretics (e.g. furosemide), macrolide antibiotics (e.g. erythromycin), nonsteroidal anti-inflammatory drugs (NSAIDs) (e.g. ibuprofen) and quinine derivatives (Wium & Gerber, 2016). Ototoxicity caused by loop diuretics, salicylate analgesics macrolide antibiotics and quinine usually resolves once the treatment is stopped, while ototoxicity caused by platinum drugs and aminoglycosides is usually irreversible (Lanvers-Kaminsky et al, 2016).

2.4.1 Aminoglycosides

2.4.1.1 Mechanism of action

Aminoglycosides (amikacin and kanamycin) are used in the treatment of life-threatening gram-negative infections such as septicaemia and MDR-TB (Bilgili, Casimir, Pickard & Lindsey, 2017). Aminoglycosides bind to the aminoaeryl-rRNA binding site of the 16s rRNA (ribosomal ribonucleic acid) in the 30s subunit of bacterial ribosomes resulting in misreading during mRNA (messenger ribonucleic acid) translation and compromise of protein synthesis (Lanvers-Kaminsky et al, 2016).

2.4.1.2 Mechanism of ototoxicity

They destroy the basal hair cells of the basilar membrane which is required for high frequency hearing and then progresses to affect the frequencies associated with speech and communication (Govender & Paken, 2015; Petersen & Rogers, 2015).
Aminoglycosides also damage the stria vascularis, marginal cells and the spiral ganglion (Lanvers-Kaminsky et al., 2016). The incidence of aminoglycoside-induced ototoxicity following drug therapy has been reported to be between 18 and 57 percent (Maluleka, Kuschke & Ramma, 2015).

2.4.1.3 Prevention of ototoxicity

Aminoglycoside-induced ototoxicity can be prevented by identifying patients that are at high risk and selecting alternative antibiotics. Patients should also avoid noisy environments for at least six months following aminoglycoside therapy as the patients will be more susceptible to noise-induced cochlear damage (Bilgili et al., 2017).

2.4.2 Platinum compounds

2.4.2.1 Mechanism of action

The platinum-based chemotherapy drugs (cisplatin, carboplatin and oxiplatin) are the most commonly used anticancer drugs for the treatment of paediatric and adult solid tumours such as neuroblastoma, brain tumours, germ cell tumours, testicular, ovarian, endometrial, lung and head and neck cancer (Lanvers-Kaminsky et al., 2016). Cisplatin induces interstrand and intrastrand crosslinks which activate signalling cascades that block replication and transcription, inhibiting the cell cycle and inducing DNA repair. Platination of mitochondrial DNA (deoxyribonucleic acid) and proteins affects cell respiration and induces the formation of reactive oxygen species which result in irreversible damage through induction of apoptosis in the affected cells (Lanvers-Kaminsky et al., 2016).

2.4.2.2 Mechanism of ototoxicity

Cisplatin is associated with a high incidence of irreversible and progressive high-frequency sensorineural bilateral hearing loss (Whitehorn, Sibanda, Lacerda, Spracklen, Ramma, Dalvie & Ramesar, 2014). Carboplatin appears to block the transduction channels within the cochlea. It is also associated with the generation of free radicals, depletion of intracellular glutathione and interferes with antioxidant enzymes in the cochlea causing cell death which leads to irreversible hearing loss (Wilmington, Konrad-Martin, Helt, Dille, Gordon & Fausti, 2011; Bilgili et al., 2017). The incidence ototoxicity is much higher in the paedriatric population, with more than 60% of paedriatric patients
receiving the platinum-based chemotherapy agents experiencing ototoxic effects (Bilgili et al, 2017).

### 2.4.2.3 Prevention of ototoxicity

Base-line audiograms and periodic follow-up audiograms are recommended while monitoring ototoxic effects; including audiometric testing up to 5 years after completion of therapy due to potential of extended drug retention (Bilgili et al, 2017). The main focus for otoprotective strategies is reduction of the formation of free radial species; this includes pretreatment with ototoprotectants and anti-oxidants such as Vitamin E (α-tocopherol), sodium thiosulphate, D-methionine, N-acetylcysteine and ebselen (Schellack & Naude, 2013; Lanvers-Kaminsky et al, 2016).

### 2.4.3 Loop diuretics

#### 2.4.3.1 Mechanism of action

Loop diuretics (furosemide, torsemide and bumetanide) are used in the treatment of congestive heart failure, hypertension and renal failure. They cause reversible blockade of the NA-K-CL co-transporter in the thick ascending limb of the loop of Henle, which is also expressed in the inner ear and regulates the ionic composition of the endolymph and mechanical transduction (Lanvers-Kaminsky et al, 2016).

#### 2.4.3.2 Mechanism of ototoxicity

The ototoxic effects of loop diuretics are associated with changes in the ionic gradient between the fluids of the inner ear in the stria vascularis, resulting in endothelial oedema (Bilgili et al, 2017). The incidence of ototoxicity by loop diuretics is estimated to occur in about 6 – 7% of patients (Bilgili et al, 2017).

#### 2.4.3.3 Prevention of ototoxicity

Loop diuretic-induced ototoxicity may be prevented by using the lowest effective dose and avoiding co-administration with other ototoxic drugs such as aminoglycosides (Bilgili et al, 2017).

### 2.4.4 Aspirin, NSAIDs and other Salicylates

#### 2.4.4.1 Mechanism of action
NSAIDs are the most commonly used analgesics for the relief of mild to moderate pain and fever. Aspirin is the most widely used and it works by irreversible inhibition of cyclo-oxygenase (COX) 1 and 2 enzymes which results in a reduction of prostaglandin synthesis and also inhibiting platelet aggregation (Bilgili et al, 2017).

2.4.4.2 Mechanism of ototoxicity

High doses induce mild to moderate hearing loss which recedes within two to three days after cessation of the drug (Lanvers-Kaminsky et al, 2016). Salicylates rapidly penetrate the cochlea, resulting in perilymph levels parallel to serum levels (Bilgili et al, 2017). The decrease in prostaglandins and increased leukotrienes results in vasoconstriction and reduced blood flow to the cochlea (Lanvers-Kaminsky et al, 2016). The incidence of salicylate-induced ototoxicity has been reported 1% of patient and most commonly in elderly patient even at lower doses (Bilgili et al, 2017).

2.4.4.3 Prevention of ototoxicity

Salicylate-induced ototoxicity may be prevented by using the lowest effective dose or using a non-salicylate alternative and avoiding concomitant use with other ototoxic agents (Bilgili et al, 2017).

2.4.5 Macrolides

2.4.5.1 Mechanism of action

Macrolide antibiotics (erythromycin, azithromycin and clarithromycin) are bacteriostatic agents inhibit protein synthesis by binding to the 50s ribosomal subunit of susceptible organisms (Bilgili et al, 2017).

2.4.5.2 Mechanism of ototoxicity

The mechanism of ototoxicity is not fully understood, but animal studies suggest cochleotoxicity and ion transport impairment within the stria vascularis which results in endothelial oedema and reversible hearing loss within three days of initiation of therapy (Bilgili et al, 2017).

2.4.5.3 Prevention of ototoxicity
Macrolide-induced ototoxicity is generally observed in patients who have other risk factors such as advanced age, renal impairment, hepatic impairment, gender (females are at higher risk), intravenous administration and those taking doses of more than four hundred milligrams per day (Bilgili et al, 2017).

2.4.6 Quinine

2.4.6.1 Mechanism of action

Quinine is approved for the treatment of chloroquine resistant malaria caused by *Plasmodium falciparum* and it acts by increasing the pH of acid vesicle in the parasite and also disrupts molecular transport phospholipase activity (Bilgili et al, 2017).

2.4.6.2 Mechanism of ototoxicity

The mechanism of ototoxicity is not fully understood, but quinine is similar to salicylates in causing vasoconstriction in the cochlea resulting in reduction in blood flow to the cochlea (Lanvers-Kaminsky et al, 2016).

2.4.6.3 Prevention of ototoxicity

A few studies have suggested the use of the calcium channel blocker, nimodipine, for the prevention of quinione-induced tinnitus in a dose dependent manner (Bilgili et al, 2017).

