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Full Length Research Paper

Ototoxicity in tuberculosis treatment in South Africa: Exploring the current status

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As a result of the known ototoxic effects of some of the medications used for tuberculosis (TB) treatment, healthcare workers involved in treating TB patients need to be aware of the ototoxic signs and when to refer to an audiologist for hearing monitoring. The main objective of the present paper was to determine the knowledge and management of ototoxicity related to TB treatment by South African healthcare workers. Telephonic interviews using a semi-structured interview schedule consisting of closed- and open-ended questions were conducted on 100 healthcare workers involved in the treatment of patients with TB. Findings were collated and analyzed via thematic analysis and quantitative descriptive statistics procedures. A large percentage of participants were not aware of what ototoxicity is and what the role of the audiologist was in the management of TB patients. All participating public health facilities do not work with an audiologist as a member of the team in the management of TB patients, and a stark lack of ototoxicity monitoring programs exists. Results highlight the need for education of health-care workers as well as patients regarding ototoxicity. Additionally, audiologists need to become more involved in establishing and implementing ototoxicity monitoring programs in facilities where ototoxic medications are prescribed.

Key words: Aminoglycosides, ototoxicity, tuberculosis, health care.

INTRODUCTION

Despite the fact that tuberculosis (TB) is a preventable and treatable disease, it is the oldest of the world's current pandemics (Dye et al., 2005). In South Africa, the TB epidemic is one of the greatest challenges facing post-apartheid South Africa, alongside the control of the concomitant human immunodeficiency virus (HIV) (Karim et al., 2009). Karim et al. (2009) assert that HIV continues to spread relentlessly, and that tuberculosis has been declared a national emergency, with the rising drug resistance and HIV co-infection, making South Africa one of the world's worst tuberculosis epidemics. The continued upsurge in the number of TB cases largely due to co-infection with HIV was earlier predicted by Clarke et al. (2006). Besides the contribution of human immuno-deficiency virus/acquired immune deficiency syndrome (HIV/AIDS), neglect of TB control also plays a role in the increased rate of TB infection, resulting in the emergence of drug resistant TB (Aziz et al., 2006), increased rate of recurrent TB (Korenromp et al., 2003), and extensively drug-resistant TB (XDR-TB) (Morbidity and Mortality Weekly Report (MMWR), 2006; Dye, 2006). Treatment therefore often consists of second-line drugs that are more costly and toxic than first-line anti-tuberculosis drugs (MMWR, 2006). Some of the drugs used in the treatment of TB fall under the umbrella term of antibiotics called 'aminoglycosides' (Smith and MacKenzie, 1997; Cohn, 1981). These antibiotics are most notorious for being ototoxic (Edmunds et al., 2006). As a result of the

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known ototoxic effects of some of the medications used for TB treatment, healthcare workers involved in treating TB patients need to be well aware of the ototoxic signs as well as know when to refer to an audiologist for hearing monitoring.

Streptomycin was the original antibacterial agent to be used successfully to combat the scourge of TB (Schuknecht, 1974), and its ototoxic effects were also documented and highlighted that early on (Talaska and Schacht, 2005), when a substantial number of TB patients treated with streptomycin were found to develop irreversible cochlear and vestibular dysfunction (Edmunds et al., 2006). Despite its documented ototoxic effects, streptomycin continues to be in wide use in the present day (de Lima et al., 2006). Symptoms of streptomycin ototoxicity include: high-frequency hearing loss (usually not affecting lower frequencies which are utilized in conversational hearing), tinnitus; as well as vestibular symptoms (Khoza-Shangase et al., 2009).

