

## LEVELS OF PARAOXONASE AND SERUM LIPID PARAMETERS IN PATIENTS WITH NOISE-INDUCED HEARING LOSS

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### ABSTRACT

To evaluate the relationship between noise induced hearing loss (NIHL) and levels of high density lipoprotein-cholesterol (HDL), low density lipoprotein-cholesterol (LDL-C) and Paraoxonase (PON1) activity in patients with NIHL compared to normal subjects.

Thirty two patients with NIHL were recruited in the study. 30 subjects with normal hearing were included in the control group. Pure tone audiometry was applied to all patients and controls. Blood samples were obtained from all subjects to determine levels of HDL-C, LDL-C and PON1.

PON1 activity and HDL-C levels were found to be significantly lower while the level of LDL-C was significantly higher in the patients with NIHL compared to healthy controls ( $p<0.05$ ). In the study group the hearing loss was starting at 4000 Hz and reached to maximum at 6000 Hz.

Present findings suggest that atherosclerosis at microlevels begin in cochlear artery. In this respect, decreasing in cochlear arterial perfusion may cause sensorineural hearing loss. Low levels of PON1 activity and HDL-C and high levels of LDL-C may aggravate the noise induced hearing loss.

**Key Words:** Noise induced hearing loss, Paraoxonase, HDL-C, LD-CL.

### ÖZET

#### Gürültüye Bağlı İşitme Kaybı Bulunan Hastalarda Paraoksanaz ve Serum Lipid Parametrelerinin Seviyeleri

Gürültüye bağlı işitme kaybı bulunan hastalar ile sağlıklı bireyler arasında yüksek dansiteli, düşük dansiteli lipoprotein-kolesterol (LDL-K) ve paraoksanaz (PON1) aktivitesi arasındaki ilişkiyi değerlendirmek.

Gürültüye bağlı işitme kaybı bulunan 32 hasta çalışmaya alındı. Kontrol grubu ise sağlıklı 30 bireyden oluşturuldu. Tüm hasta ve sağlıklı bireylere pür ton odiyometri yapıldı. HDL-K, LDL-K ve paraoksanaz seviyelerinin tespiti için tüm bireylerden kan örnekleri alındı. Bulgular: Sağlıklı bireylerle karşılaştırıldığı zaman gürültüye bağlı işitme kaybı bulunan hastalarda LDL-K seviyesi anlamlı olarak yüksek iken HDL-K seviyeleri ve PON1 aktivitesi anlamlı olarak düşük bulunmuştur ( $p<0.05$ ). Çalışma grubundaki işitme kaybı 4000 Hz'de başlamakta ve 6000 Hz'de maksimum seviyeye ulaşmıştır.

Mevcut bulgular aterosklerozun kohlear arterde mikro seviyelerde başladığını göstermektedir. Bu nedenle kohlear arter perfüzyonunda azalma sensorinöral işitme kaybına neden olmaktadır. Düşük seviyelerde PON1 aktivitesi ve HDL-K seviyesi ile yüksek LDL-K seviyesi gürültüye bağlı işitme kaybını artırabilir.

**Anahtar Kelimeler:** Gürültü, işitme, Paraoksanaz,, HDL-K, LDL-K.

### INTRODUCTION

Noise induced hearing loss (NIHL) is a common occupational disease of adult population. In NIHL, audiometrically sensorineural loss was first observed as a notch pattern at 4 kHz [1]. NIHL was demonstrated to be occurring by outcomes of metabolic effects. Patients exposed to noise for a long duration have hearing loss that especially maximal at 3-6 kHz and this hearing loss slightly

improves at high frequencies, but it is not affected at low frequencies [1].

It is known that hyperlipoproteinemia is an important ethiological factor in presbycusis and progressive sensorineural hearing loss [2]. In the body, atherosclerosis causes damage in organs that are perfused especially by end-arterial system. Cochlea is also perfused from end-arterial system, so

labyrinthin dysfunction appeared according to the degree of atherosclerosis [3].

Oxidative low density lipoprotein-cholesterol (LDL-C) is believed to play an important role in the events associated with the initiation of atherosclerosis. One current hypothesis to explain the development of the foam cell-laden fatty streaks in the arterial wall, which are believed to initiate atherosclerosis, suggests that oxidative modification of LDL-C in the artery wall is critical to the process [4]. Uptake of oxidised LDL-C via recognition of the modified apolipoprotein B at the macrophage scavenger receptor leads to the formation of lipid laden foam cells *in vitro*, resembling those in the fatty streak, the precursor of atheroma [5]. Secretion of monocyte-chemotactic protein 1 and macrophage colony stimulating factor by the foam cells may cause further recruitment and retention of lipid-laden macrophages, which further aggregate to form the fatty streak [6].

