Evaluation of cochlear involvement by transient evoked otoacoustic emission test in children with Crimean-Congo hemorrhagic fever

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1. Introduction

Clinical features of Crimean-Congo hemorrhagic fever (CCHF) show a common dramatic progression, characterized by hemorrhage, myalgia, nausea, headache, and fever [1,2]. It is a potentially fatal disease and is endemic in Africa, the Middle East, Central Asia, and Eastern Europe, with a reported mortality rate of 3–30% [1,3,4]. CCHF virus belongs to the genus Nairovirus in the family of Bunyaviridae. Humans become infected through the bites of ticks, by contact with a patient during the acute phase of infection, or through exposure to the blood or tissues of infected livestock [5].

Otoacoustic emissions testing, discovered by Kemp [6], is an important, simple, objective and non-invasive method for clinical evaluation of hearing disturbances [7]. It is mainly used in hearing screening, serial monitoring of progressive hearing loss (HL), and in differential diagnosis in impaired hearing [8]. Otoacoustic emission (OAE) test is used to evaluate the function of the outer hair cells of cochlea. A vulnerable cochlear mechanism, known as a “cochlear amplifier,” produces vibrations that are transmitted through the middle ear to the eardrum. The sounds of cochlear origin are recorded by a microphone in the external auditory canal [7]. These sounds can arise either spontaneously or via an evoking stimulus [9].

This study was designed to assess the cochlear status in child patients with CCHF using basic audiological evaluation and transient evoked otoacoustic emissions testing.

2. Materials and methods

2.1. Patients

This prospective case-controlled study was carried out at the Department of Otorhinolaryngology at Cumhuriyet University Hospital in the city of Sivas located in central Anatolia, Turkey, between April and September 2010. The study was performed upon patients hospitalized in the Pediatric Department. Twenty-eight CCHF disease patients (56 ears) and 26 sex- and age-matched healthy control subjects (52 ears) were included in the study. Pure-tone audiometry at frequencies 0.25, 0.5, 1, 2, 4, and 6 kHz, immittance measures including tympanometry and acoustic reflex testing, and transient evoked otoacoustic emission (TEOAE) testing were performed in the patients and controls.

Conclusions: CCHF disease does not impair cochlear function in children. The clinical course of CCHF among children seems to be milder than in adults.

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absence of acoustic reflexes at 1 kHz with contralateral stimulation, and (3) an air-bone gap of 5 dB at any frequency. Audiological examination and tests were performed before any medical treatment for CCHF.

2.2. Audiometry

The initial examination included otoscopy, tympanogram and complete audiological evaluation including pure-tone air and bone-conduction audiometry and otoacoustic reflex test. Pure-tone air conduction hearing thresholds were determined at audiometric frequencies (0.25, 0.5, 1, 2, 4, 6 kHz) for each of the ears of the CCHF and the control subjects. An AC-40 Diagnostic Audiometer was used in a sound-treated cabin (Interacoustic Company, Denmark). Pure tone averages (PTAs) were calculated at means of 0.5, 1, 2 and 4 kHz. Normal middle ear function was defined by immittance and acoustic reflex results using a Clinical Impedancemeter (Interacoustic AZ 26, Denmark). The CCHF and control subjects who had normal peak compliance and pressure gradient, ear canal volume and acoustic reflexes obtained by immittance measures, as defined by the American Speech Language and Hearing Association [10], were included in the study. The criterion of normal value was a hearing level of 20 dB in the tested octave frequencies.

2.3. TEOAE testing

We used the ILO88 transient evoked otoacoustic emission (TEOAE) test V5 system (Otodynamics Ltd, Hatfield, UK) in our study. A stimulus of about 80.0 dB was introduced with a 0.0 dB gain. The ear was exposed to 260 clicks and the emissions were collected. To be able to pass the TEOAE test, a response of at least 3 dB above the noise threshold with a minimum 70% reproducibility and at least 90% stability at three frequencies was needed. All patients with a suspicion of CCHF were otolaryngologically examined and underwent the TEOAE test before treatment.

The statistical analyses were performed using SPSS 14.0 for Windows. The Mann–Whitney U test was performed for the analysis of age. The proportion of TEOAE test ‘fail’ results and sex were analyzed with the Chi-square test. A p value lesser than 0.05 (p < 0.05) was used as the significant level. Student’s t-test was used to analyze the differences between CCHF patients and control groups in the audiometric frequencies 0.25, 0.5, 1, 2, 4, and 6 kHz and the PTA of the audiological tests. Statistical differences with probabilities of less than 0.05 were considered significant.

3. Results

Two of 30 CCHF patients were excluded from the study because of previous hearing loss greater than 20 dB; hence, 28 CCHF patients with normal hearing were included in the study.

