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Screening and Monitoring of Pharmacotherapy-Induced Ototoxicity in Patients at Dr George Mukhari Academic Hospital

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- Pharmacological ototoxicity monitoring
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Abstract

Pharmacotherapy-induced ototoxicity is a growing problem as highly effective and low-cost drugs are prescribed without the necessary monitoring being done. This study was done to identify and describe medicines with the potential to cause ototoxicity as part of treatment regimens. This study describes the type of ototoxicity caused and the prevalence of ototoxicity in this study population. Participants already on treatment with potential ototoxic medicine and newly initiated participants were referred to the ototoxicity clinic. Both adult and paediatric patients were included in the study. Screening of the patients' current treatment regimen with subsequent identification of medicines was done prospectively by the pharmacist and the audiological evaluations were done by audiologists. Fifty-two patients were enrolled in the study, and all of these patients' treatment regimens included one or more ototoxic agent. Irreversible cochleotoxicity in the high and lower frequencies were seen in the majority of patients treated with aminoglycosides and in patients treated with platinum compounds, although mostly in the high frequencies. High-frequency hearing loss, both reversible and irreversible, was also identified in patients treated with loop diuretics. Hearing loss in the high frequencies occurred in almost two thirds of the study population. This study highlights the need for a clinical pharmacist, together with an audiologist, functioning within a multi-disciplinary team, as well as the implementation of ototoxicity monitoring programs in South Africa.

INTRODUCTION

Specific attention should be paid to high risk-patients treated with ototoxic medications. Such patients include those with multi-drug resistant tuberculosis (MDR-TB), patients with renal failure [1], oncology patients [2] and neonates with severe infections or sepsis, treated in the neonatal intensive care unit [3]. Hearing loss in an individual can lead to poor communication and social isolation such as academic and occupational difficulties [4]. This highlights the need for establishing and implementing ototoxicity monitoring programmes in public and private sector hospitals in Gauteng, South Africa [5].

Ototoxicity is defined as *"the tendency of certain substances, either systemic or topical, 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 eighth cranial nerve"* [6]. Reference to the term 'ototoxicity' refers to both cochleo- and/or vestibulotoxicity. Ototoxicity can start with damage to the basal region of the cochlea, where the higher frequency sounds are coded, and the damage can further progress to the apex of the cochlea, where the lower frequency sounds are coded [7]. Hearing loss as a result of ototoxicity may be reversible or irreversible, depending on the type of ototoxic medicine being used for the treatment regimen of the patient. Examples of drugs causing irreversible hearing loss are

aminoglycosides and platinum compounds (e. g. cisplatin). The loop diuretics, salicylates and NSAIDs cause reversible hearing loss [8]. However, evidence exists that suggests permanent hearing loss results from the use of loop diuretics [9].

Hearing problems can start within minutes to several days after the administration of an ototoxic drug, or it can only start presenting several years after the treatment [5]. Early detection of ototoxic damage can improve the treatment outcome through minimizing hearing loss progression and by counselling and rehabilitation of the patient [10]. The standard protocol for ototoxicity monitoring is baseline and serial measurements of pure tone hearing thresholds within the 250 to 8000Hz frequency range. However, extended high frequency (EHF) pure tone thresholds (9000 - 16000Hz) as well as evoked otoacoustic emissions (OAE's) are more sensitive to initial ototoxic damage and detects changes in auditory function before ototoxicity affects hearing that is important for speech discrimination [11,12]. Tympanometry, for the evaluation of the middle ear function, is often needed to confirm site of lesion when OAE's are affected [13].

Pharmacists play an important role in the screening and monitoring of pharmacotherapy-induced ototoxicity by identifying and monitoring ototoxic agents in patients' treatment regimens and informing the treating physician and audiologist about the ototoxic medicine's characteristics. They can also perform therapeutic drug monitoring to reduce the occurrence of ototoxicity if applicable and where necessary [9]. Audiologists, in turn, has an important role and responsibility to inform and counsel patients on their hearing status and to inform the rest of the multidisciplinary team about any changes in patients' hearing [9].

METHODOLOGY

The study aimed to describe audiological findings in patients that were exposed to medicines that were potentially ototoxic. The process included the screening and monitoring of patients who are at risk for hearing loss because of such treatment regimens.

Study design

A prospective, observational study design was followed, with descriptive research analysis. Screening of the participants' current treatment regimen was done by the pharmacist and the audiological testing was done by the audiologist.

Study site

Ambulant participants were tested at the Skills laboratory of a higher education institution, or alternatively in the Department Speech Therapy and Audiology at the tertiary hospital. Patients who were in the hospital and who were too sick to walk were tested in the ward.

