

Editorial Review

Hearing in renal failure

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Introduction

The incidence of sensorineural hearing loss among patients with chronic renal failure (CRF) is considerably higher than in the general population. Bazzi *et al.* [1] found an incidence of 77% including patients with mild and very mild hearing loss. Ozturan and Lam [2] found a moderate to severe hearing loss in 46% of the tested patients. The general consensus in audiometric findings among patients with CRF claims a high frequency hearing loss [3,4] with a notch at 6 kHz [2].

Presence of hearing loss and estimation of type and degree constitute one of the most common methods used to investigate the effects of renal disease on the auditory system. Degree of hearing loss may give an indication of the extent of damage to auditory function, whereas the type of hearing loss may distinguish between lesions in the outer and middle ear (conductive hearing loss) or the cochlea and the neural pathways (sensorineural hearing loss). In addition to these indicators, the reports to be reviewed in the following sections have also described auditory function in CRF with methods such as otoacoustic emissions (OAEs) (namely transient evoked OAEs, TEOAEs and distortion product OAEs, DPOAEs), and auditory evoked potentials (AEPs).

OAEs are low level sounds emitted by the cochlea in the process of receiving the sound vibrations and transforming them to cellular and neural stimulation. Recording of OAEs implies a functioning cochlea and healthy middle ear mechanism. TEOAEs are produced by the action of the hair cells, and they reflect special characteristics of the stimulus. DPOAEs are produced when the ear is stimulated with a combination of pure tones that are close in frequency (the primary tones). DPOAEs reflect non-linear processes of hair cell

motion. Both TEOAEs and DPOAEs are generated by the active cochlear mechanisms responsible for enhancing basilar membrane vibration; this is known as the 'cochlear amplifier' [5].

AEPs represent neural activity related to auditory stimulation. They show summated neural energy at the various synaptic levels of the auditory pathway; this activity is generated by specific stimuli and extracted from the ongoing EEG activity by specialized technical manipulation. AEPs are recorded from the scalp representing activity in the cochlea and brainstem, thalamus and cortical areas. They are distinguished in early, middle and late evoked potentials, respectively.

AEPs recorded from the cochlea include the cochlear microphonic (CM), the summing potential (SP) and the auditory nerve action potential (AP). The CM originates in the outer hair cells and mirrors the incoming signal. The SP also reflects hair cell function. The auditory nerve AP represents the sum of synchronous responses of auditory nerve fibers at the level of the cochlea. The largest component of the AP is the N1, a characteristic wave that constitutes also the first identifiable component of the auditory brainstem response (ABR). The ABR is also an 'early' evoked response, as it reflects neural function along the ascending auditory pathway, from the cochlea to the inferior colliculus. The five distinct waves of the normal ABR waveform are mainly generated by successive nuclei in the ascending auditory pathway: waves I and II originate from the distal and proximal portions of the auditory nerve, respectively, wave III originates from the cochlear nucleus, wave IV originates from the superior olivary complex and wave V originates from the lateral lemniscus/inferior colliculus. Each higher level order wave receives contributions from lower levels of the pathway [6].

The AEP reflecting function from auditory cortical areas is the Auditory Late Response (ALR). Major identifiable waves of the ALR are the N1 and P2 waves. ALR measurements reflect higher-level auditory function [7]. In general, latency of AEP waves indicates speed of neural function, whereas amplitude is a variable indicator of response robustness.

The cochlea and kidney have similar physiological mechanisms, namely the active transport of fluid

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and electrolytes accomplished by the stria vascularis and the glomerulus, respectively [2,8]. They may also have common antigenicity [9,10]. These may account for similar effects of medications (i.e. nephrotoxic and ototoxic effects of aminoglycosides) and immunological factors on the two organs. Inner ear and kidney development are both influenced by similar genetic factors in hereditary conditions such as Alport's syndrome and branchio-oto-renal syndrome.

Several aetiological factors have been linked to hearing loss in renal failure [11] including use of ototoxic medications, electrolyte disturbances, hypertension [12,13] and haemodialysis treatment itself [1,14–16]. Brookes [17] suggested that vitamin D deficiency might be a contributing factor to hearing loss in renal failure. Adler *et al.* [18] found a significant reduction of Na^+ , K^+ -activated ATPase in the inner ear of uraemic guinea pigs. They also reported an inverse correlation between serum creatinine levels and Na^+ , K^+ -activated ATPase. As Na^+ , K^+ -activated ATPase in the cochlea is important for maintaining cationic gradients, they suggested that inhibition of this enzyme system may be a factor in inner ear dysfunction among uraemic patients [18]. Treatment evolution may have modified the contribution of several factors in causing hearing loss. For example, hyponatraemia, a common occurrence three decades ago [13], is no longer a concern with newer haemodialysis methods.

Other pathologies linked to renal failure may contribute to auditory dysfunction. Albertazzi *et al.* [19] documented the presence of alterations in the peripheral and central nervous system of uraemic patients demonstrating the existence of 'uraemic neuropathy'. Di Paolo *et al.* [20] indicated a very high incidence of nerve conduction dysfunction in groups of CRF patients. They found decreased conduction velocity in sensory and motor units, with the sensory units being more affected than the motor. In agreement with these studies, several ABR studies of CRF indicated dysfunction of the auditory nerve and pathways [4,15,21–27].

