



Does amikacin treatment cause subclinical hearing loss in patients with cystic fibrosis?



Fevzi Solmaz^{a,*}, Ercan Gündoğdu^a, Davut Akduman^b, Mehmet Haksever^a,
Oğuzhan Dikici^a, Fatih Ünal^c

^a Bursa Training and Research Hospital, Department of Otorhinolaryngology, Bursa, Turkey

^b Duzce University, Medical Faculty, Department of Otorhinolaryngology, Duzce, Turkey

^c Bursa Dörtcelik Children's Hospital, Department of Pediatrics, Bursa, Turkey

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ABSTRACT

Introduction: Aminoglycosides (AGs) have been widely used for potential life-threatening bacterial infections. Although AGs are well known for their ototoxic side effects, some AGs such as amikacin are considered less harmful to auditory functions; thus, auditory monitoring is mostly neglected during treatment with these drugs.

Objective: To reflect the potential auditory hazards of repeated amikacin use on the patients with cystic fibrosis (CF).

Method: 32CF patients with prior exposure to at least 3 courses of amikacin (the CF group) and 35 non-CF patients visiting the outpatient clinic with any complaint other than hearing loss and no history of treatment with any AG(the control, or C group) were compared with pure-tone audiometry(PTA). The diagnosis of CF was made by Nanoduck sweat test.

Results: The average age of the participants were 8.25 ± 2.76 years in the CF group and 8.58 ± 2.00 years in the C group (ranging from 5 to 13 years). 29 (43.28%) of the cases were female and 38 (56.71%) were male. Clinical SNHL(sensorineural hearing loss) was detected in 4 of the 32 subjects in the CF group. None of the subjects in the C group exhibited clinical SNHL. There was no statistically significant difference between the groups with regard to presence or absence of clinical SNHL ($p > 0.05$). However, hearing levels of the CF group were around 20 dB(decibel) HL(hearing loss), whereas hearing levels of the C group were around 5 dB. This difference was statistically significant for the pure tone averages of both all frequencies and speech frequencies ($p < 0.05$).

Conclusion: Repetitive exposure to AGs can cause permanent, although mild, sensorineural hearing loss. For prevention, hearing status of the patient should be closely monitored and treatment of choice should be precisely tailored according to the audiological evaluation. This is especially important in patients with CF who frequently experience medical conditions necessitating AGs use.

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1. Introduction

Aminoglycosides (AGs) are bactericidal antibiotics which have been widely used for potentially life-threatening bacterial infections since their invention in 1944 [1]. They are especially important in certain medical conditions such as cystic fibrosis (CF), mainly due to the high bactericidal activity against *Pseudomonas aeruginosa*, the ability to reach high concentrations in respiratory secretions, and the synergistic effect with beta-lactam antibiotics

[2,3]. They are also readily available worldwide, since they are cost-effective and easy to produce in large amounts. These advantages, however, are limited by the ototoxicity of this class of drugs, which is aggravated by their repeated use in these patients. Clinical studies report a rate of sensorineural hearing loss through a range of 0–17% in CF patients [4,5]. Newer AGs such as amikacin and netilmicin are considered less harmful to auditory functions; thus, in most instances auditory monitoring is neglected by physicians responsible for treating these patients. This study presents auditory evaluation of pediatric CF patients who had been repeatedly treated with amikacin and compares it to that of healthy children of the same age group.

* Corresponding author at: Bursa Training and Research Hospital, Department of Otorhinolaryngology, 16800 Yildirim, Bursa, Turkey.

E-mail addresses: solmazfevzi@hotmail.com, drfsolmaz@gmail.com (F. Solmaz).

Table 1
Comparison of the hearing results between groups.

Variables	L(left), R(right)	CF(Cystic Fibrosis)	C(Control)	P value
Audiometry mean(500, 1000, 2000,4000Hz > 25 dB)	L R	4/32 4/32	0/35 0/35	>0.05 >0.05
Audiometry mean(500, 1000, 2000, 4000Hz > 15 dB)	L R	21/32 30/32	0/35 0/35	<0.05 <0.05

Table 2
Comparison of the mean hearing levels.

