



Brazilian Journal of
OTORHINOLARYNGOLOGY

www.bjorl.org.br



ORIGINAL ARTICLE

Could the type of treatment for chronic kidney disease affect the auditory system?☆

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Received 20 May 2013; accepted 1 October 2013

KEYWORDS

Hypertension;
Diabetes mellitus;
Hearing loss;
Renal insufficiency
chronic;
Electrophysiology

Abstract

Introduction: Chronic kidney disease (CKD) is defined as the presence of renal injury that leads to the slow and progressive loss of kidney function.

Aim: To compare audiological tests between patients with CKD receiving different types of treatment.

Material and method: This was a clinical and experimental study. Groups were divided according to treatment: hemodialysis (n = 35), peritoneal dialysis (n = 15), and conservative (n = 51), and were compared to 27 healthy controls. Patients older than 60 years; those with congenital hearing loss, genetic syndromes, and middle-ear infections; and those who had been submitted to a kidney transplant were excluded. Audiologic evaluation included pure-tone audiometry, transient evoked otoacoustic emissions, and auditory brainstem response (ABR). The variables considered were gender, age, diagnosis of arterial hypertension, time since the diagnosis of diabetes and hypertension, CKD stage, duration of CKD, and duration of treatment.

Results: The variables age, presence of arterial hypertension, and time of CKD were statistically significant and controlled. The auditory thresholds measured by pure-tone threshold audiometry were worse for the conservative treatment group, and the III-V interval of the ABR of the conservative treatment group was significantly greater than that of the hemodialysis groups.

Conclusion: The conservative treatment group presented worse audiological tests, regardless of hypertension and diabetes, reinforcing that patients need to undergo a complete hearing assessment for better understanding of the disease and its effects on the auditory system.

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☆Please cite this article as: Lopez PS, Silva DPC, Martin LC, Montovani JC. Could the type of treatment for chronic kidney disease affect the auditory system? Braz J Otorhinolaryngol. 2014;80:54-9.

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PALAVRAS-CHAVE

Hipertensão;
Diabetes *mellitus*;
Perda auditiva;
Insuficiência renal
crônica;
Eletrofisiologia

O tratamento da doença renal crônica pode afetar a audição?**Resumo**

Introdução: Doença renal crônica (DRC) é definida pela presença de lesão renal levando à perda lenta e progressiva da função renal. A influência do tratamento da DRC sobre a audição ainda é inconclusiva.

Objetivo: Comparar testes auditivos entre pacientes com DRC submetidos a diferentes tipos de tratamento.

Material e método: Cohort transversal. Os grupos foram divididos de acordo com o tratamento: hemodiálise (n = 35), diálise peritoneal (n = 15), conservador (n = 51) e 27 pacientes saudáveis (controle). Pacientes com idade superior a 60 anos, perda auditiva congênita, síndromes genéticas, infecções de orelha média e transplante renal foram excluídos da pesquisa. A avaliação audiológica incluiu audiometria tonal, emissões otoacústicas evocadas transientes e Potencial Evocado Auditivo de Tronco Encefálico (PEATE); e as variáveis avaliadas foram: sexo, idade, diagnóstico de hipertensão arterial e diabetes, estadiamento da DRC, tempo de diagnóstico do diabetes e da hipertensão arterial, duração da DRC e do tratamento.

Resultados: A idade, presença de hipertensão arterial e tempo de DRC foram estatisticamente significantes e controlados. O grupo conservador apresentou piores limiares auditivos na audiometria tonal e o intervalo III-V do PEATE significativamente maior que o da hemodiálise.

Conclusão: O tratamento conservador mostrou piores resultados na avaliação auditiva, independente de diabetes e de hipertensão, reforçando que os pacientes submetidos a tratamento para DRC merecem avaliação auditiva completa para melhor compreensão da doença e de seus efeitos sobre o sistema auditivo.

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Introduction

Chronic kidney disease (CKD) is defined as the presence of renal injury that leads to the slow and progressive loss of kidney function.¹

An association between CKD and hearing loss was first described in patients with Alport syndrome.² However, anatomical, physiological, pathological, and pharmacological similarities between the nephron and stria vascularis of the cochlea may explain this association in cases that are not related to syndromes or genetic diseases.^{3,4} Sensorineural hearing loss at high frequencies is the most common type in patients with CKD, and includes both cochlear impairment and lesions to particular portions of the auditory pathway.⁵⁻⁸

However, the influence of CKD treatment on auditory function is inconclusive,⁸ and hypertension and diabetes mellitus are frequently associated with CKD and hearing loss; these variables were not considered when analyzing these findings.