Study population and sampling

The participants who were included in the study were those who were referred to the ototoxicity clinic, by health care professionals, who were already on treatment with potential ototoxic medicine, or those who were initiated on ototoxic treatment regimens. Patients initiated on any potentially ototoxic medicine, as outlined in the literature review, were included and indicated on a designed checklist for each individual participant (refer to Appendix A). Both adult (19 – 65 years) and paediatric patients (0 – 18 years) including neonates, were involved in the study. Patients who were excluded were those, who after an otoscopic examination, were found to have unilateral/bilateral/ partially impacted cerumen.

Data collection

At the clinic the participant or the parent/caregiver was provided with a participant information leaflet. The pharmacist screened the participant's prescription and assessed the risk of reversible and/or irreversible ototoxicity. Patients' history was taken of previous exposure to ototoxic medicine by screening patients' files for previous prescriptions of ototoxic medicine. An audiological history was taken by the audiologist with a questionnaire, regarding previous hearing injuries or complaints or family history. The standard protocol for ototoxicity measuring could not be followed. Baseline measurements were not possible as participants had started taking the ototoxic medicines when monitoring was initiated. Furthermore, diagnostic pure tone thresholds were not possible as testing took place in the wards and reliable equipment for diagnostic testing is not mobile. DPOAE's are especially valuable in monitoring ototoxicity in very young children who may not consistently provide reliable behavioural testing results. The measurement of DPOAE's is objective and non-invasive and does not require active participation. The audiological evaluation conducted by the audiologist therefore included otoscopic evaluation, tympanometry and diagnostic distortion product otoacoustic emission (DPOAE) testing with frequencies of up to 8000 Hz. All equipment was checked and calibration was confirmed by the audiologist. The results of the evaluation, together with suitable recommendations were presented in a combined report compiled by both the pharmacist and the audiologist. . Follow-up evaluations were requested where necessary.

Ethical considerations

Ethical consent was obtained from the relevant statutory parties, including the Research and Ethics Committee from the tertiary institution (MREC/H/101/2013: PG). An information leaflet was provided to all participants and informed consent was obtained. Informed assent was obtained from older children above seven years of age, and consent was obtained from the parents or caregivers. Adequate translators were used in cases where English could not be understood by participants, parents or caregivers.

RESULTS

Demographics

During the study period of eight months, 52 participants were enrolled in the study, with a total of 88 participant visits. Each participant had an average of 1. 7 visits to the clinic as participants could be evaluated more than once at the clinic, depending on their specific treatment regimen.

Patient Age

The total participant population (n=52) consisted of 30 (58%) adults and 22 (42%) paediatric participants, which included ten neonates, as illustrated in Figure A.

The mean age for participants in the paediatric population was 6.23 years (SD; 4.18), neonates six days (SD; 3. 8), and adults were 42.17 years old (SD; 10.59). A breakdown of the various groups is reflected in Table 1.

Ototoxicity related to age

Of the total study population 13 paediatric participants (59%, n=22) and 22 adult participants (73%; n=30) presented with a hearing deficit. There was no statistically significant difference (p = 0. 402; Fisher exact method) in the number of participants that presented with hearing deficits, as differentiated by age groups; this is illustrated by Figure B.

Participant Gender

Of the 52 participants enrolled in the study, 22 (42.3%; n=52) were female and the remaining 30 (57.7%; n=52) were male. Female participants consisted of 13 adults, five paediatric participants and four neonates. The male participants consisted of 17 adults, seven paediatric participants and six neonates (refer to Figure C). No statistically significant difference (p = 1.000; Fisher exact method) was found between the two genders.

Ototoxicity related to gender

Figure D illustrates hearing deficits in the male and the female population respectively. Slightly more male participants (18; 60%; n=30) presented with a hearing deficit than female participants, who were17 (77. 3%; n=22). There was no statistically significant difference (p = 0. 240; Fisher exact method) in hearing deficits between the male and female population.

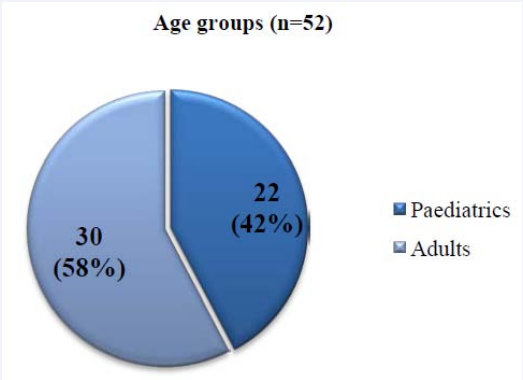

Figure A Participants divided into age groups.

