CLINICAL STUDY

RED BLOOD CELL DISTRIBUTION WIDTH: A RISK FACTOR FOR CHRONIC INFLAMMATION, INCREASED IN PATIENTS WITH PRESBYCUSIS

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SUMMARY

Objective: We aimed to investigate the relationship between presbycusis and red blood distribution width (RDW), a biochemical marker for chronic inflammation and oxidative stress.

Methods: The patient group comprised those admitted to our clinic with the complaint of hearing loss, while the control group consisted of participants over 50 years of age with normal audiograms. Hemogram parameters and audiological configurations of the participants were recorded.

Results: A total of 218 participants were included in the study (89 males, 129 females; mean age 63.6 years; age range 50-87 years). The results of our study were: 1) RDW was higher in the presbycusis group than the control group. 2) We found that RDW had a weak positive correlation with all frequencies of hearing levels. Also, RDW was found to be the only parameter in the haematology panel that showed a significant correlation with all frequencies of the audiogram; 3) Moreover, we found that MCV and Hg values had a weak negative correlation with the low frequencies of hearing loss.

Conclusion: Our study supports the fact that RDW is higher in patients with presbycusis and may be a negative prognostic parameter for presbycusis.

Keywords: Presbycusis, age related hearing loss, red cell distribution width, chronic inflammation, hemogram

PRESBİAKUZİDE ARTMIŞ KIRMIZI KÜRE DAĞILIM GENİŞLİĞİ DEĞERLERİ, KRONİK İNFLAMASYON İÇİN YENİ BİR RİSK FAKTÖRÜ

ÖZET

Giriş: Kırmızı Küre dağılım genişliği (RDW) ve presbiakuzinin ilişkisi hakkında daha önce başka bir çalışma yapılmadığı için bu çalışmada RDW ve presbiakuzi arasındaki bir ilişkiyi araştırmayı amaçladık.

Yöntem Gereçler: Hasta grubu kliniğimize işitme kaybı şikâyeti ile başvuranlardan, kontrol grubu ise 50 yaş üstü normal işitme testine sahip katılımcılardan oluşmaktaydı. Katılımcıların hemogram parametreleri ve odyolojik konfigürasyonları kaydedildi. İstatistiksel analiz, hastaların işitme değerleri ile incelenen parametreler arasındaki olası ilişkiyi saptamak amacıyla yapıldı.

Bulgular: Çalışmaya toplam 218 kişi katılmıştır (89 erkek, 129 kadın; ortalama yaş: 63.6; yaş aralığı: 50-87 yıl). Çalışmamızın sonuçları: 1. RDW, presbiakuzi grubunda kontrol grubuna göre daha yüksekti. 2. RDW'nin tüm işitme seviyeleri sıklığı ile zayıf pozitif bir korelasyon olduğu saptandı. Ayrıca, RDW, hemogram panelinde, odyogramın tüm frekansları ile anlamlı bir korelasyon gösteren tek parametre olarak bulundu 3) Ayrıca, MCV ve hemoglobin değerlerinin düşük frekans işitme kaybı ile negatif bir korelasyonu olduğunu sonucuna varıldı.

Sonuç: Bizim çalışmamız, RDW'nin presbiakuzili hastalarda daha yüksek olduğunu ve presbiakuzi için negatif prognostik bir parametre olabileceğini desteklemektedir.

Anahtar Sözcükler: Presbiakuzi, yaşa bağlı işitme kaybı, kırmızı küre dağılım genişliği, kronik inflamasyon, hemogram

INTRODUCTION

Presbycusis is a degenerative disease that emerges with aging and is characterized by bilateral, symmetrically progressive sensorineural hearing loss. As the most common cause of hearing loss in adults, it has become a major social and economic problem due to increasing life spans[1]. According to the World Health Organization, there will be 1.2 billion people over 60 years of age by 2025, of which 500 million are expected to develop presbycusis[2]. A number of etiologic factors related to presbycusis have been identified in studies, such as genetic predisposition, noise exposure, chronic middle-ear disease, cardiovascular diseases, smoking, hypertension, diabetes mellitus, hormones and ototoxic drugs[1-5]. It is known that age-related hearing loss, i.e. presbycusis, is the result of irreversible changes associated with aging tissues as well as the damaging effects of the diseases mentioned

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above to the central and peripheral hearing pathways. The level of damage caused by environmental factors is undoubtedly determined by a person's genetically determined self-renewal capacity[1,5]. Recent studies show that the pathophysiology of ageing and presbycusis is associated with increased oxidative damage at the cellular level, including mitochondrial DNA damage and molecular mediators of the cell[6,7].