In the present study, the audiological tests between patients with CKD receiving different types of treatment were compared and associated with hypertension and diabetes mellitus.

Methods**Study population**

This was a cross-sectional study conducted in a tertiary referral center. The target population consisted of patients with CKD from the region around the hospital with a non-probabilistic intentional sample.

The exclusion criteria were: previous kidney transplant, congenital hearing loss or middle ear alterations, genetic syndromes, history of excessive exposure to noise, history of use of ototoxic medications, and age greater than 60 years. These data were confirmed by the patient's clinical history or medical information.

Patients were divided into groups according to treatment: hemodialysis (n = 35), peritoneal dialysis (n = 15), and conservative (n = 51), as well as 27 healthy subjects.

Audiological assessment

This audiological evaluation consists of pure-tone audiometry (PTA), transient evoked otoacoustic emissions (TEOAEs) and auditory brainstem response (ABR).

The PTA was performed by an audiologist in a sound-treated room using standard TDH-39 earphones and an Interacoustics AD229b audiometer. Audiometric thresholds for air-conduction stimuli in both ears were established for frequencies at 250, 500, 1,000, 2,000, 3,000, 4,000, 6,000, and 8,000 Hz.

TEOAEs measurements were performed using Otodynamics ILO 288, USB II system with standard settings. The stimulus level was set to 84 dB SPL a number of 260 averages was used. Values < 3 dB amplitude were considered as negative.⁹

For the ABR analysis, the rarefaction click stimulus was presented by the 3 Ω insertion phone, with 90 dBnHL intensity and a presentation rate of 20.1 c/s with a band-pass filter of 100 and 3,000 Hz and average of 2,000 stimuli, using Interacoustics EP¹⁵ Eclipse. The ABR were captured through ECG disposable electrodes (MEDITRACE™ 200), with EEG

conductive paste (Tem 20™) placed after cleaning the skin with ECG/EEG abrasive gel (NUPREP). The impedance level was kept between 1 and 3 kΩ for the electrodes; the active electrode was positioned in Fz, the reference electrode in M₁ and M₂, and the ground electrode in F_{pz}^{10,11}

Variables

Potential confounders were considered: gender, age, race, diagnosis of arterial hypertension (yes/no), time since the diagnosis of hypertension, diagnosis of diabetes (yes/no), time since the diagnosis of diabetes, CKD stage (1/2/3/4), duration of CKD, and duration of treatment.

The outcome hearing impairment was determined as the pure-tone average of audiometric hearing thresholds at 500, 1,000, 2,000 and 4,000 Hz > 25 dB; all audiometric hearing thresholds, classification of negative TEOAEs, and parameters of ABR were analyzed.

Statistical analyses

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS), release 19.0. Nonparametric variables are expressed as the median (minimum-maximum). The chi-squared test was used to examine categorical variables. Comparisons between groups were performed with Dunn's test.

The categorical outcomes (hearing loss and negative TEOAEs) were compared by multivariable logistic regression

analysis, which was used to calculate adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for associations with CKD treatment. The numerical outcomes (audiometric hearing thresholds and ABR parameters) were compared by linear regression with a gamma response, corrected by the effect of age and the presence of hypertension. *p*-values < 0.05 were considered to be statistically significant.

Ethics

This study was approved by the Ethics Committee of the Faculdade de Medicina de Botucatu, under Protocol No. 157/2007.

Results

The characteristics of patients, comorbidities, CKD stage, and other data of the disease, stratified by treatment, were listed in Table 1. A statistical difference was observed in arterial hypertension, older patients, and duration of CKD.

No differences were observed in the percentage of hearing loss between the various types of treatment (*p* > 0.05). Corrections for hypertension and age were not necessary in this case, since the types of treatment were homogeneous. However, in other comparisons, this correction was necessary (Tables 2 and 3).

The conservative group had worse hearing thresholds when compared to the control group in all frequencies

Table 1 Comparison of demographic data, comorbidities, and characteristics of chronic kidney disease (CKD) according to groups.