Table 1: Mean values and ranges of age groups.

	Mean	Minimum	Maximum
Neonates	6 days	2 days	12 days
Paediatric	6.34 years	1.08 years	14 years
Adults	42.17 years	19 years	65 years

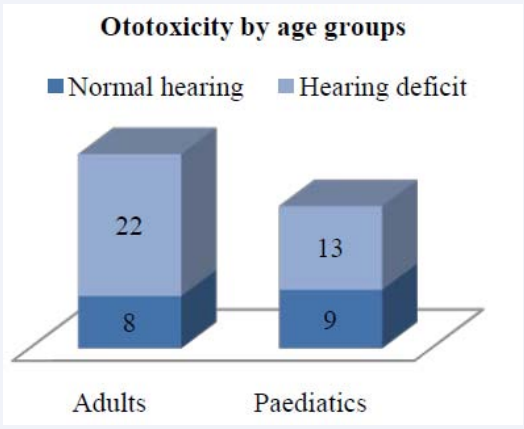

Figure B Hearing deficits in different age groups.

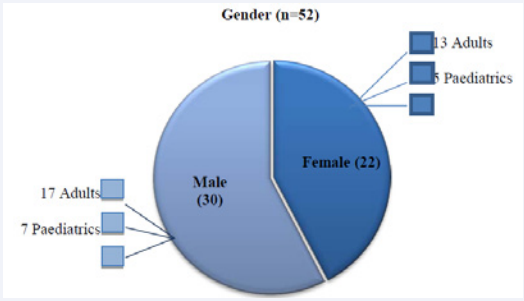

Figure C Participant gender per age group.

Diagnoses

Organ systems affected and diagnoses made are referred to as participant visits. The researcher checked diagnoses at every participant visit. Diagnoses can also affect hearing ability. The organ system mostly affected during this study was the neoplasms (C00-D49), with 37 (42%; n=88) participants visits. All of these participants were evaluated more than once. Other organ systems affected were those involved in diseases related to the genitourinary system 28 (32%; n=88); conditions originating during the perinatal period 19 (21. 6%; n=88); and certain infections and parasitic diseases. The different organ systems affected during the study period is illustrated in Figure E.

Diagnoses most commonly encountered during this study were chronic kidney disease with 28 (32%, n=88) participant visits, osteosarcoma with 14 (16%, n=88) participant visits, retinoblastoma with nine (10%, n=88) participant visits, nephroblastoma and primitive neuro-ectodermal tumour, with seven (8%, n=88) participant visits each.

Medication related to ototoxicity

Figure F, indicates the prescribing patterns of ototoxic medication in this specific study population. The medication was reviewed during each participant visit; henceforth referred to as participant visits.

The pharmacological classes that were mostly identified as part of the prescribing patterns of ototoxic medicines during

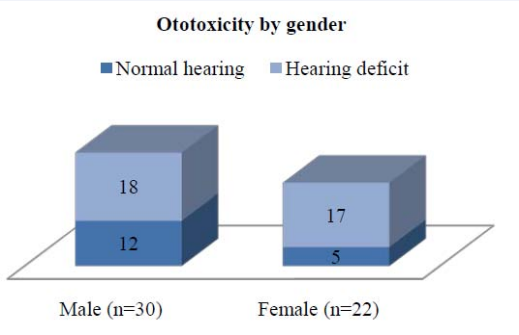

Figure D Hearing deficits related to gender.

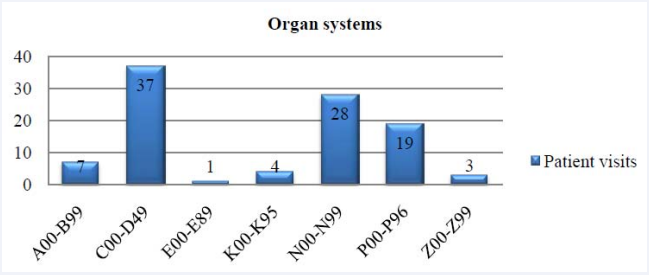

Figure E Organ systems affected during the study period.

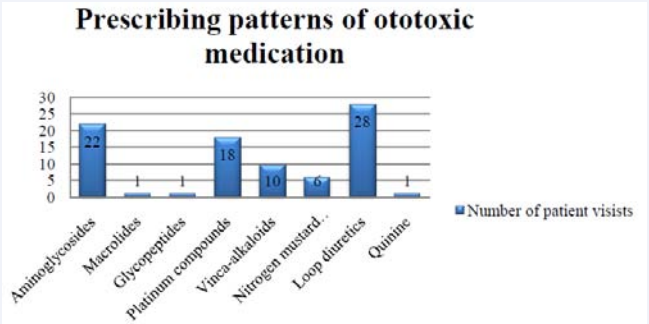

Figure F Number of participant visits per ototoxic medication class.

