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Original article

Sensorineural hearing loss in patients reaching chronic renal failure in childhood

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Abstract. The incidence of sensorineural hearing loss (SNHL) was investigated in 68 patients who reached chronic renal failure (CRF) in childhood with the aim of identifying possible risk factors. Tests were carried out by means of pure-tone and impedance audiometry. SNHL was found in 29% of patients on conservative treatment, 28% of patients on hemodialysis, and 47% after renal transplantation. Differences among groups were not significant. A significant correlation was found with the administration of ototoxic drugs (aminoglycosides and furosemide). We hypothesize that SNHL may be reduced in patients with CRF or on renal replacement therapy by strictly monitoring ototoxic therapy.

Key words: Sensorineural hearing loss – Chronic renal failure – Ototoxic drugs

Introduction

About one-third of patients who start renal replacement therapy (RRT) in childhood exhibit one or more disabilities [1]. The most common handicaps are: motor, mental, and of sight and hearing capacity. Hearing impairment was reported in 8.6% of children on RRT by the European Dialysis and Transplant Association Registry [1]. Data on hearing capacity of young patients with chronic renal failure (CRF) are scanty [2]. The aims of this study were to evaluate: (1) the prevalence of sensorineural hearing loss (SNHL) in children with CRF according to treatment; (2) possible causes of the handicap; (3) to identify a group of patients at high risk for SNHL.

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Patients and methods

Patients. The hearing capacity of 68 patients (30 females, 38 males) was studied. 14 children (mean age at the time of testing 11.6 years) were on conservative treatment [mean glomerular filtration rate (GFR) 18 ml/min per 1.73 m^2, range 10–30], 18 (mean age 14 years) were on chronic hemodialysis (HD), and 36 (mean age 16 years) had received renal transplants; 42 patients had a congenital renal disease: urinary tract malformation (24 patients), renal hypo- or dysplasia (9), cystinosis (5), Alport's syndrome (1), other (2); 24 had an acquired disease: steroid-resistant nephrotic syndrome (13), glomerulonephritis (5), hemolytic uremic syndrome (3), other (3); in 2 patients the primary renal diseases were unknown. The mean age of the whole cohort at the start of renal disease was 4.8 years (median 3.6 years, range 0–18), the mean age at the start of HD was 11 years (median 11 years, range 1–20), the mean duration of HD (including transplant patients) was 22 months (median 18 months, range 1–105), and the mean age at first transplantation 12.8 years (median 12.5 years, range 3–20). The mean duration of nephropathies was 105 months (median 96 months, range 7–252)

Methods. All patients underwent audiological assessment by means of pure-tone and impedance audiometry. Pure-tone audiometry was performed using a clinical audiometer (Amplaid 309); the signal parameters were performed in a silent room in one or more sessions, and both the air and the bone conduction was obtained in each patient using standard supra-aural earphones (TDH39 Telephonic). The hearing acuity was calculated as the air conduction threshold, for both ears, in the frequencies from 250 to 8,000 Hz. SNHL was defined as an increase both of the air and the bone threshold, while a conductive loss was defined as the gap between the bone and the air threshold. The degree of the hearing handicap was defined, according to the classification of the Bureau International de Audiophonologie [3], as the mean decibel (dB) threshold increase in the better ear (to evaluate the complete hearing function), for 500, 1,000, 2,000, and 4,000 Hz: mild, from 21 to 40 dB; moderate, from 41 to 70 dB; severe, from 71 to 90 dB; profound, greater than 90 dB.

The type of hearing loss was classified according to the prevalent frequency loss at low (250 and 500), middle (100 and 2,000 Hz), high (4,000 and 8,000 Hz), and pantonal (all) frequencies. Impedance audiometry was performed using a GS 33 middle era analyzer by Grason-Stadler and the tympanograms were typed as A, B, and C according to Jerger's classification [4]. All patients showing abnormal tympanometry (type B or C) were temporarily excluded from the study until they recovered from the conductive impairment of the middle ear following medical therapy (orally administered mucolytic and antihistamine drugs and nasal decongestants). Only patients with tympanometry type A were considered in this study.