	Groups				p-value
	Control	Conservative	Peritoneal dialysis	Hemodialysis	
Male gender	44.1	58.8	40.0	57.1	0.432 ^a
White ethnicity	0.0	7.8	13.3	14.3	0.217 ^a
Arterial hypertension	0.0 ^a	88.0 ^b	66.7 ^b	91.4 ^b	< 0.001 ^a
Diabetes mellitus	0.0	28.0	20.0	37.1	0.006 ^a
CKD stage					
1	0.0	8.2	0.0	0.0	
2	0.0	2.0	0.0	0.0	
3	0.0	24.5	0.0	0.0	
4	0.0	38.8	0.0	0.0	
5	0.0	26.5	100.0	100.0	
Age (years)	31 (20-58) ^a	51(7-60) ^b	47 (22-57) ^{ab}	53 (17-60) ^b	< 0.001 ^b
Duration of hypertension	-	8 (0.4-3.2)	5 (1.4-26.3)	11.1 (0.6-3.2)	0.202 ^b
Duration of diabetes	-	17.0 (0.6-3.1)	22.6 (18.8-24.9)	16.0 (4.2-25.0)	0.207 ^b
Duration of CKD	-	2.4 (0.3-16.9) ^a	4.2 (1.4-25.3) ^{ab}	6.9 (0.6-21.8) ^b	0.001 ^b
Treatment duration of CKD	-	2.5 (0.3-16.9)	2.3 (0.2-5.8)	2.5 (0.1-21.8)	0.484 ^b

^a Chi-squared test.

^b Kruskal-Wallis' test.

Values in the same row followed by different letters differ significantly (*p* < 0.005) by the Dunn test.

Table 2 Comparison of hearing thresholds at frequencies of 250 Hz to 8 kHz assessed by pure-tone audiometry in each ear according to group.

Groups					
Ear	Frequency	Control	Conservative	Peritoneal dialysis	Hemodialysis
Right	250 Hz	5 (0-15) ^a	10 (5-80) ^b	15 (0-40) ^{ab}	15 (0-110) ^{ab}
	500 Hz	5 (0-15) ^a	10 (0-80) ^b	15 (0-45) ^{ab}	10 (0-110) ^{ab}
	1 kHz	5 (0-15) ^a	10 (0-80) ^b	10 (0-40) ^{ab}	5 (0-120) ^{ab}
	2 kHz	5 (0-10) ^a	10 (0-85) ^b	10 (0-35) ^{ab}	10 (0-120) ^{ab}
	3 kHz	5 (0-15) ^a	15 (0-85) ^b	10 (0-35) ^{ab}	15 (0-120) ^{ab}
	4 kHz	5 (0-15) ^a	25 (0-90) ^b	20 (10-45) ^{ab}	20 (0-120) ^{ab}
	6 kHz	10 (0-25) ^a	25 (0-105) ^b	20 (0-55) ^a	25 (0-120) ^{ab}
	8 kHz	10 (0-15) ^a	30 (0-95) ^b	15 (0-65) ^a	35 (0-120) ^{ab}
Left	250 Hz	5 (0-15) ^a	10 (5-100) ^b	15 (0-60) ^b	10 (0-110) ^{ab}
	500 Hz	5 (0-15) ^a	15 (0-120) ^b	10 (0-60) ^b	10 (0-105) ^{ab}
	1 kHz	5 (0-10) ^a	10 (0-120) ^b	10 (0-65) ^b	10 (0-110) ^b
	2 kHz	5 (0-10) ^a	10 (0-120) ^b	10 (0-50) ^b	10 (0-110) ^b
	3 kHz	5 (0-10) ^a	15 (0-120) ^b	15 (0-45) ^b	15 (0-115) ^b
	4 kHz	10 (0-15) ^a	20 (0-115) ^b	10 (0-50) ^{ab}	20 (0-120) ^b
	6 kHz	10 (0-15) ^a	30 (0-100) ^b	35 (5-90) ^b	25 (0-120) ^b
	8 kHz	10 (0-20) ^a	25 (0-120) ^{ab}	25 (5-90) ^b	30 (0-120) ^{ab}

^a Values were expressed as median (range).

^b Corrected for age and hypertension.

Values in the same row followed by different letters differ significantly ($p < 0.005$) by the Wald test.

Table 3 Comparison of the parameters of the brainstem auditory response (ABR) in each ear according to group.

