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HEARING IMPAIRMENT IN PATIENTS WITH TUBERCULOSIS FROM NORTHEAST BRAZIL

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SUMMARY

The aim of this paper is to describe the auditory profile of subjects who were given streptomycin treatment for tuberculosis in the years 2000 and 2001, in Recife, Northeast Brazil. The Injury Notification Database at the Municipal Department of Health was consulted and 78 individuals who had been on streptomycin during the period under study were selected. Forty-two individuals were excluded, of whom five were over 59 years of age and two were under 18 years. Nineteen turned out to be deceased, 13 could not be found, two were serving prison terms and one refused to participate. As a result, only 36 subjects participated in the study. These 36 individuals were interviewed and underwent meatoscopy and audiometry. The mean age of the group under study was 38.8 years old and males predominated (79.4%). Twenty-seven patients (75%) showed hearing impairment, the bilateral sensorineural type (63.9%) being the most frequent, mainly affecting the high frequencies over 4000 Hz. In the light of findings showing a high percentage of hearing impairment complaints among users of streptomycin, this issue seems to warrant an in-depth investigation, as does the implementation of an auditory follow-up routine for patients undergoing such chemotherapy for tuberculosis.

KEYWORDS: Tuberculosis; Hearing impairment; Ototoxicity.

INTRODUCTION

Tuberculosis is still considered to be a public health issue. Its treatment is based mainly on chemotherapeutic agents. In Brazil, the Ministry of Health's National Program for Tuberculosis Control has established four standardized treatments[3]. Streptomycin is probably the best and most effective aminoglycoside drug still in use against tuberculosis[11], being employed in Brazil when prior treatments have failed to deliver[3].

There are many studies reporting adverse reactions to tuberculosis treatment[12,15,17]. To mention just two: patients using streptomycin have been reported to suffer from hypoacusis and dizziness[10,14].

Health-care workers prescribing or following up aminoglycoside treatment are expected to ask their patients about auditory and vestibular signs and symptoms in order to identify any alterations at an early stage, since hearing loss may turn out to be gradual and irreversible[5,8].

Recife, Northeast Brazil, despite the decreased incidence of tuberculosis over the past few years, has been classified as being of high risk for this disease since 2002, accounting for 32.5% of the total number of cases in the state. When they quit tuberculosis treatment, patients are often forced to resume it, using more toxic drugs, and even worse, for a longer period of time[13].

A study, carried out in the municipality of Recife, in 1997, revealed that 16.2% of tuberculosis cases were undergoing treatment. Cessation of therapy was the main reason for retreatment, 42% of cases having[1] undergone two or more previous treatments.

Given these facts, the aim of the present study was to evaluate the auditory profile of individuals who had undergone streptomycin treatment for tuberculosis in the years 2000 and 2001 in the municipality of Recife.

METHODS

This was a case series study covering patients treated with streptomycin for tuberculosis during 2000 and 2001 in Recife. The patients had received streptomycin sulfate at the defined daily doses, ranging from 15 to 20 mg/kg/day[3]. The Injury Notification Database, provided by the municipality's Health Department, was consulted and cases selected. The criterion for inclusion was: individuals between 18 and 59 years-old registered in the Injury Notification Database with tuberculosis who received streptomycin treatment for at least 15 days during the period under study.

This survey showed that 78 individuals had received streptomycin treatment. Forty-two individuals were excluded, of whom five were over 59 years of age and two were under 18 years. Nineteen turned out to be deceased, 13 could not be found, two were serving prison terms

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and one refused to participate. As a result, only 36 subjects participated in the study.

Information on the length of treatment was obtained from each patient by way of an interview. It was not possible to confirm these data in the Health Department records on account of the unreliability of the records or failure to trace the patient's history. Since the administration of streptomycin is parenteral and daily, it seems unlikely that there was any bias in this information. During the interview, participants were also questioned about any hearing difficulties they may have experienced prior to using streptomycin.

Home visits were scheduled so that subjects could be made aware of and encouraged to participate in the research, which included tests at the Audiology Clinic of the Audiometry and Phoniatrics Course at the Federal University of Pernambuco.

Auditory impairment was identified on the basis of both on the patient's complaints and the disturbances detected by audiometry. Pure-tone audiometry was carried out for the airways at frequencies 0.25; 1; 2; 3; 4; 6; 8; and 12 kHz and for bone conduction at frequencies 0.5; 1; 2; 3 and 4 kHz. The 12 kHz frequency was used, because, according to the literature, ototoxic alterations are easier recognized at higher frequencies[4]. Evaluations were performed using a two-channel audiometer (Damplex, model 65) calibrated to the ANSI 53.6 standard and TDM 39 phones. Auditory thresholds at or below 20 dB HL were considered normal. The absolute and relative distributions were obtained for data analysis.

The average and the standard deviations were calculated for a few numerical variables. The following tests were used for statistical analysis: Fisher's exact test, the Wilcoxon Sign Rank test, and the Student's *t* test.

The subjects were enrolled on the study after signing an informed consent form. Every individual received his/her exam results and an otolaryngological follow-up was guaranteed for those exhibiting hearing loss. The present project has been approved by the Centro de Pesquisas Aggeu Magalhães (CPqAM/FIOCRUZ) Ethics Committee.