Both study and control groups comprised 54 individuals and 108 ears. Patients’ ages ranged from 6 to 16 years (mean ± SD: 10.1 ± 3.5). The control group’s mean age was 9.8 ± 3.8 [6–15] years. Of the CCHF patients, 10 (35.7%) were male and 18 (64.3%) were female. Eleven (42.3%) in the control group were male and 15 (57.7%) were female. There was no statistically significant difference between the patient and control groups’ mean age and sex distribution (p > 0.05).

Pure tone audiometry results for the CCHF and control patients are shown in Fig. 1. Pure tone audiometry thresholds (0.25, 0.5, 1, 2, 4, and 6 kHz) and pure tone averages in the CCHF patients were not statistically significant when compared with controls (p > 0.05).

All 28 CCHF patients (100%) with normal hearing had a test result of ‘pass’ for the TEOAE test. Twenty five of 26 (96.1%) in the control group had a ‘pass’ result for the TEOAE test; one of 26 (3.9%) received a ‘fail’ (Table 1). The proportion with a result of ‘fail’ for the TEOAE test in the CCHF patients was not statistically significant from the control group (p > 0.05).

4. Discussion

In this study, we have shown through the TEOAE test that CCHF virus infection does not cause cochlear damage in children. We could not find any relation between the proportion of failed TEOAE tests and CCHF infection.

CCHF is a viral hemorrhagic disease with fever. It was first described in the Crimea in 1944 and took the name Crimean Hemorrhagic Fever. In 1969, it was detected that Crimean Hemorrhagic Fever had the same pathogen as that responsible for an illness identified in the Congo in 1956. Therefore, the disease has begun to be called Crimean-Congo Hemorrhagic Fever [5,11]. The distribution of the virus is geographically wide and the disease is regarded as a public health threat in many regions of the world, including Asia, Eastern Europe, the Middle East, and Africa [12–14]. The first CCHF case in Turkey occurred in 2002 and outbreaks have been seen in Central, Northern, and Eastern Anatolia, as well as in the Eastern Black Sea regions of Turkey, since that time [5,15,16]. Recently, CCHF has been endemic in our country. Our hospital is in an endemic region with a high level of CCHF and a large amount of cases have been seen in the service area of our training hospital during the spring and summer seasons. According to data held by the Ministry of Health of Turkey, there were, in total, 242 confirmed CCHF cases under eighteen years old in Turkey and 4 deaths were reported in 2008 and 2009 in this age group. Different outcomes among different patient groups could be seen due to the virulences of different strains, access to the health system, the sensitivity threshold for the symptoms, co-existence of infections, and host factors [17].

CCHF shares many clinical features with other types of viral hemorrhagic fever [18]. After an incubation period of about a week, our patients have the symptoms of fever, headache and muscle...
aches, nausea, diarrhea, and other nonspecific symptoms. However, none of the patients presented with vestibular symptoms or signs.

General supportive therapy is the mainstay of patient management in CCHF infection. Intensive monitoring to guide volume and blood component replacement is required [11]. Ribavirin inhibits CCHF virus in vitro, but its efficacy in clinical practice remains unconfirmed; it should be noted that there is no evidence from randomized clinical trials for the use of ribavirin to treat human CCHF virus infections. Treatment options for CCHF in children are also limited. Supportive therapy is the most essential part of case management and includes intensive monitoring for volume control and administration of platelets, fresh frozen plasma, and erythrocyte preparations [5,12].

Viral infections such as mumps, rubella, rubella, herpes zoster, and cytomegaloviruses are known causes of hearing loss in humans. These infections usually lead to the loss of hair and supporting cells of the cochlea during the active phase of the infection. The tectorial membranes are disrupted and the stria vascularis atrophy, leading to end-vessel thrombosis and inner-ear fibrosis. Direct invasion of the spiral ganglion may also result in the loss of integrity of the vestibulocochlear nerve [19]. However, the mechanism underlying the pathogenesis of CCHF is not well described and there is limited data in the literature [20]. Impairment of endothelial cell function can cause a wide range of vascular effects that lead to changes in vascular permeability or hemorrhage [21,22]. Bodur et al. indicate that vascular endothelial damage in CCHF patients is probably indirect and may be caused by inflammatory cell activation [23]. In other study, half of the patients were detected with reactive hemophagocytosis, and it was suggested that hemophagocytosis might have a role in the pancytopenia in CCHF infection [16].

TEOAs are highly sensitive to cochlear pathology in a frequency-specific way with the potential for preclinical detection of damage to the cochlea. Frequencies at which hearing thresholds exceed 20–30 dB HL are typically absent in the TEOA response [24,25]. In our study, we evaluated the cochlear damage caused by CCHF in children with the TEOAE test.

In a study performed in adults, the proportion of TEOAE test ‘fail’ results in CCHF patients was significantly higher than in the control group [26]. However, in our study, the proportion of TEOAE test ‘fail’ results in children with CCHF was not significantly different from the control group. The clinical course of CCHF among children seems to be milder than in adults [17].

In conclusion, it appears that CCHF disease does not impair cochlear function in children.

References


