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MAIN ARTICLE

Influence of lipoproteins and fibrinogen on pathogenesis of sudden sensorineural hearing loss

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Abstract

Aim: To evaluate the relationship between lipoproteins, fibrinogen and sudden sensorineural hearing loss in a Croatian population. Since pathological derangement of lipoproteins and fibrinogen could be one of the causes of sudden sensorineural hearing loss, we hypothesised that patients with sudden sensorineural hearing loss would have more abnormal fibrinogen and lipoprotein concentrations, compared with subjects with normal hearing.

Methods: Plasma concentrations of cholesterol, fibrinogen and triglycerides in patients with sudden sensorineural hearing loss were compared with those in a control group (i.e. subjects with normal hearing function).

Results: Patients with sudden sensorineural hearing loss had significantly higher plasma concentrations of cholesterol and low density lipoprotein cholesterol, compared with controls.

Conclusion: Higher cholesterol and low density lipoprotein cholesterol concentrations were found in patients with sudden sensorineural hearing loss, within a Croatian population. Cholesterol and low density lipoprotein cholesterol concentrations may be important factors in the pathogenesis of sudden sensorineural hearing loss, and should be assessed during the investigation of patients with this condition.

Key words: Sudden Hearing Loss; Cholesterol; Low Density Lipoprotein Cholesterol; Fibrinogen; Triglycerides; Atherosclerosis; Hearing Loss; Croatia

Introduction

Sudden hearing loss is defined as sensorineural hearing loss (SNHL) of more than 30 dB, over three or more speech frequencies, which develops in less than three days.[1] Damage is usually unilateral. The first manifestation of disease is sudden hearing loss, sometimes accompanied by tinnitus in the damaged ear. Diagnosis is based on anamnesis (i.e. sudden development) and audiometric testing. Sudden SNHL resolves spontaneously in 65 per cent of patients,[2] and there is no treatment method which guarantees successful recovery in all cases.

Suckfull[3] found that decreasing pathological lipoprotein and cholesterol concentrations in patients with sudden SNHL resulted in a statistically significant hearing improvement, compared with standard therapy (i.e. corticosteroids, vasodilators and parenteral crystalloid fluids).[4,5]

Lipoproteins and fibrinogen are very important factors in the development of atherosclerosis, and are the basic pathophysiological elements in the development of many other disorders. For this reason, many treatment modalities for hyperlipoproteinaemia have been developed.[6]

There are two different mechanisms by which hyperlipoproteinaemia and hyperfibrinogenaemia could cause sudden SNHL. The first is the influence on the blood vessels of the inner ear,[7] while the second is the influence on the outer hair cells in the organ of Corti.[8] Hyperlipoproteinaemia and hyperfibrinogenaemia may cause spasm of the spiralis modiolic artery and the vestibulocochlear artery.[8,9] The pathophysiological mechanism may involve nitric oxide,[10] altered rheological characteristics of plasma,[11] atherosclerotic plaque development, and local hypercoagulability of blood adjacent to a cholesterol plaque.[12] High cholesterol levels cause changes in outer hair cell rigidity which alter these cells' ability to actively contract. This reduces the radial movement of endolymph towards the outer hair cells, and diminishes their activation. Finally, hearing loss and/or tinnitus results.[8]

This study aimed to evaluate the relationship between lipoprotein and fibrinogen concentrations and sudden SNHL pathogenesis, within a Croatian population. Since pathological levels of lipoproteins and fibrinogen may be one possible cause of sudden SNHL, we expected that patients with sudden SNHL

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would have more abnormal fibrinogen and lipoprotein concentrations, compared with subjects with normal hearing.

Materials and methods

This prospective study included patients admitted between 2000 and 2007 to a single clinical hospital. In all patients, standard laboratory tests and audiological diagnostic procedures were used.

The study was done in accordance with the ethical standards of, and was approved by, the hospital ethics committee. Written, informed consent was obtained from all patients.

