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

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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.© 2014 Associação Brasileira de Otorrinolaringologia e Cirurgia Cérvico-Facial. Published by Elsevier Editora Ltda. All rights reserved.

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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. An association between CKD and hearing loss was first described in patients with Alport syndrome. 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. 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.

However, the influence of CKD treatment on auditory function is inconclusive, 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.
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 Fpz.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 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

| Groups                      | Control | Conservative | Peritoneal dialysis | Hemodialysis | p-value   |
|-----------------------------|---------|--------------|---------------------|--------------|-----------|
| Male gender                 | 44.1    | 58.8         | 40.0                | 57.1         | 0.432a    |
| White ethnicity             | 0.0     | 7.8          | 13.3                | 14.3         | 0.217a    |
| Arterial hypertension       | 0.0b    | 88.0b        | 66.7b               | 91.4b        | < 0.001a  |
| Diabetes mellitus           | 0.0     | 28.0         | 20.0                | 37.1         | 0.006a    |
| 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 | < 0.001b  |
| Duration of hypertension    | -       | 8 (0.4-3.2)  | 5 (1.4-26.3)       | 11.1 (0.6-3.2) | 0.202b    |
| Duration of diabetes        | -       | 17.0 (0.6-3.1) | 22.6 (18-24.9) | 16.0 (4.2-25.0) | 0.207b    |
| Duration of CKD             | -       | 2.4 (0.3-16.9)a | 4.2 (1.4-25.3)ab | 6.9 (0.6-21.8)b | 0.001b    |
| Treatment duration of CKD   | -       | 2.5 (0.3-16.9) | 2.3 (0.2-5.8) | 2.5 (0.1-21.8) | 0.484b    |

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.
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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)ab |
|                               | 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.

| ABR | Groups | Ear Frequency | Control     | Conservative | Peritoneal dialysis | Hemodialysis |
|-----|--------|---------------|-------------|--------------|---------------------|--------------|
| I-V | Right  | 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 |
| I-V | Left   | 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, 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. 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. Additionally, transplantation is usually the treatment of last resort, and thus patients who 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, 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 ion concentrations of sensory cells. However, most studies did not demonstrate a significant effect of a single dialysis session on hearing. 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. and by Nikolopoulos et al. 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 & Lam and by Naderpour et al. Although hemodialysis may be a more aggressive method regarding the cochlea by possibly causing ionic changes in the cell membrane, 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.

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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