Ear	ABR	Groups		Grupos	
		Control	Conservative	Peritoneal dialysis	Hemodialysis
Right	I	1.37 (1.17-1.60) ^a	1.40 (1.17-1.90) ^a	1.40 (1.20-1.57) ^a	1.47 (0.93-1.83) ^a
	III	3.47 (3.23-3.90) ^a	3.60 (3.27-4.07) ^a	3.67 (3.37-3.90) ^a	3.62 (3.20-4.53) ^a
	V	5.50 (5.27-5.93) ^a	5.77 (5.20-6.60) ^a	5.77 (5.27-6.23) ^a	5.70 (5.13-6.60) ^a
	I-III	2.10 (1.83-2.43) ^a	2.17 (1.77-2.73) ^a	2.23 (2.00-2.43) ^a	2.20 (1.73-2.70) ^a
	III-V	2.07 (1.50-2.40) ^{ab}	2.13 (1.73-2.80) ^a	2.10 (1.60-2.73) ^{ab}	2.07 (1.87-2.53) ^b
	I-V	4.20 (3.77-4.67) ^a	4.30 (3.80-5.43) ^a	4.33 (3.97-4.97) ^a	4.25 (3.77-4.77) ^a
Left	I	1.37 (1.20-1.53) ^a	1.37 (1.17-1.87) ^a	1.40 (1.17-1.57) ^a	1.43 (1.17-2.00) ^a
	III	3.49 (3.20-3.70) ^a	3.57 (3.37-4.07) ^a	3.62 (3.43-3.97) ^a	3.67 (3.27-4.43) ^a
	V	5.47 (5.27-5.90) ^a	5.73 (5.30-7.43) ^a	5.69 (5.47-6.23) ^a	5.80 (5.27-6.43) ^a
	I-III	2.12 (1.77-2.47) ^a	2.20 (1.77-2.80) ^a	2.25 (2.03-2.63) ^a	2.27 (2.00-2.90) ^a
	III-V	2.07 (1.73-2.37) ^{ab}	2.10 (1.83-3.67) ^a	2.09 (1.67-2.30) ^{ab}	2.09 (1.77-2.27) ^b
	I-V	4.12 (3.80-4.67) ^a	4.33 (3.87-5.87) ^a	4.35 (4.03-4.90) ^a	4.33 (3.90-5.00) ^a

ABR, auditory brainstem response.

^a Values were expressed as median (range).

^b Corrected for age and hypertension.

Values in the same row followed by different letters differ significantly ($p < 0.005$) by the Wald test.

tested. In contrast, no significant difference was observed between the other treatments (Table 2). The percentage of negative TEOAEs did not differ significantly among the groups ($p > 0.05$).

In the ABR, the conservative group had bilateral symmetric increased III-V interval compared to the hemodialysis group, with a statistically significant difference (Table 3).

Discussion

The present study was motivated by the inconclusive literature findings regarding the effect of the type of CKD treatment - conservative, peritoneal dialysis, and hemodialysis - on auditory acuity, and by the possible correlations of arterial hypertension and diabetes,^{12,13} which are frequently associated with CKD and hearing loss.

To this end, certain criteria were adopted to reduce the interference of other factors with auditory alterations. Subjects older than 60 years were excluded, since 25% of individuals in this age range show alterations in auditory tests due to age.⁸ Individuals submitted to previous kidney transplantation were excluded due to the use of immunosuppressive drugs pre- and post-transplantation, which may exert an ototoxic effect.^{5,14} Additionally, transplantation is usually the treatment of last resort, and thus patients have been submitted to other treatments, hindering the analysis of their effects.

Arterial hypertension and diabetes mellitus are the main causes or consequences of CKD,¹ and therefore were maintained in the study and considered in the data analysis.

Possible changes in hearing assessment have been described by some authors soon after dialysis; these findings could be attributed to the drugs used or to the ionic concentrations of sensory cells.^{15,16} However, most studies did not demonstrate a significant effect of a single dialysis session on hearing.¹⁵⁻¹⁸ For this reason, and because patients are usually tired and stressed after a dialysis session, subjects were not evaluated at this time.

When the type of CKD treatment was considered, the subgroups were found to be similarly affected by hearing loss, as also reported by Mancini et al.¹⁹ and by Nikolopoulos et al.²⁰ However, the results show that audiometry findings of the conservative group were significantly worse than those of the control group. The authors believe that the conservative therapy may cause accumulation of toxic substances in the bloodstream, since these substances are not efficiently eliminated by the kidneys or by dialysis, consequently impairing auditory functions.

The peritoneal dialysis group was least affected by negative TEOAEs, and the hemodialysis group was the most affected, although the difference was not significant, as also reported by Ozturan & Lam¹⁵ and by Naderpour et al.²¹

Although hemodialysis may be a more aggressive method regarding the cochlea by possibly causing ionic changes in the cell membrane,^{19,20,22,23} this finding was not observed in the present study when using TEOAEs.

In the ABR, the conservative group differed from the hemodialysis group, with an increased III-V interval, suggesting injury in central portions of the brainstem auditory pathway.²⁴

Conclusion

The conservative treatment group presented worse hearing threshold and abnormal ABR, reinforcing that patients undergoing treatment for chronic renal disease need a complete hearing assessment for better understanding of the disease and its effects on the auditory system.

Conflicts of interest

The authors declare no conflicts of interest.

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