Audiometric evaluation of patients treated for pulmonary tuberculosis*

Avaliação audiométrica de pacientes em tratamento para tuberculose pulmonar

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Abstract

Objective: To evaluate the hearing status of patients being treated for pulmonary tuberculosis at referral hospitals in Brazil. **Methods:** This was a descriptive study involving 97 male and female inpatients/outpatients between 18 and 60 years of age who were undergoing treatment for active pulmonary tuberculosis at one of two referral hospitals in the state of Rio de Janeiro. After being interviewed, all of the patients underwent pure tone audiometry. **Results:** Of the 97 patients studied, 65 (67%) were male, 52 (54%) were receiving first-line treatment, and 45 (46%) were receiving second-line treatment, which included aminoglycosides. Smoking, alcohol consumption, exposure to noise, and ototoxic medication use were identified in 65 (67%), 51 (53%), 53 (55%), and 45 (46.4%) of the patients, respectively. The most common auditory and vestibular complaints were dizziness, in 28 patients (28.8%); tinnitus, in 27 (27.8%); and hypoacusis, in 23 (23.7%). **Conclusions:** Due to the great number of patients with hearing loss in the present study, we recommend that all patients with active pulmonary tuberculosis be submitted to auditory monitoring.

Keywords: Audiometry; Hearing loss; Tuberculosis; Drug toxicity.

Resumo

Objetivo: Analisar a condição auditiva de uma população em tratamento para tuberculose pulmonar em dois hospitais de referência no Brasil. **Métodos:** Estudo descritivo envolvendo 97 pacientes de ambos os sexos, com idade entre 18 anos e 60 anos, que estivessem em tratamento para tuberculose pulmonar ativa, internados ou em acompanhamento ambulatorial em dois hospitais de referência no estado do Rio de Janeiro. Os participantes foram entrevistados e realizaram audiometria tonal liminar. **Resultados:** Na população estudada, 65 pacientes (67%) eram homens, 52 (54%) estavam em tratamento de primeira linha e 45 (46%) estavam em tratamento de segunda linha, o qual incluía aminoglicosídeos. Tabagismo, uso de bebidas alcoólicas, exposição a ruído e uso de medicamentos ototóxicos foram identificados respectivamente em 65 (67%), 51 (53%), 53 (55%) e 45 (46,4%) pacientes. As queixas auditivas e vestibulares mais frequentemente mencionadas foram tontura, em 28 (28,8%); zumbido, em 27 (27,8%); e hipoacusia, em 23 (23,7%). **Conclusões:** Devido ao elevado número de casos de perda auditiva encontrado neste estudo, recomenda-se que todos os pacientes em tratamento para tuberculose sejam submetidos a monitoramento auditivo.

Descritores: Audiometria; Perda auditiva; Tuberculose; Toxicidade de drogas.

Introduction

According to data from the World Health Organization, the incidence rate of tuberculosis continues to increase in Africa, in the Eastern Mediterranean region, and in Asia.[1] It is estimated that, in 2009, there were 9.4 million new cases of tuberculosis, 1.7 million deaths, and 500,000 cases of multidrug-resistant tuberculosis (MDR-TB) worldwide. The emergence of MDR-TB is a cause for concern, because these cases involve patients with strains of the tuberculosis bacillus that are resistant to the most effective drugs for the treatment of the disease (rifampin and isoniazid). In these situations, it is necessary to use second-line medications, which are less

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effective, are associated with higher failure and mortality rates, and can increase the occurrence of adverse (gastrointestinal, hepatotoxic, ototoxic, etc) effects.

Brazil ranks 19th among the 22 countries with the highest tuberculosis burden worldwide. A World Health Organization report on tuberculosis in Brazil estimated that, in 2009, there were 92,000 cases. A cohort study conducted between 2000 and 2007 reported 2,690 cases of MDR-TB, 14% of which died. The treatment of MDR-TB lasts 18 to 24 months and consists of an alternative pharmacological regimen, made available by the Brazilian National Ministry of Health and consisting of a combination of drugs, which is based on sensitivity testing results.[2] Among the medications used in special regimens and in regimens for MDR-TB, aminoglycosides (streptomycin and amikacin) are of note because of their ototoxic potential.[1]

Aminoglycosides can cause great damage to the cochlear or labyrinthine hair cells, causing permanent hearing losses and labyrinthine lesions.[3,4] The lesion caused by ototoxic medication use can lead to different degrees of neurosensory hearing loss. This type of loss is characterized by being irreversible, i.e., it is not possible to return to previous auditory thresholds even after the medication is discontinued. The variation in the degree of loss depends on various factors, such as medication type/dose and genetic predisposition. In these situations, it is recommended that the drug be discontinued and replaced.[1]