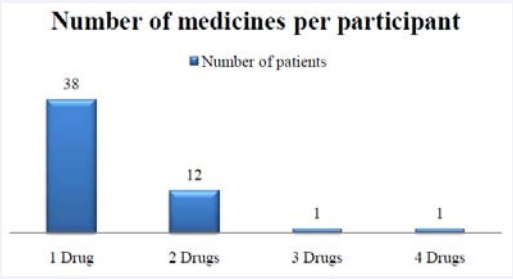

Figure G Number of ototoxic agents per participant.

the data collection process were: aminoglycosides with 22 participant visits (25%; n=88), platinum compounds with 18 participant visits (20. 5%; n=88) and loop diuretics with 28 participant visits (32%; n=88).

Table 2 provides information on the route of administration, the mean daily dose (DD) with the minimum and maximum dose of each ototoxic drug, and the mean duration of treatment (DOT) of the ototoxic drugs. Amikacin was the most often prescribed agent, with a mean DD of 133. 1mg IV in one adult and 13 paediatric patient visits and 750mg IM in one adult patient visit and a mean DOT of 5.3 days for the participants that received IV amikacin, and 180 days for the participant receiving IM amikacin. Macrolide antibiotics, i. e. erythromycin had a mean DD of 2000mg IV and a mean DOT of five days for one adult patient visit. Vancomycin had a mean DD of 1000mg IV and a mean DOT of seven days in one adult patient visit. Although vincristine was the most often prescribed antineoplastic agent, with a mean DD of 0.9mg IV and a mean DOT of 1.2 days in 10 paediatric patient visits, cisplatin resulted in more cases of hearing loss, with a mean DD of 123mg IV and a mean DOT of only one day in nine paediatric patient visits. Furosemide, a loop diuretic, had a mean DD of 232.7mg per mouth and a mean DOT of 1092.4 days. The long duration of treatment with loop diuretics was due to chronic renal failure. The antimalarial, quinine, had a mean DD of 900mg IV and a mean DOT of 5 days in one paediatric patient visit.

Number of ototoxic medicines per participant

The majority of participants (38; 73. 1%; n=52) were treated with only one ototoxic agent and 12 (23.1%; n=52) participants were treated with two ototoxic agents. One (1.9%; n=52) participant was treated with three and another one (1.9%; n=52) was treated with four ototoxic agents, as illustrated in Figure G.

Incidence of pharmacotherapy-induced ototoxicity

Figure H illustrates the effect of the medicine on hearing for the 88 patient visits for the 52 participants.

Of the 21 participants treated with aminoglycosides, 13 (61.9%) participants presented with decreased DPOAE's bilaterally. Of these 13 participants cochlear damage was mostly seen in high frequencies (4000 – 8000Hz) in five neonates who received IV amikacin, in three paediatric participants who received IV amikacin or gentamicin and in three of the five adults who received IV amikacin or gentamicin. The other two adult MDR-TB participants received IM amikacin or streptomycin

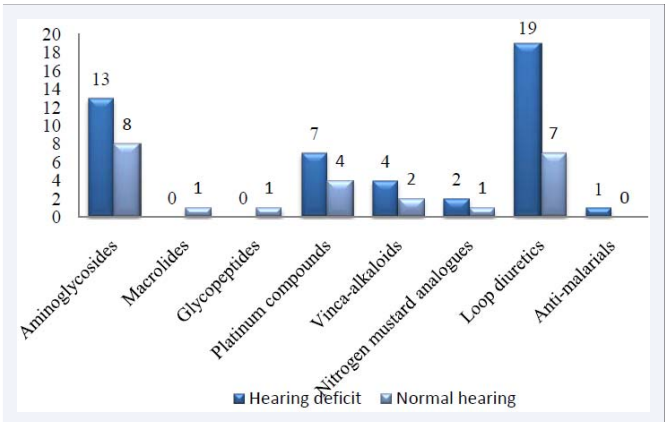

Figure H Hearing deficits versus normal hearing in participants related to each class of ototoxic agents.

