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Journal of Ear, Nose and Throat Disorders

Research Article

Ototoxic Hearing Loss in Paediatrics – Knowledge and Perceptions Amongst Medical Professionals - *L'habit Ne Fait Pas Le Moine*

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Submitted: 19 May 2017

Accepted: 16 June 2017

Published: 18 June 2017

ISSN: 2475-9473

Keywords
- Ototoxicity
- Paediatric
- Oncology
- Knowledge
- Physicians

Abstract

Background: The incidence of ototoxicity has become a major challenge in the vulnerable paediatric population, especially with the increasing survival rates. The objective of the study was to determine the knowledge and perceptions of medical practitioners on pharmacotherapy-induced ototoxicity.

Method: The study followed a descriptive quantitative design, and was conducted prospectively. Purposive sampling was done on all medical practitioners who rotated through the paediatric oncology unit at a large teaching hospital in Gauteng.

Results: The majority of medical practitioners obtained a result of ≥ 50%. The section with the most correct answers were section D that handled about the prescribing of ototoxic medication and the least correct answers section C that handled about the monitoring of ototoxicity.

Conclusion: It is evident from the results that medical practitioners had an overall good knowledge of ototoxicity and the prescribing of ototoxic medication. They were, however, much less knowledgeable on ototoxicity monitoring.

ABBREVIATIONS

AIDS: Acquired Immunodeficiency Syndrome; CEO: Chief Executive Officer; DGMAH: Dr George Mukhari Academic Hospital; HIV: Human Immunodeficiency Virus; ICU: Intensive Care Unit; MDT: Multi-Disciplinary Team; Ndoh: National Department Of Health; SA: South Africa; SADC: Southern African Development Community; SMU: Sefako Makgatho Health Sciences University; TB: Tuberculosis; TDM: Therapeutic Drug Monitoring

INTRODUCTION

Sub-Saharan Africa has the highest prevalence of drug-resistant tuberculosis (TB) [1] and Human Immunodeficiency Virus (HIV)/Acquired immunodeficiency syndrome (AIDS) in the world [2]. In HIV-infected individuals a significant cause of mortality and morbidity is cancer. According to statistics obtained from a recent study, up to 40% will develop a malignancy during their lifetime [3]. Certain types of cancer affect HIV-positive people and are those established as AIDS-defining: Kaposi's sarcoma, non-Hodgkin's lymphoma, and invasive cervical cancer [3]. A recent study showed that HIV-positive children in South Africa (SA) were at high risk of developing cancer with an overall incidence rate of 82/100,000 person-years [4].

The standard treatment for paediatric malignancies are the platinum compounds, cisplatin and carboplatin [5-7]. Although these drugs have proven higher survival rates [8-10] they do present with numerous side-effects that negatively impacts on the quality of life, and in this instance, ototoxicity [8,11,12]. Health care professionals in SA should therefore be trained on information regarding certain treatment regimens that cause ototoxicity [13-16].

The younger the paediatrics is when affected by hearing loss, the more serious the effects on the paediatric's process of speech and language development will be [17]. To this effect, the earlier cochlear impairment is identified and quantified, and intervention initiated, the less serious the ultimate impact on language and speech development will be. Children who present with mid- to high-frequency hearing loss, which is typical in ototoxicity, experience difficulty in hearing in certain situations (e.g. noisy environments in class rooms, softly-spoken people) [17].

It is therefore imperative that health care professionals in SA are knowledgeable about the impact of hearing loss caused by chemotherapeutic agents, including aminoglycosides, thereby

enabling appropriate management of affected individuals and thus increasing the overall quality of life [1].

Trends

Several studies have shown that ototoxic agents, such as medication, industrial chemicals and noise can cause sensorineural hearing loss [18]. The most common ototoxic medications used in clinical practice include: aminoglycoside and macrolide antibiotics, quinoline anti-malarials, platinum analogues antineoplastics, loop diuretics, and acetylsalicylic acid [18]. Risk of cisplatin ototoxicity appears to increase at extremes of age, with elderly patients and the paediatric population being particularly at risk [19].

There is a need for the pharmacist, medical practitioners, nurses, specialists and physicians as part of the multi-disciplinary team (MDT), to be involved in direct patient care with the audiologist focussing on the risk of ototoxicity in each individual patient [1].[1]Clinically risk–benefit evaluations should be undertaken to balance the need for intervention against the risk of permanent, irreversible hearing loss and the ramifications of living with such a disability. The use of available clinical guidelines should encourage clinicians to evaluate their practice with aminoglycosides [1].