2.5 PHARMACOTHERAPY-INDUCED OTOTOXICITY EDUCATION IN UNDERGRADUATE CURRICULUM

2.5.1 International trends

According to the World Health Organisation (WHO) reports, it is suggested that a large percentage of hearing impairment caused by ototoxic medication results from inappropriate use of ototoxic medication by health care providers due to lack of awareness from the prescriber (Khoza-Shangase & Jina, 2013). It is important that healthcare practitioners have adequate knowledge regarding ototoxicity in order to appropriately manage and refer patients (Petersen & Rogers, 2015). Musleh et al (2016) also adds that nurses are essential for the successful implementation of ototoxicity-monitoring protocols, especially for cancer chemotherapy patients, while Petersen and Rogers (2015) report that in a small study conducted among ICU nurses in Brazil, nurses showed gaps in knowledge with regard to identifying ototoxic drugs.
2.5.2 National trends

Given the high prevalence of HIV/AIDS, TB and malaria in South Africa, there is a strong need for ototoxicity monitoring (Wemmer, 2008). An effective monitoring program should detect ototoxic damage before the patient starts experiencing symptoms to allow healthcare providers to consider alternative treatments such as dosage modifications or changing to less toxic drugs (Musleh et al, 2016).

Wium and Gerber (2016) state that the roles of an audiologist include the prevention, identification, assessment, diagnosis, rehabilitation, counselling, consultation as well as education, research and administration related to hearing and balance disorders. In a study by Naidoo (2006) on audiological practice and service delivery in South Africa, the majority of the respondents were of the opinion that their undergraduate clinical training had left them completely or poorly prepared to implement ototoxicity monitoring services. In the same study, South African audiologists stated that they don’t provide ototoxicity monitoring due to insufficient case load. This indicates a strong need to implement pharmacotherapy-induced ototoxicity education at undergraduate level.

Pharmacists can also play an active role in identifying and monitoring ototoxicity agents and where applicable perform therapeutic drug monitoring to reduce ototoxicity (Schellack et al, 2015). Ethical practice with regards to ototoxicity requires that patients be made aware of the name, dosage and administration of the drug and also include how the drug is absorbed, excreted, kidney and liver function and potential ototoxic risks (Wium & Gerber, 2016).

Doctors are also required to have knowledge on pharmacotherapy-induced ototoxicity as they have to disclose this information when they obtain informed consent from the patients prior to treat because if the information is not disclosed it can be considered as unethical practice (Wium & Gerber, 2016). However, a studies conducted by Khoza-hangase and De Andrade et al in 2013 and 2009 respectively, reveal that doctors do not have adequate knowledge of ototoxicity symptoms or treatment (Wium & Gerber, 2016).

With limited literature on implementing pharmacotherapy-induced ototoxicity at undergraduate level, the need to conduct a study of this kind is important.
2.6 CONCLUSION

A comprehensive literature review was given regarding all aspects of pharmacotherapy-induced ototoxicity. The importance of implementation of pharmacotherapy-induced ototoxicity education at undergraduate level was also highlighted. The importance of a multidisciplinary approach to patient care was also outlined. The next chapter will give a systematic description of the methodology applied in the completion of this study.
3.1 INTRODUCTION

This chapter outlines the methodology of this study in detail, starting with a discussion of the study design and the study population and the sample selection used. A full description of the data collection and data collection instruments is explained followed by a description of the data analysis. Lastly the reliability and validity are discussed and the chapter ends off with the ethical considerations that were taken into account.

3.2 STUDY DESIGN

A descriptive cross-sectional study was conducted where quantitative data was collected prospectively.

3.3 STUDY POPULATION AND SAMPLE SELECTION

The target population for this study included all final year pharmacy, medicine, audiology and nursing students across South African universities. Table 3.1 indicates the universities in South Africa that offer pharmacy, medicine, audiology and nursing. Purposive quota sampling was conducted, and for this purpose heads of schools were contacted regarding their numbers of final year students as soon as clearance from SMUREC was received. Once ethical approval was obtained, requests were sent to the various Universities requesting study population numbers. Subsequent to this the sample sizes were calculated.

<table>
<thead>
<tr>
<th>University</th>
<th>Pharmacy</th>
<th>Medicine</th>
<th>Audiology</th>
<th>Nursing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nelson Mandela Metropolitan University (NMMU)</td>
<td>X</td>
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</tr>
<tr>
<td>University Of Forte Hare (UFH)</td>
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<tr>
<td>Walter Sisulu University</td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>North-West University (Potchefstroom Campus)</td>
<td>X</td>
<td>*</td>
<td>*</td>
<td>X</td>
</tr>
<tr>
<td>University Of Free State (UFS)</td>
<td>*</td>
<td>X</td>
<td>*</td>
<td>X</td>
</tr>
</tbody>
</table>
The following inclusion and exclusion criteria applied for the purposes of the study

3.3.1 Inclusion criteria

- Students who were currently doing their final year in pharmacy, medicine, audiology and nursing
- Students who were willing to participate in the study following implied consent

3.4 COLLECTION AND DATA COLLECTION INSTRUMENT

All data was collected using an online questionnaire, which was used to assess final years students’ knowledge regarding pharmacotherapy-induced ototoxicity. The following aspects of knowledge were observed:

- General knowledge on pharmacotherapy-induced ototoxicity
• Prevention of pharmacotherapy-induced ototoxicity
• Monitoring on patients using ototoxic drugs
• Prescribing of ototoxic drugs

3.4.1 Data collection instrument

The questionnaire (Appendix 1) was adapted into an online questionnaire format was sent through email to the respective department heads. It was designed on an online tool called Typeform™, which is an easy-to-use form that also provides periodic statistics and allows the researcher to view and download the responses on a spreadsheet.

3.5 QUESTIONNAIRE DEVELOPMENT

The online questionnaire was developed and compiled by the researcher in accordance with the objectives based on an article by Schellack and Naude (2013) on the overview of pharmacotherapy-induced ototoxicity. Section A includes demographic information (Age, gender, course, university). Section B consisted of questions in line with the objectives, which includes questions regarding:

• General knowledge on pharmacotherapy-induced ototoxicity
• Prevention of pharmacotherapy-induced ototoxicity
• Monitoring on patients using ototoxic drugs
• Prescribing of ototoxic drugs

The aim of the of the questionnaire was to assess the knowledge of the students regarding drugs that cause ototoxicity, the signs of ototoxicity, the type of damage caused by the drugs and discipline specific questions.

The questionnaire was designed to capture the following information:

• Participant information and demographic: This included the age, gender, race, course they are currently doing and name of university they are doing their course.

• Participant general knowledge regarding pharmacotherapy-induced ototoxicity: This included questions regarding the definition of ototoxicity and signs and symptoms of ototoxicity. This was to determine if all the final year students had basic knowledge about ototoxicity.

• Participant knowledge regarding prevention of pharmacotherapy-induced ototoxicity: This was to determine whether final year pharmacy, audiology and
medicine students had sufficient knowledge about the prevention of pharmacotherapy-induced ototoxicity

- **Participant knowledge regarding the monitoring of pharmacotherapy-induced ototoxicity**: This was to determine whether final year audiology students had sufficient knowledge about the prevention of pharmacotherapy-induced ototoxicity
- **Knowledge regarding prescribing of ototoxic drugs**: This was to determine whether final year medicine students had sufficient knowledge about prescribing of ototoxic drugs

### 3.6 QUESTIONNAIRE DISTRIBUTION

A link to the questionnaire was sent to the designated staff member at the university whose responsibility was to disseminate the link to the final year students in the respective department. Reminder emails, pertaining to the online questionnaire were sent to a designated staff member at the university departments/schools on a weekly basis throughout the 24 week data collection period. The aim with this communication was for the designated staff member to remind students to submit and complete the questionnaire on the online platform.

### 3.7 PILOT STUDY

A pilot study was conducted with students from each department (pharmacy, medicine, audiology and nursing) from Sefako Makgatho Health Sciences University as it offers all of the four courses under study. The aim of the pilot study was to determine the relevance of the data collection tool and to identify problems that the participants might encounter so that modifications and adjustments could be made to the questionnaire accordingly. The questionnaire was restructured following the results and feedback from the pilot study. The researcher ensured that all the questions are well understood by the average student which will allow consistency in the responses by different participants (10 students per school).

### 3.8 DATA CAPUTRING AND ANALYSIS

The questionnaire was assessed against a memorandum (see Attached Appendix 2). All data was captured onto a Microsoft Excel® spread sheet and the data was kept for backup and record purposes. The statistical analysis was of a descriptive nature with responses to the questions summarised by frequency counts and percentages, with graphical representations. The subgroups in the sample were analysed separately as appropriate. All
statistical procedures were performed on Microsoft Excel® 2010, running under Microsoft Windows for a personal computer and analysed using IBM SPSS Statistics version 24. The percentage of correct answers of the general questions in the questionnaire was calculated for each student who completed the questionnaire.

3.9 RELIABILITY AND VALIDITY

Reliability was ensuring that the questionnaire was repeatable and this was done by ensuring that the questions were consistent. Internal validity was ensured by testing the questionnaire in a pilot study before the actual data collection, to ensure that all the questions asked were understood correctly and that the research team was satisfied with the responses to the questions.

