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Short Communication

Detection of HSV Infection in Patients with Sudden Sensory-Neural Hearing Loss (SSNHL) by Real-time PCR

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Abstract

Background and Aims: Sudden sensorineural hearing loss (SSNHL) is a common disorder diagnosed in otologic and audiologic practices. Its accompanying symptoms include tinnitus, dizziness, and permanent hearing loss affecting negatively the life quality of affected patients. Many viruses have been involved in the occurrence of SSNHL especially Herpes simplex virus (HSV) type I and II. This study was attempted to explore the association between SSNHL and HSV infection using RT-PCR.

In this case- control study, 56 patients with SSNHL occurring within a 72-hr period were selected as case group and 56 participants who had no recent history of this disease were assigned into control group. Applying real-time PCR, we tracked the genome of the HSV virus and measured its loading.

Control group comprised of 31 (55.4%) male and 25 (46.6%) female and the case group included 26 (46.4%) male and 30 (53.6%) female. The genomic DNA of HSV was measured by Real-time PCR in both groups, and no viral genome was detected.

The findings of the current investigation suggest no relation between HSV and SSNHL. Further research conducting on larger population is recommended to obtain more detailed results.

Keywords: Sudden sensorineural hearing loss, Herpes simplex virus, PCR.

Introduction

Sudden sensorineural hearing loss (SSNHL) is a common disorder diagnosed in otologic and audiologic practices (1, 2). Commonly, SSNHL is defined as sensorineural hearing loss of 30dB or greater over at least three contiguous audiometric frequencies happening within a 72-hr period (3). Delayed diagnosis and treatment of hearing impairment can affect the development of language skills and social interaction, which form important part of human life (4). Despite extensive research, there is a lot of debate about the cause and appropriate treatment of idiopathic SSNHL. SSNHL affects 5-20 per 100000 individuals annually (1, 5, 6). The actual incidence of SSNHL may exceed these estimates since affected individuals who recover quickly do not refer to medical centers (7). Accompanying symptoms include tinnitus, and dizziness, and perineal sensation (1, 5, 8, 9). Different pathologies have been suggested for SSNHL. These include infection, cardiovascular causes,

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immunological disorders, damage to the tympanum, genetic disorders and mutation, inheritance factors, systemic stress, auto-immune disorders, side effects from ototoxic medications such as salicylates and amino-glycosides, damage to the ears due to aging, perinatal complications, tumors of the inner ear, exposure to loud noise, temporal arthritis, coagulation disorders, local histamine production, neoplasm, prothrombotic risk factors, and the unusual effects of some surgical procedures such as cardiopulmonary bypass surgery (10).

Mostly, the etiology of SSNHL is not recognized in affected patients and therefore their hearing loss is classified as idiopathic. One of the widely accepted reasons for idiopathic SSNHL is viral infections. Herpes simplex virus (HSV) types I and II are one of the most common human pathogens, and are capable of causing early, latent, and recurrent infections (11). About one third of the world's population is affected with HSV creating a major public health problem. This infection can also occur in various parts of the body such as the ears (12).

HSV is a neurotropic virus that invades the spiral ganglion and the eighth cranial nerve. HSV is suspected to be responsible for acute facial paralysis, sudden SSNHL, vestibular neuritis, and Meniere's disease. The prevalence of HSV in the eighth cranial nerve is 39% to 61% on the basis of PCR analysis (13). Obtaining the basic knowledge and performing research on the role of this virus in hearing loss is very important to discover its appropriate treatment (14). Performing research in this field; on the other hand, involves serologic diagnostic methods based on the detection of IgG and IgM antibodies against the virus (15).

However, these methods have a number of disadvantages such as not able to diagnose the disease in the early stages and have the probability of yielding false-negative/positive results. Consequently, molecular detection methods such as PCR / REAL TIME PCR are more suitable because they can accurately detect the early stages of infection, latent infection, pathogenicity, and low-titer virus (16-18). In several studies to detect the different viruses in patients with SSNHL, PCR / real time pcr have been used.

For example for the detection of enterovirus infection in patients with SSNHL, Mentel et al used reverse transcriptase polymerase chain reaction (RT-PCR), a highly sensitive method, which can identify viral infections in samples where neither intact virus nor viral antigens can be detected when standard techniques are used (19). The real-time polymerase chain reaction assay has been developed to detect and quantify even a minimal amount of viral DNA. This system has been shown to be useful for clinical studies because of its wide dynamic range and high reproducibility (13).

The objective of this study was to determine whether idiopathic SSNHL is indeed associated with HSV1&2 infections using RT-PCR.

