Evaluation of cochlear functions in children with Familial Mediterranean Fever

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ABSTRACT

Objectives: To evaluate cochlear functions in patients with Familial Mediterranean Fever in relation to the disease severity score and treatment duration.

Methods: 50 patients (4–18 years) who had been followed-up with the diagnosis of FMF and regularly receiving appropriate colchicine treatment and 39 healthy controls were included in the study. All the patients and controls were evaluated by audiologic evaluation, including high-frequency pure-tone audiometry and distortion product otoacoustic emission tests (DPOAE). The disease severity was determined by scoring system developed by Pras et al.

Results: Fifty patients (52% female, 48% male; mean age12.2 ± 4.1 years) and 39 controls (58.9% female, 41.1% male, mean age 11.1 ± 3.4 years) were enrolled the study.

The pure tone average of FMF patients was significantly higher than that of the control group at 500, 4000, and 8000 Hz frequencies. The patients' DPOAE signal values at 6 kHz, 8 kHz frequencies and SNR values at 8 kHz were significantly higher than control group.

The patients' audiometry and DPOAE results were compared with the disease severity scores. Pure tone average was significantly higher in severe and moderate patient groups compared to the mild patient group at 2000 Hz frequency. DPOAE signal values showed statistically significant differences between the patient severity scores at 1.4 and 2.8 kHz frequencies. The mean colchicine treatment duration was found to be 5.1 ± 3.7 years. There were significant differences at 250 and 500 Hz frequencies when patients' audiometry results were compared with the treatment periods.

Conclusions: FMF affects cochlear functions particularly at high frequencies.

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1. Introduction

Familial Mediterranean Fever (FMF) is an autosomal recessive disease characterized by recurrent episodes, usually manifested with fever and pain due to peritoneal, pleural or synovial inflammation and/or skin rashes [1]. The incidence rate of the disease was reported to be 1/1075 in Turkey [2]. The disease is diagnosed according to the Tell-Hashomer criteria which were defined in 1967 [3,4]. Pras et al. developed severity scoring system which divides the disease into three groups; mild, moderate and severe, based on clinical findings [5]. Familial Mediterranean Fever is categorized within the systemic auto-inflammatory group of diseases [6]. This group has been described as causing visual and hearing impairment [7]. There are a limited number of studies about the effects of Familial Mediterranean Fever on auditory functions. The majority of these studies were conducted in adults. Familial Mediterranean Fever is thought to affect cochlear function due to increased inflammatory cytokines [7]. Loss of hearing adversely affects the development of language skills such as verbal communication and reading and as a result academic and professional success. This study aims to evaluate auditory function in children with FMF in relation to the disease severity score and the duration of treatment.

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2. Materials and methods

This study is a case control study performed in two medical centers; Pediatric Nephrology Department of Dr. Sami Ulus Obstetrics, Child Health and Diseases Training and Research Hospital and Ear Nose Throat Department of Kecioren Training and Research Hospital. A total of 50 patients between the ages of 4–18 years who had been followed-up with the diagnosis of FMF and who had been regularly receiving appropriate colchicine treatment.

without signs and symptoms of ear infection were enrolled the study. The diagnosis of FMF was made according to Tell-Hashomer criteria [4]. 39 healthy volunteers were enrolled the study as a control group. The study was approved by Institutional Ethics Board. Informed consent was obtained from parents.

Exclusion criterias were to have another chronic illness besides FMF, during attack period, those who had developed amyloidosis, those who had outer and middle-ear related diseases, those with a history of exposure to high levels of noise, head trauma, usage of ototoxic drugs or had undergone ear surgery. Patients below 4 years of age were also excluded from the study due to their inability to cooperate with audiometry.

Patients were grouped according to the severity of Familial Mediterranean Fever using the severity scoring system developed by Pras et al. [5]. Taking into consideration the starting time of the symptoms, frequency of attacks, colchicine doses, arthritis, the presence of erysipelas-like erythema and amyloidosis. The severity scores 3–5, 6–8 and 9 ≤ were evaluated as mild, moderate and severe scores of the disease, respectively.

The study group were evaluated by a detailed ear, nose and throat (ENT) examination with audiologic evaluation including audiometry and Distortion product otoacoustic emission (DPOAE) tests separately for the right and the left ear. The tests were done once at attack free period. Madsen Orbiter 922-2 Clinical audiometry (Denmark) device was used for pure tone and speech audiometry. TDH-39 standard headphones were used for airway thresholds, speaking tests and radio ear B-71 vibrators were used for bone conduction thresholds. Airway thresholds were examined at 250, 500, 1000, 2000, 4000 and 8000 Hz.

The pure tone average (PTA) air conduction thresholds were calculated separately for each ear. Conductive hearing loss patients were excluded from the study due to its effects on the OAE result.