Renal failure is linked to hearing loss irrespective of the treatment method; it has been difficult, however, to separate the effects of disease duration, haemodialysis treatment, possible contributions of medication ototoxicity, age, exposure to noise and possible interactions. As treatments become more efficient and patients' life span increases, there is a better chance of observing co-existing conditions as well as the added factors of geriatric concerns. This issue is circumvented when children with CRF are observed [27–32]. Antonelli *et al.* [4] present a detailed review of possible causes of hearing loss in patients with CRF; they stipulate that even with strict control for confounding variables, there remains evidence of sensorineural hearing loss among these patients. Published research exploring hearing loss in CRF presents common directions that will be reviewed in the following sections.

Induced acute renal failure

Study of animal models with induced renal failure offered more specific description of the disease and effects. Although methodologies of inducing renal failure and time of measurements of auditory function vary among studies, the general consensus seems to be that the site of auditory lesion in induced CRF is the cochlea. Ohashi *et al.* [33] found that with greater renal damage, amplitudes of the cochlear potentials N1 and CM were smaller and latency of N1 was prolonged, while AP was within normal range. This pattern points to the sensory cells of the cochlea as the site of damage caused by the disease, although light microscopy of the cochlea did not reveal alterations. The authors attributed the hearing loss to metabolic disturbances, electrolyte imbalance and endocrine dysfunction due to the disease.

Ikedo *et al.* [34] induced renal failure to guinea pigs and measured cochlear potentials at 1, 2 and 3 months post-operatively. They initially found small changes in the compound AP and CM, which were exacerbated with time; they found no change in the endocochlear potentials similar to Ohashi *et al.* [33]. They concluded that CRF affects the cochlear hair cells. Furthermore, they observed a synergy between CRF and noise exposure because animals with CRF did not recover from exposure to broadband noise as did controls. This may suggest that patients with CRF, apart from the associated hearing loss, might be susceptible to additional noise-induced hearing loss [34]. Shvili *et al.* [24] reported similar findings by inducing CRF in rats and measuring ABRs after 3 months. They found prolongation of wave I, with normal I–V interpeak latency, suggesting a site of damage either at the cochlea or along the proximal part of the acoustic nerve.

Anteunis and Mooy [35] presented a case of acute renal failure and hearing loss. Hearing loss and neural function of the auditory nerve recovered after therapy indicating that acute renal failure causes reversible cochlear and neural dysfunction.

Chronic renal failure and hearing loss

Incidence and aetiology, site of lesion

Hearing loss among patients with CRF has been a common finding in studies investigating the effects or renal failure on auditory function. Despite differences in methodologies and indices of auditory function, existence of hearing loss has been a common thread (Tables 1 and 2). The higher incidence of hearing loss among children with CRF has long been established and is constantly being verified by new studies [27]. Bergstrom *et al.* [36] reported hearing loss in 40% of the CRF patients on haemodialysis. Bergstrom and Thompson [28] reported that 47% of 151 paediatric end-stage renal patients had hearing loss. Hearing loss is a more commonly reported finding than

Table 1. Studies on effects of haemodialysis treatment on hearing (1HD: one haemodialysis treatment session)

Study	# subjects	Age (years)	Duration of study	Audiometry method	hearing loss	Effects of haemodialysis on hearing
Ozen <i>et al.</i> [48]	7	Adults	1 HD	PT	yes	20 dB improvement
Visencio and Gerber [50]	8	Adults	5 HD	PT	yes	no
Klingerman <i>et al.</i> [45]	12	Adults	1 yr	PT	yes	No
Rossini <i>et al.</i> [15]	2		1 HD	ABR	yes	yes
Pratt <i>et al.</i> [51]	38	Adults	1 HD	ABR	yes	yes
Magliulo <i>et al.</i> [52]	20	Adults	1 HD	ABR	yes	yes
Gartland <i>et al.</i> [12]	31	Adults	1HD	PT	yes	improved on 1/3 of pts
Pagani <i>et al.</i> [49]	98	Adults	<5->10 yrs	ABR	yes	No
Bazzi <i>et al.</i> [1]	91	Adults	<5->10 yrs	PT	yes	No
Nikolopoulos <i>et al.</i> [30]	9	Children	1 HD	PT	yes	No
Ozturan and Lam [2]	15	Adults	1HD	PT + DPOAEs	yes	No
Niedzielska <i>et al.</i> [47]	7	Children	1HD	ABR	yes	yes
Stavroulaki <i>et al.</i> [32]	9	Children	1HD	PT-DPOAEs	yes	No
Serbetcioglu <i>et al.</i> [16]	19	Children+adults	1HD	PT	yes	No
Orendorz-Fraczkowska <i>et al.</i> [27]	20	Children	1 HD	ABR+DPOAE	yes	Yes, subclinical changes
Yassin <i>et al.</i> [13]	71	Adults	3 yrs	PTA	yes	improvement
Kusakari <i>et al.</i> [53]	37	Adults	4 years/by 3-12 months	PTA	yes	No
Heinrich <i>et al.</i> [46]	20	Adults	1-4 years	PTA	yes	No
Mirahmadi and Vaziri [54]	23	Adults	1-5 years	PTA	yes	No
Johnson and Mathog [3]	61	Adults	1 HD	PTA	yes	No