HDL-C has been shown to prevent oxidative modification of LDL-C *in vitro* [7], as well as *in vivo* [8]. Paraoxonase (PON1) is a serum enzyme that is entirely complexed to HDL-C. A recent hypothesis suggests an antioxidant role of PON1 in the protection of LDL-C from oxidative modifications [9]. Gail *et al.* reported that increased activity of PON1 was predicted by increased vitamin C and E intake [10].

The aim of the present study was to evaluate possible relationship between NIHL and levels of HDL-C, LDL-C and PON1 activity.

## MATERIAL and METHODS

Workers in a local hydroelectric powerhouse (Keban, Elazig, Turkey) were recruited to form the study group. Control group was consisted of 30 voluntary males with similar age who are working in the same powerhouse with normal hearing who were. Study and control groups were composed of 40 patients (mean age 37±5 year) and 37 subjects (mean age 36±4 year), respectively. All of the subjects in study and control groups were male. Eight patients from study and seven patients from control group who have history of cigarette smoking is excluded from this study and it was created with 32 study patients (mean age 37±3 year) and 30 study subject. (mean age 36±6 year)

A questionnaire form was applied to all subjects in the study. In the questionnaire; date of the birth, age of initializing to work, duration of working, daily working and resting times were compiled. The patients who have history of using ototoxic drugs,

previous ear diseases, trauma to head and the ear and familial history of hearing diseases were excluded from the study.

Noise levels were measured by a noise measurer (Bruel and Kjaer 2235, Copenhagen, Denmark). The mean level of noise was determined to be altering between 95-116 dB in the hydroelectric powerhouse. The period being exposed to noise is 8 hours per day. The mean duration of working in the power house of workers with NIHL was 18±5 year.

The audiometric tests were performed in a sound-proof chamber with an Interacoustics AC-40 audiometer (Denmark) that was calibrated according to ISO 1964 standards as we reported previously [11]. Pure tone audiometry was applied to all patients and controls. For the escape from temporary threshold alteration induced by noise, hearing measures were taken after 24 hours with noiseless resting period. Frequencies at octave intervals from 250 to 8000 Hz were tested for air conduction and from 500 to 4000 Hz for bone conduction. Hearing level was accepted as abnormal if the hearing threshold was 25 dB or more below than the age-corrected level at two or more test frequencies. In our criterion for NIHL, hearing threshold is normally at 1 kHz but hearing loss is more than 25 dB at 4-6 kHz.

Fasting blood samples were obtained from all subjects for biochemical analysis. Levels of HDL-C and LDL-C were measured by an autoanalyzer (Olympus AU 600) using commercially available kits (Olympus Optical Co. Ltd., Japan). For determination of PON1, modified methods of Ecerson [12], Juretic [13] and Mackness [14] were used as we recently reported [15]. Statistical analyses were performed using SPSS program for windows, version 10.0 (SPSS Inc., Chicago, IL, USA). All test used were two-tailed and P less than 0.05 was considered as significant. The data are given as mean ± standard deviation (SD). Comparison between groups were performed using the Student's *t* test. Pearson correlation coefficient was used to assess the relationship between variables.

## RESULTS

PON1 and HDL-C levels were determined to be lower whereas levels of LDL-C were higher in the patients with NIHL. These data were statistically significant ( $p < 0.05$ ) (Table 1). In the study group, the hearing loss was started at 4 kHz and reached to maximum at 6 kHz (Figure 1).

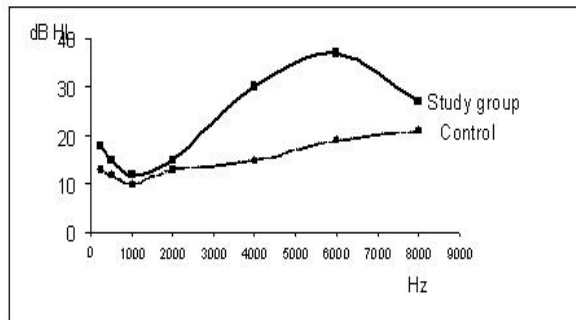
In the study group, there was no significant correlation between the levels of PON1 activity and