On the other side, red cell distribution width (RDW) is a parameter that expresses the variation in the size of erythrocytes in blood circulation in hemogram parameters. It is used with mean cell volume (MCV) in the classification of anaemias, such as iron deficiency anaemia, thalassemia and chronic anaemia. Recently, RDW has been investigated in relation to microcirculation changes in chronic inflammatory events. Oxidative damage and the inflammation related to oxidative stress affect the erythropoiesis and lead to an increase in RDW levels by causing the release of immature cells into the blood, a result of the shortened survival life of red blood cells due to oxidative stress[8-10]. Several studies have shown that RDW increase is a poor prognostic of acute coronary disease and cerebral stroke[11-13]. Two recent studies investigated the prognostic value of RDW in facial-nerve paralysis and acute sensorineural hearing loss, and the researchers found that elevated RDW levels were a poor prognostic factor for these two common disease in the otologic field[14,15].

To the best of our knowledge, there has been no other study about RDW levels and presbycusis. Thus, we aimed to investigate the relationship between presbycusis and RDW.

MATERIAL and METHODS

We conducted our study at the Otorhinolaryngology Department of Ankara Numune Training and Research Hospital between January 2017 and December 2017. The approval of the Local Ethics Committee was obtained (E-17/1232), and all investigations were performed in accordance with the Declaration of Helsinki on biomedical studies involving human subjects.

The patient group comprised those admitted to our clinic with the complaint of hearing loss, while the control group consisted of participants over 50 years of age with normal audiograms.

Individuals with a history of noise damage, middle-ear hearing loss and cognitive function disability were excluded. Also not included in the study were individuals who had been treated with ototoxic medications, exhibited serious medical health problems or neurological medical conditions, or had been diagnosed with Meniere's disease or labyrinthitis. Hemogram parameters and audiological configurations of the participants were recorded. Pure tone audiometry was measured at 0.5, 1, 2, 4, and 8 kHz to detect the hearing threshold at each frequency, using an AC40 clinical audiometer (Interacoustics, Assens, Denmark) in a sound-isolated room standardized according to the manufacturer's instructions. Air-conduction thresholds between 0.5 and 8 kHz were measured using TDH-39 earphones and an MX41/AR cover. Bone-conduction thresholds between 0.5 and 4 kHz were measured using an Oticon 60273 vibrator. The pure tone average (PTA) was determined based on the air-conduction average threshold levels in each ear at 0.5, 1, 2, and 4 kHz. In the haematology panel, white blood cell (WBC), haemoglobin (Hg), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), platelet, mean platelet volume (MPV) and red blood distribution width (RDW) were recorded. All the haematological examinations were performed in the same device (Sysmex XT-1800i).

Statistical Analysis

The SPSS 16.0 program was used for statistical analysis. The Kolmogorov-Smirnov test was used to determine whether the distribution of the data in the study groups was normal or not. Because the distribution was normal, parametric tests were used to evaluate the study data. The chi-square or t-test was used to evaluate whether there was a statistically significant difference between the group with presbycusis and the control group with normal hearing in terms of the parameters studied. Pearson correlation analysis was also performed

to determine the possible relationship between the hearing values of the patients and the parameters examined. P value of <0.05 was considered statistically significant.

RESULTS

A total of 218 participants were included in the study (89 males, 129 females; mean age 63.6 years; age range 50-87 years). The participants were divided into two groups according to their average hearing threshold. An average hearing threshold in the range of -10 to 20 dB was considered to be normal. Participants with normal hearing levels formed the control group, whereas participants with average hearing threshold levels above 20 dB formed the presbycusis group. The haematological parameters and audiological findings were used for statistical analysis. The descriptive statistical analysis of the study groups is shown in Table 1 and Table 2. As shown in Table 1, there was a significant difference between the presbycusis and control groups in terms of gender and age. However, we did not find a statistically significant difference between the study groups in terms of calculated haematological parameters, with the exception of RDW. A Pearson correlation analysis was performed to determine the statistical relationship between hearing levels and haematological parameters (Table 3). We found that RDW had weak positive correlation with all of the calculated hearing-level frequencies for both the right and left ear. Also, we found that MCV had a weak positive correlation with the low hearing-level frequencies for both the right and left ear. Moreover, Hg levels had weak negative correlation with the frequencies of 500 dB and 1000 dB for both the right and left ear. We did not find any significant correlation between hearing levels and other hematologic parameters such as platelet levels, WBC, MCH, MCHC and MPV. A multivariate analysis of variants was performed to determine the effect of RDW on the hearing-level frequencies independent of age and gender. In all hearing-level frequencies, increasing RDW levels were associated with increased hearing thresholds ($p<0.001$ for all frequencies for both for right and left ears). As expected, increased age was associated with an increased hearing threshold for all frequencies ($p<0.001$).

Table 1. The descriptive statistical analysis of the study groups.