and a decrease in DPOAE's was noticed at all frequencies. One participant treated with IV macrolides and IV glycopeptides presented with measurable DPOAE's within normal limits when either of the two agentswere taken. Overall 11 paediatric participants were treated with IV platinum compounds of which seven (63.6%) presented with cochleotoxicity, especially at the higher frequencies (4000 – 8000Hz) as decreased DPOAE's were measured bilaterally. The results showed that from those participants who were treated with vinca-alkaloids (n=6) and with nitrogen mustard-analogues (n=3), there were four (66.7%; n=6) and two (66.7%; n=3) participants respectively who presented with decreased DPOAE's, which indicated cochlear damage in the high frequencies (4000 – 8000Hz). Loop diuretics were administered to the adult participants (n=27) mostly orally, apart for one participants who received IV furosemide. Of the 28 participants, there were 19 (67.9%) who presented with decreased DPOAE's and cochleotoxicity. Hearing loss was mostly observed in the high frequencies (4000 – 8000Hz), although in eight of the 19 participants (42%)the lower frequencies seem to have been affected (500 - <4000Hz). In the single paediatric participant who was treated intravenously with the antimalarial quinine, presented with decreased DPOAE's, with cochleototoxicity observed only at 8000Hz.

Pharmacist and Audiologist interventions and recommendations

Most of the interventions and recommendations made by the pharmacist included the monitoring and screening of patients when they were identified as being treated with an ototoxic medication (19; 36.5%; n=52), or when treated with a combination of ototoxic agents (8; 15.4%; n=52). Patients were re-evaluated according to their specific treatment regimen (20; 38.5%; n=52). The discontinuation of ototoxic medicine was suggested for two patients (3.8%; n=52). Six patients (11.5%; n=52) were referred for diagnostic audiological evaluations. Therapeutic drug monitoring (TDM) was initiated with peak and trough levels in four patients (7. 8%; n=52), of whom one patient (1.9%; n=52) was treated with vancomycin. The other three patients (5.8%; n=52) were treated with amikacin of whom one had inconclusive results, and in another only the trough level was obtained and no calculations could be done. The last patient's dose was calculated correctly and increased. More than one intervention (range: 1–3) could be made per patient.

DISCUSSION

Demographics and demographics related to ototoxicity

The study population consisted of more adult (58%) than paediatric participants. The neonatal population was included in the paediatric population. Half (50%) of the neonates included in the paediatric population presented with decreased DPOAE's at frequencies of 4000-6000Hz. Hearing loss in these frequencies affect speech discrimination and therefore will have a detrimental effect on children's language development and learning abilities [14]. All of the neonates included in this study were treated with amikacin for at least five days. Such results are contrary to previous research [15] which reported the incidence of aminoglycoside-induced ototoxicity in neonates as only 2%, although this could have been influenced by other factors. These include underlying diseases and severe infections, including birth asphyxia, hypoxia, neonatal sepsis, and prematurity, which are known indicators of high risk for dysfunction of the auditory pathway [16].

Two-thirds of the paediatric population (66. 7%) in this study, excluding the neonates, presented with decreased or absent DPOAE's. Most of these paediatric participants were treated with platinum compounds. Children who have an increased risk of ototoxicity include those who are younger than the age of five years, those with renal dysfunction and with concomitant treatment of more than one ototoxic agent [11]. Although a few studies stated that children of a younger age are at a higher risk of developing ototoxicity from treatment with platinum compounds than the adult population [17,18], these also stated that all adult participants may experience a progression of hearing loss over time and this may relate to other hearing insults or presbycusis

Table 2: Ototoxic medicine with their route of administration, daily dose and the number of participant visits per drug.

	Pharmacological classification	Drug	ATC code	ROA	Mean DD (mg)	Min dose (mg)	Max dose (mg)	Mean DOT (days)	Number of adult participant visits	Number of paediatric participant visits
Antibiotics	Aminoglycosides	Amikacin	J01GB06	IV	133.1	20	550	5.3	1	12
				IM	750	750	750	180	1	
		Gentamicin	J01GB03	IV	87.1	40	150	3.1	3	4
		Streptomycin	J01GA01	IM	750	750	750	9	1	
	Macrolides	Erythromycin	J01FA01	IV	2000	2000	2000	5	1	
	Glycopeptides	Vancomycin	J01XA01	IV	1000	1000	1000	7	1	
Antineoplastic agents	Platinum Compounds	Cisplatin	L01XA01	IV	123	45	162	1		9
		Carboplatin	L01XA02	IV	212.3	100	430	1.9		9
	Vinca alkaloids	Vincristine	L01CA02	IV	0.9	0.7	1.2	1.2		10
	N-mustard analogues	Ifosfamide	L01AA06	IV	2170	1800	2300	3		6
Diuretics	Loop diuretics	Furosemide	C03CA01	Oral	232.7	20	500	1092.4	28	
Antimalarials	Antimalarial	Quinine	P01BC01	IV	900	900	900	5		1

[18,19]. Even though the majority of the adult population (73%) in this study had some form of cochleotoxicity, literature stated that hearing loss is more detrimental in children than in adults because of the effect on their social, language and academic development [20].

