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ORIGINAL ARTICLE

Is Tympanosclerosis Effected by Risk Factors for Atherosclerosis?

Aydin Acar, Adil Eryilmaz, Celil Gocer, Umut Genc, Fatih Bakir, Suleyman Boynuegri, Muharrem Dagli

Ankara Numune Education Hospital 3rd ENT Department. (AA, AE, GG, UG, SB, MD) Ankara, Turkey
Ankara Numune Education Hospital Biochemistry Department. (FB) Ankara, Turkey

Objective: Etiology and pathogenesis of tympanosclerosis is still unclear. Risk factors for atherosclerosis have been well known and guided in preventing strategies for reducing cardiovascular disease prevalence. The probable association of atherosclerosis with tympanosclerosis may open a new frontier in reducing tympanosclerosis development and related hearing loss. The purpose of the present study was to evaluate association of some of the commonly accepted risk factors for atherosclerosis with tympanosclerotic patients.

Materials and Methods: Fifty patients with tympanosclerosis and 50 patients without tympanosclerosis undergoing surgical treatment included in the study. Of the risk factors commonly accepted for atherosclerosis, positive family history for cardiovascular disease (CVD), high density lipoproteine (HDL), low density lipoproteine (LDL), cholesterol, high sensitive C- reactive proteine (CRP) and homocysteine levels determined and compared between tympanosclerotic and non-tympanosclerotic groups.

Results: Only high homocysteine levels were found statistically significant in tympanosclerotic patients ($p<0.05$). A positive family history for cardiovascular disease was found at a rate of 18/50 in patients with tympanosclerosis and 10/50 in patients without tympanosclerosis.

Conclusions: High homocysteine levels which was shown as a risk factor in atherosclerosis in many reports, were found also as a risk factor in patients with tympanosclerosis.

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Tympanosclerosis is a degenerative process characterized by a hyaline degeneration of the middle ear and mastoid mucosa.[1] Degenerative process starts in the submucosal connective tissue layer and progresses to involve all connective tissue sublayers.[2] Although there are many investigations on this issue, etiology and pathogenesis of tympanosclerosis are still unclear. Immunological hypersensivity reaction, infection, genetic tendency or trauma have been suggested as causative factors for tympanosclerosis.[3-8]

Koc and Uneri have pointed similarities between tympanosclerosis and atherosclerosis.[9] They reported the incidence of tympanosclerosis in atherosclerotic patients in comparison with the normal population. On otoscopic examination of 1,024 atherosclerotic patients, myringosclerosis was revealed in 66.6%. Myringosclerosis was found in 12% of 300 nonatherosclerotic patients. The high incidence of tympanosclerosis observed in atherosclerotic patients was an impressive datum. Pirodda et al examined 50 patients who were undergoing carotid endarterectomy and compared them with 50 healthy persons.[10] They observed tympanosclerosis at a rate of 18/50 (36%) in the study group and at a rate of 6/50 (12%) in the control group. According to results of both reports, high rate of tympanosclerosis in the presence of atherosclerosis in comparison to its presence in the normal population was found to be statistically significant. These findings indicate that there must be similar risk factors triggering pathogenesis in tympanosclerosis and atherosclerosis.

Numerous investigations have focused on risk factors for atherosclerotic vascular disease. Many of the risk factors for atherosclerosis are well known and there has been a concensus on some of them.

Corresponding address:
Aydin Acar. MD
Ankara Numune Eğitim ve Araştırma Hastanesi
Samanpazarı 06100- Ankara, Turkey
Phone:+90.312.5085079; Fax:+90.312.3111121; E-mail: acara66@yahoo.com

A positive family history of cardiovascular disease is known to be a strong independent risk factor for atherosclerosis for many years. With addition of risks such as lifestyle, smoking, and diabetes, likelihood for coronary hearth disease increases significantly.[11]

High cholesterol levels are strongly associated with atherosclerosis.[12]

CRP is the most extensively studied potential biomarker for atherosclerosis. Prospective studies have demonstrated that high CRP levels are associated with an increase in cardiovascular risk in apparently healthy men.[13]

Elevated plasma homocysteine levels have been associated with an increased risk of atherosclerotic vascular disease.[14]

We aimed in this study to investigate relationship of these well known atherosclerotic risk factors with tympanosclerosis.

Materials and Methods

Fifty patients with tympanosclerosis and 50 patients with chronic otitis media showing no sign of tympanosclerosis were included in the study. All patients underwent surgery for chronic otitis media or its sequelae. A written informed consent was obtained from patients. Tympanosclerosis has been defined as significant calcification of the middle ear mucosa or restricted movement of the ossicular chain resulting from tympanosclerotic plaques. A detailed family history for cardiovascular disease was questioned. After overnight fasting venous blood samples were obtained and sent for laboratory analysis.

