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Cochlear sensitivity in children with chronic kidney disease and end-stage renal disease undergoing hemodialysis

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ABSTRACT

Objectives: Auditory system abnormalities commonly occur in patients with chronic renal disease and end-stage renal disease undergoing hemodialysis. The aim of this study was to determine the relationship between cochlear sensitivity and hemodialysis in dialytic and non-dialytic chronic kidney disease patients.

Methods: The study included children aged 6–18 years that were divided into 3 groups: 36 non-dialytic patients with chronic kidney disease, 16 end-stage renal disease patients undergoing hemodialysis, and 30 healthy controls. Blood urea nitrogen, serum cystatin C levels, duration of chronic kidney disease, and the duration of hemodialysis were compared between the chronic kidney disease patients and end-stage renal disease patients undergoing hemodialysis. Hearing health was measured via tympanometry, pure-tone audiometry and distortion product otoacoustic emissions testing.

Results: Distortion product otoacoustic emission amplitudes and signal-to-noise ratios were significantly lower at all frequencies tested in the non-dialytic and dialytic groups than in the control group ($p < 0.05$). Patients with normal hearing had significantly lower distortion product otoacoustic emission amplitudes and signal-to-noise ratios than the healthy controls ($p < 0.05$). The duration of CKD, the cystatin C level, and the blood urea level were not associated with hearing loss. The present findings suggest that there was a significant association between the duration of HD and hearing loss.

Conclusion: The present findings show that there was impaired cochlear function in the dialytic and non-dialytic patient groups, regardless of hearing loss, as compared to the control group. Patients with chronic renal disease—both dialytic and non-dialytic—should be monitored to prevent any further deterioration by avoiding potential ototoxic agents, even if their hearing thresholds are within normal limits.

1. Introduction

Chronic kidney disease (CKD) is defined as irreversible kidney damage and/or reduction in kidney function that can result in a further decrease in kidney function [1]. CKD affects several organs [2]. Auditory system abnormalities are common in CKD patients [3]. Although the pathophysiology of hearing loss in CKD patients remains unclear, many factors have been suggested, including ototoxic drug use, elevated serum urea, electrolyte disturbance, edema and atrophy of hair cells, neuropathy, hypoxia and hypotension, and changes in blood pressure during hemodialysis (HD) [2,4,5].

Hearing loss can become more severe over time in pediatric patients and negatively affect the ability to communicate with other people, resulting in social isolation, anger, low self-esteem, and depression [6–8]. HD might play a role in the development of hearing loss in CKD patients, although earlier studies on the effects of HD have yielded inconsistent findings regarding its role in hearing loss [2,9]. The association between CKD and hearing loss was first described in patients with Alport syndrome [10], which was followed by several studies on hearing loss in CKD patients [3,11–14], but few studies have investigated the effect of HD versus conservative treatment on hearing in pediatric CKD patients [15,16].

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Otoacoustic emissions require a healthy middle and inner ear for detection. Otoacoustic emissions are sounds of cochlear origin that can be recorded using a microphone fitted in the ear canal. Otoacoustic emissions are simple, objective, and non-invasive indicator of outer hair cell function, which is indicative of cochlear function. These emissions can be used to monitor cochlear changes, such as those that occur in patients receiving ototoxic medication [17]. In addition, as otoacoustic emissions testing is objective, it is suitable for use with non-compliant patients, including newborns, children, and cognitively impaired elderly patients. There are two types of otoacoustic emissions used for clinical testing: transient evoked otoacoustic emissions (TEOAEs) and distortion product otoacoustic emissions (DPOAEs).

DPOAEs are generated in the cochlea in response to two simultaneous tones of different frequency. DPOAEs are measured in individuals to obtain frequency-specific and quantitative data regarding cochlear sensitivity [18]. When hearing loss is detected via pure-tone audiometry (PTA), a decrease line in the same frequency region is observed via DPOAE testing. The high test–retest reliability of DPOAE testing enables monitorization of dynamic changes in the cochlea. It is well known that DPOAEs are more useful for detecting inner ear dysfunction and early changes in hearing acuity than PTA and auditory brainstem response (ABR) [19,20]. DPOAEs can be used in patients with diminished attention to differentiate tones in PTA. DPOAE testing is often more useful than TEOAE testing, because DPOAEs can be obtained over a wider frequency range typically (1–6 kHz and can be recorded up to 10 kHz). High frequency assessment is extremely important in young patients who initially suffer from high frequency hearing loss.

The literature includes a limited number of studies that have reported cochlear sensitivity (based on DPOAEs) in patients with CKD [15,21]. To the best of our knowledge no study to date has evaluated signal-to-noise ratios (SNRs) or distortion product (DP) levels at 1–8 kHz in dialytic and non-dialytic CKD patients. The aim of the present study was to determine the relationship between cochlear sensitivity and CKD in dialytic and non-dialytic pediatric CKD patients. Hearing function was measured via DPOAE testing and PTA. An additional aim was to determine the effect of CKD and HD on inner ear function.