Table 2. Studies on effects of CRF on hearing

Study	# of subjects	Age (years)	Audiometry method	Hearing loss/auditory dysfunction
Henrich <i>et al.</i> [46]	20	Adults	PT	yes
Charachon <i>et al.</i> [39]	54	Adults	PT	yes
Risvi and Holmes [43]	1	Adults	PT	yes
Johnson <i>et al.</i> [3]	71	Adults	PT	yes
Jonhson and Mathog [52]	61	Adults	PT	yes
Kusakari <i>et al.</i> [53]	229	Adults	PT	yes
Bergstrom and Thompson [36]	151	Children	PT	yes
Rossini <i>et al.</i> [15]	17	Adults	ABR	yes
Komsuoglu <i>et al.</i> [21]	36	Adults	ABR	yes
Marsh <i>et al.</i> [22]	27	Adults	ABR+ERP	yes
Anteunis, Mooy [35]	1	Adult	PT	yes
Baldini <i>et al.</i> [25]	19	Adults	ABR	yes
Antonelli <i>et al.</i> [4]	46	Adults	PT+ABR	yes
Warady <i>et al.</i> [26]	14	Children	PT+ABR	yes
Mancini <i>et al.</i> [29]	68	Children	PT	yes
Nikolopoulos <i>et al.</i> [30]	46	Children	PT	yes
Samir <i>et al.</i> [31]	34	Children	TEOAE	yes
Stavroulaki <i>et al.</i> [32]	9	Children	PT+DPOAE	yes
Zeigelboim <i>et al.</i> [40]	37	Adults	PT	yes
Orendorz-Fraczkowska <i>et al.</i> [27]	20	Children	PT+OAE+ABR	yes

vestibular dysfunction. Kusakari *et al.* [37] reported on inner ear function of 229 patients on chronic haemodialysis. They found that 60% had hearing loss, 36% had vestibular dysfunction and 26% had a combination of both. Johnson and Mathog [38] noted high frequency hearing loss in 61 adults early in the course of haemodialysis. Charachon *et al.* [39] reported that 75% of 54 patients with CRF had hearing loss. Zeigelboim *et al.* [40] measured thresholds between 9 and 18 kHz in 37 patients with CRF undergoing conservative treatment and a control group with normal hearing function. Age ranges in both groups were 30-59 years. They found a more severe

high-frequency hearing loss in the group with CRF. Hearing loss among patients with CRF seemed to deteriorate further a year after the first evaluation. Related research is briefly summarized in Table 2.

Bergstrom *et al.* [36] compared a group of patients with hearing loss of unknown aetiology, one with stria deposits and one with neither. They found no difference between the groups. Cochlear stria deposits were not related to vascular disease or calcium metabolism, but their size could be related to the presence of hearing loss. Histopathological studies of the inner ear in renal failure are sparse and provide valuable insight to how the disease may affect the

auditory pathway [41,42]. Charachon *et al.* [39] applied the surface preparation method on temporal bones from this group. They reported on a case with bilateral deafness associated with demyelination of the pre-ganglionic cochlear fibres, and a cell loss of about 25% in the spiral ganglion. The high incidence of hearing loss in this group was attributed to the premature aging caused by renal failure.

Risvi and Holmes [43] reported a patient with progressive hearing loss parallel to progression of CRF, peritoneal dialysis and haemodialysis. They found anatomic changes in the labyrinth (collapse of the endolymphatic system, oedema and atrophy), which they attributed to osmotic disequilibrium caused by haemodialysis. However, the finding of progressive hearing loss is not consistent with published reports.

Antonelli *et al.* [4] investigated auditory function in older adults using pure tone measurements and ABR. They compared pure tone thresholds, ABR wave latencies and interpeak latency differences of patients with CRF undergoing haemodialysis with a control group of gender and age-matched subjects. They also compared ABR findings of the patients with CRF with a second control group matched additionally by degree of hearing loss. They reported that pure tone hearing loss as well as wave I latency of the CRF group was correlated with age and negatively correlated with serum albumin level. Wave I was additionally correlated with calcaemia. These findings were interpreted as effects of age and CRF. The correlations with albumin and calcium might explain some of the changes observed in histopathological temporal bone studies of patients with CRF including sedimentations in the stria vascularis and loss of outer hair cells and spiral ganglion cells [41], as well as strial deposits [42]. A contradictory finding was reported by Bergstrom *et al.* [36], who found no correlation between cochlear strial deposits and calcium metabolism. After controlling for age, Antonelli *et al.* [4] found that the group with CRF still had a significantly longer wave I–III interpeak latency difference. Because this difference reflects conduction time from the cochlea to the level of the cochlear nucleus, it was interpreted as a subclinical dysfunction of the VIII nerve caused by axonal uraemic neuropathy. CRF would then seem to exacerbate hearing loss and prolong neural conduction even further than aging itself, although it would be difficult to distinguish between the effects of uraemic neuropathy and accelerated aging because of cardiovascular disease. Komsuoglu *et al.* [21] also reported differences in ABR latency between 36 patients with CRF on haemodialysis and 10 controls. These findings indicated neural involvement in the auditory dysfunction associated with renal failure and dialysis. Similarly, Baldini *et al.* [25] reported ABR measures from patients on chronic dialysis in comparison with a control group. They found significant prolongations of waves III and V.