Patients may present with unsteadiness, ataxia, nausea and/or vomiting (Wofford, 1981; Catlin, 1981; De Jager and van Altena, 2002). These symptoms can have a significant impact on the patient's quality of life and therefore, early diagnosis and management is important (de Lima et al., 2006). It is the belief of the current author that pre-treatment counseling around these symptoms could also contribute toward adherence and compliance with treatment plans. Hence, it is essential that health care workers involved in TB treatment are aware of the ototoxic effects so that they can be in a better position to educate patients who may not notice ototoxic hearing loss until a communication problem becomes apparent, signifying that hearing loss within the frequency range which is critical for understating speech has already occurred. Similarly, by the time a patient complains of dizziness due to the medication, permanent vestibular system damage may have probably already occurred (Cohn, 1981; Edmunds et al., 2006). Furthermore because late and slowly progressive hearing loss occurring several months and years later through synergic effects between drugs and other known toxic agents such as noise exposure is possible (Edmunds et al., 2006; Martini et al., 2003), patients need to be educated and pre-counseled to avoid excessive noise exposure during and post-exposure to ototoxic drugs, at least for some time.

When a deadly disease necessitates treatment with ototoxic drugs, preserving the quality of the patient's remaining life develops into an important objective. This is particularly serious where documented aminoglycosides which are infamous for their ototoxic effects have to be used; where high prevalence of infectious, life-threatening diseases such as TB makes their use understandable and often unavoidable. It can be argued that hearing loss is not a life-threatening condition; however, Khoza-Shangase et al. (2009) argue that it is a threat to essential quality of life indicators unless intervention occurs early. These authors emphasize the adverse effects of a hearing loss on cognitive-linguistic skills and psychosocial behaviour, as well as the vocational, social, and interpersonal consequences for the patient (Khoza-Shangase et al., 2009). It is thus important that the patient is educated about what to expect so that they are aware of possible side-effects and know what management options are available.

The aim of the current study was therefore to determine the knowledge and management of ototoxicity related to TB treatment by South African healthcare workers. The analysis was made in three relevant perspectives:

1. To determine the TB treatment protocol followed by health care workers.
2. To determine the health care workers' awareness of ototoxicity and its management
3. To determine the extent of involvement of an audiologist in the treatment of TB

MATERIALS AND METHODS

Subjects

A total of 100 healthcare workers were interviewed for this study (Table 1). Convenient sampling of health care workers from five healthcare facilities involved in TB treatment in Gauteng was done (Lavrakas, 1987). For the purpose of this study, all participants had to be familiar with the running of the TB clinic, including the medications used; and had to be fluent in English since the interviews were conducted in English. Semi-structured telephonic interviews, consisting of open- and closed-ended questions were used. This design allowed for a large geographic coverage (Salant and Dillman, 1994) and was less expensive than personal interviews (Lonsbury-Martin and Martin, 2001). Ethical clearance was obtained from the University of the Witwatersrand, Human Research Ethics Committee (medical) before the study could be conducted and the ethical considerations of consent, anonymity, confidentiality, and feedback provision were observed.

Interview schedule

The interview questions were developed in accordance with the aims of the study, and were divided into 5 subsections:

1. General occupation: aimed at determining the position the participant held at the health site as well as the amount of experience they had dealing with TB patients.
2. TB treatment: aimed to determine the participants' awareness of the treatment currently used to treat TB, multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB), including knowledge of alternative drugs with less severe side effects.
3. Ototoxicity: focused on participants' awareness of ototoxicity, including the ototoxic effects of the TB medication.
4. Audiology and TB management: to ascertain the participants' awareness of audiology as a profession and services offered by an audiologist as well as to establish the perceived role of an audiologist in TB management programs.

Table 1. Description of participating healthcare professionals (N = 100).

Occupation	Participant's number
Clinical director	5
Clinical executive	5
Deputy director	3
Assistant director	4
Doctor	5
Pharmacist	11
Senior nurse	19
Professional nurse	26
Enrolled nurse	13
Community care worker	9

Table 2. Participants' responses to the medication used for treating TB (N = 100).