Bias can be defined as any systematic error with a tendency for selectivity or influence, meaning that the research findings deviate from the ‘true findings’. Bias can occur at any stage of the research (Pannucci & Wilkins, 2010). Bias was ruled out and limited by using the data collection sheet after the pilot test had been successfully completed. As noted during the discussion on internal and external validity, various biases could have an influence on the current research study. These have been accounted for and, as far possible, various techniques were employed to decrease or minimise the effect of bias on the data obtained.

Sampling bias occurs when the sample is collected in such a way that some members of the intended population are less likely to be included than others. These were minimised through the means of using the same protocol and the same data collection and survey sheet for all sampled medical practitioner participants, throughout the research. Purposive sampling was also done to include all students who met the inclusion criteria.

Analytical bias results from differences in methods and techniques used to evaluate the results. All results were evaluated using the same method and technique to capture and analyse data.

Table 3.2: Threats to internal validity

<table>
<thead>
<tr>
<th>Threat</th>
<th>Definition</th>
<th>Applicability to current study</th>
<th>What was done to minimize the effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implementation</td>
<td>Occurs when the</td>
<td>Can occur if the</td>
<td>The protocol was</td>
</tr>
</tbody>
</table>
**bias**
protocol designed for the intervention is not followed in the intended manner
protocol used for all patients are not the same for example time of measurement, environment for measurement, etc.
followed to the intended manner

**Attrition**
Occurs when participants who have been selected to take part in the study, do not take part at all or fail to take part during every stage of the research process.
Can occur when potential research participants or participant’s parents/guardians do not give consent for the participation in the study, or participants pass away after they have been selected or during the research process.
Participation in the study is voluntary and anonymous

**Researcher bias**
Occurs when the researcher has a personal bias/preference towards a technique.
The researcher may create a predetermined hypothesis regarding the results that were obtained with the various testing procedures.
Researcher has no personal bias preference towards a certain technique. The study is in the form an online questionnaire

**Effect size**
It is the incorrect interpretation of statistical significance and related failure to interpret intervals.
$P$-values can be over or under interpreted if the sample size is not correct.
The sample size has been estimated as accurately as possible

<table>
<thead>
<tr>
<th>Table 3.3: Threats to external validity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Threat</strong></td>
</tr>
<tr>
<td><strong>Population validity</strong></td>
</tr>
</tbody>
</table>
Chapter 3: Methodology

| Ecological validity | The extent to which the findings from a given study can be generalised across settings, conditions, variables and contexts. | The data and final results in this study are dependent on the setting and the location in which it is obtained in. | The study reached as many students from the different universities as possible to provide a big sample |

3.10 ETHICAL CONSIDERATIONS

Ethical approval was sought from Sefako Makgatho University Research Ethics Committees (SMUREC) before commencement of data collection (SMUREC/H/246/2016: PG) (Appendix 4). Permission for the study was obtained from the Head of each department and research ethics committees at the different universities.

3.10.1 Respect for autonomy

Implied consent was used for the purposes of the study, and was stated as part of the DCI (See Appendix 1). The completion of the questionnaire will thus imply consent to participate in the study. Students could withdraw from the study without negative consequences. Questionnaires were completed anonymously and the identity of the students were not disclosed and students were informed of this. Data was handled with confidentiality.

3.10.2 Beneficence

The Declaration of Helsinki principles also mention that medical research involving human participants may only be conducted if the importance of the objective outweighs the inherent risks and burdens to the research subjects. There were no inherent risks involved in this study.

3.11 CONCLUSION

This study was conducted among final year medical, pharmacy, nursing and audiology students across South African universities. The study was in the form of a descriptive cross-sectional design where quantitative data was collected prospectively. Data was captured from the online questionnaire tool into Microsoft Excel® spread. A systematic discussion of the study’s methodology was given, as well as informative descriptions of the study design, study site and sample selection. The data collection instruments used in this study were described. This chapter ended with a definition and explanation of reliability, validity and
bias, as well as the necessary ethical considerations, implemented throughout the study period. Chapter 4 will cover the results obtained in this study with a relevant discussion of the findings.
4.1 INTRODUCTION

The results and discussion of this discussion is presented in a manuscript format and will be submitted to a peer reviewed journal.

4.2 MANUSCRIPT FOR PUBLICATION

Pharmacotherapy-induced ototoxicity: Do final year medical, pharmacy, audiology and nursing students in South Africa have enough knowledge?

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Department of audiology, University of Cape Town²

Corresponding author: Omphile Mogole (Omphile.mogole@gmail.com)

Abstract

BACKGROUND AND OBJECTIVES: The growing disease burden in South Africa results in detrimental side-effects from the drugs used to treat these conditions. HIV, TB and malaria have a high prevalence in South Africa and the drugs used to treat these conditions are ototoxic. It is therefore important that healthcare professionals are able to identify these drugs and their effects to ensure effective care of the patient. The aim of the students was to assess the knowledge of final year pharmacy, medicine, audiology and nursing students across South African universities regarding pharmacotherapy-induced ototoxicity.

METHODS: A descriptive cross-sectional study was conducted where quantitative data will be collected prospectively. A structured, self-administered online questionnaire was administered and was structured according to the objectives

RESULTS: An overall response rate of 41% (n=720) was obtained. Majority of the respondents were female between the ages of 21 – 25. A Vast majority of the respondents (95%) understood the general concept of what pharmacotherapy-induced ototoxicity was,
with only a few (39%) knowing the general signs and symptoms of ototoxicity. Very few of respondents could identify ototoxic medication and the type of damage caused by ototoxic medicine

CONCLUSION: There were significant differences between the respondents with regards to undergraduate education on pharmacotherapy-induced ototoxicity. In order minimise pharmacotherapy-induced ototoxicity, a multidisciplinary healthcare team must have sufficient knowledge about ototoxicity. Therefore efforts should be made to extensively introduce concepts of pharmacotherapy-induced ototoxicity into the undergraduate curricula of pharmacy, medicine, nursing and audiology programs.

INTRODUCTION

The global incidence of Multidrug-Resistant tuberculosis (MDR-TB) by 2015 was 580 000.\textsuperscript{1} In South Africa, this rapid spread in MDR-TB is usually seen among Human Immunodeficiency Virus (HIV) infected patients due to the impaired ability of their immune system to contain the MDR-TB bacilli.\textsuperscript{2} South Africa has the highest rate of new HIV infections in the world and is one of the five countries in the world with the largest incidence of active tuberculosis (TB).\textsuperscript{3,4,5} In developing countries, there is usually a co-infection of TB and HIV, which warrants a simultaneous administration of highly active antiretroviral therapy (HAART) and ototoxic TB drugs, thus increasing the potential for ototoxicity.\textsuperscript{6}

Pharmacotherapy-induced ototoxicity is a growing problem, especially in developing countries like South Africa.\textsuperscript{7} The prevalence of TB, HIV and malaria in South Africa predisposes these patients to hearing loss which is induced by some agents used to treat these conditions.\textsuperscript{7} Neonates, particularly premature ones, are more prone to infections due to their immunocompromised nature and the antibiotics used to treat these infections are ototoxic, e.g. amikacin.\textsuperscript{8}

Pharmacists, along with medical professionals and nurses, play an integral role in identifying and monitoring ototoxic agents, while audiologists often only get involved after the patients has completed therapy and start experiencing hearing loss.\textsuperscript{7} This can be rectified as early identification of hearing loss and balance problems is of paramount importance to prevent or minimize permanent impairment and therefore improve quality of life post treatment.\textsuperscript{9}

Interprofessional education (IPE) refers to healthcare students learning from and about one another to improve collaboration and the quality of patient care.\textsuperscript{10} IPE is an important
approach to develop healthcare students as the trained students are more likely to become collaborative interprofessional team members who show respect and positive attitudes towards each other and work towards improving patient outcomes.\textsuperscript{11} Nursing, medicine, pharmacy and other allied health professions are required to work together in a clinical environment, which requires effective teamwork and communication skills. The majority of the university-based health professional education currently deliver a discipline specific model of teaching.\textsuperscript{12}

A relationship between the physician (as the prescribers) and nurses (as the care takers) needs to be established and supported by education regarding the importance and benefits of monitoring and evaluation which should be discussed with the patients.\textsuperscript{13} Many physicians do not understand the importance of otolaryngologist and audiologists in pre-treatment counselling and evaluation and the need for follow-up assessments of the patient’s auditory function.\textsuperscript{14}

A multidisciplinary team approach is integral in collaborative patient’s education programs with physicians, pharmacist, nurses and audiologists regarding ototoxic medication, considering that most primary care clinicians and clinical pharmacists have seen patients who have suffered from ototoxicity at some point in their careers.\textsuperscript{7} However literature pertaining to the core curriculum or knowledge and perceptions of these healthcare workers in training is limited especially in the South African context. The following key concepts are depicted in box 1.
Box 1: Key concepts in ototoxicity