Slightly more males (57.7%) than female participants were admitted to the study. The results showed a higher prevalence (77.3%) of hearing impairment in the female population, which was not statistically significant. Previous research [18] with humans, however, found males to be four times more likely to develop hearing loss than the females.

Diagnoses

Chronic conditions, such as chronic kidney disease and various neoplasms were the most common diagnoses during the patient visits. There are a number of studies supporting the relationship between chronic kidney disease and toxicity with furosemide [21]. Diagnoses seen in cancer participants in this study relates to common diagnoses seen in literature [11]. Only a few participants with MDR-TB were evaluated during this study period, as Dr George Mukhari Academic Hospital is not a referral treatment center. Patients with MDR-TB need expert monitoring of therapy and should therefore be managed in specialized centers [22].

Medicine related to ototoxicity

The ototoxic medications mostly prescribed in this study were the aminoglycosides (25%), the platinum compounds (20.5%) and the loop diuretics (32%), which are in accordance to the ototoxic medication that have been studied and described most in literature[15,21,23,24], refer to Appendix A.

Aminoglycosides were given intravenously for three to five days, and intramuscularly for nine to 180 days. Participants that received aminoglycoside therapy for a period of more than five days (n=12) with mean doses of amikacin at 133.1mg IV, gentamicin 87. 1mg IV and streptomycin 750mg IM, showed weaker responses in audiological evaluations, especially in the high frequencies (4000-8000Hz) as tested with OAEs. MDR-TB participants (n=2) that were treated with high doses of aminoglycosides (750mg daily) for long periods of time (180 days) showed a cochleotoxicity at all emissions and at all frequencies. Literature states that aminoglycoside-induced ototoxicity is more likely to occur with higher dosages, high blood concentration levels, or prolonged duration of therapy [15,25], which correlates well with the results found in this study. No cochleotoxicity was observed in participants treated with erythromycin 2000mg IV for five days or with vancomycin 1000mg IV for seven days.

Paediatric participants were the only participants treated with intravenous platinum compounds (mean dose of cisplatin 123mg or carboplatin 212.3mg) in this study. They presented with decreased DPOAE's, mostly in the high frequencies after one to two doses in almost every cycle of treatment. Such results correlates well with previous research [15] where cumulative and high dosages of platinum compounds were found to be factors indicating a high risk for cochleotoxicity in the high frequencies first, then the lower frequencies with higher or cumulative dosages [26]. Even though ototoxicity in children is poorly described, studies have shown that because the effects on hearing is often permanent it can have a significant impact on a child's social development, understanding of language and production of speech, academic achievements and quality of life [20]. Although literature states that both vinca-alkaloids and nitrogen mustard analogues are ototoxic [27], all of the participants' treatment regimens that included either one of these two agents, included a platinum compound as well. Thus, the cochleotoxicity noticed in these participants cannot be directly related to either one of these two classes on its own, but rather to the combination of ototoxic agents in the treatment regimens. All the participants treated with loop diuretics received furosemide orally, except for one patient who received it IV. It was noted that the participants treated with furosemide mostly presented with cochleotoxicity in the high frequencies when on treatment for five years or longer and when on very high dosages of 250mg to 500mg daily. These findings correlate with literature stating that high-dose (≥240mg) oral furosemide therapy has been associated with ototoxicity [21]. The participants that presented with cochleotoxicity in the lower frequencies might have been due to previous exposure to other ototoxic agents (e. g. aminoglycosides, salicylates) as indicated in literature [20]. The patient treated with intravenous quinine 900mg presented with cochleotoxicity in the high frequencies after five days of treatment, which is in accordance with literature indicating that hearing loss usually appears in the high frequencies and is reversible [28].

The number of ototoxic agents per patient (range: 1–4) is indicative of individual variability in susceptibility to ototoxicity of different ototoxic agents. Ototoxicity should thus be monitored for each individual patient due to the fact of individual variability in susceptibility in ototoxicity [11], especially for participants who may present with ototoxicity presumably due to genetic predisposition for aminoglycosides [29].