Parameter	TB	MDR-TB	XDR-TB
Rifafour	82	-	-
Ethambutol	16	9	-
Isoniazid	9	-	9
Rifampicin	14	9	-
Refinah	27	5	5
Pyrazinamide	9	9	-
Streptomycin	18	14	9
Pyrodoxin	21	-	-
Don't know	18	50	59

5. Protocols and regulations: aimed at determining what protocols were available in health settings concerning assessment and monitoring of renal function, blood-serum level, and hearing function during treatment as well as to determine recommendations provided to patients. According to Sharma and Mohan (Burns and Grove, 2001), patients receiving treatment for TB should be closely followed-up through reviewing clinical, radiological, laboratory and microbiological parameters to assess the patients' response to treatment.

Pilot study

Prior to the commencement of the study, a pilot study was conducted to assess the suitability and applicability of the research tool (Greeff, 2002). The pilot study proved the tool to be appropriate following minor changes to some of the questions in the interview schedule.

Data analysis

After the researcher transcribed the interviews, data was analyzed using a qualitative statistical approach through descriptive statistics and content analysis (Altman et al., 2005; Lancaster et al., 2004; Flick, 2002).

RESULTS AND DISCUSSION

The results of the study are reported following the format of the interview schedule.

General occupation

Participants' occupation included clinical directors, clinical executives, and deputy directors, assistant directors, doctors, pharmacists, senior nurses, professional nurses, enrolled nurses, and care workers. The range of length of experience working with the TB population was from 1.1 years to 10 years, with an average length of experience of 4 years.

TB treatment

Participants' responses to the question on the treatment protocols followed with TB patients were varied. As shown in Table 2, 82% indicated that Rifafour was used in the initial phase of treatment for a period of two months. Drugs that were reported to be used during the continuation phase were ethambutol (16%), isoniazid (9%), rifampicin (14%), refinah (27%), pyrazinamide (9%), streptomycin (18%), and pyrodoxin (21%). These responses are in accordance with literature on TB treatment. Rifafour is reported as the first line of treatment against TB (Clarke et al., 2006), while Refinah is used during the continuation phase. The rest of the 'single drugs', including streptomycin, are used to re-treat cases or when a patient develops resistance against one of the other drugs (Clarke et al., 2006). The remaining 18% of participants indicated that they were not sure of the treatment for TB, however, they were aware that drugs such as pyradoxin (21%), ethambutol (16%), and Refinah (27%) were used. This was of significant concern since lack of this knowledge could negatively impact on the healthcare workers' ability to properly counsel patients regarding treatment side effects. It further implied that they would in turn not be aware of the side-effects and as a result, would be unable to neither offer proper counseling nor refer patients for monitoring for symptoms of side effects such as ototoxicity.

Furthermore, as can be noted in Table 2, a higher percentage (50%) of the participants indicated that they did not know which drugs are currently being used to treat MDR-TB, and a similarly high number (59%) did not know what treatment was used for XDR-TB. This is of concern since health care workers' knowledge is crucial in the successful implementation of the South African government's plan to contain and eradicate TB as one of the infectious diseases that it has to manage. Upon further investigation, it was found that healthcare workers with minimal knowledge pertaining to treatment of MDR-

Table 3. Participants' awareness of ototoxicity (N = 100).

Questions	Participants' responses (%)	
	Yes	No
Do you know anything about medications causing a hearing loss (referred to as ototoxicity)?	26	74
Of the participants who responded 'yes' to the question above (n=26)	**Yes**	**No**
Are you aware of the ototoxic effects of some TB medications?	40	60
Do you know the symptoms a patient with ototoxicity would present with?	22	78
Do you ask patients about family history of hearing loss (ototoxicity)?	18	82
Do you ask patients about their ears and hearing status while on TB treatment?	0	100
Do you have an ototoxicity-monitoring program in place?	0	100
Is there documentation of the ototoxic effects of various medications available for professionals to read?	0	100
Do you routinely consider patients' renal function during treatment?	42	58
Do you routinely monitor patients' blood-serum levels during treatment?	26	74

TB and XDR-TB were predominantly those working in healthcare facilities where there was minimal contact with patients infected with MDR-TB and XDR-TB. Currently in Gauteng, health facilities refer MDR-TB and XDR-TB patients to a specialized facility, where a diagnosis is confirmed. The patient's treatment is then specifically instituted, and once rendered non-infectious; the patient is then referred back to the local health facility to continue treatment.