**Key concepts**

**Ototoxicity**

Ototoxicity is damage to the inner ear after exposure to a toxic chemical or agent

**Cochleotoxicity**

Cochleotoxicity is hearing loss that may be permanent and presents with tinnitus, hyperacusis (increased sensitivity to sounds) and difficulty in speech discrimination especially in the presence of background noise

**Vestibulotoxicity**

Vestibulotoxicity is damage to the inner ear that presents with general disequilibrium, unsteadiness when walking, ataxic gait (lack of voluntary coordinated muscle movement), oscillopia (sensation that the environment is moving)

**Interprofessional education**

Interprofessional education refers to healthcare students learning from and about one another to improve collaboration and the quality of patient care

**Methods**

**Study design and population**

A descriptive cross-sectional study was conducted where mainly quantitative data was collected prospectively. The target population for this study included all final year pharmacy, medicine, audiology and nursing students across South African universities. Table 1 indicates the universities in South Africa that offer pharmacy, medicine, audiology and nursing.
Table 1: Universities offering pharmacy, medicine, audiology and nursing

<table>
<thead>
<tr>
<th>University</th>
<th>Pharmacy</th>
<th>Medicine</th>
<th>Audiology</th>
<th>Nursing</th>
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</thead>
<tbody>
<tr>
<td>Nelson Mandela Metropolitan University (NMMU)</td>
<td>X</td>
<td>*</td>
<td>*</td>
<td>X</td>
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<tr>
<td>University Of Forte Hare (UFH)</td>
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<td>X</td>
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<tr>
<td>Walter Sisulu University</td>
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<tr>
<td>University Of Free State (UFS)</td>
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<tr>
<td>Rhodes University</td>
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<tr>
<td>Tshwane University Of Technology (TUT)</td>
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<td>*</td>
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<tr>
<td>University Of Limpopo (Turfloop Campus)</td>
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<td>*</td>
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<td>University of the Western Cape (UWC)</td>
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<tr>
<td>Sefako Makgatho Health Sciences University (SMU)</td>
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<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>University Of Pretoria (UP)</td>
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<td>Durban University Of Technology (DUT)</td>
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<td>University Of Kwazulu Natal (UKZN)</td>
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<tr>
<td>University Of Cape Town (UCT)</td>
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</tr>
</tbody>
</table>

*Department/school did not participate in the study

Data collection instruments and procedures

An electronic questionnaire was used to evaluate the final year pharmacy, medicine, nursing and audiology students’ knowledge on pharmacotherapy-induced ototoxicity. The following themes of knowledge were investigated: general knowledge on pharmacotherapy-induced ototoxicity, prevention of pharmacotherapy-induced ototoxicity, monitoring on patients using ototoxic drugs and prescribing of ototoxic drugs. The online questionnaire was developed and compiled in accordance with the objectives based on an article by Schellack and Naude (2013) on the overview of pharmacotherapy-induced ototoxicity.\(^\text{15}\)

A link to the questionnaire was sent to a designated staff member at the university whose responsibility was to disseminate the link to the final year students in the respective department. Reminder emails, pertaining to the online questionnaire were sent to a
designated staff member at the university departments/schools on a weekly basis throughout the 24 week data collection period. The aim with this communication was for the designated staff member to remind students to submit and complete the questionnaire on the online platform.

**Data analysis**

All statistical procedures were performed on Microsoft Excel® 2010, running under Microsoft Windows for a personal computer and analysed using IBM SPSS Statistics version 24. Prior to analysis, universities were de-identified and recorded as “A”, “B”, “C”, “D”, “E”, “F”, “G”, “H”, “I”, “J”, “K”, “L”, “M”. Frequencies and percentages were calculated for all variables. The Fisher exact test or the Chi-Square test was used to test for differences in responses between the different universities. Statistical significance was set at $p \leq 0.05$.

**Ethical Considerations**

Ethical approval was sought from Sefako Makgatho University Research Ethics Committees (SMUREC) before commencement of data collection (SMUREC/H/246/2016: PG). Permission for the study was obtained from the Head of each department and research ethics committees at the different universities. Implied consent is used for the purposes of the study, and has been stated as part of the DCI. The completion of the questionnaire will thus imply consent to participate in the study. Participation was voluntary and the responses were anonymous.

**Results**

**Response rate**

Seven hundred and twenty final year students from all courses across South African universities participated in the study. This only included schools/departments who chose to participate in the study. From the schools and departments that participated, two hundred and sixty six (42%) of the 634 final year pharmacy students completed the survey. Two hundred and ten (38%) of the 557 final year medicine students completed the survey. One hundred and eighty eight (41%) of the 459 final year nursing students completed the survey. Fifty six (64%) of the 88 final year audiology students completed the survey. The overall response rate was 41%, ranging from 25% to 86% across the different universities and courses. The response rates by institution and course are shown in Table 2.
Table 2: Response rate by university and course

<table>
<thead>
<tr>
<th>University</th>
<th>NUMBER (n) AND RESPONSE RATE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PHARMACY (n = 266)</td>
</tr>
<tr>
<td>A</td>
<td>*</td>
</tr>
<tr>
<td>B</td>
<td>46 (39%)</td>
</tr>
<tr>
<td>C</td>
<td>35 (25%)</td>
</tr>
<tr>
<td>D</td>
<td>49 (77%)</td>
</tr>
<tr>
<td>E</td>
<td>*</td>
</tr>
<tr>
<td>F</td>
<td>*</td>
</tr>
<tr>
<td>G</td>
<td>*</td>
</tr>
<tr>
<td>H</td>
<td>38 (44%)</td>
</tr>
<tr>
<td>I</td>
<td>31 (48%)</td>
</tr>
<tr>
<td>J</td>
<td>39 (39%)</td>
</tr>
<tr>
<td>K</td>
<td>28 (46%)</td>
</tr>
<tr>
<td>L</td>
<td>*</td>
</tr>
<tr>
<td>M</td>
<td>*</td>
</tr>
</tbody>
</table>

*Department/school did not participate in the study

Demographics

Overall, 64.03% of the respondents were female. Over two-thirds (68.19%) of the students were between the ages of 22-25 years, 6.94% were younger than 22 years and 24.72% were over the age of 25 years.

General knowledge on pharmacotherapy-induced ototoxicity

Respondents’ general knowledge of pharmacotherapy-induced ototoxicity are summarised in Table 3. A vast majority of the respondents (95%) had an understanding about what ototoxicity was, however only a small number of the respondents (28%) could identify the signs of ototoxicity (p < 0.001), with responses of 39% for pharmacy, 35% for medicine, 18% for nursing and 21% for audiology. Only 21% of the respondents knew the risk factors of pharmacotherapy-induced ototoxicity, with responses ranging from 18% to 23% and significant differences between the different courses (p < 0.001).

Table 3: General knowledge of final year pharmacy, medicine, nursing and students on pharmacotherapy-induced ototoxicity

| Percentage of students per university |
### Drugs causing ototoxicity

Respondents knowledge on drugs that cause ototoxicity are summarised in Table 4. Just under half of the respondents (48%) could identify ototoxic drugs, with responses of 62% for pharmacy students, 53% for medicine students, 44% for nursing students and 32% for audiology students. Only 36% of the respondents knew how NSAID-induced ototoxicity occurred (p < 0.001) and about 43% of the respondents accurately reported that hearing loss caused by aminoglycosides was irreversible, with significant differences between the different courses (p < 0.001). Close to a fifth of the respondents (19%) could identify ototoxic anti-hypertensive medication (p < 0.001), with responses 23% from both pharmacy and medicine students, and 14% for both nursing and audiology students. A few of the respondents (43%) were able to identify ototoxic anti-tuberculosis medication, with significant difference in responses between the different courses (p < 0.001).