In the international literature, the rates of ototoxicity as an adverse reaction to aminoglycoside use vary greatly (5-64%), since they depend on various factors, such as medication type/dose, duration of use, patient age, comorbidities, genetic predisposition, alcohol abuse, smoking, and living/working conditions (homeless individuals or construction workers, who are exposed to environmental noise), as well as on the diversity in the design of the studies in which these factors are described.[3-8]

In Brazil, there have been few studies on the hearing status of the general population and of patients with tuberculosis.[9,10] Hearing loss prevalence and psychosocial impairments (occupational difficulties, isolation, reduced quality of life, and depression) were reported in one study, in which 6.8% of the population, most of whom were low-income males over 60 years of age who had a low level of education, exhibited hearing loss classified as disabling. One group of authors evaluated tuberculosis patients receiving streptomycin and found that, in 75% of the cases, there was some type of hearing loss.[4]

The objective of the present study was to evaluate the hearing status of patients being treated for pulmonary tuberculosis at one of two referral hospitals for tuberculosis in the state of Rio de Janeiro, Brazil.

Methods

This was a descriptive study conducted between November and December of 2008 at two referral hospitals for tuberculosis in the state of Rio de Janeiro, Brazil: *Instituto Estadual de Tórax Ary Parreiras* and *Hospital Estadual Santa Maria*.

We included all inpatients/outpatients between 18 and 60 years of age who were undergoing treatment for active pulmonary tuberculosis and who agreed to participate in the study. The volunteers gave written informed consent and responded to a standardized interview, followed by otoscopy for assessment of the internal acoustic meatus and tympanic membrane and by pure tone audiometry for determination of auditory thresholds.

We excluded patients who were not physically able to complete all stages of the study and those who declined to participate. Patients in whom the audiometric findings showed tracings consistent with changes or impairment of the external or middle ear were excluded from the analysis of the study.

The tests were performed in a portable soundproof booth with an Amplaid 460 A audiometer (Amplifon S.p.A, Milan, Italy) and TDH-39 headphones (Telephonics Corporation, Farmingdale, NY, USA). All tests were performed by only one trained technician. The limit of normality was defined as a maximum intensity of 25 dB for all frequencies. When one or more frequencies showed values equal to or greater than 30 dB, the test was considered abnormal, even if unilaterally.[11]

Although the objectives of this study did not include determining the causal factor of the hearing impairment, we performed a statistical analysis to investigate a potential association between the variables of interest (smoking, alcohol consumption, ototoxic medication use, gender,

and exposure to noise) and the audiometric findings. The patients were divided into two groups: patients aged 18 to 40 years (group 1) and patients aged 41 to 60 years (group 2). The evaluation was performed using two age groups to prevent age from being a confounding factor, since the auditory losses resulting from advancing age affect most of the population and show the same audiometric tracing as that of the variables studied.[3]

For categorical variables, percentage distribution was used. The Mann-Whitney test was used for evaluating the two groups, and, when this test was not applicable, Fisher's exact test was used. The analyses were performed with the Epi Info statistical package, version 3.5.1. Values of $p < 0.05$ were considered statistically significant.

The study protocol was analyzed and approved by the Medical Ethics Committee of the Federal University of Rio de Janeiro Clementino Fraga Filho University Hospital (Protocol no. 065/07).

Results

We evaluated 114 subjects, 17 of whom were excluded from the statistical analysis because of the type of audiometric curve found (mixed or conductive—losses that have conductive components and are therefore inconsistent with the variables studied). Therefore, we included 97 patients who either had normal audiometric findings or had neurosensory hearing loss. Of those 97 patients, 52 were receiving first-line treatment and 45 were receiving second-line treatment, which included aminoglycosides.

Previous aminoglycoside use was reported by 27 (27.8%) of the 97 patients included in the study. Ototoxic medication use was observed in 45 patients, streptomycin and amikacin being used by 11 and 34 patients, respectively. The use of these medications for at least 15 days was identified in 43 cases. Statistical analysis of this variable by type of medication was not performed because of the small sample size.