When asked whether the health care workers were aware of alternative medications that could be used in the treatment of TB if the patient had severe side effects, 87% of participants stated they were not aware of any alternative medications. Only 13% of the participants indicated that there were alternative drugs, however, these respondents were of the belief that these drugs are not as cost-effective and as efficient as drugs currently used. This response is in accordance with literature, which states, for an example that, although streptomycin has adverse ototoxic effects it is the most commonly used aminoglycoside in the fight against TB, especially in developing countries, because of its efficiency and cost-effectiveness (MMWR, 2006).

Ototoxicity

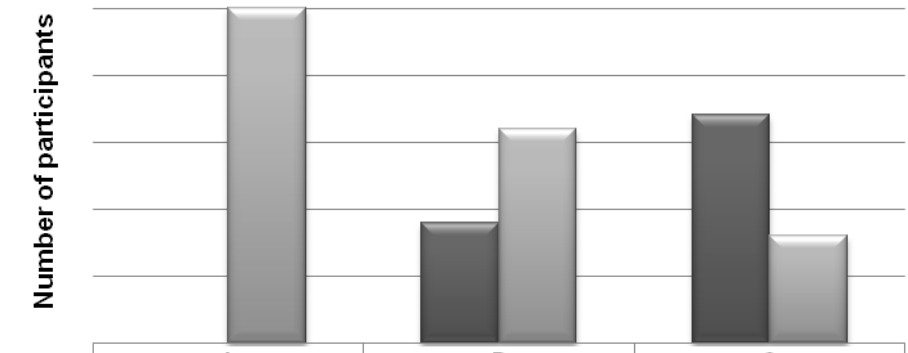
Table 3 reveals particularly concerning results about the healthcare workers' awareness of ototoxicity. These results highlight the amount of educational campaigns required from audiologists aiming at marketing the profession as well as in ensuring that patients receive the appropriate audiological services when required. The results in Table 3 indicate that a large number of health-care workers (74%) lack awareness in terms of ototoxicity and the symptoms a patient may present with as a result of exposure to ototoxic drugs. Out of those health-care workers who were aware of ototoxicity (n = 26), only 40% were aware of the ototoxic effects of the TB drugs, while only 22% were aware of the type of symptoms to look out for in the case of exposure to ototoxic drugs. From Table 3, it is also evident that there were no formal ototoxicity monitoring programs in place at health facilities where the current study was conducted nor were there available protocols for healthcare workers to refer to regarding ototoxicity.

These results reveal that healthcare workers, particularly those working in non-specialized TB treatment facilities, lack knowledge in terms of ototoxicity, symptoms of ototoxicity as well as management of patients on potentially ototoxic medications. Without the necessary knowledge of ototoxicity, ototoxic medication and the presenting symptoms, these healthcare workers are in no position to impart this knowledge to their patients or to refer to an audiologist or an otorhinolaryn-gologist when a patient presents with symptoms such as tinnitus, vertigo or hearing loss.

The fact that a large majority of the healthcare workers that were aware of ototoxicity (82 to 100%) reported that they did not enquire about family history of hearing impairment nor about patients' ear and hearing status is also of concern. If no formal audiological assessments exist at the TB clinics that patients can access; and minimal or no subjective inquiries are made regarding patients' hearing status, the disjuncture between what established theoretical knowledge has proven and what is being practiced is highlighted.

Audiology and TB management

Comprehensive management of TB patients that includes identification and treatment of side effects of drugs (in this case, ototoxicity) can only be done if the healthcare



	A	B	C
YES	0	36	68
NO	100	64	32

Figure 1. Summary of participants' responses to audiology and TB management sub-section (A = Do you have an audiologist as part of the TB management team? B = Do you refer TB patients to an audiologist? C= Do you know what the role of an audiologist is?).

workers know what audiologists are, what role the audiologists play in patient management, when to refer to audiologists, and work with audiologists as part of the TB management team. Figure 1 reveals that audiologists are not routine members of the TB management team. This again highlights the need for more active lobbying by audiologists to have posts created in such institutions so that ototoxicity monitoring programs can be established. Furthermore, Figure 1 indicates that even though 68% of the participants reported that they knew what the role of an audiologist is, only 36% actually refer patients to an audiologist. This again brings to the fore the need for audiologist to educate other healthcare workers about their many roles.