<table>
<thead>
<tr>
<th>Percentage of students per university</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ALL (n = 266)</strong></td>
</tr>
<tr>
<td>________________</td>
</tr>
<tr>
<td>Which of the following drugs does not cause ototoxicity</td>
</tr>
<tr>
<td>NSAIDs (Ibuprofen) induced ototoxicity may occur when</td>
</tr>
</tbody>
</table>
Type of damage caused

Respondents’ knowledge on the type of damage caused by ototoxic drugs are summarised in Table 5. Only a quarter of the respondents (25%) knew the ototoxic side effects caused by aspirin ($p < 0.001$), with responses of 25% for pharmacy, 26% for medicine, 14% for nursing and 36% for audiology. Just over fifty percent of the medical students (52%) could identify the most ototoxic medicine from a list of ototoxic medication ($p < 0.001$). Pharmacy students showed poor knowledge regarding the signs of damage to the cochlea and vestibular system, with 25% of them knowledgeable regarding the signs of damage to the vestibular system and only 21% of them knowledgeable regarding the signs of damage to the cochlea ($p < 0.001$). Just over a third of the pharmacy students (34%) indicated that medicine that causes reversible hearing loss do not require monitoring ($p < 0.001$) and just under half of the them (47%) could identify the frequencies (higher or lower) that are affected by ototoxic medicines. Only 23% of pharmacy students knew which hair cells in the ear are most susceptible to ototoxic damage. Both pharmacy (42%) and audiology students (43%) showed a fair understanding of the type of hearing loss caused by cisplatin and vancomycin, with both pharmacy (13%) and audiology (27%) also showing insufficient knowledge regarding the cause of sensorineural hearing loss ($p < 0.001$).

Table 5: Final year pharmacy, medicine, nursing and audiology students’ knowledge on the type of damage caused by ototoxic medicine

<table>
<thead>
<tr>
<th>Which TB medication is likely to cause hearing loss</th>
<th>43%</th>
<th>47%</th>
<th>40%</th>
<th>44%</th>
<th>41%</th>
<th>0.063$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertensive patients are at risk of ototoxicity when using a high dose of which of the following anti-hypertensives</td>
<td>19%</td>
<td>23%</td>
<td>23%</td>
<td>14%</td>
<td>14%</td>
<td>&lt;0.001$^b$</td>
</tr>
<tr>
<td>Aminoglycoside-induced ototoxicity is reversible</td>
<td>43%</td>
<td>35%</td>
<td>53%</td>
<td>42%</td>
<td>41%</td>
<td>&lt;0.001$^b$</td>
</tr>
</tbody>
</table>

$^a$Chi-Square test  
$^b$Fisher exact test
Respondent’s discipline specific knowledge is summarised in Table 6. Under half of the respondents (45%) knew the steps to take when a patient starts experiencing ototoxic side effects, with responses of 42% for pharmacy students, 55% for medicine students, 36% for nursing students and 46% for audiology students. Just over half of the pharmacy students (54%) knew the ototo-protective antioxidant properties N-acetylcysteine ($p < 0.001$), while 23% of them knew the strategies involved to minimize drug-induced ototoxicity. The majority of both pharmacy (61%) and audiology (75%) students understood what otoacoustic emissions were, however only 16% of pharmacy students and

<table>
<thead>
<tr>
<th>Question</th>
<th>Pharmacy (n=23)</th>
<th>Medicine (n=26)</th>
<th>Nursing (n=18)</th>
<th>Audiology (n=20)</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most ototoxic drugs</td>
<td>*</td>
<td>52%</td>
<td>*</td>
<td>*</td>
<td>&lt;0.001$^a$</td>
</tr>
<tr>
<td>Damage vestibular organ</td>
<td>25%</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>&lt;0.001$^a$</td>
</tr>
<tr>
<td>Reversible hearing loss (erythromycin)</td>
<td>34%</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>&lt;0.001$^a$</td>
</tr>
<tr>
<td>Pharmacotherapy-induced hearing loss</td>
<td>47%</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>&lt;0.001$^a$</td>
</tr>
<tr>
<td>Cochlea damage</td>
<td>21%</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>&lt;0.001$^a$</td>
</tr>
<tr>
<td>Hair cell susceptibility</td>
<td>23%</td>
<td>*</td>
<td>*</td>
<td>45%</td>
<td>0.530$^a$</td>
</tr>
<tr>
<td>Cisplatin and vancomycin</td>
<td>42%</td>
<td>*</td>
<td>*</td>
<td>43%</td>
<td>0.041$^a$</td>
</tr>
<tr>
<td>High frequency sensorineural hearing loss</td>
<td>13%</td>
<td>*</td>
<td>*</td>
<td>27%</td>
<td>0.234$^a$</td>
</tr>
<tr>
<td>Hair cell susceptibility</td>
<td>23%</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>&lt;0.001$^a$</td>
</tr>
</tbody>
</table>

*Department/school did not participate in study  
$^a$Chi-Square test  
$^b$Fisher exact test
14% of audiology students being able to identify what they are used for in determining hearing loss, with significant differences in the responses between the different courses (p < 0.001). Fourteen percent (14%) pharmacy students and 29% of audiology students knew what pure tone audiometry tests are used for in determining hearing loss. Both pharmacy and audiology students showed slight knowledge regarding when baseline audiometric tests should be performed when patients are taking ototoxic medication, 36% and 39% respectively. Upon further investigation, pharmacy students seemed to have a better understanding of when audiometric monitoring should initiated (46%) then audiology students (30%). Just over half of the medicine students (54%) reported that a patient should not receive more than one ototoxic medicine at a time and with only 31% of them being able to identify what to do in the event of ototoxicity.

Just over sixty percent of medicine students (66%) indicated that the risk to benefit ratio should also be taken into account when prescribing ototoxic medication, with significant differences between the individual universities (p < 0.001). Just over half of the medicine students (52%) also indicated that patients who experience ototoxic effects should only be referred for audiological monitoring only once the therapy has been completed (p < 0.001). Very few of the medicine students (11%) could identify N-acetylcysteine as an oto-protective agents in patients receiving ototoxic medications (p < 0.001). A few of the medical students (35%) reported that patients should be counselled before treatment of the possible ototoxic side effects of the medicine and 59% of them reported that most ototoxic medicine will not cause hearing loss when given at therapeutic doses. Only 33% of pharmacy students indicated that patients with a past history of hearing loss should not take ototoxic drugs, and sixty percent of medical students (60%) agreed with them (p < 0.001).

Table 6: Discipline specific knowledge of final year pharmacy, medicine, nursing and audiology students on pharmacotherapy-induced ototoxicity

<table>
<thead>
<tr>
<th>Percentage of students per university</th>
<th>Pharmacy (n = 266)</th>
<th>Medicine (n = 210)</th>
<th>Nursing (n = 188)</th>
<th>Audiology (n = 56)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>As a healthcare professional, when you suspect that a patient may be showing some ototoxic signs/symptoms, you must</td>
<td>42%</td>
<td>55%</td>
<td>36%</td>
<td>46%</td>
<td>0.058&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>N-acetylcysteine can be used as a protective agent in patients treated with ototoxic drugs</td>
<td>54%</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>&lt;0.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>What are the strategies used to minimize</td>
<td>23%</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>&lt;0.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>ototoxicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---------------------------------------------------------------------------</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>Otoacoustic emissions are sounds generated by the cochlea’s sensory hair cells in response to auditory stimulation</td>
<td>61%</td>
<td>*</td>
<td>*</td>
<td>75%</td>
<td>0.049&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>What are otoacoustic emissions used for</td>
<td>16%</td>
<td>*</td>
<td>*</td>
<td>14%</td>
<td>(&lt;0.001)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Baseline testing should be performed ___ treatment has started</td>
<td>36%</td>
<td>*</td>
<td>*</td>
<td>39%</td>
<td>(0.037)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>What are pure tone audiometry tests used for</td>
<td>14%</td>
<td>*</td>
<td>*</td>
<td>29%</td>
<td>(0.01)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Monitoring of ototoxicity can only be done once the patient starts experiencing ototoxic effects</td>
<td>46%</td>
<td>*</td>
<td>*</td>
<td>30%</td>
<td>(0.250)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Pharmacotherapy-induced hearing loss affects which frequencies?</td>
<td>47%</td>
<td>*</td>
<td>*</td>
<td>64%</td>
<td>0.757&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>A patient can receive more than one ototoxic drug as long as the doses are not high</td>
<td>*</td>
<td>54%</td>
<td>*</td>
<td>*</td>
<td>0.067&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>What should be done if a patient starts experiencing ototoxic side effects</td>
<td>*</td>
<td>31%</td>
<td>*</td>
<td>*</td>
<td>&lt;0.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>When prescribing ototoxic drugs, the risk to benefit ration should be taken into account</td>
<td>*</td>
<td>66%</td>
<td>*</td>
<td>*</td>
<td>&lt;0.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Patients experiencing ototoxic effects should be referred for audiologic monitoring only after the treatment has finished</td>
<td>*</td>
<td>52%</td>
<td>*</td>
<td>*</td>
<td>&lt;0.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Which of the following drugs can be used concurrently with ototoxic medicine to try and minimize the ototoxic effects</td>
<td>*</td>
<td>11%</td>
<td>*</td>
<td>*</td>
<td>&lt;0.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
**Discussion**

The study evaluated final year pharmacy, medicine, nursing and audiology students’ knowledge on pharmacotherapy-induced ototoxicity. To the best of our knowledge, this study is the first to assess these aspects amongst pharmacy, medicine, nursing and audiology students across South African universities. The response rate for this study was relatively good, despite lack of participation from some schools/departments from the different universities. The reasons for the lack of participation was either because the relevant head/dean did not respond to the numerous emails that was sent out, or because some of the heads/deans refused to participate in the study. The response rate was boosted through sending weekly reminder emails over the 24 week data collection period.