Incidence of pharmacotherapy-induced ototocixicity

The incidence of hearing impairment in participants treated with aminoglycosides (61.9%) is higher as compared to literature which states that hearing loss varies between a few percent up to 33% [3,30]. Platinum compound-induced hearing impairment showed a prevalence (63.6%) that was equal to what was described in literature (22-70%) [18]. Although the data suggesting the incidence of furosemide-induced hearing impairment is poor and it only suggests a low incidence, the prevalence of furosemide-induced hearing impairment was much higher (73.1%) in this study population than what was described in literature [21]. This might be due to patients on treatment with furosemide for extended periods of time due to chronic kidney disease. Comparing the one patient in this study population that was treated with quinine to the literature available on quinine-induced hearing impairment [28] does not reflect a reliable correlation. Vestibulotoxicity could not be tested as some of the participants were not ambulant.

Pharmacist and Audiologist interventions and recommendations

Interventions and recommendations most commonly made by the pharmacist focused on the monitoring and screening of patients on ototoxic medication; these interventions included

discontinuation or referral. TDM was done successfully in only one patient where dosage adjustments were made, the other three patients had inconclusive results thus no interventions could be made [9]. Interventions by the audiologist included counseling patients on their hearing status and further diagnostic audiological evaluations and interventions if necessary. Such monitoring of patients with ototoxicity by the pharmacist as well as the audiologist was previously described in literature [9].

Limitations and challenges

The referral rate from physicians for ototoxicity monitoring was low as this study was done prospectively and the ototoxicity clinic was a new initiative. The audiology equipment used in this study was noise sensitive, which made audiological evaluations to be challenging, especially when testing was done in the wards where there was a lot of background noise. Pure tone measurements could not be performed due to limitations in mobility of diagnostic audiological equipment. The equipment used for the audiological testing in this study was only able to test up to 8000Hz and extended high frequency (EHF) pure tone measurements are recommended in ototoxicity protocols as ototoxicity can appear in frequencies higher than 8000Hz. Vestibulotoxicity was not evaluated in this study and should be considered in future research. Baseline audiological evaluations could not be done for all patients due to the fact that patients were only referred to the clinic by physicians after initiation of the ototoxic medications. The results of this study cannot be generalized to other contexts because of the limited sample size that was available in this specific context.

RECOMMENDATIONS

The importance of timely referrals should be emphasized to health care practitioners (e. g. doctors, nurses, pharmacists and audiologists), as baseline audiograms need to be performed prior to commencing with the treatment. The use of state-of-the art audiology equipment that is less noise sensitive, a sound level meter, as well as EHF pure tones should be considered for a follow-up study. A follow-up study with baseline audiological assessments of the medicines highlighted in this study, with higher frequency audiometry monitoring and with a larger sample size should be conducted. Future studies should include testing for vestibulotoxicity using appropriate equipment, as some of the medicines highlighted in this study (e. g. streptomycin, gentamicin, quinine, etc.) could be vestibulotoxic as well as cochleotoxic.

CONCLUSION

The need for a clinical pharmacist together with an audiologistin the management of ototoxicity is not well discussed in literature. The effect of ototoxic medication on hearing has been emphasized in this study, which in turn highlights the need for a multidisciplinary team including both a clinical pharmacist and audiologist for the identification, evaluation and monitoring of patients treated with ototoxic medicine. It is evident from this study that patients treated with ototoxic medication such as aminoglycosides and loop diuretics have a higher incidence of ototoxicity than was previously described in literature. The incidence of platinum compound-induced ototoxicity is in line with current literature. Two thirds of the patients treated with ototoxic medication presented with a cochleartoxicity making them high-risk patients for future treatments with such agents. The clinical pharmacist has an important role in drug monitoring and/or interventions for high-risk patients when it comes to risk-versus-benefit for the use of ototoxic medication in patients. This study also emphasizes the importance of collaboration between the members of the inter-disciplinary team, particularly the pharmacist and the audiologist. In turn, audiologists should closely monitor hearing, particularly in patients who use medication that could cause irreversible hearing loss. It is important that there is a clear line of communication between the pharmacist, the audiologist and the doctor.