Samir *et al.* [31] recorded TEOAEs in 34 children with CRF, 27 on haemodialysis and seven on conservative treatment. They found four children with conductive hearing loss (11.8%) and five children (14.7%) with bilateral moderately severe sensorineural hearing loss. The remaining 25 patients had normal hearing when assessed with pure tone audiometry. This finding is seemingly in contrast to findings of studies with adult CRF patients (Gartland *et al.* [12] found 53% incidence of high frequency hearing loss, while Morton *et al.* [44] found 50% incidence of ultra high frequency hearing loss). However, TEOAE testing revealed subclinical signs of cochlear pathology: children with CRF had overall lower echo levels and reproducibility than controls. Forty-six percent of these patients had partial or no TEOAEs. In other words, even among normal hearing children with CRF, OAEs revealed certain signs of cochlear pathology not yet detected by pure tone testing, indicating an increased susceptibility to later-developing hearing loss. It would be expected that cochlear dysfunction would evolve to the hearing loss measured among adults with CRF, especially because the incidence of cochlear dysfunction in children was similar to the incidence of hearing loss in adults. The discrepancy in these findings is that cochlear dysfunction among children was observed in the low-frequency area (<2000 Hz), whereas the consensus among adults with CRF points to a high frequency hearing loss. [12,40,43].

Stavroulaki *et al.* [32] found hearing loss in 55.5% of the children with CRF, with hearing mainly affected in the high frequencies (12 kHz). Children with CRF had poorer hearing in all frequencies above 1000 Hz. DPOAE amplitudes were smaller among children with CRF, even in frequencies where hearing was normal. OAEs were absent or smaller among the CRF children. These findings are in accordance with evidence of cochlear dysfunction as reported by Samir *et al.* [31] corroborating the hypothesis that children with CRF (on haemodialysis) may have signs of adverse effects on cochlear function, which is predictive of upcoming hearing loss. Furthermore, Orendorz-Fraczkowska *et al.* [27] reported that latencies of ABR wave I, III, V and interpeak latencies I–III and I–V were longer than controls', indicating a retrocochlear involvement in addition to cochlear dysfunction.

Warady *et al.* [26] obtained pure tone thresholds and ABRs from 14 children on long-term peritoneal dialysis associated with aminoglycoside therapy. Overall hearing was worse among CRF patients than in controls. They found no evidence that progressive hearing loss was associated with intraperitoneal aminoglycoside therapy. Furthermore, they concluded that PTA is a better indicator of hearing function than click-evoked ABR.

In summary, auditory function is affected by CRF in all reported studies. Cochlear as well as retrocochlear findings are reported.

Association of hearing loss, disease duration and blood tests

An association between measures of renal and hearing function would specify how hearing is affected by CRF. Several studies have investigated correlations between duration of the disease, blood levels and hearing. Mancini *et al.* [29] reported hearing loss in 47.5% of patients with congenital disease and in 21% of children with acquired renal disease. Henrich *et al.* [45] found that 75% of the patients showed no deterioration of hearing during the 4-year time of follow-up. They concluded that hearing loss is common in renal failure, but it does not worsen with duration of treatment. Samir *et al.* [31] found no correlation between pure tone audiometry findings and OAE measures with serum electrolyte levels. Kusakari *et al.* [37] reported that inner ear dysfunction (including hearing loss and vestibular dysfunction or a combination) was not correlated with Hct, BUN and serum creatinine levels or with duration of haemodialysis treatment. Johnson *et al.* [3] found no relationship between fluctuations of hearing and serum urea nitrogen, creatinine, K^+ , Na^+ , Ca^{++} and glucose. In a similar report, Jorgenson . [42], found that hearing loss was not related to changes in creatinine, K^+ , Na^+ , Ca^{++} , glucose, BUN, blood pressure, weight or hyperlipidaemia.

Gafter *et al.* [23] recorded ABRs from patients with CRF before initiation of dialysis treatment and from patients on long-term dialysis. They found that both groups had delayed latencies of waves III and V. Furthermore, the second group had prolonged inter-peak latency I–V. There was no correlation between ABR measures and serum urea, creatinine, PTH or duration of haemodialysis. In agreement with Mancini *et al.* [29], they suggested that neural conduction along the auditory pathway is delayed irrespective of haemodialysis onset, basically due to the disease. Baldini *et al.* [25] found no correlation between ABR wave prolongation measures and plasma level of vitamin B12, folic acid, PTH and β -20microglobulin.

Duration of disease and/or blood measures do not seem to have a significant impact on auditory function.