RESULTS

Of the 36 subjects who participated in the study, 27 (75%) were males and nine (25%) females. The age of the patients ranged from 27 to 57 years, with a mean of 38.8 years.

Auditory disorders were identified in 27 individuals (75%), sensorineural hearing loss being the most frequent type of disorder (23 patients). Those without hearing loss represented one quarter of the study sample. Conducive and other forms of hearing impairment were seen in two cases each.

The audiometric examinations for frequencies up to 3,000 Hz showed means ranging between 16 and 18 dB HL in the right ear, and between 14 and 20 dB HL in the left ear. For frequencies from 4,000 to 12,500 Hz, the means ranged between 22 and 46 dB HL in the right ear, and between 21 and 38 dB HL in the left ear. Comparing right and left ears, the largest mean differences occurred at 12,500 Hz, 8,000 Hz and 1,000 Hz, the highest values being found in the right ear. Except for the 3,000 Hz and 6,000 Hz frequencies, all other mean values were higher in the right ear, and at 12,500 Hz, the right ear was significantly impaired compared to the left ($p < 0.01$) (Table 1).

Table 1
Summary audiometric data, for each ear, of individuals using streptomycin for tuberculosis treatment, during 2000 and 2001 in Recife

Frequency (Hz)	Statistical data	Ear		
		Right	Left	*p* value
250	Mean [3]	18.13	17.42	p [1] = 0.5410
	Standard deviation [3]	8.01	7.19	
	Variation coefficient (%)	44.18	41.29	
500	Mean	16.25	15.61	p [1] = 0.4782
	Standard deviation	7.73	7.26	
	Variation coefficient (%)	47.54	46.54	
1,000	Mean	16.88	14.70	p [1] = 0.1153
	Standard deviation	8.30	6.95	
	Variation coefficient (%)	49.21	47.31	
2,000	Mean	16.41	15.91	p [1] = 0.6383
	Standard deviation	10.94	11.56	
	Variation coefficient (%)	66.70	72.63	
3,000	Mean	18.59	20.00	p [1] = 0.0918
	Standard deviation	13.33	13.92	
	Variation coefficient (%)	71.71	69.60	
4,000	Mean	22.34	21.52	p [2] = 0.6624
	Standard deviation	16.51	14.66	
	Variation coefficient (%)	73.89	68.12	
6,000	Mean	30.28	31.06	p [2] = 0.2304
	Standard deviation	20.67	17.44	
	Variation coefficient (%)	68.25	56.16	
8,000	Mean	30.00	27.12	p [2] = 0.7721
	Standard deviation	24.70	19.57	
	Variation coefficient (%)	82.33	72.15	
12,500	Mean	45.97	38.03	p [1] = 0.0051*
	Standard deviation	26.96	25.65	
	Variation coefficient (%)	58.65	67.44	

* Significant difference at p = 0.05; (1) Wilcoxon Sign Rank test; (2) Student's paired *t* test; (3) Mean in dB; Two conductive and two mixed forms of hearing impairment were excluded.

The audiometric measurements according to the type of frequency, low or high, per individual ear, demonstrated that the mean audiometric values were significantly higher at the high frequencies than at the lower ones ($p < 0.01$) (Table 2).

Fifty percent of the study participants had received treatment for a period of more than two months, while the remainder had been treated for shorter periods of time. However, differences in hearing impairment between these groups were not significant (77.8% versus 72.2, respectively) (Table 3).

Individuals between 40 to 59 years-old exhibited higher percentages of hearing loss (81.3%) than those between the ages of 20 to 39 (70%), ($p > 0.05$), as depicted in Table 4. Most patients (77.8%) had not complained of hearing loss prior to treatment with streptomycin. The

patients who had complained of hearing loss prior to treatment showed 16.1% greater hearing impairment than those who had no such complaints ($p > 0.05$).

Table 2
Audiometry in people treated with streptomycin. High and low frequencies for each ear, Recife, 2000-2001

		Audiometry		
	Statistics	Low	High	p value
Right ear	Mean (2)	16.91	27.72	p (1) < 0.001 *
	Standard deviation (2)	7.87	18.31	
	Variation coefficient (%)	46.51	66.06	
Left ear	Mean	15.91	27.55	p (1) < 0.001 *
	Standard deviation	6.76	16.06	
	Variation coefficient (%)	42.51	58.30	

* Significant difference at p = 0.05; (1) Wilcoxon Sign Rank test; (2) Mean in dB; Two ears with conductive and two with mixed forms of hearing loss were excluded.