Statistical analysis was performed using chi-squared and Student's *t*-tests. Significance was defined as $P<0.05$. We defined as ototoxic at least one treatment with aminoglycoside (at least 7 days of full therapy adjusted to GFR [5]) and/or treatment with furosemide (≥1 mg/kg) for more than 1 week.

Results

Twenty-six patients (38.2%) had SNHL; 25 had a high-frequency hearing loss which was mild in 9 patients (36%), moderate in 7 (28%), and severe in 9 (36%); 10 of these patients (including the 1 with Alport's syndrome) also had middle-frequency impairment which was mild in 1 (10%), moderate in 6 (60%), and severe in 3 (30%). Only 1 patient on HD had a mild hearing loss at low frequency. Six patients needed a hearing aid: 4 showed bilateral moderate SNHL, while 2 had bilateral severe hearing loss; all patients complained of a lack of speech discrimination.

SNHL was identified in 29% of patients with CRF, 28% of those on HD, and in 47% of patients with transplants (Table 1). SNHL was found in 47.5% of patients with congenital renal disease compared with 21% with acquired renal disease [P=0.03, relative risk (RR)=2.3] (Table 2). The mean age at the start and the mean duration of nephropathies or of HD did not significantly influence SNHL prevalence. Previous ototoxic therapy was known in 20 patients (29%): 15 had received at least one course of aminoglycoside (in 9 two or more courses were identified); 5 patients received furosemide intravenously. A precise correlation between SNHL and previous exposure to ototoxic drugs is not possible from our retrospective study. In almost all cases drugs were administered when patients were still on conservative treatment. Doses were adjusted to GFR as indicated in the literature [5], but plasma levels were only measured occasionally. Of these patients, 70% showed SNHL compared with only 25% of those in whom ototoxic drugs had not been identified (P=0.01, RR=1.7) (Table 2). If we compare only patients with urinary tract malformation (n=24), 92% of those who received ototoxic therapy showed SNHL compared with only 8% of those in whom no ototoxic therapy was identified (P=0.0002, RR=11).

Table 1. Prevalence of sensorineural hearing loss (SNHL) according to treatment and renal disease

	n	SNHL				No SNHL		*P**
		High frequencies		Middle frequencies				
		n	(%)	*n*	(%)	*n*	(%)	
CRF	14	4	(29)	2	(14)	10	(71)	
HD	18	4	(22)	1	(5)	13	(72)	NS
TP	36	17	(47)	7	(19)	19	(53)	
Congenital renal disease	42	20	(48)			22	(52)	0.03
Acquired renal disease	24	5	(21)			19	(79)	

CRF, Chronic renal failure; HD, hemodialysis; TP, renal transplant
* Chi-squared test

Table 2. Relationship of SNHL to ototoxic therapy

Ototoxic therapy	SHL		No SHL	
	n	%	*n*	%
Yes	14*	70	6*	30
No	12	25	36	75

* P = 0.001, odds ratio = 6.81, chi-squared test

Discussion

An association between RRT and SNHL has long been described in adult patients on conservative treatment [6], on HD, and after renal transplantation [7], with an incidence of SNHL ranging from 20% to 87% mostly (which is higher than in the normal population) depending on the different criteria for sample selection (excluding or including patients with SNHL due to known causes) and for hearing loss detection (pure-tone audiometry, brain stem auditory evoked potentials) [8, 9]. There is general agreement that almost 80% of cases of SNHL are due to known causes: diabetes, infections, trauma, congenital nephropathies leading to SNHL (such as Alport's syndrome), and ototoxic drugs (aminoglycosides, erythromycin, furosemide, ethacrynic acid) [10–12]. In the remaining 20% of cases, a cause for SNHL has not been identified.