Levels of homocysteine were measured in plasma collected into EDTA which was in turn analyzed by Shimadzu HPLC analyzer (Shimadzu Corporation, Kyoto/Japan) using recipe commercial kits (Recipe Chemical and Instruments GMBH, Munich, Germany) with a reference range of 5.5-17 µmol/l.

Analysis for CRP was done by nephelometric method using Dade-Behring NB II nephelometer (Dade-Behring GmbH, Marburg, Germany). Reference levels for CRP was 0-5 mg/L. Cholesterol, HDL and LDL measurements were done with Abbott Aeroset Autoanalyser by spectrophotometric method using Abbott commercial kits (Abbott Laboratories. Abbott Park, Illinois/USA). Reference levels for cholesterol, HDL and LDL were 112-200 mg/dL, 28-75 mg/dL and 0-160 mg/dL respectively.

The study was approved by local ethic committee.

Statistical Analysis

Statistical analyses were performed by Statistical Package for the Social Sciences (SPSS) version 11.5 software for Windows. Normality was tested by Shapiro Wilk test. Nominal variables were evaluated by Chi-square test Continuous variables were evaluated by Student's t test, stated as mean ± standard deviation. Categorized variables were expressed as %. Differences in mean values between groups were analysed with Student's t test. Comparison of categories was done by Chi-square or Fisher's Exact test. Odds ratio and 95% dependence gap were calculated after single variable analyses of risk factors expected to effect tympanosclerosis development. A p value of <0.05 was considered significant.

Results

Both tympanosclerotic and non-tympanosclerotic groups included 50 patients. In the tympanosclerotic group, mean age was 39.8 years (range 13-70); 44% of them were male and 56% of them were female. Mean age of non-tympanosclerotic group was 34.4 years (range14-71); 58% of them were male and 42% of them were female.

Between groups, analysis of ages and genders revealed no statistical difference. (Chi-Square test) (Table 1).

Mean blood levels of homocsyteine in tympanosclerotic and non-tympanosclerotic groups were 18.6 µmol/l and 15.7 µmol/l respectively. In comparison, this was found statistically significant. (Student's t test) ($p<0.01$). In the tympanosclerotic group, homocysteine was above normal ranges in 64% of patients; whereas it was found above normal ranges in 34% of non-tympanosclerotic group (Figure 1).

Table 1. Comparison of the genders and ages of tympanosclerotic and non-tympanosclerotic groups revealed similar results.

	Male	Female	Age
tympanosclerotic (n=50)	22(%44)	28(%56)	39±16.69
non-tympanosclerotic (n=50)	29(% 58)	21(% 42)	34±13,17

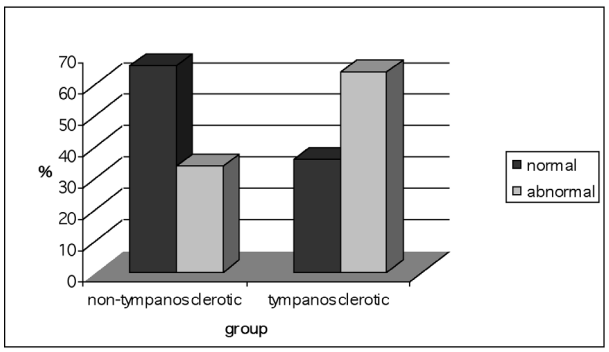

Figure 1. Percentages of normal and abnormal levels of homocysteine in tympanosclerotic and non-tympanoslerotic patients.

CRP was found with a mean level of 6.2 mg/L in the tympanosclerotic group and 5.7 mg/L in the non-tympanosclerotic group. Although high levels were found in the tympanosclerosis group, comparison between groups was not statistically significant. (Student's t test) (p>0.05).

Mean levels of LDL were similar in both groups. It's concentration was found 123.25 mg/dL in the study group and 124.95 mg/dL in the non-tympanosclerotic group. Comparison of LDL concentrations between the groups were not statistically significant .(Student's t test) (p>0.05).

Both HDL and cholesterol contcentrations were similar in study and control groups. Mean HDL concentrations in the tympanosclerotic and non-tympanosclerotic groups were 42.5 mg/dL and 42.8 mg/dL respectively. Mean cholesterol levels in the tympanosclerotic and non-tympanosclerotic groups were 189 mg/dL and 193 mg/dL respectively. In comparison between the groups, both cholesterol and HDL levels were not statistically significant. (Student's t test) (p>0.05) (Table 2).

A positive family history for cardiovascular disease was found in 36% (18 patients) of the tympanosclerotic group. In the non-tympanosclerotic group 20% (10 patients) of patients had a positive family history. Statistical analysis did not reveal a significant difference between groups (p>0.05) (Figure 2).