With particular reference to ototoxicity, there has been a call for easy ototoxicity grading systems to be made available to the MDT, to apply and understand and be standardised [1]. Hearing loss and tinnitus have the potential to cause severe social, vocational, and educational consequences [19]. An effective ototoxicity monitoring programme detects cochlear injury prior to the onset of symptoms, allowing potential intervention to halt the progression of inner ear damage [19].

A relationship between the members of the MDT, including medical practioners (as the prescribers) nurses (as the caretakers), pharmacists (as the guardians of medicines) and audiologists, needs to be established and supported by education regarding the importance and benefits of monitoring evaluations which should be discussed with the patients [20]. Many medical practioners do not understand the importance of otolaryngologists and audiologists in pre-treatment counselling and evaluation and the need for follow-up assessments of the patient's auditory function [21].

Pharmacists are integral in strengthening pharmaceutical care and services in South Africa's district-based health system [22]. Therefore pharmacists also play an important role in the screening and monitoring of pharmacotherapy-induced ototoxicity. Pharmacists can identify and monitor ototoxic agents in the participants' treatment regimens. They can also perform Therapeutic Drug Monitoring (TDM) to reduce ototoxicity in the instance of antimicrobial agents that cause ototoxicity [14].

Implementation of initial baseline and periodic hearing monitoring can improve treatment outcome by identifying and minimising hearing loss progression. It also provides the medical practioner an opportunity to monitor or adjust the therapeutic treatment in order to minimise or prevent permanent hearing loss warranting rehabilitation [23].

National core standards

In 2011, the National Department of Health (NDoH) of SA established the domain of patient safety, clinical governance and clinical care, which provided guidelines 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 [24].

According to the NDoH (2011) core standards for patient safety is a main responsibility of the health care provider, as well as promoting health, reducing further patient complications and ensuring that adverse events are identified and managed through an effective, integrated patient management plan [24]. A closer look at identified medications that cause ototoxicity and are used regularly in the paediatric oncology unit is needed. Various authors identified that the health care worker in SA should become an active member of the health care team in the management of ototoxicity [13-16].

It is therefore the responsibility of the health care provider to ensure that: pharmacotherapy-induced ototoxicity identified as part of patient safety incidents are instantly acknowledged and managed to minimise patient harm and loss of hearing, and to ensure that early hearing loss is routinely investigated and managed to prevent repetition and to learn from those identified [24].

Contribution to the field

There is a need for ototoxicity monitoring in SA, given the prevalence of HIV/AIDS, TB and malaria [1,2], as both the medicines used in treatment of these diseases and the condition itself, can cause hearing loss. Further to this, a study undertaken in 2006 on audiological practice and service delivery in SA, identified a need for undergraduate clinical training in ototoxicity, to enhance implementation of ototoxicity monitoring services [25].

MATERIALS AND METHODS

Study design, population and setting

The study followed a descriptive quantitative cross-sectional design, and was conducted prospectively to elicit information on the knowledge and perceptions on ototoxicity amongst medical practitioners who worked and rotated in the paediatric oncology ward at Dr George Mukhari Academic Hospital (DGMAH). This facility is a rural public sector academic hospital (teaching facility) with 1,500 active beds and utilises a paper-based patient management system and is situatedin Ga-Rankuwa in the Gauteng Province of SA. DGMAH comprises 28 clinical departments, rendering all three levels of service. It is one of the four academic institutions in the province and provides a service to the surrounding populations of sub-districts 1-4 of approximately 1.7 million people. This excludes the catchment population from the other provinces that it services. DGMAH also receives referrals from Limpopo, North West and Mpumalanga Provinces. In addition, this facility receives referrals from Southern African Development Community (SADC) countries, other tertiary academic hospitals, local specialists and general

practitioners. The hospital has 1,500 active beds, 20 approved Intensive Care Unit (ICU) beds, 60 high care beds and 17 theatres.

All medical practitioners working at DGMAH (rotating through the paediatric oncology unit) were asked to complete the questionnaire.