Some hypotheses have been proposed to explain these cases of SNHL: the kidney and cochlea share common antigens and an autoimmune origin of the double defect has therefore been proposed [13]. Ultrastructural, anatomical, and pathophysiological similarities between the kidney and cochlea have been demonstrated [13]. Other authors have proposed a possible common defect in electrolyte transport through membranes [9]. Hearing evoked potentials have been used to test patients with CRF [6, 14]; these tests demonstrated an involvement of both the central and peripheral nervous systems, but this was already present before HD began and is possibly due to uremic neuropathy. Others have proposed involvement of the acoustic nerve as a cause of hearing loss [15]. The role of dialysis is unclear. Patients on HD showed a higher incidence of SNHL than those on conservative treatment [16]. Alterations in the organ of Corti (vascular alteration and cellular loss) have been related to the number of HD sessions, and it has been proposed that long-term HD treatment may cause electrolyte, osmotic, and biochemical alterations leading to SNHL [7].

The effect of kidney transplantation on hearing function is controversial. It has been suggested that kidney transplantation improves hearing function initially but, in the long term, leads to worsening of hearing capacity [17]. This has been attributed to vascular changes in the inner ear due to hyperlipemia induced by steroid therapy, to ototoxic treatment, or recurrence of renal disease [14], and not to transplantation per se. Only one abstract has been published on children which confirms pathological changes in acoustic evoked potentials (prolonged latency of wave V) in CRF, HD, and transplant groups [2].

The present paper is to our knowledge the only study of SNHL prevalence in children on RRT. SNHL was identified in 38% of patients with RRT or CRF. In 15% of cases the damage affected mean frequencies and therefore influences social life. In 9% of all patients in this study it was a real handicap, and was not always corrected by a hearing aid. Patients with CRF and those on HD show the same prevalence of SNHL, which supports an early origin of the impairment. SNHL prevalence in the transplant group, although higher than in the HD and CRF groups, was not significantly different.

Patients with congenital nephropathies are more at risk for SNHL. The duration of nephropathy and HD treatment do not appear to influence the damage; ototoxic therapy, however, is highly related to the prevalence of SNHL. Patients with a urinary tract malformation are at higher risk. This is probably due to antibiotic treatment received early in life (which explains the higher risk for SNHL of congenital nephropathies). It must be stressed that in general antibiotic treatment was reduced according to renal function [5]. It is possible that individual patients react differently to the same treatment. Recently it has been demonstrated that a ribosomal RNA mutation led to an increase in susceptibility to aminoglycoside-induced SNHL in several patients with familial aminoglycoside-induced deafness [18].

We must stress that this is a prevalence study: ototoxic treatment was evaluated retrospectively, which makes it difficult to quantify the doses of drugs administered. In almost 25% of cases of SNHL, the previous use of ototoxic drugs was not demonstrated. We can not explain the causes of impairment in these patients, but we feel that at least in some patients hearing loss could be prevented by making available more information for pediatricians about the correct use of drugs for patients with CRF, monitoring plasma levels of drugs and whenever possible not using ototoxic drugs.

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Literature abstract

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Familial membranoproliferative glomerulonephritis

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Four and two male sibs of two separate families who had biopsy-proven membranoproliferative glomerulonephritis (MPGN) are presented. In the first family four sibs of the first-degree consanguineous marriage showed the clinical picture of nephrotic syndrome without hypocomplementaemia at initial laboratory findings. In the second family two affected sibs showed nephrotic and nephritic syndromes on admission. Family investigations showed normal serum complement, immunoglobulins. T-cell subsets, urine analysis, and serum biochemistry. HLA typing in the two families revealed a common antigen HLA A2 in all affected sibs. Some other reports give suggestive evidence of MPGN in siblings but this is the first report that showed the occurrence of MPGN in four sibs. Our data strengthened the concept that genetic factors are involved in the development of MPGN but additional immunogenetic studies will shed light on the genetic aspects of the disease.