	Presbycusis group (N= 145)	**Control group (N=73)**	**P value**
Age	66 ± 9	59 ± 8	*<0.001*$^{+}$
Gender (male/female)	67/78	22/51	*0.03**
Hemoglobin	13.4 ± 1.7	13.5 ± 1.6	0.5^{+}
White blood cell	9.01 ± 4.8	7.8 ± 2.8	0.3^{+}
Platelet	252 ± 75	269 ± 65	0.09^{+}
Mean platelet volume	9.7 ± 1.2	9.7 ± 1.3	0.9^{+}
Mean Corpusculer Volume	85.6 ± 4.9	84.2 ± 8.6	0.1^{+}
Red blood cell distribution width	13.8 ± 1	13.3 ± 1.2	*0.005*$^{+}$

*chi square test, + Independent sample t test

Table 2. The audilogical findings of the study groups.

Audilogical findings	Presbycusis group (N= 145)	Control group (N=73)	P value *
R500	28.5 ± 14	9.9 ± 4.2	*<0.001*
R1000	32.8 ± 16	9.8 ± 4	*<0.001*
R2000	42 ± 17	11 ± 5	*<0.001*
R4000	53 ± 17	18.3 ± 14	*<0.001*
R8000	63 ± 19	27 ± 18	*<0.001*
R average	31 ± 11	7 ± 4	*<0.001*
L500	27 ± 14	9.6 ± 4	*<0.001*
L1000	32 ± 16	9.6 ± 3.8	*<0.001*
L2000	41 ± 17	10.8 ± 5.6	*<0.001*
L4000	53 ± 17.5	17.8 ± 13.5	*<0.001*
L8000	64.6 ± 20	27.7 ± 18	*<0.001*
L average	31 ± 11	7.6 ± 3.8	*<0.001*

* Independent sample t test, (R= right ear, L= left ear)

Table 3. The correlation analysis between frequencies of hearing levels and hematologic parameters (only statistically significant data was shown in the table).

Frequency	P value / Pearson correlation coefficient, r		
	RDW	Hg	MCV
R500	0,01 / 0.17	0.009 / - 0.18	0.04 / 0.14
R1000	0,02 / 0.16	0.01 / - 0.18	0.009 / 0.18
R2000	0,007 / 0.18		0.03 / 0.14
R4000	0,008 / 0.18		
R8000	0,02 / 0.16		
Rmean	0,008 / 0.18		0.03 / 0.14
L500	0,01 / 0.17	0.01 / - 0.17	
L1000	0,02 / 0.16	0.01 / - 0.17	0.009 / 0.18
L2000	0,02 / 0.16		0.02 / 0.16
L4000	0,018 / 0.16		
L8000	0,022 / 0.16		
Lmean	0,012 / 0.17		0.02 / 0.15

DISCUSSION

Hearing loss is one of the most common chronic conditions that affect people with advancing age. In the literature, studies have found many etiologic factors related to presbycusis, such as genetics, noise exposure, chronic middle-ear disease, cardiovascular diseases, smoking, hypertension, hormones and ototoxic drugs. The biological mechanism underlying presbycusis, however, has not been established[16]. There are studies indicating that chronic inflammation and other life factors may lead to presbycusis. Dietary folic acid, B12 and homocysteine levels were found to be associated with presbycusis. Since the blood supply to the inner ear is provided from the end artery, vascular diseases and sensorineural hearing impairment are thought to be closely related[1,16].

In recent studies, RDW was found to be associated with sudden sensorineural hearing loss and Bell's palsy as a prognostic factor. In patients with sudden sensorineural hearing loss, RDW values before and after treatment were significantly higher in the nonresponders" group.

Similarly, RDW was significantly higher in patients who did not recover from Bell's palsy than in recovered patients. These studies suggested that RDW was a prognostic factor for sudden sensorineural hearing loss and Bell's palsy[14,15]. Also, RDW was found to be a novel predictive indicator as an inflammatory marker, especially for cerebral and cardiovascular diseases[8-10]. Considering the effects of oxidative stress and chronic inflammation on presbycusis, the correlation between the RDW and presbycusis was investigated in our study.

The results of our study were: 1) RDW was higher in the presbycusis group than the control group. Although average RDW values for both study groups were within the normal limits (i.e. between 12.1-14.3%), this difference was statistically significant; 2) we found that RDW had a weak positive correlation with all frequencies of hearing levels. Also, RDW was found to be the only parameter in the haematology panel that showed a significant correlation with all frequencies of the audiogram; 3) Moreover, we found that MCV and Hg values had a weak negative correlation with the low frequencies of hearing loss.

Current literature suggests that age-related hearing loss, or presbycusis, is related to oxidative stress, which causes impaired cellular functioning through the peripheral and central hearing pathways[16]. An increased RDW value may be a result of chronic inflammation and oxidative stress. The survival rate of red blood cells can be reduced due to oxidative stress and chronic inflammation, which are conditions mutually triggering of each other[6].

This study had some limitations. First, we have a single centre and a relatively small sample size. Second, we could not have an age-appropriate and gender-matched control population, so we included the age group of 50 years or older in the control group. Further research is needed to confirm our findings in larger populations.

CONCLUSION

In conclusion, our study supports the fact that RDW is higher in patients with presbycusis and may be negative prognostic parameter for presbycusis.

Compliance with Ethical Standards: All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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