Effect of treatment method on auditory function

Mancini *et al.* [29] investigated sensorineural hearing loss in three groups of children with CRF: 14 on conservative treatment, 18 on haemodialysis and 36 with renal transplants. They found sensorineural hearing loss in 29% of the children on conservative treatment, 28% of the children on haemodialysis and 47% of the children with renal transplants. There were no correlations between hearing loss, duration of nephropathy and haemodialysis treatment. The authors concluded that, as the incidence of hearing loss was identical in the conservative treatment

and haemodialysis groups, there must be an early onset of the impairment, suggesting that the disease is causatively linked to hearing loss, but not the treatment.

Samir *et al.* [31] found a significantly higher incidence of cochlear dysfunction among children on haemodialysis compared with children on conservative treatment, in contrast to [29] despite overall similar median duration of haemodialysis. However, renal function among patients on dialysis is worse than among patients on conservative treatment, which further complicates the distinction between the effects of a more severe renal impairment from effects of the treatment. Albeit novel and interesting, this finding should be interpreted with caution, in light of the small number of subjects in the conservative treatment group.

Nikolopoulos *et al.* [30] evaluated auditory function among 46 children with CRF, 22 with pre-end stage renal disease, 15 on haemodialysis, and 9 on continuous ambulatory peritoneal dialysis (CAPD). They found that a total 41.3% had hearing loss. Conductive hearing loss and ototoxicity accounted for 11%, whereas 30.4% was of unknown aetiology, therefore, it could be attributed to CRF or haemodialysis. Hearing was mostly impaired in the high frequencies, with 30% of the ears affected to a lesser degree in the middle and low frequencies. Forty-seven percent of the children in the haemodialysis group had hearing loss, compared with 32% in the pre-end stage of renal insufficiency group and none in the CAPD group. However, when adjusted for small samples, the difference between the two methods of dialysis was not statistically significant. The finding that children on haemodialysis suffer hearing loss more often than those on conservative treatment, was consistent with Samir *et al.* [31].

Marsh *et al.* [22] recorded AEPs from two groups of patients: 13 CAPD patients and 14 patients on haemodialysis and compared them with those from a control group. They found some differences in brainstem responses; however, the most striking findings occurred in the later potentials. In the chronic dialysis group, middle latency wave N1-P2 was delayed and its amplitude was smaller than controls and CAPD patients for the low-task demand, whereas both CRF groups had smaller amplitudes under the high-task. The authors concluded that the CAPD group showed function closer to normal than the chronic dialysis patients [22].

Rossini *et al.* [15] recorded ABRs from 17 CRF patients on conservative treatment and 11 on chronic dialysis. They found abnormal responses in 32.15% of the patients. Waveform morphology was normal in most of the patients, with latency prolongation of all waves following wave I. Altered ABRs were more frequent in the conservative treatment group.

The above studies showed that method of treatment may influence the impact of the disease on hearing, a topic yet to be conclusively investigated.

Effects of a single session and short term haemodialysis

Early and more recent reports present conflicting findings concerning possible contributions of haemodialysis treatment to hearing loss in renal failure. Methodology of these investigations includes reports on the effects of a single session on hearing function [2,12,16,46,47] and comparisons of patient groups with varying duration on the treatment [1,12,48]. Many studies are briefly summarized in Table 1.

Ozen *et al.* [47] reported an improvement of 20 dB in the hearing of patients following haemodialysis. They suggested that changes in serum somolality, BUN and fluid retention may reverse the hearing impairment post-dialysis. However, as changes in the dialysis method alleviated wide fluctuations of these parameters, hearing may not be as affected from haemodialysis today as it was at that time. There are several more recent reports in the literature contradicting the 'hearing improvement' finding. Visenscio and Gerber [49] reported that pure tone thresholds did not change significantly after haemodialysis. They did observe individual threshold shifts which they attributed to temporary imbalance in the labyrinth caused by haemodialysis.

Gartland *et al.* [12] recorded pure tone thresholds on 31 patients before and after a session of haemodialysis. They included 125 Hz in the audiograms and documented a low frequency hearing loss, which improved significantly on one-third of the patients after dialysis. As low-frequency sensorineural hearing loss is related to endolymphatic hydrops, they postulated that changes in fluid balance during haemodialysis may be accountable for the low frequency hearing improvement. However, there was no correlation between weight and hearing changes after haemodialysis. Ozturan and Lam [2] found a notch at 6 kHz among CRF patients not related to haemodialysis indices. Therefore, the frequency specificity of possible CRF/haemodialysis effects remains inconclusive.

Serbetcioglu *et al.* [16] tested pure tone thresholds of 19 patients 14–87 years of age prior to and 1 and 24 h following a randomly selected session of haemodialysis. They noted a permanent high frequency hearing loss, but no specific effects of haemodialysis. Similarly, Nikolopoulos *et al.* [27] found no effect of a single haemodialysis session on the hearing of nine haemodialysed children.