Patients

The test group included all patients with sudden SNHL who were hospitalised between 2000 and 2007 and who were willing to participate in the study. The control group comprised patients scheduled for cosmetic surgery procedures (e.g. nasal septum deviation), without any hearing problems, who were hospitalised between 2000 and 2007, and who were willing to participate in the study. In the test group, all patients had sudden-onset SNHL that commenced seven days or less before hospitalisation. Patients with an average hearing loss of more than 30 dB for speech frequencies were included. Hearing loss was determined by comparing audiograms of healthy and deaf ears.

We excluded patients with other hearing diseases, those with psychiatric illness, dementia, heart failure (i.e. New York Heart Association stage III or IV), hepatitis B or C, human immunodeficiency virus infection, clotting or coagulation disorders, hereditary lipoprotein disorders, malignant neoplastic disease, or arrhythmias, and also those receiving haemodialysis. Patients were excluded based on questionnaire answers and laboratory test results.

In the control group, the inclusion criterion was normal hearing in both ears, measured by audiometry. The exclusion criteria were the same as for the test group.

The test group comprised 54 patients (23 females and 31 males), with a mean age ± standard deviation of 55 ± 14 years (range 16–78 years).

The control group comprised 55 patients (29 females and 26 males), with an average age ± standard deviation of 40 ± 15 years (range 19–70 years).

Test procedures

Hearing was evaluated by tonal audiometry, conducted in an audiological laboratory using an AC 40 Interacoustic clinical audiometer (Interacoustics A/S, Assens, Denmark). The evaluation was performed during hospital admission. Audiometric testing included pure tone audiometry (conducted at the frequencies 0.125, 0.25, 0.5, 1, 2, 3, 4, 6 and 8 kHz). Audiograms of deaf and healthy ears were compared.

Laboratory parameters were evaluated, including: total cholesterol concentration, low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol, triglycerides, fibrinogen, haematocrit, prothrombin time (PT) and activated partial thromboplastin time (APTT) in plasma. Patients with plasma viscosity disorders were excluded by measuring haematocrit values. Patients with coagulation disorders were excluded by measuring PT and APTT. Other standard tests were also performed.

Following ranges were considered normal: fibrinogen: 1, 8–3, 5 g/L, total cholesterol: 3, 8–5, 2 mmol/L, LDL cholesterol: <4,0 mmol/L, HDL cholesterol: >1,5 mmol/L, triglycerides: <2,0 mmol/L.

Statistical analysis

The following descriptive statistical elements were defined for each variable: arithmetic mean, median, range and standard deviation. The distribution of defined variables was tested by the Shapiro-Wilk test. Variables with a normal distribution (i.e. total cholesterol and LDL cholesterol levels) were tested using the *t*-test. Variables with an abnormal distribution (i.e. HDL cholesterol, fibrinogen and triglyceride levels) were tested using the Mann–Whitney U test. A p value of 0.05 or less was considered significant.

Results and analysis

Of 68 patients with a diagnosis of sudden SNHL, 14 were excluded for various reasons (two refused to participate in the study, and the remainder met the exclusion criteria).

Tables I to V show plasma total cholesterol levels, plasma LDL cholesterol levels, plasma HDL cholesterol levels, plasma fibrinogen levels and plasma triglyceride levels for the test and control groups. The test group patients had significantly higher levels of plasma total cholesterol (Table I) and plasma LDL cholesterol (Table II), compared with the control group patients. There were no statistically significant

TABLE I
PLASMA TOTAL CHOLESTEROL

Group	X ± SD (mmol/l)	Median (range) (mmol/l)	p^*
Test	5.9 ± 1.1	6.0 (3.7–8.8)	0.000049
Control	5 ± 1.0	5.2 (2.9–7.2)	

*t-test. X = arithmetic mean; SD = standard deviation

TABLE II
PLASMA LDL CHOLESTEROL

Group	X ± SD (mmol/l)	Median (range) (mmol/l)	p^*
Test	3.7 ± 0.9	3.8 (1.8–5.5)	0.000046
Control	2.9 ± 0.8	2.9 (1.2–5.0)	