Table 3
Hearing impairment in people receiving treatment for tuberculosis using streptomycin throughout treatment in Recife, 2000-2001

Duration of treatment	Hearing impairment					
	Yes		No		Total	
	N	%	N	%	N	%
15 days - 2 months	13	72.2	5	27.8	18	100
> 2 - 8 months	14	77.8	4	22.2	18	100
Total group	27	75.0	9	25.0	36	100

Fisher's exact test: p = 1.000; Ratio between proportions of loss: RP = 1.08; IC = (0.74 to 1.57)

Table 4
Hearing impairment in people who underwent treatment for tuberculosis with streptomycin according to age group, Recife, 2000-2001

Age group (years)	Hearing impairment					
	Yes		No		Total	
	N	%	N	%	N	%
40 - 59	13	81.3	3	18.7	16	100
20 - 39	14	70.0	6	30.0	20	100
Total	27	75.0	9	25.0	36	100

Fisher's exact test: p = 0.70003; Ratio between proportions of loss: RP = 0.71; CI + (0.40 - 1.26).

DISCUSSION

Tuberculosis treatment interruption is a source of concern for public health managers. Usually the long treatment periods, the lack of an appropriate follow-up and the occurrence of adverse reactions to therapy lead patients to quit treatment, although afterwards they will be forced to undergo retreatment. The resumption of treatment frequently entails subjects having to be put on potentially ototoxic and vestibulotoxic medication.

The audiometric measurements taken in our study population showed hearing impairment, although, in most cases, hearing loss was restricted to the higher frequencies. These results are in accordance with the data found in the literature, which point out that the higher the frequency, the more severe is the impairment found. According to some authors[1,2,4], hearing loss due to the use of ototoxic agents is triggered at high frequencies and, generally, confined to these.

In this study, hearing impairment was found to be bilateral in 62.9% of the patients. Hearing impairment caused by ototoxic medication is of the sensorineural uni- or bilateral type[9].

The study found that hearing loss was more prevalent in females and this differs from the data published elsewhere[16], in which 80% of the hearing impairments occurred in males. It should be noted that most studies on ototoxicity do not mention the patient's gender as a risk factor.

Individuals over 59 years of age were excluded from our study due to the fact that they may display hearing impairments mimicking those caused by ototoxicity. Somewhat higher percentages of hearing impairment were found in individuals between 40 and 59 years of age, a predictable finding, since older people tend to display higher susceptibility to ototoxic agents[14].

Despite the fact that hearing impairment occurred in a high percentage of subjects, one should not overlook the fact that this group had very special socioeconomic traits, being made up of alcohol abusers, unemployed and homeless people and the like. Although socioeconomic and cultural factors were not analyzed, they are known to influence the outbreak, exacerbation and persistence of any disease.

The treatment strategy currently recommended by the National Tuberculosis Control Program is to use streptomycin daily for three months. In the present study, the minimum period for streptomycin therapy was 15 days and the maximum, eight months. The duration of use of any given drug is considered to be an important factor for adverse reactions. The effects of streptomycin have been analyzed elsewhere in people who used it for six months. The initial symptoms occurred during the 4th and 5th weeks of therapy and continued for periods varying from one week to several months[6]. In our study there were no significant differences in hearing impairment between the groups who had received treatment for more or less than two months. On the other hand, the effect of the daily dose given to each patient was not studied because this information was not given either in the database consulted or by the patients in the interview. Hearing impairment was more commonly present in those individuals who took streptomycin for more than two months. In fact, data found elsewhere also associate hearing loss with the daily dosage and the length of treatment using streptomycin[7].

CONCLUSION

The high percentage of hearing impairment found in this population points to the need for further studies, using larger samples and a study design with greater analytical power, which could more accurately reflect the real situation. Every year, streptomycin is prescribed for about 40 new patients in the municipality of Recife, a number small enough to allow for systematic follow-up. The implementation of

auditory monitoring for patients who undergo treatment with this drug is therefore recommended. Special attention should be paid to both the treatment strategy and the complaints reported during treatment. In this way, possible sequelae may be avoided or lessened, thereby encouraging greater compliance with the treatment of a disease that brings social stigma and causes problems of control for the health system.

RESUMO

Alteração auditiva em pacientes com tuberculose no nordeste do Brasil

Este trabalho teve por objetivo descrever o perfil auditivo de pessoas que realizaram tratamento para tuberculose com estreptomicina em Recife nos anos de 2000 e 2001. Para tal foi utilizado o banco de dados do Sistema de Informação de Agravos de Notificação, fornecido pela Secretária de Saúde deste município, sendo selecionadas 78 pessoas que usaram a droga no período em estudo. Do total de pacientes selecionados sete eram menores de 18 anos ou maiores de 58 anos, 19 haviam falecido, 13 não foram localizados, dois eram presidiários, um negou-se a participar, restando, pois 36 indivíduos que puderam ser submetidos a uma entrevista, a meatoscopia e a audiometria. No grupo estudado predominou o sexo masculino (79,4%) e a média das idades era de 38,8 anos. Dos 36 pacientes, 27 (75,0%) apresentaram alteração auditiva, sendo a mais freqüente a sensório-neural bilateral (63,9%), com predomínio de freqüências agudas, a partir de 4000 Hz. Os achados com elevados percentuais de alteração auditiva entre os usuários de estreptomicina, apontam para a necessidade de aprofundamento deste tema em outros estudos, e também sugerem a necessidade de estruturação de um sistema de monitoramento auditivo para a população de pacientes submetidos a esse quimioterápico no tratamento para tuberculose.

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