HDL-C ( $r:0.226$ ,  $p>0.05$ ). No significant correlation between levels of PON1 and HDL-C ( $r:0.226$ ,  $p<0.077$ ), LDL-C ( $r:0.287$ ,  $p<0.0226$ ) were found but

there was a significant but weak correlation between PON1 activity and LDL-C ( $r:-0.287$ ,  $p<0.05$ )

**Table 1.** The levels of PON1, HDL-C and LDL-C in study (patients with NIHL) and healthy control groups. All of the subjects in both study and control groups were male

Parameter	Study group (n=32)	Control group (n=30)	P
HDL-C (mg/dL)	37±80	48±60	<0.0001
LDL-C (mg/dL)	163±37	79±10	<0.0001
PON1 (nmo14-nitrophenol/sec/ml)	205±100	252±44	<0.005



**Figure 1.** The audiograms of study (n:32) and control (n:30) groups. (dB: Decibel, Hz: hertz)

## DISCUSSION

Because of rapid industrialization, widespread increase of noise sources and increased population being exposed to noise, NIHL is one of the most important cause of sensorineural hearing loss.

Spencer demonstrated that exact hyperlipoproteinemia was present in 42.3 % and border hyperlipoproteinemia was seen in 8.66% of 300 patients who had inner ear disease with cochlear and/or vestibular symptoms [2]. The possible reversing effects on hearing loss of a low-cholesterol diet after a person develops hearing loss associated with high blood cholesterol levels was studied by Rosen *et al.* [16]. They reported that a change of diet from a cholesterol-rich diet to a low-cholesterol diet actually improved the hearing loss at 4 kHz hearing in subjects after four years. Kojima *et al.* [17] reported that hearing improvement were observed after therapy for hyperlipidemia in patients with chronic-phase sudden deafness. Suzuki *et al.* [18] suggested that the low serum HDL-C levels are associated with atherosclerosis-related micro-circulatory disturbances of the cochlear vasculature and increased susceptibility of the cochlea to noise. When a low HDL-C combined with daily exposure to noise, this combination can lead to hearing loss [18]. It is reported that hyperlipoproteinemia is seen

together with sudden fluctuant or progressive vestibular and hearing disorders and probably hyperlipoproteinemia causes anoxia on the sensitive cells in the inner ear by the vascular blockage [17]. It has been reported that hypoxia alone did not cause hearing loss and hair cells loss, the combined exposure to noise and hypoxia causes more hearing loss and hair cell loss than the noise alone [19].

Saito *et al.* [20] showed a mild increase in the auditory brainstem response-induced hearing threshold in 40% of Guinea pigs fed with a high-fat diet. Electron microscopic studies of the inner ear revealed structural changes, such as vacuolar degeneration and parenchymal protrusions of the stria vascularis and the surface of Corti's organ, vacuolar degeneration around capillaries in the stria vascularis, and the formation of crevices beneath marginal cells. Sikora *et al.* exposed chinchillas fed with a high-fat diet to noise. In the hyperlipidemic group, NIHL in the high frequency range was more severe and the loss of inner hair cells was significantly greater than those in chinchillas fed with a normal diet [21].

The generation of reactive oxygen species is thought to be part of the mechanism underlying NIHL. There are studies which indicate that two enzymes associated with HDL-C, PON1 and platelet-activating factor acetylhydrolase, are responsible for its antioxidative and anti-inflammatory properties [22]. There is considerable evidence that the antioxidant activity of HDL-C is largely due to the PON1 located on HDL-C. Experiments with transgenic PON1 knockout mice indicate the potential for PON1 to protect against atherogenesis. This protective effect of HDL-C against LDL-C peroxidation is maintained longer than the protective effects of antioxidant vitamins [23]. Fortunato *et al.* reported that PON2 polymorphisms could predispose to NIHL by exerting variable local tissue antioxidant roles but any association was not detected for PON1 and NIHL (24).

In the present study, PON1 and HDL-C levels were found to be lower and level of LDL-C was higher in the patients with NIHL. In the study group, there was a weak negative correlation between LDL-C and PON1. Low levels of PON1 activity and HDL-C and high levels of LDL-C may contribute to the development of NIHL.

In conclusion we think that, evaluation of pure tone audiograms and levels of lipid parameters such as HDL-C and LDL-C in routine control of the workers who are employed in a noise environment such as a hydroelectric powerhouse may be helpful in the management of possible development of NIHL.

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