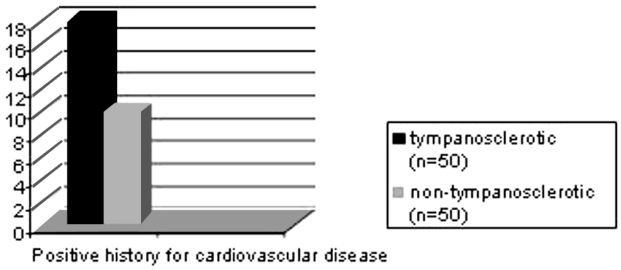

Figure 2. Presence of cardiovascular disease history in tympanosclerotic and non-tympanosclerotic patients.

Discussion

Many studies have been reported on the pathogenesis of tympanosclerosis in both humans and animals. Suggestion of a common origin of tympanosclerosis and atherosclerosis is new in otolaryngology literature. Koc and Uneri investigated incidence of tympanosclerosis in atherosclerotic patients and compared it with its incidence in the normal population.[9] They found a very high rate of

Table 2. Mean blood concentrations of LDL, HDL, Total Cholesterol and CRP in tympanosclerotic and non-tympanosclerotic patients.

	LDL (mg/dL)	HDL (mg/dL)	Total Cholesterol (mg/dL)	CRP (mg/L)L)
tympanosclerotic (n=50)	123.24±41.05	42.46±9.87	189.02±46.78	6.2±6.22
non-tympanosclerotic (n=50)	124.94±39.17	42.76±9.58	193.08±42.50	5.7±5.71

tympanosclerosis in atherosclerotic patients. After Koc and Uneri's report, Pirodda et al investigated 50 patients effected by atherosclerosis who underwent carotid endarteroctomy.[10] In comparison to the healthy group, they found higher rates of tympanosclerosis. (36% and 12% respectively). Koc and Uneri also investigated light and electron microscopic appearences of atherosclerotic and tympanosclerotic plaques and they found similar ultrastructural properties. In another study analysing biochemical composition of tympanosclerotic deposits, cholesterol was found similar to atherosclerotic plaques.[15] Both diseases are last reactions of inflammation in connective tissue and pathogenesis may follow the same route.

Reported similarities between atherosclerosis and tympanosclerosis rises the question whether these two clinical diseases are effected by similar risk factors. Risk factors for atherosclerosis have been investigated in numerous clinical and experimental studies. Identification and reduction of risk factors for atherosclerosis have been the main goal in preventing cardiovascular disease for many years. Understanding the pathogenesis and risk factors for tympanosclerosis may play a role in preventing tympanosclerosis development. Commonly accepted risk factors for atherosclerosis, such as family history for cardiovascular disease, CRP levels, lipid levels and homocysteine levels were therefore investigated in patients with tympanosclerosis.

Only homocysteine levels were found to be significantly high in tympanosclerotic patients compared to the control group. Since homocysteine levels are lowered with folic acid, studying the effect of folic acid supplemantation on development of tympanosclerosis may provide additional insight into the role of homocysteine in the pathogenesis of tympanosclerosis. In a study, plasma homocysteine was proposed as an intermediate risk factor for coronary heart disease development.[16] They suggested that plasma homocysteine levels may express a clinical importance as a marker in coronary heart disease. Use of homocysteine as a marker for tympanosclerosis development may be studied further. History for cardiovascular disease was found higher in number (18/50) in tympanosclerotic patients compared to the control group (10/50). This difference was statistically insignificant (p>0,05). However, this must investigated in a study enrolling higher numbers of patients. Since a positive family history for cardiovascular disease is an independent strong risk factor for atherosclerosis, to elucidate similarities of atherosclerosis and tympanosclerosis it should be studied with cohort investigations.[11,17]

Blood cocentrations of cholesterol and LDL were not significantly different than the control group in tympanosclerosis.

Some authors claim that CRP is a promoter of atherosclerosis and coronary heart disease and some report association of CRP and atherosclerosis is not so reliable.[13,18,19] Mean CRP levels of tympanosclerosis and control groups were not significantly different in our study (p>0,05). It was within normal ranges in 68% of the study group and in 70% of the control group. This high ratio of normal values in both groups indicates that there is no need for further investigating CRP. On the other hand there are some reports which some differences can be sought out between atherosclerosis and tympanosclerosis. There has been suggestions of a possible role of certain type of human leucocyte antigens (HLAs) in the genesis of tympanosclerosis.[20] In another study atherosclerosis was not associated with particular HLA alleles.[21] Furthermore some differences can be outlined concerning the age of presentation, although even it is difficult to present precise data on this aspect, and the sex prevalence, which is controversial in tympanosclerosis although a greater incidence of atherosclerosis in males is generally accepted until the age of 50-60 years.[5,22,23] Patients with tympanosclerosis generally present themselves at a younger age than atherosclerotic patients.

Conclusion

High homocysteine levels which was shown as a risk factor in atherosclerosis in many reports, were found also as a risk factor in patients with tympanosclerosis.

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