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Determination of hearing levels in patients with Familial Mediterranean Fever

Cengiz Cevik [a,*], İbrahim Silfeler [b], Vefik Arica [b], Erhan Yengil [c], Ercan Akbay [a], Tuba Sarac [a], Fatmagul Basarslan [b], Ertap Akoglu [a]

[a] Mustafa Kemal University School of Medicine, Department of Otolaryngology, Turkey
[b] Mustafa Kemal University School of Medicine, Department of Pediatric, Turkey
[c] Mustafa Kemal University School of Medicine, Department of Family Medicine, Turkey

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ABSTRACT

Objective: Familial Mediterranean Fever is the most common congenital, periodic fever condition that affects over 100,000 people worldwide. In the literature, there is limited number of studies about hearing levels in children with Familial Mediterranean Fever. In the present study, we aimed to investigate hearing levels and cochlear functions by using Distortion product Otoacoustic Emission and High Frequency Audiometry (250–20,000 Hz) in pediatric patients with Familial Mediterranean Fever.
Methods: The study included 62 children with Familial Mediterranean Fever and 27 healthy children with similar age and gender. After otoscopic examination, both groups underwent audiological evaluation including High Frequency Audiometry (250–20,000 Hz) and Distortion product Otoacoustic Emissions. The results obtained were assessed among groups. In addition, these results were compared regarding colchicine use, age at the onset of disease and duration of the diseases in the Familial Mediterranean Fever group.
Results: Of the Familial Mediterranean Fever patients, 93.5% were on colchicine therapy and mean duration of colchicine use was 19.9 ± 13.9 months. The mean age at diagnosis was 6.57 ± 2.86 years (min–max: 2–14) and mean duration of disease was 23 ± 17 months (min–max: 6–84). Pure tone audiometry values, and hearing levels between 9000 and 20,000 Hz were similar and within normal range in both groups. The Distortion product Otoacoustic Emissions responses at the frequencies of 1020, 2040, 3000, 4080 and 5040 Hz were similar for both groups.
Conclusion: To the best of our knowledge, this is the first study evaluating hearing levels at the frequencies of 18 kHz and 20 kHz in children with Familial Mediterranean Fever in the literature. In children with Familial Mediterranean Fever, Pure tone audiometry values, hearing values obtained at all frequencies from 250 to 20,000 Hz, and Distortion product Otoacoustic Emissions levels were within normal range. Furthermore, hearing levels were found to be similar to those in healthy children.

1. Introduction

Familial Mediterranean Fever (FMF) is the most common congenital periodic fever condition with autosomal recessive inheritance and affects over 100,000 individual worldwide [1,2]. It has been reported that the prevalence of the diseases is 1% in Turkey [3]. The disease is more prevalent among Jewish, Arabian, Turkish and Armenian populations [3,4]. This disease is characterized by recurrent fever with abdominal pain, pleurisy, arthritis and skin lesion [5–7]. The symptomatic period is termed as "attack" [5,7]. The patients have no symptom at the intervals between attacks which is an important feature for diagnosis.

It has been reported that clinical characteristics of FMF does not exhibit significant variations across different ethnic groups. However, in several studies, it was emphasized that the disease has a more severe clinical course and higher risk for amyloidosis in Turkish population [8]. FMF could be seen together with many diseases. The vasculitis (particularly polyarteritisnodosa and Henoch-Schönleinpurpura) are the most important ones [7].

The frequent association of amyloidosis and vasculitis with FMF suggests that these clinical conditions influencing many organs can also affect hearing [9]. Otoacoustic emission is an important test that allows to determine cochlear component and to observe cochlear status in an objective manner [10]. In recent years, High Frequency Audiometry (HFA) becomes particularly helpful in the

* Corresponding author. Tel.: +90 3262291000.
E-mail address: drccevik@yahoo.com (C. Cevik).

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diagnosis and management ototoxicity and presbycusis [11]. Moreover, it is possible to recognize cochlear injury at early period by HFA. In the present study, we aimed to investigate the hearing levels and cochlear functions in children with FMF by using DPOAE and HFA.

2. Method

The study included children diagnosed as FMF according to Tell-Hashomer criteria and healthy children recruited from Pediatrics Clinics of Mustafa Kemal University, Medicine School [12]. Overall, 62 children with FMF and 27 healthy controls were included to the study.

Otoscopic examination was performed in all subjects included. The children with active ear infections, acute otitis media, otitis media with effusion, chronic otitis media and otitis externa, those with a positive history of ototoxic agent use and those not eligible for hearing testswere excluded. In children with FMF and controls, high frequency audiometry and otoacoustic emission tests were performed in both ears. Audiometric evaluations were performed in sound-proof room compatible with Industrial Acoustic Company (IAC) standards and double-channel high frequency audiometer (GrasonStadler, GSI) and Telephonics TDH-39P headphones were used in tests. Air-conduction and bone-conduction thresholds were measured at frequencies of 125–20,000 Hz interval by using TDH-39 speakers and Radio Ear B 71 vibrator according to 1969 ANSI standards. In the study, Pure Tone Audiometry (PTA) values were estimated for each ear by using average of thresholds including 500–1000–2000 Hz. PTA averages were used to determine the presence or absence of hearing loss. Hearing levels below 25 dB were considered as normal.