2. Methods

2.1. Patients

This cross-sectional study included children aged 6–18 years who were referred due to CKD and divided into three groups: 36 non-dialytic CKD patients (ND CKD group) ($15 <$ glomerular filtration rate (GFR) < 90 mL min$^{-1} \times 1.73$ m^{-2}), 16 dialytic end-stage renal disease patients (HD ESRD group) (GFR < 15 mL min$^{-1} \times 1.73$ m^{-2}), and 30 age- and gender-matched healthy controls. GFR was measured via the Schwartz equation using height (cm) and serum creatinine (mg dL^{-1}) [22]. Additional variables studied were blood urea nitrogen (BUN), serum cystatin C, duration of CKD, and duration of HD. This study was conducted at Antalya Research and Education Hospital, Department of Pediatric Nephrology, Antalya, Turkey, between December 2014 and April 2015.

Children with a history of otological and audiological dysfunction, chronic systemic disease, a history of ear surgery, exposure to noise, head trauma, acute or chronic otitis media, or effusion with otitis media were excluded from the study. The age- and gender-matched controls included patients that presented to the hospital for such minor illness as conjunctivitis and dermatitis. All the controls were free of autoimmune-related disease, kidney disease including patients who should be Alport syndrome and prior aminoglycoside treatment, and endocrine disorder, and were not using any medications. All the participants were negative for a history of renal transplantation, chronic disease, active infections, neoplastic diseases, and inflammatory diseases. Written informed consent was obtained from the parents of each participant and the study protocol was approved by the Antalya Education and Training Hospital Ethics Committee.

2.2. Audiometric procedures

Otoscopic examinations were performed before audiometric testing, followed by tympanometry to rule out middle ear pathologies. Tympanometry was performed using an impedance audiometer (AZ26, impedance audiometer, Interacoustics, Assens, Denmark) and an 85-dB sound pressure level tone set at 226 Hz to measure middle ear function. Patients and controls with normal peak compliance, peak pressure, gradient, and ear canal volume, according to American Speech-Language-Hearing Association criteria, were included in the study [23]. After evaluation of the middle ear, PTA (AC-40 Clinical Audiometer, Interacoustics, Assens, Denmark) was performed in a soundproof booth by the audiologist. The audiometer was calibrated in decibels hearing level (dB HL), according to International Organization for Standardization [24] and American National Standard Institute standards [25]. PTA thresholds were measured bilaterally at 0.5–8 kHz (0.5, 1, 1.5, 2, 3, 4, 6, and 8 kHz) using the modified Hughson-Westlake procedure and a pair of Telephonics TDH-39P headphones [26]; this procedure is detailed in ANSI S3.21-1978 (R-1992) [27]. All thresholds were calculated in dB HL; the actual threshold was set after 2 of 3 responses were consistent.

Calibration of DPOAE testing equipment was performed and a correct fit of the probe in each participant's external ear canal was confirmed before each evaluation. DPOAEs were documented using a Madsen Capella otoacoustic emission device (Otometrics, Copenhagen) at $2f1 - f2$ frequencies. Two simultaneous pure-tone signals were administered to the cochlea at two different frequencies ($f1$ and $f2$) and the greatest intensity of the distortion product response was documented using the formula: $2f1 - f2$. Once the responses were received, they were presented in graphic form. The recordings were obtained using a ratio of $f2$:$f1$. The ratio between the two frequencies was fixed at 1:22, based on varying mean values of 1, 1.5, 2, 3, 4, 6, and 8 kHz. Stimulus intensities were both 65 dB for $L1$ and $L2$ (the intensity level of $f1$ and $f2$ are, respectively $L1$ and $L2$); these levels primarily obtain DPOAEs from those with hearing impairment. SNRs were defined as signal to mean noise ratio. SNRs and DP amplitudes were recorded via a microphone to obtain cochlear sensitivity data, according to the diminished intensity of the signals.

2.3. Statistical analysis

Statistical analysis was performed using SPSS v.22.0 for Windows (IBM Corp., Armonk, NY). The Shapiro–Wilks test was used to determine the normality of the distribution of data. The Kruskal–Wallis test was used to compare the three groups (ND CKD, HD ESRD, and control) and the Mann–Whitney U-test was used to compare ND CKD and HD ESRD patients without hearing loss. Dunn's test of multiple comparisons was performed for post hoc testing after a significant Kruskal–Wallis test. Categorical variables were measured using Fisher's exact test and Pearson's chi-square test. The level of statistical significance was set at $p < 0.05$.

3. Results

The study included 36 non-dialytic CKD patients, 16 dialytic ESRD patients (27 females [51%] and 25 males [49%]), and 30