The results indicated that the majority of the students across the different universities and courses don’t have adequate basic general knowledge regarding pharmacotherapy-induced ototoxicity. Across all universities, the students were only able to define what ototoxicity is, but could not identify the signs of ototoxicity and risk factors involved. The results also concur with those reported by Khoza-Shangase & Jina (2013) and De Andrade et al (2009), which revealed that doctors do not have adequate knowledge of ototoxicity symptoms and treatment. Pharmacy students did however score much better (97%) than students from other courses in terms general knowledge on pharmacotherapy-induced ototoxicity and this might be attributed to the fact that they have more extensive pharmacology training at undergraduate level than the other courses.
More so, most of the respondents could not adequately identify medicine that cause ototoxicity. Audiology students obtained the lowest scored the lowest for this (32%), which can be explained by the fact that they do not have pharmacology training at undergraduate level. This supported a study conducted by Naidoo in 2006 in which majority of the audiologists were of the opinion that their undergraduate clinical training had left them unprepared to implement pharmacotherapy-induced ototoxicity monitoring services. The respondents knowledge regarding the type of damage caused by ototoxic medicine was shown to be poor. Respondents could not adequately identify whether certain medicines caused reversible or irreversible hearing loss. The respondents could not also determine the signs that arise as a result of damage to a specific structure of the ear (cochlea and vestibular system) as well as which drugs cause damage to which structure. This is in contrast to a paper by Schellack and Naude in 2013 that highlighted the importance of a coordinated and cooperative healthcare team in the early detection of cochleotoxicity.

Discipline specific questions were aimed at assessing what the students needed to know regarding pharmacotherapy-induced ototoxicity within their specific disciplines of pharmacy, medicine, nursing and audiology. This included steps to follow when a patient starts experiencing signs of ototoxicity. Pharmacy and medicine students performed relatively well in terms of identifying the steps to follow if a patient starts experiencing preventative measures that can be taken, including the pre-treatments that can be used when a patient is receiving ototoxic medicine. This is in line with a report by the World Health Organisation (WHO) which suggested that a large percentage of hearing impairment was attributed to ototoxic medication as a resulted of inappropriate use by healthcare providers, most especially from prescribers. Knowledge was slightly inadequate regarding when audiologic monitoring should be initiated, including prevention and pre-treatment of pharmacotherapy-induced ototoxicity. Nursing students showed poor knowledge in terms of steps to be taken when a patient starts experiencing ototoxic side effects. Audiology students scored fairly with regards to the steps that need to be followed when a patient starts experiencing ototoxic side effects and showed slight knowledge regarding when audiologic monitoring should be initiated as majority of them indicated that audiologic monitoring can only be done once a patient has completed treatment.

Strengths of the study were that the survey was anonymous and voluntary, which reduced the tendency of the respondents to provide socially desired answers. The study was conducted among final year undergraduates students when they had completed their formal academic curriculum to provide a better estimate of their education close to completion of the degree. Limitations of the study was the use of an online survey, which reduced the
response rate and difficulty obtaining ethical clearance from the different universities. Another limitation was the large sample size which consisted of 13 universities and four different course around South Africa, which resulted in a less than describable response rate.

Conclusion

The study demonstrated that final year pharmacy, medicine, nursing and audiology students across South African universities lack sufficient knowledge regarding pharmacotherapy-induced ototoxicity. The gaps in knowledge regarding the topic indicate that there is insufficient undergraduate training pertaining to ototoxicity. The results suggest that pharmacy, medicine, nursing and audiology students should be adequately trained at undergraduate level to handle cases of pharmacotherapy-induced ototoxicity once they get into the professional multidisciplinary healthcare environment to ensure patient safety. This holds especially true for a country such as South Africa that has a high disease burden that is treated with drugs that could be potentially ototoxic.

References


5.1 INTRODUCTION

The limitations and recommendations of this study are discussed, followed by a conclusion. A summary for the study ends this chapter.

5.2 LIMITATIONS OF THE STUDY

5.2.1 Online response rate

According to Nulty (2008), response rates from online surveys are less likely to achieve response rates as high as surveys administered on paper. In order to keep the patients in the study anonymous, the universities did not share student information such as email address. This meant that the survey had to be distributed to a designated staff member in the specific school/department and the investigator would have to rely on the staff member to distribute the survey to the students. Therefore the researcher could not be certain that the questionnaires were disseminated to the students as requested.

5.2.2 Obtaining ethical clearance from participating universities

In order to conduct research in other universities, some of the universities require your protocol to be submitted for ethical clearance. This process took months to complete for certain universities as amendments to the protocol needed to be made. This was also one of the reason some schools/departments did not participate as the ethical clearance process continued until the completion of the study.

5.3 RECOMMENDATIONS

5.3.1 Early application for ethical clearance

If a study of this kind, an online survey at universities, will be conducted in the future, ethical clearance need to be applied for as early as possible.

5.4 CONCLUSIONS

The study demonstrated that final year pharmacy, medicine, nursing and audiology students across South African universities lack sufficient knowledge regarding
pharmacotherapy-induced ototoxicity. The gaps in knowledge regarding the topic indicate that there is insufficient undergraduate training. The results suggest that pharmacy, medicine, nursing and audiology students should be adequately trained at undergraduate level to handle cases of pharmacotherapy-induced ototoxicity once they get into the professional multidisciplinary healthcare environment to ensure patient safety.
REFERENCES

Bilgili, E., Casimir, J., Pickard, K. and Lindsey, W., Drug-Induced Ototoxicity


References


Streubert, H.J. and Carpenter, D.R., 1999. Qualitative research in nursing: Advancing the humanistic perspective,(2"^ ed.).
References


Appendices

APPENDICES

Appendix 1: Questionnaire on Pharmacotherapy-Induced Ototoxicity

Dear Candidate

Please choose the sections applicable to you

Section A: Demographics

(To be completed by everyone)

Please tick the appropriate box or give the necessary information in the space provided

Gender:
Male
Female

Age:
18 - 21
22 - 25
26 - 30
30 +

Which course are you currently doing?

Pharmacy
Medicine
Audiology
Nursing

Which university are you enrolled at?

<table>
<thead>
<tr>
<th>University</th>
<th>Mark with ‘x’</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nelson Mandela Metropolitan University (NMMU)</td>
<td></td>
</tr>
</tbody>
</table>
Section B: General knowledge on pharmacotherapy-induced ototoxicity

(To be completed by everyone)

(1) Ototoxicity is
   (A) A side effect of medicine resulting in auditory and/or vestibular dysfunction resulting in hearing loss and disequilibrium
   (B) A toxic reaction resulting from an interaction between two or more drugs
   (C) Renal impairment due to medicine overdose
   (D) A side effect of medicine resulting in severe skin rash
   (E) I don’t know

(2) Signs of ototoxicity include
   (A) Hearing loss
   (B) Disequilibrium
   (C) Renal impairment
   (D) A & B
   (E) A, B & C
(3) Which of the following drugs does not cause ototoxicity
   (A) Vancomycin
   (B) Cisplatin
   (C) Penicillin
   (D) I don’t know

(4) Which patients are at risk of developing ototoxicity
   (A) Patients with renal impairment
   (B) MDR-TB patients
   (C) Heart failure patients
   (D) All of the above
   (E) I don’t know

(5) Aminoglycosides induced ototoxicity is reversible
   (A) True
   (B) False
   (C) I don’t know

(6) NSAID’s (e.g. ibuprofen) induce ototoxicity may occurs when
   (A) Patients use the medication for a prolonged period
   (B) Double the normal dose is administered
   (C) Patients take a normal dose for a few days
   (D) All of the above
   (E) I don’t know

(7) Aspirin causes the following ototoxic effects
   (A) Hearing loss
   (B) Tinnitus
   (C) Disequilibrium
   (D) Earache
   (E) All the above
   (F) I don’t know

(8) Which medicine used for TB is likely to cause hearing loss

(F) I don’t know
(A) Rifampicin
(B) Ethambutol
(C) Amikacin
(D) Isoniazid
(E) None of the above
(F) I don’t know

(9) Hypertensive patients are at risk of ototoxicity when using high dose of which antihypertensive
(A) hydrochlorothiazide
(B) Enalapril
(C) Ilosartan
(D) Furosemide
(E) I don’t know

