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Clinical investigation of the transient evoked otoacoustic emission test in Crimean—Congo hemorrhagic fever

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Summary
Objective: The aim of this study was to investigate cochlear damage in Crimean—Congo hemorrhagic fever (CCHF) infection.
Methods: Thirty-two CCHF patients (study group) and 13 healthy people (controls) were included in the study. CCHF patients were also grouped for the presence of fever. CCHF was diagnosed with the presence of CCHF virus-specific IgM antibody or CCHF virus (CCHFV) antigen by ELISA. Cochlear damage was determined by a 'fail' in the transient evoked otoacoustic emission (TEOAE) test.
Results: The proportion of TEOAE test 'fail' results in the CCHF patients was significantly higher than in the control group ($p < 0.05$). We found no increase in the proportion of TEOAE test 'fail' results related to fever in the study group.
Conclusions: CCHF disease damages cochlear function regardless of fever.

Introduction

Crimean—Congo hemorrhagic fever (CCHF) is a severe, potentially fatal disease in humans; it is caused by infection with the CCHF virus (CCHFV).[1] CCHF is described in about 30 countries, and it has the most extensive geographic distribution of the medically important tick-borne viral diseases.[2] The average mortality rate is often cited at 30—50%. Mortality rates of nosocomial infections are often much higher than those acquired naturally through tick bites.[1]

CCHFV is a member of the *Nairovirus* genus of the family *Bunyaviridae*.[3] CCHF viruses are transmitted by *Hyalomma* genus ticks, particularly by *Hyalomma marginatum marginatum*.[2] Human beings become infected through tick bites, by

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crushing infected ticks, after contact with a patient with CCHF during the acute phase of infection, or by contact with blood or tissues from viremic livestock.[1,3] The most important clinical features are fever and hemorrhage.

Otoacoustic emissions (OAEs) have been suggested as a sensitive measure of cochlear function with the potential for preclinical detection of damage.[4] The primary purpose of otoacoustic emission (OAE) tests is to determine cochlear status, specifically hair cell function. This information can be used to: (1) screen hearing (particularly in neonates, infants, or individuals with developmental disabilities); (2) partially estimate hearing sensitivity within a limited range; (3) differentiate between the sensory and neural components of sensorineural hearing loss; and (4) test for functional (feigned) hearing loss. The information can be obtained from patients who are sleeping or even comatose because no behavioral response is required.[5,6] The normal cochlea does not just receive sound; it also produces low-intensity sounds called OAEs.[7] OAEs are sounds caused by the motion of the eardrum in response to vibrations from deep within the cochlea and organ of Corti, and can be recorded in the ear canal using a specialized microphone.[8] There is significant interest in the clinical usefulness of evoked otoacoustic emissions (EOAEs) for early identification of sensorineural (cochlear) hearing loss that is undetectable by other audiologic methods. OAEs are present in essentially all healthy ears but are absent in ears with sensorineural (cochlear) hearing loss of greater than approximately 30 dB.[9,10]

In this prospective study we have evaluated the cochlear damage caused by CCHFV with the OAE test.

Materials and methods

We conducted a prospective analysis of 32 patients with a diagnosis of confirmed CCHF infection; 13 healthy volunteer adults acted as controls. The control group consisted of volunteers from the Cumhuriyet University staff. CCHF patients were also grouped for the presence of fever. Fever was defined as the presence of body temperature (axillary) $\geq$38 °C.

Thirty-two patients diagnosed with CCHF infection and followed up at the Department of Infectious Diseases and Clinical Microbiology at Cumhuriyet University Hospital (an 800-bed teaching hospital) in the city of Sivas located in central Anatolia, Turkey, between May and September of 2005, were included in this study. The diagnosis of CCHF infection was based upon typical clinical and epidemiological findings and serological tests with ELISA. Serum samples of the patients were sent to the Virology Laboratory of Refik Saydam Hygiene Central Institute, Ankara, Turkey for microbiological testing for CCHF virus infection. Anti-CCHF IgM and IgG antibodies and CCHF viral antigen were tested in sera samples of patients by ELISA. Twenty-five of 32 (78.1%) CCHF patients had CCHF virus-specific IgM antibodies, and seven of 32 (21.9%) had CCHF virus antigen.

An otolaryngologist examined the patients to determine any other otological manifestations that could impair the OAE. Pure tone audiometry was performed in the patient's room and in a silence environment with a MAICO portable audiometer and TDH 39 headphones. Those patients with hearing loss greater than 30 dB and those having any other otological manifestations that could impair the OAE were excluded from the study. The ILO88 transient evoked otoacoustic emission test (TEOAE) V5 system (Otodynamics Ltd, Hatfield, UK) was used for the study. TEOAE tests were conducted on the same day as the pure tone test. The test stimulus approximated 80.0 dB and the gain was 0.0 dB. Two hundred and sixty click sweeps were sent to the ear and the emissions were collected by a microphone in a probe. A response at three frequencies of 3 dB or greater above the noise floor with a minimum 70% reproducibility at each frequency and 90% or greater stability was required for passing the TEOAE test. An otolaryngological examination and TEOAE test were performed in all patients with a suspicion of CCHF infection before any medical treatment was given. Those not serologically confirmed as a CCHF infection were not included in the study. Pure tone audiometry and the TEOAE test were performed in all of them.

The Mann–Whitney test was performed for the analysis of age. The proportion of TEOAE test 'fail' results and sex were analyzed with the Chi-square test. Fisher's exact test was performed for the effect of fever on the TEOAE test in our study group.

Results

Of the CCHF patients, 18 (56.2%) were male and 14 (43.8%) were female, and the mean age was 49.2 $\pm$ 20.8 years. Six (46.2%) in the control group were male and seven (53.8%) were female, and the mean age of the healthy people was 47.6 $\pm$ 7.1 years. There was no significant difference between the study and control groups with regard to sex and age ($p > 0.05$).

Eight of 32 CCHF patients were excluded from the study because of previous hearing loss greater than 30 dB; hence 24 CCHF patients with normal hearing were included in the study. Fourteen of 24 CCHF patients (58.3%) with normal hearing had a test result of 'pass' for the TEOAE test; 10 of 24 (41.7%) had a test result of 'fail'. Twelve of 13 (92.3%) in the control group had a 'pass' result for the TEOAE test; one of 13 (7.7%) received a 'fail'. The proportion with a result of 'fail' for the TEOAE test in the CCHF patients was significantly higher than in the control group ($p < 0.05$).

Of the 24 CCHF patients, 17 were exposed to fever and seven were not. Of those exposed to fever, 12 CCHF patients

Table 1 TEOAE test results and fever exposure in the CCHF and control groups

Study groups	TEOAE test passed	TEOAE test failed	Exposed to fever	No fever
CCHF patients (N = 24)	14	10	17	7
Control group (N = 13)	12	1	0	12

TEOAE, transient evoked otoacoustic emission test; CCHF, Crimean–Congo hemorrhagic fever.