Kligerman *et al.* [50] evaluated the hearing of patients with CRF, following 12 of them for 1 year as they were going through haemodialysis. A second group of patients not on haemodialysis were re-evaluated at the end of the year; a third group having received haemodialysis for 1.5, 2, 3 and 6 years was included in the study. Similarly, Bazzi *et al.* [1] reported pure tone audiometric findings on three groups of patients: patients on haemodialysis for <5 years, for 5–10 years and for more than 10 years. Both studies found a permanent high-frequency hearing loss

in all groups related to the disease and treatment. They did not report a correlation between haemodialysis duration and severity of hearing loss. Therefore, duration on haemodialysis treatment did not appear to affect the degree of hearing loss in the CRF patient population.

Auditory evoked responses and OAEs were used to evaluate auditory function in several studies. OAE and ABR offer a direct glimpse to cochlear and VIII nerve function, allowing a better exploration of the auditory pathway in CRF.

Ozturan and Lam [2] examined the effects of a single session of haemodialysis on pure tone thresholds and DPOAEs. They tested 15 patients of 19–45 years of age prior to and following a session of haemodialysis in a similar study with Stavroulaki *et al.* [32]. There were no significant changes in the pure tone thresholds or the DPOAE amplitude in either study.

Pratt *et al.* [51] obtained ABRs from 38 patients before and after haemodialysis along with blood chemistry data. They found abnormal ABRs in 24% of the patients at slow stimulus presentation rate (10/s) and in 44% of the patients at the fast presentation rate (55/s). These abnormalities consisted of prolonged latencies and interpeak latency differences indicating both a cochlear and a retrocochlear involvement. The temporary effect of haemodialysis on peaks III and V at the slow rate and I and V at the fast rate were correlated with changes in calcium levels. These findings are consistent with Rossini *et al.* [12], who found a decrease in I–V interpeak latency 26 h following haemodialysis. However, this finding was noted in only two patients, which precludes generalization.

Magliulo *et al.* [52] found that brainstem function was below normal in 30% of the 20 patients evaluated. They reported a temporary improvement of brainstem conduction lasting about 24 h after the treatment. Of the five transplanted patients they examined, three had abnormal brainstem responses. Brainstem function returned to normal after renal transplantation.

Gafer *et al.* [23] recorded ABRs from patients with CRF before onset of dialysis, compared them with those of patients on long-term dialysis, and they evaluated the effects of a single session of haemodialysis. They found that wave latencies were affected in both groups. A single session led to a slight shortening of wave III latency. This finding was probably a temporary change with no lasting effect on neural conduction of patients on long-term dialysis.

Pagani *et al.* [48] recorded auditory evoked responses from patients on haemodialysis for <5 years, between 5 and 10 years and more than 10 years. They found prolongation of wave and interwave latencies when compared with a group of non-CRF controls, but no difference between the groups with CRF. In other words, they found evidence of pathology along the auditory pathway in the CRF groups, with no indication that the length of dialysis treatment or the length of the disease may exacerbate this pathology.

Niedzielska *et al.* [46] analysed the ABR of seven children between the ages of 6 and 17 years. They found that latencies of waves I, III and V were shorter after a session of haemodialysis. They suggested that this temporary improvement of ABR latencies might signal a protective role of haemodialysis on hearing. However, even with the improvement of wave latencies, the ABR waveform was not in the normal range. There was no correlation between uraemic toxic products, fluid overload and the observed changes in the ABR. Based on these findings, they concluded that there was no effect of a haemodialysis session on the ABR of the observed children. Orendorz-Fraczkowska *et al.* [27] corroborated the previous ABR findings and added that interpeak latencies I–III and I–V were significantly shorter after a session of haemodialysis. They also noted appearance of DPOAEs after the haemodialysis session in frequencies where they were non-detectable before the session. Overall emission amplitude increased following haemodialysis. They concluded that normalization of blood parameters might help improve neural conduction and restores hair cell function.

As haemodialysis treatment has changed over the years, it is becoming clear from the most recent literature that there is no correlation between a single session or short-term treatment and changes in the patients' hearing sensitivity or auditory function. The report to the contrary [12] did not find a correlation between low-frequency hearing improvement and parameters measured, in order to explain the observed link between haemodialysis and improvement of low-frequency hearing. As there are no reported studies to corroborate this finding, it remains to be seen whether the prevalent view, that haemodialysis does not affect hearing status, will be changed.

Conclusion

The high incidence of hearing loss among children and adults with CRF is well-documented in published reports. Duration on haemodialysis treatment does not seem to have a significant impact, although the method of treatment may influence the impact of the disease on hearing. The literature concurs that the main site of lesion is cochlear with some retrocochlear findings in auditory brainstem audiometry. However, lack of correlation between hearing function and blood measures precludes a detailed description of the mechanisms causing hearing loss in CRF. Changes in the dialysis treatment have eliminated the temporary effects of single session of dialysis on hearing function. Therefore, based on recent literature, it is evident that there is no correlation between a single session or short-term treatment and changes in the patients' hearing sensitivity or auditory function.

Conflict of interest statement. None declared.