(10) As a nurse, when you suspect that a patient may be showing some ototoxic signs/symptoms, you must:
(A) Observe the patient for a while before referring them
(B) Refer to an audiologist for confirmation
(C) Inform the treating physician
(D) Wait until the end of the treatment before referring the patient
(E) I don’t know

Section C: Prevention of pharmacotherapy-induced ototoxicity

(To be answered by pharmacy students)

(1) N-acetylcysteine (ACC-200®) can be used as a protective agent in patients treated with ototoxic drugs
(A) True
(B) False
(C) I don’t know

(2) Which of the following is the most correct preventative measure for patients receiving ototoxic medicine
(A) Change medication
(B) Counsel patient
Appendices

(C) Change dosage
(D) All of the above
(E) I don’t know

(3) The protective anti-oxidant effects of which drug is related to its action as a free radical scavenger
(A) Paracetamol
(B) N-acetylcsteine
(C) Sodium chloride
(D) Adrenaline
(E) None of the above
(F) I don’t know

(4) Patients can receive more than one ototoxic drug as long as the doses are not too high
(A) True
(B) False
(C) I don’t know

(5) Damage to the vestibular organ results in which side effects
(A) Tinnitus
(B) Hearing loss
(C) Dizziness
(D) Loss of balance (disequilibrium)
(E) A & B
(F) C & D
(G) I don’t know

(6) Patients with a past history of hearing loss should not take any ototoxic medicine
(A) True
(B) False
(C) I don’t know

(16) Which of the following patients are at a higher risk of aminoglycoside ototoxicity
(A) Those taking therapy for more than 5 days
(B) Those taking higher doses
(C) Elderly patients with renal insufficiency
(D) All of the above
(E) I don’t know

(17) Drugs that cause reversible hearing loss (erythromycin) do not have to be monitored for ototoxic effects
(A) True
(B) False
(C) I don’t know

(18) Strategies to minimize ototoxicity include
(A) Keep patients hydrated
(B) Dosage instructions should be strictly followed
(C) Noisy environments should be avoided for at least 6 months after treatment
(D) A & B
(E) A, B, C
(F) I don’t know

Section D: Monitoring of pharmacotherapy-induced ototoxicity

(To be completed by audiology and pharmacy students)

(1) Otoacoustic emissions are sounds generated by the cochlea’s sensory hair cells in response to auditory stimulation
   (A) True
   (B) False
   (C) I don’t know

(2) Pharmacotherapy-induced hearing loss affects
   (A) Lower frequencies first then progresses to the higher frequencies
   (B) Higher frequencies first then progresses to the lower frequencies
   (C) Both lower and higher frequencies at the same time
   (D) I don’t know

(3) Otoacoustic emissions are used to
(A) Monitor effects of treatment
(B) Treat ototoxicity before it progresses
(C) Determine which medicine caused the ototoxicity
(D) Change the sound generated by the cochlea
(E) I don't know

(4) Damage to the cochlea results in which side effects
   (A) Tinnitus
   (B) Hearing loss
   (C) Dizziness
   (D) Loss of balance (disequilibrium)
   (E) A & B
   (F) C & D
   (G) I don't know

(5) Which hair cells are more susceptible to ototoxic damage
   (A) Inner hair cells
   (B) Outer hair cells
   (C) Middle hair cells
   (D) All of the above
   (E) I don't know

(6) Cisplatin and vancomycin causes which type of hearing loss
   (A) Reversible
   (B) Irreversible
   (C) I don't know

(7) High frequency sensorineural hearing loss is caused by damage to the
   (A) Cochlea
   (B) Vestibular organ
   (C) Tympanic membrane
(D) Ear drum
(E) I don't know

(8) Baseline testing should be performed __________ treatment has started
   (A) 2 hours before
   (B) 24 hours before
   (C) 2 hours after
   (D) 24 hours after
   (E) I don't know

(9) Pure tone audiometry tests determine
   (A) Absence or presence of hearing loss
   (B) Extent of hearing loss
   (C) The cause of hearing loss
   (D) All of the above
   (E) I don't know

(10) Monitoring of ototoxicity can only be done once the patient starts experiencing ototoxic effects (e.g. tinnitus)
   (A) True
   (B) False
   (C) I don't know

Section E: Prescribing of ototoxic medicine

(To be completed by medicine students)

(1) A patient can receive more than two ototoxic medicine as long as the doses are not high
   (A) True
   (B) False
   (C) I don't know

(2) If a patient starts experiencing ototoxic effects, the following should be done
   (A) Change the medicine to less toxic ones
   (B) Counsel the patient
(C) Change the dose of the medicine
(D) All of the above
(E) I don't know

(3) When prescribing ototoxic drugs, the risk to benefit ratio should always be taken into consideration
(A) True
(B) False
(C) I don't know

(4) Patients experiencing ototoxic effects should be referred for audiologic monitoring only after the treatment has finished
(A) True
(B) False
(C) I don't know

(5) Which of the following drugs can be used concurrently with ototoxic medicine to try and minimize the ototoxic effects
(A) Adrenaline
(B) N-acetylcysteine
(C) Sodium chloride
(D) Paracetamol
(E) None of the above
(F) I don't know

(6) Audiologic monitoring should be initiated
(A) Before treatment, during treatment and after treatment
(B) Only before treatment to assess hearing
(C) Only after treatment to assess effect of treatment
(D) Only during course of treatment
(E) None of the above
(F) I don't know

(7) Patients receiving ototoxic drugs should not be counselled about the possible effects as this will prevent treatment compliance
(A) True
(B) False
(C) I don’t know

(18) Most ototoxic drugs do not cause hearing loss when given at therapeutic doses

(A) True
(B) False
(C) I don’t know

(19) Which of the following drugs are the most ototoxic

(A) Furosemide
(B) Erythromycin
(C) Vancomycin
(D) Aspirin
(E) I don’t know

(20) Patients with a past history of hearing loss should not take any ototoxic medicine

(A) True
(B) False
(C) I don’t know
Appendices

Appendix 2: Memorandum

Section B: General knowledge on pharmacotherapy-induced ototoxicity

(To be completed by everyone)

(11) Ototoxicity is

(A) A side effect of medicine resulting in auditory and/or vestibular dysfunction resulting in hearing loss and disequilibrium
(B) A toxic reaction resulting from an interaction between two or more drugs
(C) Renal impairment due to medicine overdose
(D) A side effect of medicine resulting in severe skin rash
(E) I don’t know

(12) Signs of ototoxicity include

(A) Hearing loss
(B) Disequilibrium
(C) Renal impairment
(D) A & B
(E) A, B & C
(F) I don’t know

(13) Which of the following drugs does not cause ototoxicity

(A) Vancomycin
(B) Cisplatin
(C) Penicillin
(D) I don’t know

(14) Which patients are at risk of developing ototoxicity

(A) Patients with renal impairment
(B) MDR-TB patients
(C) Heart failure patients
(D) All of the above
(E) I don’t know

(15) Aminoglycosides induced ototoxicity is reversible

(A) True
(B) False
(C) I don’t know

(16) NSAID’s (e.g. ibuprofen) induce ototoxicity may occurs when
(A) Patients use the medication for a prolonged period
(B) **Double the normal dose is administered**
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(17) Aspirin causes the following ototoxic effects
(A) Hearing loss
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(D) Earache
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(F) I don’t know

(18) Which medicine used for TB is likely to cause hearing loss
(A) Rifampicin
(B) Ethambutol
(C) **Amikacin**
(D) Isoniazid
(E) None of the above
(F) I don’t know

(19) Hypertensive patients are at risk of ototoxicity when using high dose of which antihypertensive
(A) hydrochlorothiazide
(B) Enalapril
(C) Losartan
(D) **Furosemide**
(E) I don’t know

(20) As a nurse, when you suspect that a patient may be showing some ototoxic signs/symptoms, you must:
(A) Observe the patient for a while before referring them
(B) Refer to an audiologist for confirmation
(C) **Inform the treating physician**
(D) Wait until the end of the treatment before referring the patient
(E) I don’t know

*Section C: Prevention of pharmacotherapy-induced ototoxicity*

*(To be answered by pharmacy students)*

(7) N-acetylcysteine (ACC-200®) can be used as a protective agent in patients treated with ototoxic drugs
   (A) **True**
   (B) False
   (C) I don’t know

(8) Which of the following is the most correct preventative measure for patients receiving ototoxic medicine
   (A) Change medication
   (B) Counsel patient
   (C) Change dosage
   (D) **All of the above**
   (E) I don’t know

(9) The protective anti-oxidant effects of which drug is related to its action as a free radical scavenger
   (A) Paracetamol
   (B) **N-acetylcysteine**
   (C) Sodium chloride
   (D) Adrenaline
   (E) None of the above
   (F) I don’t know
(10) Patients can receive more than one ototoxic drug as long as the doses are not too high
    (A) True
    (B) False
    (C) I don’t know