Regarding gender, 65 patients (67%) were male, with a median age of 40 years (interquartile range [IQR]: 33-52 years) and 32 (33%) were female, with a median age of 38 years (IQR: 26-42 years). Smoking, alcohol consumption, exposure to noise, and use of ototoxic medication were identified in 65 (67%), 51 (53%), 53 (55%), and 45 (46%) of the patients, respectively. The most common auditory and vestibular complaints were dizziness, in 28 patients (28.8%); tinnitus, in 27 (27.8%); and difficulty in hearing (hypoacusis), in 23 (23.7%); Figure 1).

Group 1 comprised 54 patients (median age = 32 years; IQR: 27-36 years), whereas group 2 comprised 43 patients (median age = 51 years; IQR: 47-56 years).

Abnormal audiometric findings (irreversible hearing loss) were more common in group 2 than in group 1, being observed in 30 (69.7%) and 24 (44.4%) of the 43 and 54 patients, respectively ($p = 0.02$; OR = 2.8; 95% CI: 1.15-7.35). The auditory abnormalities were of varying degrees, ranging from mild to severe loss, and a common characteristic to all of the results was worse auditory thresholds at high frequencies (Figure 2).

In group 1, we found a statistically significant association between abnormal audiometric findings and exposure to ototoxic medications ($p = 0.03$). In group 2, abnormal audiometric findings were associated with male gender ($p = 0.001$) and smoking ($p = 0.028$; Table 1).

Discussion

Ototoxicity can cause, in addition to balance disturbances, varying degrees of permanent hearing loss. The frequencies responsible for speech discrimination are usually the last to be affected, and this can prevent patients from noticing their hearing loss promptly.[3] With audiometric evaluations, timely identification of hearing loss is possible, which allows appropriate interventions.

Although audiometric abnormalities were more common in the population over 40 years of age (69%), they were also quite common in those under 40 (44%). The damages caused by acquired hearing loss are many and result from

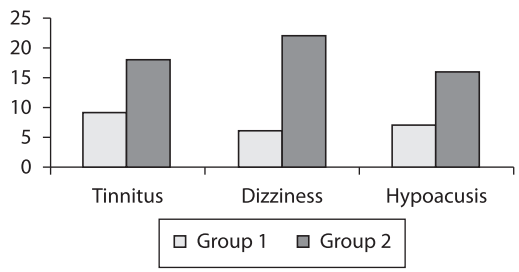

Figure 1 - Distribution of auditory and vestibular complaints in group 1 (patients aged 18 to 40 years) and in group 2 (patients aged 41 to 60 years).

communication impairment. Auditory or vestibular symptoms, such as tinnitus, dizziness, or even reports of slight difficulty in hearing, should be taken into consideration by the professionals involved. Therefore, appropriate referral can take place in order to preserve the sense of hearing and the balance of the population treated.

The choice to analyze two distinct age groups was based on previous studies on presbycusis,[3,10] i.e., increased auditory thresholds resulting from advancing age. The aging process can affect the auditory sensitivity initially in the higher frequencies, which are decoded in the basal region of the cochlea.[3] Hearing damage caused by aminoglycoside use or by any of the variables analyzed in the present study has an audiometric configuration similar to that of presbycusis, and, therefore, age could present as a confounding factor. Although the older population had a high frequency of auditory complaints, there was no significant association between age and hearing loss. It should be borne in mind that the older

Table 1 - Statistical analysis of risk variables for hearing loss by pure tone audiometry findings in the study groups.

Variable	Abnormal audiometry findings		Normal audiometry findings		Total		OR (95% CI)	p*
	n	%	n	%	n	%		
Group 1 (18-40 years of age)								
Gender								
Female	7	30.4	16	69.6	23	100.0	0.36 (0.10-1.18)	0.077
Male	17	54.8	14	45.2	31	100.0		
Smoking								
Yes	15	46.9	17	53.1	32	100.0	1.27 (0.37-4.42)	0.061
No	9	40.9	13	59.1	22	100.0		
Alcohol consumption								
Yes	15	57.7	11	42.3	26	100.0	2.88 (0.83-10.26)	0.061
No	9	32.1	19	67.9	28	100.0		
Exposure to noise								
Yes	13	46.4	15	53.6	28	100.0	1.18 (0.35-3.99)	0.763
No	11	42.3	15	57.7	26	100.0		
Ototoxic medication use								
Yes	15	60.0	10	40.0	25	100.0	3.33 (0.95-12.7)	0.034
No	9	31.0	20	69.0	29	100.0		
Group 2 (41-60 years of age)								
Gender								
Female	2	33.3	7	66.7	9	100.0	0.06 (0.01-0.46)	0.001
Male	28	82.4	6	17.7	34	100.0		
Smoking								
Yes	26	78.8	7	21.2	33	100.0	5.57 (0.99-33.89)	0.021
No	4	40.0	6	60.0	10	100.0		
Alcohol consumption								
Yes	19	76.0	6	24.0	25	100.0	0.02 (0.45-9.26)	0.300
No	11	61.1	7	38.9	18	100.0		
Exposure to noise								
Yes	18	72.0	7	28.0	25	100.0	1.29 (0.29-5.79)	0.710
No	12	66.7	6	33.3	18	100.0		
Ototoxic medication use								
Yes	14	70.0	6	30.0	20	100.0	1.02 (0.23-4.56)	0.976
No	16	69.6	7	30.4	23	100.0		