References

- Bazzi C, Venturini C, Pagani C, Arrigo G, D'Amico G. Hearing loss in short and long-term haemodialyzed patients. *Nephrol Dial Transpl* 1995; 10: 1865–1868
- Ozturan O, Lam S. The effect of hemodialysis on hearing using pure-tone audiometry and distortion-product otoacoustic emissions. *ORL J of Oto Rhino lary* 1998; 60: 306–313
- Johnson DW, Wathen RL, Mathog RH. Effects of hemodialysis on hearing threshold. *ORL J Oto Rhino lary* 1976; 38: 129–139
- Antonelli A, Bonfiolii F, Garrubba V *et al.* Audiological findings in elderly patients with chronic renal failure. *Acta Otolaryngologica* 1991; 476 [Suppl]: 54–68
- Glatke TJ, Robinette MS. *Otoacoustic Emissions, Clinical Applications*. 2nd edn, Thieme Publishers, 2002
- Hall JW, III. *Handbook of Auditory Evoked Responses*. Allyn and Bacon Publishers, 1992
- Jacobson JT. *Principles and Applications of Auditory Evoked Potentials* 1994 Allyn and Bacon Publishers 1994
- Arnold W. Inner ear and renal diseases. *Ann Oto Rhino Lary* 1984; 112 [Suppl]: 119–124
- Quick CA, Fish A, Brown C. The relationship between cochlea and kidney. *Laryngoscope* 1973; 83: 1469–1482
- Arnold W. Experimental studies in the pathogenesis of inner ear disturbances in renal diseases. *Archives of Otorhinolaryngology* 1975; 211: 217
- Bergstrom L, Jenkins P, Sando I, English G. Hearing loss in renal disease: Clinical and pathological studies. *Ann Oto Rhino Lary* 1973; 82 [Suppl]: 555–574
- Gartland D, Tucker B, Chalstrey S, Keene M, Baker L. Hearing loss in chronic renal failure – hearing threshold changes following hemodialysis. *J Roy Soc Med* 1991; 84: 587–589
- Yassin A, Badry A, Fatthi A. The relationship between electrolyte balance and cochlear disturbances in cases of renal failure. *J Laryngol Otol* 1970; 84: 429–435
- Hutchinson J, Klodd D. Electrophysiological analysis of auditory, vestibular, and brainstem function in chronic renal failure. *Laryngoscope* 1982; 92: 833–843
- Rossini M, Stefano D, Febbo A, Paolo D, Bascini M. Brainstem auditory responses (BAERs) in patients with chronic renal failure. *Electroen Clin Neuro* 1984; 57: 507–514
- Serbetcioglu B, Erdogan S, Sifil A. Effects of a single session of Hemodialysis on Hearing Abilities. *Acta Otolaryngol* 2001; 121: 836–838
- Brookes GB. Vitamin D deficiency and deafness: 1984 update. *Am J Otol* 1985; 6: 102–107
- Adler D, Fiehn W, Ritz E. Inhibition of Na⁺, K⁺-stimulated ATPase in the cochlea of the guinea pig. A potential cause of disturbed inner ear function in terminal renal failure. *Acta Otolaryngol* 1980; 90: 55–60
- Albertazzi A, Cappelli P, Di Marco T, Maccarone M, Di Paolo B. The natural history of uremic neuropathy. *Contrib Nephrol* 1988; 65: 130–137
- Di Paolo B, Di Marco T, Cappelli P *et al.* Electrophysiological aspects of nervous conduction in uremia. *Clin Nephrol* 1988; 29: 253–260
- Komsuoglu SS, Mehta R, Jones LA, Harding GF. Brainstem auditory evoked potentials in chronic renal failure and maintenance hemodialysis. *Neurology* 1985; 35: 419–423
- Marsh JT, Brown WS, Wolcott D, Landsverk J, Nissenson AR. Electrophysiological indices of CNS function in hemodialysis and CAPD. *Kidney Int* 1986; 30: 957–963
- Gafter U, Shvili Y, Levi J, Talmi Y, Zohar Y. Brainstem auditory evoked responses in chronic renal failure and the effect of hemodialysis. *Nephron* 1989; 53: 2–5
- Shvili Y, Gafter U, Zohar Y, Talmi YP, Levi J. Brainstem auditory evoked responses in rats with experimental chronic renal failure. *Clin Sci* 1989; 76: 415–417
- Baldini S, Radicioni R, Melappioni M *et al.* Utility of electrophysiologic study using the blink reflex and brainstem