Key aspects

Ototoxicity: The tendency of certain substances to cause functional impairment and cellular damage to the tissues of the inner ear and especially to the end organs of the cochlear and vestibular divisions of the eight cranial nerve [26].

Consultant: A doctor working at a hospital of senior rank within a specific field [27].

Registrar: A middle-ranking hospital doctor undergoing training as a specialist [27].

Chemotherapeutic agents: The treatment of a disease or cancer, using chemical agents or drugs that are selectively toxic to the causative agent of the disease, such as a virus, bacterium, or other microorganism [28,29].

Study procedures and instruments

Data was collected using a self-administered questionnaire in the form of multiple-choice questions. The questions were based on the 2013 ASHA ototoxicity monitoring guideline in the screening and monitoring for ototoxicity [30] and were designed to evaluate the knowledge and perceptions of ototoxicity of medical practitioners working in the Paediatric Oncology Unit at DGMAH. The questionnaire had been structured in accordance with the objectives of the study and was validated using content validity. Subject-matter experts were provided with access to the data collection instrument and were asked to provide feedback on how well each question measures the construction thereof. The questionnaire was pretested for readability, length and relevance of the questions amongst five medical interns from the Oncology Unit. No amendments were made. Their feedback was then analysed, and informed decisions were made about the effectiveness of each question and amended accordingly. The form was divided into four sections, as follows:

Assessing the level of knowledge and perception of ototoxicity

Section A: This section focussed on the general knowledge on pharmacotherapy-induced ototoxicity.

Section B: In this section physicians had to indicate how to prevent pharmacotherapy-induced ototoxicity.

Section C: This section was about monitoring pharmacotherapy-induced ototoxicity, which includes measures to refer a patient for ototoxicity monitoring.

Section D: This section enabled physicians to reflect on the prescribing of ototoxic medicines.

Ethical considerations

DGMAH is affiliated to Sefako Makgatho Health Sciences University (SMU) and approval to conduct the study was obtained from the Research Ethics Committee (SMUREC/H/137/2015: PG) before commencement of the study. Permission to conduct the study was requested and obtained from the Chief Executive Officer (CEO) of DGMAH and the Head of the Paediatrics Department. Medical practitioners provided signed consent if they were willing to partake in the study. Consent involves a participant in making a decision and becoming committed to the decision [31].

Data analysis

All data was captured on Microsoft Excel™ spread sheets and were checked for accuracy and completeness by a second person. Corrections were made prior to data analysis. Data was statistically analysed in consultation with a statistician via a Statistical Analysis System® using SAS® Release 9.3. Demographic and clinical data were expressed as frequency percentages, with confidence intervals, where feasible, and as means, medians, inter-quartile ranges, minimum and maximum values, where appropriate.

All four sections, comprising ten questions each, were counted and a percentage was calculated from a total of 40 marks. Results ≥ 50% were considered to be valuable and participants were deemed to be competent in the monitoring, prevention and prescribing of ototoxic medication. Those who scored less than 50% were deemed to be lacking knowledge. There was not a statistical significant correlation between the ages and the number of participants who passed as determined by the Pearson and Spearman correlation ($p=0.4466$).There was no statistical significance in the correlation of designation and the number of participants that passed as determined by the Pearson and Spearman correlation ($p=0,5296$).

RESULTS AND DISCUSSION

Results

The number of medical practitioners in the paediatric department totalled 30, of which 24 gave consent to partake in the study. The response rate was therefore 80% for the medical practitioners who completed the questionnaire and could therefore be evaluated for the study site.

Socio-demographic characteristics

The majority of participants (15: 62,5%) were female medical practitioners . All the participants were practising as medical practitioners and registered with the Health Professions Council of South Africa (HPCSA). Each of these participants was allocated to the paediatric wards where they were specialising and therefore rotated through the oncology ward. The majority of participants (17: 70,83%) were registrars and the remaining seven (29%) were consultants. The group of participants were of different ethnicity, 21 (88%) were African, two (8%) were white and one (4%) participant was coloured. The majority of participants were between the ages of 31-40 years and were equally spread between the 31-35 year age group (29%) and 36-40 year age group (29%). The remaining participants were either younger than 30 years (25%) or older than 40 years (16%).

Pharmacotherapy Induced Ototoxicity

Table 1 illustrates the participant's response to Section A of

Table 1: General knowledge on pharmacotherapy-induced ototoxicity.