*Mantel-Haenszel chi-square test or Fisher's exact test when the chi-square test was not applicable.

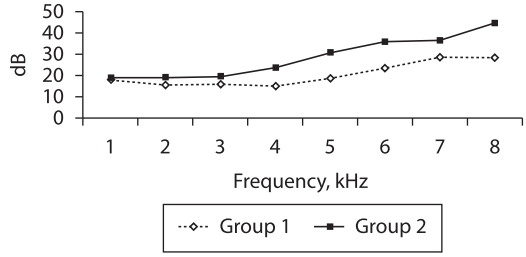

Figure 2 - Mean auditory thresholds in group 1 (patients aged 18 to 40 years) and in group 2 (patients aged 41 to 60 years).

population resorts to the use of medications (other than those used for the treatment of tuberculosis) more often and that multisensory deficits and systemic diseases are more common among them; in addition, it is necessary to mention the fact that most patients had poor health status, which required hospital care.[10] All these factors should be considered at the time of the evaluation of the auditory/vestibular complaints, especially dizziness. The findings of the present study were similar to those reported by Carmo et al.,[10] who evaluated elderly individuals and found that the most common complaint was tinnitus, followed by common reports of dizziness.

In the present study, the sociodemographic and clinical characteristics of the study population were similar to those described in patients treated at referral hospitals for tuberculosis in Brazil.[7,9,12] There was a high proportion of male patients, patients receiving second-line medications, smokers, patients who consumed alcohol, and homeless individuals. Regarding gender, the results are similar to those found in the general population, hearing loss being more common among males, in both groups.

Exposure to noise is the factor that is most harmful to hearing in working adults.[13] In the present study, despite the high rate of exposure to noise in the workplace (55.2%), there was no association between exposure to noise and audiometric abnormalities. This association was not observed probably because we did not obtain precise information, either from patients or from medical charts, about sound intensity level or duration of exposure to noise.

In our study, the ototoxic medications used for the treatment of tuberculosis were streptomycin and amikacin, in accordance with the recommendations of the Brazilian National Ministry of Health for a standard second-line regimen.[2] Typically, causal studies on ototoxicity should be longitudinal, and auditory thresholds should preferably be determined prior to medication use. Although the objective of the present study was not to determine the cause of the hearing impairment in this population, we analyzed the data on the patients receiving ototoxic medications in the two groups. An association between abnormal audiometric findings (neurosensory hearing loss) and ototoxic medication use occurred only in group 1 ($p = 0.034$). Similar findings in younger populations have been described by some authors.[5,6] Despite not having been investigated, the duration of exposure to smoking, noise, and alcohol is estimated to be shorter in group 1 than in group 2, and, therefore, the association between auditory abnormalities and exposure to ototoxic medication in group 1, which was observed in our study, is more plausible. In contrast, we observed a significant association between smoking and audiometric abnormalities only in the patients in group 2, which is similar to the findings reported by some authors,[14,15] but different from the findings reported by others.[16] Although we did not quantify smoking history in our study, we estimate that there is a direct relationship between increasing age and smoking history. Habitual alcohol consumption was not related to audiometric abnormalities in either of the two groups studied. Although the relationship between hearing loss and alcohol consumption is not yet well established, some authors suggest this association.[17-19]

In conclusion, due to the great number of patients with permanent hearing loss in our sample, we suggest that patients undergoing antituberculosis treatment be submitted to auditory monitoring in order to confirm (or not) the findings of the present study.

Auditory monitoring by means of appropriate auditory tests, such as otoacoustic emission and high-frequency audiometry, should be initiated prior to ototoxic medication use. Therefore, it is expected that auditory abnormalities can be detected as early as possible, thus contributing to the maintenance of one of the most important human representations, which is communication.

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