REFERENCES

1. Xie J, Talaska AE, Schacht J. New developments in aminoglycoside therapy and ototoxicity. Hear Res. 2011; 281: 28-37.
2. Handelsman JA. Vestibular Ototoxicity: The Importance and Pragmatics of Monitoring. Seminars in Hearing. 2011; 32: 262-272.
3. Huth ME, Ricci AJ, Cheng AG. Mechanisms of aminoglycoside ototoxicity and targets of hair cell protection. Int J Otolaryngol. 2011: 937861.
4. Peer S, Fagan JJ. Hearing loss in the developing world: evaluating the iPhone mobile device as a screening tool. S Afr Med J. 2015; 105: 35-39.
5. De Andrade V, Hajat F, Khoza-Shangase K. Perceptions of oncologists at two state hospitals in Gauteng regarding the ototoxic effects of cancer chemotherapy: A pilot study. Afr J Pharm Pharmacol. 2009; 3: 307-318.
6. Roland PS, Rutka JA. Preface in: Roland, PS &Rutka, JA. Ototoxicity. London: Hamilton; 2004.
7. Dunckley KT, Fausti SA, Gordon JS, Konrad-Martin D, Leigh-Paffenroth E, et al. Objective Measures of Ototoxicity. Hearing and Hearing Disorders: Research and Diagnostics. 2005; 9: 10-16.
8. Blockman M, Sinxadi P. Clinical Pharmacology: Drug induced ototoxicity. Continuing Medical Education. 2009; 27: 372-373.
9. Schellack N, Naude A. An overview of pharmacotherapy-induced ototoxicity. S Afr Fam Pract. 2013; 55: 357-365.
10. Bratt GW, Coleman LL, Fausti SA, Gordon JS, Helt WJ, Konrad-Martin D, et al. Ototoxicity: Early Detection and Monitoring. The ASHA Leader. 2005.
11. Kraemer DF, Knight KR, Neuwelt EA, Winter C. Early changes in Auditory Function As a Result of Platinum Chemotherapy: Use of Extended High-Frequency Audiometry and Evoked Distortion Product Otoacoustic Emissions. J of Clin Oncolo. 2007; 25: 1190-1195.
12. Kemp DT. Otoacoustic emissions, their origin in cochlear function, and use. Br Med Bull. 2002; 63: 223-241.
13. Adlin D, Duffy J, Mikolai TK. A Guide to Tympanometry for Hearing Screening. 2006.
14. Audiology Department and Learning and Development Department, BC Children's Hospital. Effects of hearing loss on the ability to hear speech. 2006.
15. Mudd PA, Campbell KCM, Edmunds AL, Glatz FR, Rybak LP. Ototoxicity. 2012.
16. Chayasirisobhon S, Yu L, Griggs L, Westmoreland SJ, Leu N. Recording of brainstem evoked potentials and their association with gentamicin in neonates. Pediatr Neurol. 1996; 14: 277-280.

17. Grewal S, Merchant T, Reymond R, McInerney M, Hodge C, Shearer P. Auditory late effects of childhood cancer therapy: a report from the Children's Oncology Group. Pediatrics. 2010; 125: 938-950.

18. Egbelakin A, Gilbert J, Harris MS, Pisoni DB, Renbarger J, Yancey A. Risk Factors for Cisplatin-Associated Ototoxicity in Paediatric Oncology Patients. Pediatr. Blood Cancer. 2012; 59: 144-148.

19. Roland PS. Presbycusis. 2014.

20. Anderson K, Matkin N. Relationship of Degree of Longterm Hearing Loss to Psychosocial Impact and Educational Needs. 2007.

21. Baldwin KA, Budzinski CE, Shapiro CJ. Acute Sensorineural Hearing Loss: Furosemide Ototoxicity Revised. Hospital Pharmacy. 2008; 43: 982-987.

22. Njaramba P, Naidoo S. Managing multi-drug resistant tuberculosis in hospitalized patients: a review of treatment outcomes. South Afr J Epidemiol Infect. 2007; 22: 39-44.

23. Matz GJ, Schuman RM. Ototoxicity. Head & Neck Surgery – Otolaryngology. Fourth edition. 2006.

24. Li H, Steyger PS. Systemic aminoglycosides are trafficked via endolymph into cochlear hair cells. Sci Rep. 2011; 1: 159.

25. Duggal P, Sarkar M. Audiologic monitoring of multi-drug resistant tuberculosis patients on aminoglycoside treatment with long term follow-up. BMC, Ear, Nose and Throat Disorders. 2007; 7: 1-7.

26. Constine LS, Hobbie WL, Ruccione KS, Schwartz CL. Survivors of Childhood and Adolescent Cancer: A Multidisciplinary Approach. [Online]. Germany: Springer-Verslag. 2006.

27. Prepageran N, Rutka JA, Scott AR. Iron-Chelating and Other Chemotharepeutic Agents: The Vinca Alkaloids, (Chapter seven) in: Roland, PS & Rutka, JA. Ototoxicity. London: Hamilton. 2004.

28. Selimoglu E. Aminoglycoside-induced ototoxicity. Curr Pharm Des. 2007; 13: 119-126.

29. Rybak LP, Ramkumar V. Ototoxicity. Kidney Int. 2007; 72: 931-935.

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