No	Perception	Correct answer	Incorrect answer	Total n=24
1	What is ototoxicity	24 (100%)	0 (0%)	24 (100%)
2	Signs of ototoxicity	21 (87,5%)	3 (12,5%)	24 (100%)
3	Drug that doesn't cause ototoxicity	15 (62,5%)	9 (37,5%)	24 (100%)
4	Patients at risk for ototoxicity	16 (66,7%)	8 (33,3%)	24 (100%)
5	Aminoglycoside ototoxicity reversible	12 (50,0%)	12 (50,0%)	24 (100%)
6	When does NSAIDS cause ototoxicity	15 (62,5%)	9 (37,5%)	24 (100%)
7	What ototoxic related side-effect does Aspirin cause	10 (41,7%)	14 (58,3%)	24 (100%)
8	What cancer drug causes ototoxicity	6 (25,0%)	18 (75,0%)	24 (100%)
9	What antibiotic causes ototoxicity	21 (87,5%)	3 (12,5%)	24 (100%)
10	Ototoxicity is caused by	11 (45,8%)	13 (54,2%)	24 (100%)
TOTAL		**151**	**89**	**240**

the questionnaire. From the responses 151 (63%) were correct. The entire group of medical practitioners (100%) knew what ototoxicity was and the majority of practitioners seemed to have a very good understanding of the antibiotics that caused ototoxicity (87,5%) and what the signs of ototoxicity were (87,5%). The majority (75%) however did not know which of the chemotherapeutic agents caused ototoxicity. Exactly half of the medical practitioners (50%) answered that aminoglycoside ototoxicity is irreversible. This section however indicated that the majority of participants had a good general knowledge on pharmacotherapy-induced ototoxicity.

Prevention of pharmacotherapy-induced ototoxicity

Table (2) illustrates the responses to Section B of the questionnaire. This provides an overview of the preventive measures for pharmacotherapy-induced ototoxicity. The average for correct responses for this section was more than 50% (128; 53%). Less than half (41,7%) of medical practitioners knew that *N*-acetylcysteine is otoprotective. However, 87.5% had a clear understanding of the *N*-acetylcysteine's properties of a free radical scavenger that protects a patient from the effects of ototoxicity. The minority (16,7%) of medical practitioners knew what duration of treatment with aminoglycosides caused ototoxicity.

Monitoring of pharmacotherapy-induced ototoxicity

Table (3) focuses on monitoring of pharmacotherapy-induced ototoxicity which includes signal measures to refer a patient for ototoxicity monitoring. It represents Section C of the questionnaire, and respondents scored just below 50% (48%). The majority (75%) of medical practitioners knew that OtoacousticEmissions (OAEs) were sounds generated by the hair cells in the cochlea and also knew what type of hearing loss cisplatin and vincristine causes. However 95,8% could not identify the type of hair cells in the cochlea that are affected by ototoxicity.

Prescribing Principles of Ototoxic Medicine

Table 4focuses specifically on the medical practitioner as Section D of the questionnaire reflected on the prescribing of ototoxic medicine. In this section 173 (72%) responses were correct. The majority (95,8%) of medical practitioners had a very good understanding of risk vs benefit ratio when prescribing ototoxic medication, as well as when to refer a patient while on ototoxic medication and counselling the patient about the effects of ototoxicity. However, 37,5% of medical practitioners did not clearly understand that ototoxicity could occur at therapeutic dosages.

Correlations between knowledge, perceptions and participant characteristics

The majority of medical practitioners (21: 87,5%) had an overall mark of ≥ 50 %. Those who failed were spread over the following age groups: Two (8%) were in the age group of 31-35 and one (4%) was in the 25-30 year age group.

Another correlation was drawn between the numbers of medical practitioners who passed according to their designation. None of the consultants failed, whereas three (12,5%) of the registrars failed.

The section with the most correct answers (173: 72,08%) was Section D, which addressed prescribing ototoxic medication. The section with the least number of correct answers (115: 47,92%) was Section C, which pertained to the monitoring of pharmacotherapy-induced ototoxicity.

DISCUSSION

The study evaluated medical practitioner's knowledge and perceptions on pharmacotherapy-induced ototoxicity. To the best of our knowledge, this study is the first to assess these aspects amongst paediatric registrars and consultants working in a paediatric oncology unit.