Protocols and regulations

This section aimed at determining protocols that were being followed for ototoxicity monitoring. As can be seen in Table 3, none of the participating facilities had protocols for ototoxicity monitoring that was prescribed when and how often the patients' hearing status can be evaluated. Furthermore, over half (58%) indicated that the patients' renal functioning was not considered and 74% indicated that the patients' blood-serum levels were not monitored during TB treatment. The main reason provided by a majority of respondents for lack of monitoring was that it was the attending doctor's responsibility to refer the patient. Of concern here is that a significant number of patients on TB treatment are not always seen by doctors, but rather by nurses, therefore shifting the responsibility to the doctors may negatively impact on the patients' quality of life.

Recommendations for TB patients

As can be seen in Figure 2, a significant amount (46%) of information provided to patients focused on adherence to the treatment regimen, with the other recommendations covering establishing and maintaining a healthy lifestyle (24%), reporting side effects such as skin rash, nausea and vomiting (21%), with only 9% focusing on ototoxicity and hearing conservation. Recommendations concerning hearing conservation were only made to patients complaining of hearing loss prior to discharge from the health facility.

Conclusion

The results of this study have highlighted the lack of awareness of ototoxicity amongst the healthcare workers from various health facilities involved in the treatment of TB. Healthcare workers are not aware of the symptoms of ototoxicity and as a result symptoms are attributed to side-effects that will wear-off and are therefore not investigated further. Healthcare workers also lack knowledge with regards to the role of the audiologist and as a result do not refer patients to an audiologist and/or employ the services of an audiologist during management of patients exposed to ototoxic drugs. The fact that audiologists do not form part of the treatment team involved in TB treatment influences the healthcare workers' knowledge as well as the referral rate of patients to audiologists for ototoxicity monitoring. Audiologists are responsible for imparting knowledge to healthcare workers as well as advocating for their role within the TB treatment team. They are responsible for ensuring that

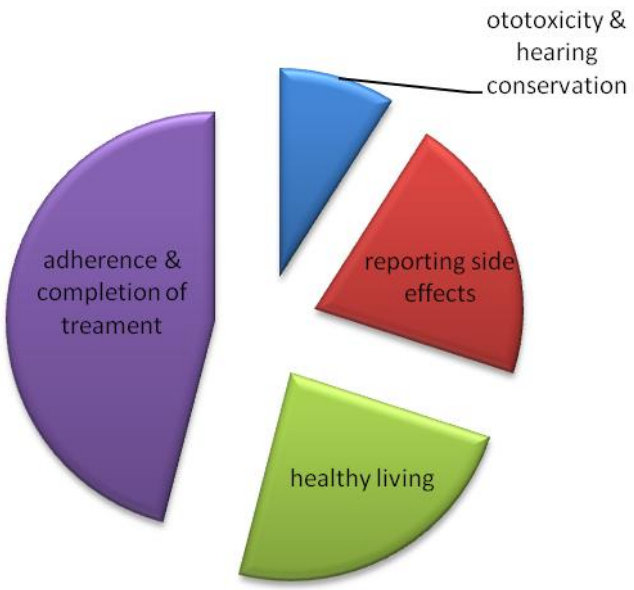


Figure 2. Summary of recommendations made to TB patients.

they get involved as one of the key members of the team that manages patients receiving ototoxic drugs, including implementing and managing ototoxicity-monitoring programs in healthcare facilities involved in treating diseases using ototoxic drugs. Without proper facilities and monitoring programs, patients are at a risk of the adverse psychological, social and occupational impacts that result from the presence of an unidentified and untreated hearing impairment.

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