- evoked potentials for the evaluation of the course of uremic polyneuropathy. *Minerva Urol Nefrol* 1995; 47: 13–17
26. Warady BA, Reed L, Murphy G *et al*. Aminoglycoside ototoxicity in pediatric patients receiving long-term peritoneal dialysis. *Pediatric Nephrol* 1993; 7: 178–181
 27. Orendorz-Fraczkowska K, Makulska I, Pospiech L, Zwolinska D. The influence of haemodialysis on hearing organ of children with chronic renal failure. *Otolaryngol Pol* 2002; 56: 597–602
 28. Bergstrom L, Thompson P. Hearing loss in pediatric renal patients. *Int J Pediatr Otol* 1983; 5: 227–234
 29. Mancini M, Dello Strologo L, Bianchi P, Tieri L, Rizzoni G. Sensorineural hearing loss in patients reaching chronic renal failure in childhood. *Pediatr Nephrol* 1996; 10: 38–40
 30. Nikolopoulos TP, Kandiloros DC, Segas SV *et al*. Auditory function in young patients with chronic renal failure. *Clin Otolaryngol* 1997; 22: 222–225
 31. Samir M, Riad H, Mahgoub M, Awad Z, Kamal N. Transient otoacoustic emissions in children with chronic renal failure. *Clin Otolaryngol* 1998; 23: 87–90
 32. Stavroulaki P, Nikolopoulos TP, Psarommatis I, Apostolopoulos N. Hearing evaluation with distortion-product otoacoustic emissions in young patients undergoing hemodialysis. *Clin Otolaryngol* 2001; 26: 235–242
 33. Ohashi T, Kenmochi M, Kinoshita H, Ochi K, Kikuchi H. Cochlear function of guinea pigs with experimental chronic renal failure. *Ann Oto Rhinol Laryn* 1999; 108: 955–962
 34. Ikeda K, Kusakari J, Arakawa E, Ohyama K, Inamura N, Kawamoto K. Cochlear potentials if guinea pigs with experimentally induced renal failure. *Acta Otolaryngologica* 1987; 435 [Suppl]: 40–45
 35. Anteunis LJ, Mooy JM. Hearing loss in a uraemic patient: indications of involvement of the VIIIth nerve. *J Laryngol Otol* 1987; 101: 492–496
 36. Bergstrom L, Thompson P, Sando I, Wood R. Renal disease. Its pathology, treatment, and effects on the ear. *Arch Otolaryngol* 1980; 106: 567–572
 37. Kusakari J, Kobayashi T, Rokugo M *et al*. The inner ear dysfunction in hemodialysis patients. 1981; 135: 359–369
 38. Johnson DW, Mathog RH. Hearing function and chronic renal failure. *Ann Oto Rhinol Laryn* 1976; 85: 43–49
 39. Charachon R, Moreno-Ribes V, Cordonnier D. Deafness due to renal failure. Clinicopathological study. *Ann Otolaryngol Chir Cervicofac* 1978; 95: 179–203
 40. Zeigelboim B, Mangaberia-Albernaz P, Fukuda Y. High Frequency Audiometry and Chronic Renal Failure. *Acta Otolaryngol* 2001; 121: 245–248
 41. Oda M, Preciado MG, Quick CA. Labyrinthine pathology of chronic renal failure patients treated with hemodialysis and kidney transplantation. *Laryngoscope* 1974; 84: 1489–1506
 42. Jorgenson MG. Changes in aging in the inner ear and the inner ear in diabetes mellitus. Histologic studies. *Acta Otolaryngol* 1963; 188 [Suppl]: 125–128
 43. Risvi SS, Holmes RA. Hearing loss from hemodialysis. *Arch Otolaryngol* 1980; 106: 751–756
 44. Morton L, Reynolds L, Zent R, Rayner B. Hearing thresholds in CAPD patients. *Advances in Peritoneal Dialysis* 1992; 8: 150–152
 45. Henrich W, Thompson P, Bergstrom L, Lum GM. Effect of dialysis on hearing acuity. *Nephron* 1977; 18: 348–351
 46. Niedzielska G, Katska E, Sikora P, Szajner-Milart I. ABR differences before and after dialyses. *Int J Pediatr Otorhi* 1999; 48: 27–29
 47. Ozen M, Sandalci O, Kadioglu A, Sandalci M, Agusoglu N. Audiometry in chronic renal failure before and after intermittent haemodialysis. *Proceedings of the European Dialysis Association* 1975; 11: 203–209
 48. Pagani C, Bazzi C, Arrigo C, Venturini C, D'Amico G. Evoked Potentials (VEPs and BAEPs) in a large cohort of short- and long-term haemodialyzed patients. *Nephrol Dial Transpl* 1993; 8: 1124–1128
 49. Visencio LH, Gerber SE. Effects of hemodialysis on pure-tone thresholds and blood chemistry measures. *J Speech Hear Res* 1979; 22: 756–764
 50. Kligerman AB, Solangi KB, Ventry IM, Goodman AI, Weseley SA. Hearing impairment associated with chronic renal failure. *Laryngoscope* 1981; 91: 583–592
 51. Pratt H, Brodsky G, Goldsher M *et al*. Auditory brain-stem evoked potentials in patients undergoing dialysis. *Electroencephalogr Clin Neurophysiol* 1986; 63: 18–24
 52. Magliulo G, Gagliardi M, Ralli G, Persichetti S, Muscatello M. BSR audiometry in haemodialysis patients. *Clin Otolaryngol* 1987; 12: 249–254
 53. Kusakari J, Hara A, Takeyama M, Suzuki S, Igari T. The hearing of patients treated with hemodialysis: a long-term follow-up study. *Auris Nasus Larynx* 1992; 19: 105–113
 54. Mirahmadi MK, Vaziri ND. Hearing loss in end-stage renal disease – effect of dialysis. *J of dialysis* 1980; 4: 159–165

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