DPOAE test was performed in a soundproof room. A hand held Echocheck brand instrument, which uses ILO 88 system based recording, was used for testing. The instrument's probe portion which comprises of two speakers and a microphone was placed in the clean external ear canal. Then two stimuli were created in the cochlea at 60 dB and higher intensity resulting in two different progressive waves. The DPOAE (signal and SNR) results of the patients were recorded by measuring the overlapping parts of these waves in the cochlea.

All of the patients' age, gender, age at onset of FMF, follow-up records, colchicine treatment period, genetic mutation analysis results, disease severity scores and hearing tests results (audiometry, DPOAE separately for the right and the left ear) were recorded. The data of averages of both ears were compared with control group.

"Statistical Package for Social Sciences- SPSS 17" (Chicago, USA) program was used for the evaluation of results. Student's *t*-test was used for normally distributed quantitative variables whereas Mann-Whitney *U* test was used for numerical variables. Chi-square test was used for the comparison of categorical variables. Results were evaluated within the 95% confidence interval at $p < 0.05$ significance level, and reevaluated at $p < 0.01$ and $p < 0.001$ significance level.

3. Results

Fifty patients (52% female, 48% male) with FMF and 39 healthy controls (58.9% female, 41.1% male) were enrolled the study. The mean age was 12.2 ± 4.1 years in patient group and 11.1 ± 3.4 years in control group. There were no significant differences between the patient and the control group in respect to age and gender distribution ($p > 0.05$).

According to disease severity score developed by Pras et al.; 16% (n = 8) patients were placed in the mild group, 72% (n = 36) were placed in moderate group, and 12%(n = 6) were placed in severe group. Patients had a median disease severity score of 7 [4–10].

The audiogram data were analyzed separately for the right and the left ear in both groups. The mean pure tone average (PTA) values of patient group were significantly higher than control group at 500, 4000 and 8000 Hz frequencies ($p < 0.05$) (Table 1).

DPOAE and SNR values were evaluated at different frequencies in both groups. The signal values of FMF patients at 6 kHz and 8 kHz frequencies were significantly higher than control group ($p < 0.05$) (Table 1).

SNR values were evaluated in the DPOAE test. The FMF patients had significantly lower SNR values than the control group at 1 and 1.4 kHz ($p < 0.05$). The SNR values of FMF patients were detected to be significantly higher than the control group at 8 kHz ($p < 0.05$). (Table 1).

The patients' audiometry results were compared with the disease severity scores. Pure tone average was significantly higher in severe and moderate patient groups compared to the mild patient group at 2000 Hz frequency ($p < 0.05$) (Table 2).

The patients' DPOAE test results at different frequencies were compared with the disease severity scores. There were statistically significant differences between the patient severity scores at 1.4 and 2.8 kHz frequency ($p < 0.05$) (Table 2).

The patients' SNR ratio results at different frequencies were compared with the disease severity scores. There were no statistically significant differences between the SNR results and the patient severity scores ($p > 0.05$) (Table 2).

All the patients were taking colchicine treatment. Durations were <5 years in 52% (n = 26) and, 5≤ in 48% (n = 24). The mean

Table 1
Comparison of the audiometry, DPOAE and SNR results between the patient and the control group.

Tests	Patient group	Control group	P Value
PTA			
250	12.5(10–15)	10(5–15)	0.097
500	10(6.25–15)	10(5–11,25)	0,008
1000	10(5–15)	10(5–15)	0.799
2000	10(5–10)	10(5–15)	0.749
4000	10(5–15)	10(5–10)	0.009
8000	15(10–20)	10(5–15)	0.001
DPOAE			
1 khzsignal	6.5(-1.75–11.75)	6.75(-1.075-11.075)	0.799
1.4 khzsignal	7.35(3.8-15.175)	12.35(4.05-16.85)	0.108
2 khzsignal	9.35(1.2-15.6)	8.35(0.275-14.55)	0.721
2.8 khzsignal	7.8(0.25-12.35)	5.95(1.75–10,125)	0.156
4 khzsignal	11.8(4.925–15.325)	9.85(3.675–13.1)	0.084
6 khzsignal	12.65(4.45–15.75)	6.45(-0.1–11.3)	<0.001
8 khzsignal	−5.9(−22.65−−0.45)	−21.65(-30−−6275)	<0.001
SNR			
1 khzsnr	7.95(-2–15.725)	12.35(2875–20.825)	0.011
1.4 khzsnr	14.55(5.4–23.175)	18.1(11.325–27.2)	0.020
2 khzsnr	17.05(8.95–23.6)	16.75(9.6–25.6)	0.618
2.8 khzsnr	19,6(8125–24.875)	18.2(11.75–22.625)	0.616
4 khzsnr	24.05(17.45–28.3)	22.25(17.3–27.125)	0.312
6 khzsnr	23.75(16.4–29.55)	21.05(14,85–26.325)	0.063
8 khzsnr	9,7(-8.725–15.975)	−4.05(-10.45–11.2)	0.022