Methods

After approval by ethics committee and obtaining informed consent, this prospective case-control study was done on 56 patients referred to ENT ward and suffered from SSNHL. Patients participating in this study met the following criteria: (Inclusion criteria)

1) sensorineural hearing loss of unknown cause; 2) hearing loss of at least 30 dB hearing level for 3 subsequent frequencies in the standard pure tone audiogram; 3) blank otologic history; and 4) hearing loss occurring within a period of 72 hours. Participants were excluded if they had acute inflammation, infection, acute or chronic renal failure, acute or chronic pulmonary thrombosis, coronary artery disease, and inflammatory bowel disease, history of ocular surgery, history of ear or head trauma, hematologic disease, or history of any viral diseases.

In order to exclude a known cause of hearing loss, we submitted the patients to a diagnostic protocol that included a complete history and physical examination, audiological tests, magnetic resonance imaging of the temporal bone, and laboratory workup. Fifty six patients with SSNHL occurring within a 72-hr period were selected as case group and 56 participants who had no recent history of disease were assigned into the control group.

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Then, blood sample was taken from each participant. EDTA-treated peripheral blood samples were kept frozen at –80 °C until DNA extraction. DNA extraction was done using a Russian PCR template purification kit (Ampli-sens HSV 1, 2 FR KIT-110 Rxn) according to the manufacturer's instructions.

All the collected data were registered using a form and analyzed using SPSS (version 20) and running descriptive statistics, Chi-square, and T-Test.

To explain the relationship between the sudden hearing loss and the amount and presence of HSV I and II infection, Spearman and Pearson correlation tests were applied. P value <0.05 was considered as significant level.

Results

The aim of this study was to detect HSV virus in patients with SSNHL. This study was conducted on 112 individuals, of whom 56 had no history of infectious or systemic disease (control group), and 56 had SSNHL (case group). Control group comprised of 31 (55.4%) male and 25 (46.6%) female and the case group included 26 (46.4%) male and 30 (53.6%) female. The mean age of participants in the control group was 36.2 ± 13.4 and was 40.80 ± 13.37 in the case group. The prevalence of SSNHL was not significantly different in terms of gender (p value = 0.54) and age (p value = 0.07). The genomic DNA of HSV was measured by Real-time PCR in both groups, and no viral genome was detected.

Discussion

Hearing loss is a common, escalating disorder worldwide, which has multiple negative consequences on the afflicted. Only 10–15% of the SSNHL cases have specified causes, while more than 85% are of unknown etiology—idiopathic sudden sensorineural hearing loss (ISSNHL). Many aspects of SSNHL are still unknown, and its etiology, risk factors, prognostic factors and treatment protocols remain controversial. Probable etiologies of SSNHL have been suggested by various authors. However, each of these etiologies have either been confirmed or rejected in follow-up studies. So far, several studies have been conducted on the correlation between viral infections such as HSV 1&2 and the occurrence of SSNHL (10). The real-time polymerase chain reaction assay has been developed to detect and quantify even a minimal amount of viral DNA. This system has been shown to be useful for clinical studies because of its wide dynamic range and high reproducibility (13). The objective of this study was to determine whether idiopathic SSNHL is indeed associated with HSV 1&2 infections using RT-PCR. According to the current study, using Real-time PCR, no viral DNA genome of HSV virus was detected in patients with SSNHL. Westerlaken BO et al investigated HSV infection by serologic evaluations in 500 human cases suffering from SSNHL and similar to our findings, they found no cases of HSV indicating the pathogenicity of this infection (20). Mishra B et al also explored HSV IgM antibodies to herpes simplex virus using micro ELISA in 32 patients with SSNHL and none of the samples were found to be positive for herpes simplex virus specific IgM antibodies (4). Saiko Sugiura et al investigated Herpes virus DNAs in perilymph obtained from 15 patients with Sensorineural Hearing Loss by Real-Time Polymerase Chain Reaction and HSV DNA was not detected in the perilymph of the patients with SSNHL(13).

In the above mentioned studies researchers did not detect the HSV virus by serologic and PCR method that these findings are in line with our findings. Schweinfurth's JM et al assessed 84 cases for the presence of antibody titer and diagnosed HSV in 14 cases (16.6%) (21). In a study by Noorbakhsh et al. on viral infections in 119 patients with idiopathic sensorineural hearing loss, they detected HSV virus (detected by DNA-PCR, confirmed by serology) in 16.6% of SSNHL cases (22). In a study by Sang Man Park on patients with SSNHL, detection of IgM to herpes simplex virus was performed using (ELISA) and HSV IgM was positive in 33 of 232 patients (14.2%) (23). These contradictions with our study can be due to limited sample size.

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Conclusion

According to the results of this study, it can be concluded that HSV infection is not associated with SSNHL. Establishing an association between viral agent and SSNHL disease seems difficult and further prospective studies in larger populations, in different seasons and epidemiological settings using direct and sensitive molecular assays are required to verify the role of viral infections in SSNHL.

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