The majority (63%) of medical practitioners were females and of African ethnicity (88%). In recent years the number of female medical practitioners has grown immensely [32]. The majority (58%) of participating medical practitioners were between 31 and 40 years of age and the majority (71%) were registrars.

For all sections, medical practitioners performed the best (72%) in the section on prescribing of ototoxic medication and scored 63% in the section on general knowledge on pharmacotherapy-induced ototoxicity. The section on the

Table 2: General Knowledge on Prevention of Pharmacotherapy-induced Ototoxicity.

No	Perception	Correct answer	Incorrect answer	Total n=24
1	ACC is otoprotective when using ototoxic medication	10 (41,7%)	14 (58,3%)	24 (100%)
2	Measures that are preventive for patients receiving ototoxic medication	17 (70,8%)	7 (29,2%)	24 (100%)
3	Which drug's properties of protection a free radical scavenger	21 (87,5%)	3 (12,5%)	24 (100%)
4	Is it okay to use more than one ototoxic drug in low dosages	8 (33,3%)	16 (66,7%)	24 (100%)
5	Aminoglycoside ototoxicity presents after how long	4 (16,7%)	20 (83,3%)	24 (100%)
6	Damage to the vestibular organ causes which side-effects	13 (54,2%)	11 (45,8%)	24 (100%)
7	Past history of hearing loss should not take ototoxic drugs	9 (39,1%)	15 (62,5%)	24 (100%)
8	Patients that are susceptible to aminoglycoside ototoxicity	20 (83,3%)	4 (16,7%)	24 (100%)
9	Reversible hearing loss should not be monitored for ototoxic effects	18 (75,0%)	6 (25,0%)	24 (100%)
10	Strategies to minimize ototoxicity	8 (33,3%)	16 (66,7%)	24 (100%)
TOTAL		**128**	**112**	**240**

Table 3: General Knowledge on Monitoring of Pharmacotherapy-induced Ototoxicity.

No	Perception	Correct answer	Incorrect answer	Total n= 24
1	OAE's are sounds generated by the cochlea's sensory hair cells in response to auditory stimulation	18 (75,0%)	6 (25,0%)	24 (100%)
2	Pharmacotherapy-induced hearing loss affects	5 (20,8%)	19 (79,2%)	24 (100%)
3	OAEs are used to	10 (41,7%)	14 (58,3%)	24 (100%)
4	Side-effects related to damage to the cochlea	12 (50,0%)	12 (50,0%)	24 (100%)
5	Hair cells are more susceptible to ototoxic damage	1 (4,2%)	23 (95,8%)	24 (100%)
6	Cisplatin and Vincristine causes which type of hearing loss	18 (75,0%)	6 (25,0%)	24 (100%)
7	High frequency sensorineural hearing loss is caused by damage to the	16 (66,7%)	8 (33,3%)	24 (100%)
8	When should baseline audio be done	11 (45,8%)	13 (54,2%)	24 (100%)
9	Pure-tone audiometry tests determine	6 (25,0%)	18 (75,0%)	24 (100%)
10	Start monitoring when patient experiences side-effects	18 (75,0%)	6 (25,0%)	24 (100%)
TOTAL		**115**	**125**	**240**

Table 4: General Knowledge on Prescribing of Ototoxic Medication.

No	Perception	Correct answer	Incorrect answer	Total n=24
1	A patient can receive more than two ototoxic medicine as long as the doses are not high	12 (50,0%)	12 (50,0%)	24 (100%)
2	What should be done if a patient starts experiencing ototoxic effects	18 (75,0%)	6 (25,0%)	24 (100%)
3	When prescribing ototoxic drugs, the risk to benefit ratio should always be taken into consideration	23 (95,8%)	1 (4,2%)	24 (100%)
4	Patients with ototoxic effects should be referred after the treatment has finished	23 (95,8%)	1 (4,2%)	24 (100%)
5	Which of the following drugs can be used concurrently with ototoxic medicine to try and minimize the ototoxic effects	19 (79,2%)	5 (20,8%)	24 (100%)
6	Audiologic monitoring should be initiated	23 (95,8%)	1 (4,2%)	24 (100%)
7	Patients receiving ototoxic drugs should not be counselled about the possible effects as this will prevent treatment compliance	23 (95,8%)	1 (4,2%)	24 (100%)
8	Most ototoxic drugs do not cause hearing loss when given at therapeutic doses	9 (37,5%)	15 (62,5%)	24 (100%)
9	Which of the following drugs are the most ototoxic	9 (37,5%)	15 (62,5%)	24 (100%)
10	Patients with a past history of hearing loss should not take any ototoxic medicine	14 (58,3%)	10 (41,7%)	24 (100%)
TOTAL		**173**	**67**	**240**

prevention of pharmacotherapy-induced ototoxicity scored 53% and the section that handled monitoring pharmacotherapy-induced ototoxicity scored the least at 48%.