(11) Damage to the vestibular organ results in which side effects
    (A) Tinnitus
    (B) Hearing loss
    (C) Dizziness
    (D) Loss of balance (disequilibrium)
    (E) A & B
    (F) C & D
    (G) I don’t know

(12) Patients with a past history of hearing loss should not take any ototoxic medicine
    (A) True
    (B) False
    (C) I don’t know

(13) Which of the following patients are at a higher risk of aminoglycoside ototoxicity
    (A) Those taking therapy for more than 5 days
    (B) Those taking higher doses
    (C) Elderly patients with renal insufficiency
    (D) All of the above
    (E) I don’t know

(14) Drugs that cause reversible hearing loss (erythromycin) do not have to be monitored for ototoxic effects
    (A) True
    (B) False
    (C) I don’t know

(15) Strategies to minimize ototoxicity include
    (A) Keep patients hydrated
    (B) Dosage instructions should be strictly followed
Noisy environments should be avoided for at least 6 months after treatment

A & B

A, B, C

I don’t know

Section D: Monitoring of pharmacotherapy-induced ototoxicity

(To be completed by audiology and pharmacy students)

(11) Otoacoustic emissions are sounds generated by the cochlea’s sensory hair cells in response to auditory stimulation

(A) True
(B) False
(C) I don’t know

(12) Pharmacotherapy-induced hearing loss affects

(A) Lower frequencies first then progresses to the higher frequencies
(B) Higher frequencies first then progresses to the lower frequencies
(C) Both lower and higher frequencies at the same time
(D) I don’t know

(13) Otoacoustic emissions are used to

(A) Monitor effects of treatment
(B) Treat ototoxicity before it progresses
(C) Determine which medicine caused the ototoxicity
(D) Change the sound generated by the cochlea
(E) I don’t know

(14) Damage to the cochlea results in which side effects

(A) Tinnitus
(B) Hearing loss
(C) Dizziness
(D) Loss of balance (disequilibrium)
(E) A & B
(F) C & D
(G) I don’t know

(15) Which hair cells are more susceptible to ototoxic damage
(A) Inner hair cells
(B) **Outer hair cells**
(C) Middle hair cells
(D) All of the above
(E) I don’t know

(16) Cisplatin and vancomycin causes which type of hearing loss
(A) Reversible
(B) **Irreversible**
(C) I don’t know

(17) High frequency sensorineural hearing loss is caused by damage to the
(A) **Cochlea**
(B) Vestibular organ
(C) Tympanic membrane
(D) Ear drum
(E) I don’t know

(18) Baseline testing should be performed _________ treatment has started
(A) 2 hours before
(B) **24 hours before**
(C) 2 hours after
(D) 24 hours after
(E) I don’t know

(19) Pure tone audiometry tests determine
(A) **Absence or presence of hearing loss**
(B) Extent of hearing loss
(C) The cause of hearing loss
(D) All of the above
(E) I don’t know

(20) Monitoring of ototoxicity can only be done once the patient starts experiencing ototoxic effects (e.g. tinnitus)
(A) True
(B) False
(C) I don’t know

Section E: Prescribing of ototoxic medicine

(To be completed by medicine students)

(8) A patient can receive more than two ototoxic medicine as long as the doses are not high
(A) True
(B) False
(C) I don’t know

(9) If a patient starts experiencing ototoxic effects, the following should be done
(A) Change the medicine to less toxic ones
(B) Counsel the patient
(C) Change the dose of the medicine
(D) All of the above
(E) I don’t know

(10) When prescribing ototoxic drugs, the risk to benefit ratio should always be taken into consideration
(A) True
(B) False
(C) I don’t know
(11) Patients experiencing ototoxic effects should be referred for audiologic monitoring only after the treatment has finished
   (A) True
   (B) **False**
   (C) I don't know

(12) Which of the following drugs can be used concurrently with ototoxic medicine to try and minimize the ototoxic effects
   (A) Adrenaline
   (B) **N-acetylcysteine**
   (C) Sodium chloride
   (D) Paracetamol
   (E) None of the above
   (F) I don't know

(13) Audiologic monitoring should be initiated
   (A) **Before treatment, during treatment and after treatment**
   (B) Only before treatment to assess hearing
   (C) Only after treatment to assess effect of treatment
   (D) Only during course of treatment
   (E) None of the above
   (F) I don't know

(14) Patients receiving ototoxic drugs should not be counselled about the possible effects as this will prevent treatment compliance
   (A) True
   (B) **False**
   (C) I don't know

(15) Most ototoxic drugs do not cause hearing loss when given at therapeutic doses
   (A) **True**
   (B) False
   (C) I don't know

(16) Which of the following drugs are the most ototoxic
Appendices

(A) Furosemide
(B) Erythromycin
(C) **Vancomycin**
(D) Aspirin
(E) I don't know

(17) Patients with a past history of hearing loss should not take any ototoxic medicine

(A) **True**
(B) False
(C) I don't know

Section A

(1) A  (2) D  (3) D  (4) C  (5) B  (6) A  (7) E  (8) C  (9) D  (10) A

Section B


Section C


Section D

(1) B  (2) D  (3) A  (4) B  (5) B  (6) A  (7) B  (8) B  (9) C  (10) B
Appendices

Appendix 3: Letter to head of Pharmacy

To the Head of Pharmacy,

I am a first year master's students at Sefako Makgatho University. I am doing a research study under the topic: “Final year students’ knowledge on pharmacotherapy-induced ototoxicity in medicine, pharmacy, audiology and nursing students across South African universities”

The aim of the study is to assess the knowledge of final year pharmacy, medicine, audiology and nursing students across South African universities regarding pharmacotherapy-induced ototoxicity. All the results and knowledge gained will be used to make recommendations to the relevant authorities to include more information about pharmacotherapy-induced ototoxicity.

We there for kindly request your permission to conduct the study at your school. Please find attached a copy of the protocol.

The study has been approved by the Sefako Makgatho University and Ethics committee, and Human Resource Department.

We will be very thankful if you will be prepared to take part in this study.

Please feel free to contact me on 083 757 0065 or my supervisor, Prof N Schellack on 012 5214312, if you have any further questions regarding this study.

Email addresses:

Student: Omphile Mogole, omphile.mogole@gmail.com

Supervisor: Natalie Schellack, natalie.schellack@smu.ac.za

Yours truly,

Omphile Mogole
Appendices

Appendix 4: SMUREC Clearance certificate

Sefako Makgatho Health Sciences University
Research & Postgraduate Studies Directorate
Sefako Makgatho University Research Ethics Committee
(SMUREC)

Molotlegi Street, Ga-Rankuwa 0208
Tel: (012) 521 5617/3698 | fax: (012) 521 3749
Email: lorato.phiri@smu.ac.za
P.O. Box 163 Medunsa 0204

06 October 2016

Mr O Mogale
Department of Pharmacy
P.O Box 218
Medunsa, 0204

MEETING:
08/2016

SMUREC Ethics Reference Number:
SMUREC/246/2016: PG

The New Application received on 09 September 2016, was reviewed by members of Sefako Makgatho University Research Ethics Committee 06 October 2016 and was approved on 06 October 2016.

Title: Final year student’s knowledge on pharmacotherapy-induced ototoxicity among medical, pharmacy, audiology and nursing students across South Africa Universities

Researcher:
Mr O Mogale

Supervisor:
Prof N Schellack

Co-supervisor:
Prof L Ramna

Department:
Pharmacy

School:
Health Care Sciences

Degree:
Masters of Pharmacy (Clinical Pharmacy)

Please note the following information about your approved research protocol:

Protocol Approval Period: 06 October 2016 – 06 October 2017

Please remember to use your protocol number (SMUREC/246/2016: PG) on any documents or correspondence with the REC concerning your research protocol.

Please note that the REC has the prerogative and authority to ask further questions, seek additional information, require further modification, or monitor the conduct of your research and the consent process.

After Ethical Review: Please note a template of the progress report is obtainable in the Research Office and should be submitted to the Committee before the year has expired. The Committee will then consider the continuation of the project for a further year (if necessary). Annually a number of projects may be selected randomly for an external audit. Translation of the consent document in the language applicable to the study participants should be submitted.

International Organisation (IORG00008691), Institutional Review Board (IRB000010386) Expiry date: 09 December 2018, Federal Wide Assurance (FWA000023943) Expiry date: 31 August 2017 and NHREC No: REC 216408-003

Sincerely

DR C BAKER
DEPUTY CHAIRPERSON SMUREC

Chairperson

Date: 01/10/2016