Variables	L(left), R(right)	CF(Cystic Fibrosis) (Mean ± SD)	C(Control) (Mean ± SD)	P value
Audiometric mean of all frequencies	L (dB) R(dB)	17.96 ± 5.27 21.39 ± 4.20	5.86 ± 2.58 5.43 ± 2.78	0.00004 0.01018
Audiometric mean of 500, 1000, 2000, 4000 Hz frequencies	L(dB) R(dB)	16.25 ± 4.91 20.52 ± 4.52	5.32 ± 2.71 5.15 ± 2.80	0.00048 0.00366

Table 3
The Mean ± SD of 250, 500, 1000, 2000, 4000 and 8000 Hz frequencies in the CF group.

Case	250 Hz		500 Hz		1000 Hz		2000 Hz		4000 Hz		8000 Hz	
	Left (dB)	Right(dB)	Left (dB)	Right(dB)	Left (dB)	Right(dB)	Left (dB)	Right(dB)	Left (dB)	Right(dB)	Left (dB)	Right(dB)
1	18	22	18	21	15	22	17	24	28	25	30	25
2	20	27	21	24	10	36	16	30	22	32	25	33
3	14	25	10	25	17	22	16	21	18	20	20	23
4	13	25	10	25	15	16	15	17	15	21	21	20
5	22	20	22	24	20	16	16	13	21	22	24	22
6	20	21	27	20	21	23	23	21	29	25	31	24
7	21	20	20	19	14	17	13	18	15	22	16	23
8	16	18	15	15	15	18	11	17	17	21	20	22
9	17	19	15	23	13	17	15	20	16	26	20	24
10	16	14	14	23	16	12	15	15	20	17	22	20
11	22	13	19	25	13	13	11	12	24	16	27	18
12	10	22	10	23	12	18	10	19	16	22	18	21
13	30	19	30	18	27	17	25	19	27	21	29	21
14	15	23	14	25	12	16	12	20	15	22	18	24
15	21	25	21	24	20	15	23	15	22	19	22	23
16	26	25	25	26	26	25	25	25	26	25	30	26
17	15	20	14	15	15	15	18	25	17	18	20	20
18	13	20	11	15	15	15	16	22	20	18	23	20
19	18	21	14	22	15	15	22	20	21	18	25	20
20	15	22	12	24	13	15	16	17	17	18	20	20
21	12	19	11	19	23	16	15	18	17	18	20	19
22	11	20	10	18	13	25	15	21	22	18	23	18
23	12	21	12	21	13	20	13	22	17	18	19	19
24	14	21	15	20	12	21	16	22	16	28	18	25
25	17	19	16	17	14	17	18	18	18	20	22	22
26	17	18	12	18	15	16	13	18	14	22	17	24
27	12	18	10	15	14	17	13	16	15	25	17	23
28	19	20	19	21	20	19	18	18	20	22	20	23
29	21	20	20	18	23	19	21	18	22	20	22	21
30	27	26	25	25	25	25	25	25	26	26	32	27
31	26	26	25	24	25	24	25	25	26	26	26	26
32	20	23	19	22	17	18	18	16	19	19	21	21
Mean ± SD	17.00 ± 4.81	21.56 ± 3.34	16.18 ± 5.77	21.50 ± 3.54	16.06 ± 4.68	19.87 ± 5.86	16.50 ± 4.50	20.18 ± 3.97	19.62 ± 4.44	22.25 ± 4.10	22.43 ± 4.76	23.00 ± 3.66

2. Material and methods

2.1. Groups

The study design was approved by the ethics committee of the study center. This study was designed prospectively with two groups. A total of 67 subjects were enrolled. The first group (*the CF group, or cystic fibrosis*) was composed of 32CF patients who had history of at least three courses of intravenous treatment with amikacin 10–30 mg/kg daily for at least 10 days per episode, mostly because of pulmonary infections but not for meningitis. The second group (*the control group, or C group*) consisted of 35 children who had visited the pediatric outpatient clinic for any reason other than hearing loss and had no history of exposure to any AGs.

2.2. Diagnosis of CF

For the diagnosis of CF, Nanoduck sweat test was performed three times to every patient in the CF group. The test was accepted as positive, suspicious and negative when the result was over 80 mmol/l, between 60 and 80 mmol/l and under 60 mmol/l respectively. Sweat test results ranged between 50 and 122 mmol/l. An informed consent was taken from the patient's parents and a protocol was filled.

2.3. Auditory evaluation

All subjects were examined otoscopically (HEINE® K-100 Diagnostic Otoloscope, HEINE Optotechnic, Herrsching, Germany) to

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