*t-test. X = arithmetic mean; SD = standard deviation

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TABLE III
PLASMA HDL CHOLESTEROL

Group	X ± SD (mmol/l)	Median (range) (mmol/l)	p^*
Test	1.4 ± 0.5	1.3 (0.6–3.5)	0.746195214
Control	1.4 ± 0.4	1.3 (0.8–2.4)	

*Mann–Whitney U test. X = arithmetic mean; SD = standard deviation

TABLE V
PLASMA TRIGLYCERIDE

Group	X ± SD (mmol/l)	Median (range) (mmol/l)	p^*
Test	1.6 ± 0.8	1.5 (0.5–3.7)	0.527845789
Control	1.6 ± 0.9	1.3 (0.6–5.5)	

*Mann–Whitney U test. X = arithmetic mean; SD = standard deviation

differences between the two groups regarding plasma HDL cholesterol levels (Table III), plasma fibrinogen levels (Table IV) or plasma triglyceride levels (Table V).

Discussion and conclusion

These results indicate that our test group patients had higher plasma total cholesterol levels than the normal reference range. Our control group patients had plasma total cholesterol levels within the normal range. The difference in plasma total cholesterol levels between the two groups was statistically significant ($p < 0.0001$).

Plasma LDL cholesterol levels were within the reference range in both groups, but were significantly higher in the test group compared with the control group ($p < 0.0001$). Since the two groups differed in average age (the test group was on average 15 years older than the control group), and since total cholesterol and LDL levels tend to increase with age, our results could be partly explained by observed age differences.[13] Turek *et al.*[13] found that, in a Croatian population, a total cholesterol increase of 0.39 mmol/l and an LDL cholesterol increase of 0.33 mmol/L could be expected for the observed age difference. In our test group, we found a 0.8 mmol/l increase in total cholesterol and a 0.9 mmol/l increase in LDL cholesterol, compared with the control group, which could not be explained solely by age difference. This result suggests that there is a strong connection between higher plasma cholesterol and LDL cholesterol levels and the appearance of sudden SNHL.

A recent Croatian study found that 43.1 per cent of that population had pathological levels of LDL cholesterol.[13]

Since pathological levels of lipoproteins and fibrinogen are one possible cause of sudden SNHL, we expected that patients with sudden SNHL would have more abnormal lipoprotein and fibrinogen levels, compared with normal hearing subjects. Based on our findings, we propose that abnormal lipoprotein and fibrinogen levels may represent a new and potentially important aetiological factor in the development of sudden SNHL. This theory suggests potential new avenues for treatment of this disease, as many drugs have been developed for the treatment of hypercholesterolaemia. Plasmapheresis may also be relevant as a treatment method, enabling quick removal of cholesterol from plasma.[14] Interventions designed to reduce the incidence of hypercholesterolaemia, such as promotion of dietary and life-style changes, may also reduce the incidence of sudden SNHL.

- **Sudden sensorineural hearing loss has a variety of aetiological factors; the cause is frequently not detected**
- **This study assessed the prevalence of abnormal lipoprotein and fibrinogen levels in patients with sudden sensorineural hearing loss**
- **Sudden sensorineural hearing loss patients had higher plasma levels of cholesterol and low density lipoprotein cholesterol, compared with controls**
- **Abnormal cholesterol and low density lipoprotein cholesterol levels may constitute a significant aetiological factor in the development of sudden sensorineural hearing loss**

Our results suggest that cholesterol may be an important factor in the aetiology of sudden SNHL, and that cholesterol levels should be evaluated during the investigation of patients with sudden SNHL. Furthermore, we believe that the standard treatment of sudden SNHL should include all the current therapeutic modalities for the reduction of raised cholesterol levels.

TABLE IV
PLASMA FIBRINOGEN

Group	X ± SD (g/l)	Median (range) (g/l)	p^*
Test	3.8 ± 1.1	3.5 (1.6–6.6)	0.579313014
Control	3.9 ± 1.1	3.7 (2.2–6.6)	

*Mann–Whitney U test. X = arithmetic mean; SD = standard deviation

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