Further to this, in Section A the majority (87,5%) of medical practitioners knew that the signs of cochleotoxicity included hearing loss and/or tinnitus, while those of vestibulotoxicity consisted of disequilibrium and dizziness [33]. Seventy percent of medical practitioners did not know that cisplatin is the cancer drug that causes severe ototoxicity. According to literature, cisplatin-related ototoxicity in paediatrics occurs in up to 70% [34]. The severity of hearing loss appears to be worse at high frequencies (4–8 kHz) and is related to the cumulative dose of cisplatin. Half the participants (50%) are under the impression that aminoglycoside ototoxicity is reversible. However, aminoglycosides cause irreversible damage to both the auditory and vestibular organs [33].

In Section B, less than half (41,7%) of medical practitioners knew that *N*-acetylcysteine is otoprotective. According to literature several trials tested the efficacy of otoprotective treatments against the ototoxic effects of cisplatin. Drugs, such as sodium thiosulfate, amifostine, *N*-acetylcysteine, salicylate, ebselen, lactate, dexamethasone, and Ginkobiloba extract were tested. Literaturereported positive otoprotection evidence for intra-thecal *N*-acetylcysteine [12]. However, the vast majority of medical practitioners (87,5%) had a good understanding of the free radical scavenger properties of *N*-acetylcysteine.

In Section C, the majority of medical practitioners knew what OAEs were used to evaluate the cochlear outer hair cell system, and that early changes in the OAE may reflect on cochlear damage [35]. With normal functioning of the middle ear, the OAE reflects the functional status of the cochlea [35]. The minority of medical practitioners (4,2%) knew that the outer hair cells of the cochlea are first to be affected by ototoxicity.

In Section D, the majority (95,8%) of medical practitioners knew that, when prescribing ototoxic drugs, referral to audiology should happen before, during and after treatment. According to literature monitoring before, during and after treatment is an important component in the early detection and management of hearing loss in young cancer patients [36]. However, medical practitioners scored an overall of 72% for the section on prescribing, and the majority (62,5%) were not aware that ototoxicity can occur at therapeutic dosages.

In similar research studies the findings indicated that the majority (88%) of the participants knew and understood pharmacotherapy-induced ototoxicity. The findings from a study indicated that even though general practitioners were aware of their role in ototoxicity monitoring, they did not appear to carry out monitoring strategies [37]. These findings are also in line with this study's findings, as the section that dealt with the monitoring of pharmacotherapy-induced ototoxicity, scored the least correct answers (48%).

CONCLUSION

The medical practitioner, as part of the MDT treating and caring for these patients, should be knowledgeable of and understand the degrading consequences that potential hearing loss could have in this vulnerable population. Therefore, the medical practitioner should also be knowledgeable of the monitoring parameters related to ototoxicity. Baseline audiometry is of absolute importance to enable the audiologist to monitor the decline in hearing due to damage of the cochlea. Ototoxicity monitoring guidelines should be standardised to equip the medical practitioner on when to refer a patient and how to monitor the patients.

LIMITATIONS

The study only focussed on pharmacotherapy-induced ototoxicity in the paediatric oncology population. Therefore, the number of participants was small. It also excluded other ototoxic medication such as macrolide antibiotics, diuretics, other aminoglycosides and quinolones.

RECOMMENDATIONS

It is recommended that similar studies be performed with all medical practitioners in all specialities across different hospitals. A multi-centre approach would give a clearer view of the knowledge medical practitioners have about ototoxicity.

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Cite this article

Smith N, Schellack N, Ehlert K, Gous AGS (2017) Ototoxic Hearing Loss in Paediatrics – Knowledge and Perceptions Amongst Medical Professionals - L'habit Ne Fait Pas Le Moine. J Ear Nose Throat Disord 2(2): 1022.