Stimulus presentation, data recording, and spectrum analysis for Distortion product Otoacoustic Emissions (DPOAEs) were carried out using a Labat Otoacoustic Emission Test Instrument, Model Eclipse. The data were processed and evaluated with otoacoustic emission (OAE) software (Labat Audiological Platform/Labat Master and Data Management Software, Version 1.0.0.478 or upper, ITALY). The participants were seated in a sound-proof room during the test. Once the probe was placed with a good seal in the ear canal, the measurements were done. Equilevel primary tones $f1$(65 dB) and $f2$(55 dB) was fixed at $f1/f = 1.22$ and DPOAEs were measured at five different frequencies ranged from 1000 to 4000 Hz (1020, 2040, 3000, 4080 and 5040 Hz).

All audiometric evaluations were performed at the same center by same audiologist.

2.1. Statistical analysis

All statistical analyses were performed by using SPSS (Statistical Package for Social Sciences) for Windows 13.0 software. Descriptive statistics were expressed as percentage, mean ± SD (standard deviation) and number. Continues variables were expressed as mean ± SD, whereas categorical variables as number and frequency. Chi-square or Fischer's test was used for comparisons between categorical variables. Normal distribution of continues variables were tested with Kolmogorov-Smirnov test. Student's t test and Mann Whitney U test were used in the comparisons between groups. $P < 0.05$ was considered as significant for all statistical analyses.

3. Results

3.1. Demographic characteristics

The mean age was 8.39 ± 3.19 years in FMF group and 7.77 ± 3.25 years in control group. There were 23 boys and 39 girls in FMF group, whereas 11 boys and 16 girls in control group. The groups were found to be similar regarding age and sex ($P = 0.745$ and $P = 0.396$, respectively). Of the children with FMF, 58 (93.5%) were using colchicine whereas 4 (6.5%) not using. Mean duration of colchicine use was 19.9 ± 13.9 months. The mean age at diagnosis was 6.57 ± 2.86 years (min–max: 2–14). The mean duration of disease was 23.0 ± 17.0 months (min–max: 6–84). Of the children with FMF, 43 (69.4%) had a first degree relative with FMF, while 19 (30.6%) not.

3.2. Genetic outcomes

In the genetic evaluations, it was found that there were mutations in 52 patients, whereas no mutation in one patient. The mutations detected were as follows: A165A (30Het, 15Hom) in 60 alleles, G138G (29Het, 15Hom) in 59 alleles, R202Q (22Het, 14Hom) in 50 alleles, M694V (10Het, 1Hom) in 12 alleles, E148Q (11Het) in 11 alleles, V726A (4Het) in 4 alleles, M680I (3Het) in 3 alleles, P706P (2Het) in 2 alleles, R761H (1Het) in 1 allele and D102D (1Het) in 1 allele, respectively.

3.3. Audiometry outcomes

In children with FMF, PTA values were 8.59 ± 3.00 dB in right ear and 9.09 ± 3.88 dB in left ear. In control group, they were 9.50 ± 2.80 and 3.32 ± 10.46 dB, respectively. PTA values were within normal range (<25 dB) in both groups. Regarding PTA values, there was no significant difference between children with FMF and healthy controls ($P = 0.116$ for right ear and $P = 0.051$ for left ear). Moreover, high (8000, 9000, 10,000, 12,500, 14,000, 16,000, 18,000, 20,000 Hz) and low (250, 500, 1000, 2000, 4000, 8000 Hz) frequency audiometry values were within normal range (<25 dB). There was no significant

Table 1
The distribution of audiometry values according to frequency in right ear.

Audiometry frequency (Hz)		Hearing levels in DB		P values
		FMF (n:62)	Control (n:27)	
250	Mean ± std dev	12.18 ± 6.07	12.77 ± 4.87	0.554
	Min–max	0–25	5–20	
500	Mean ± std dev	9.00 ± 4.46	10.37 ± 4.14	0.080
	Min–max	5–20	5–20	
1000	Mean ± std dev	9.29 ± 4.66	10.37 ± 4.36	0.202
	Min–max	5–30	5–20	
2000	Mean ± std dev	7.48 ± 3.64	7.77 ± 3.20	0.443
	Min–max	0–15	0–10	
4000	Mean ± std dev	5.74 ± 5.07	7.03 ± 4.65	0.113
	Min–max	0–25	0–15	
8000	Mean ± std dev	8.64 ± 6.18	8.88 ± 5.93	0.941
	Min–max	0–20	0–30	
9000	Mean ± std dev	8.62 ± 8.10	8.51 ± 7.44	0.927
	Min–max	0–35	0–25	
10,000	Mean ± std dev	9.04 ± 8.98	5.74 ± 7.29	0.072
	Min–max	0–35	0–25	
12,500	Mean ± std dev	8.96 ± 10.81	11.11 ± 9.74	0.182
	Min–max	0–45	0–30	
14,000	Mean ± std dev	7.50 ± 9.57	6.11 ± 7.76	0.746
	Min–max	0–30	0–30	
16,000	Mean ± std dev	5.64 ± 9.16	4.44 ± 10.03	0.253
	Min–max	0–30	0–35	
18,000	Mean ± std dev	4.27 ± 7.98	2.59 ± 6.41	0.277
	Min–max	0–35	0–30	
20,000	Mean ± std dev	1.46 ± 3.77	1.29 ± 3.27	0.774
	Min–max	0–20	0–10	
PTA	Mean ± std dev	8.59 ± 3.00	9.50 ± 2.80	0.116
	Min–max	3.33–18.33	5–16.67	