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A New Hematological Marker for Idiopathic Tinnitus: Monocyte/HDL ratio

Nowy marker hematologiczny dla idiopatycznych szumów usznych: współczynnik monocyty/HDL

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ABSTRACT:

Aim: The aim of this study was to evaluate the association between the monocyte/HDL ratio (MHR) and idiopathic tinnitus.

Study Design: Retrospective case-control study.

Material-method: Eighty-nine patients with idiopathic tinnitus diagnosed on an outpatient basis between March 2015 and June 2016 and 87 healthy individuals who presented to our hospital for a routine health examination and had normal audiometry and otoscopy results were included in the study. Blood samples were obtained from patients during the first examination. The MHR was calculated as the ratio of the monocyte count to the HDL level. MHR ratios were compared statistically between the groups.

Results: The monocyte count and the MHR were higher and HDL was lower in the study group compared to the control group ($p< 0.05$). The cut-off value of MHR for diagnosing tinnitus was 11.

Conclusion: The MHR ratio was high in patients with idiopathic tinnitus, which supports the fact that atherosclerotic events and oxidative stress are implicated in the etiology of tinnitus.

KEYWORDS: Monocyte, HDL, tinnitus, ratio, blood count

STRESZCZENIE:

Cel: Celem niniejszego badania było zbadanie związku, o ile on istnieje, między wartością MHR a idiopatycznym szumem usznym.

Projekt badania: Prospektywne badanie kliniczno-kontrolne.

Materiał i metody: Do badania włączono 89 pacjentów (grupa badana), u których od marca 2015 roku do czerwca 2016 roku w ambulatorium przyklinicznym zdiagnozowano idiopatyczne szumy uszne oraz 87 zdrowych osób, które zgłosiły się do szpitala w celu przeprowadzenia rutynowego badania lekarskiego i uzyskały prawidłowe wyniki badania audiometrycznego i otoskopowego (zdrowa grupa kontrolna). Próbki krwi pobierano od pacjentów podczas pierwszego badania. Współczynnik HDL (MHR – Monocyte/HDL rate) uzyskano przez prosty podział liczby monocytów przez poziom HDL. Współczynniki MHR uzyskane dla obu grup poddano analizie statystycznej. Wyniki: Liczba monocytów i wartość MHR były większe w grupie badanej, a poziom stężenia HDL był niższy w porównaniu z grupą kontrolną ($p<0,05$). W niniejszym badaniu wartość odcięcia dla MHR w odniesieniu do szumów usznych ustalono na 11.

Wniosek: Współczynnik MHR okazał się wysoki u pacjentów z idiopatycznymi szumami usznymi. Uzyskany wynik wskazuje na udział zdarzeń miażdżycowych i stresu oksydacyjnego w etiologii szumów usznych.

SŁOWA KLUCZOWE: monocyt, HDL, szumy uszne, współczynnik, morfologia krwi

INTRODUCTION

Tinnitus is defined as hearing sounds in the ears or the head without any external acoustic stimuli. Some patients do not seek medical help since they are comfortable with their symptoms or are used to them. Others present to physicians due to occupational problems, sleeplessness, restlessness, anxiety, or depression[1]. The prevalence of tinnitus is 10-15%, while unemployment due to tinnitus affects 1-2% of the general population. The etiology of tinnitus is multifactorial and still not fully elucidated. Tinnitus may be secondary to cochlear hair cell damage due to metabolic diseases such as dyslipidemia, hyperinsulinemia, and diabetes mellitus[3]. Dyslipidemia has been reported to be associated with sensorineural hearing loss, dizziness, and tinnitus [4-5]. Low high-density lipoprotein (HDL) levels have also been demonstrated to be associated with decreased auditory function [3].

Monocytes and macrophages are the most important cells that release proinflammatory and prooxidant cytokines during inflammation [6]. In contrast, high-density lipoproteins (HDL) have been demonstrated to protect endothelial cells from adverse effects of low-density lipoproteins (LDL) and prevent oxidation of LDL molecules. Therefore, HDL cholesterol has been suggested to have both anti-inflammatory and anti-oxidative effects [7]. The ratio of the monocyte count to the HDL cholesterol level (MHR) has been suggested as a new cardiovascular prognostic marker reflecting inflammation and oxidative stress, which can be easily calculated based on the above-mentioned values [7-13].

The aim of this study was to evaluate a potential association between the MHR and idiopathic tinnitus.

MATERIAL AND METHOD

The study was retrospective, and was approved by the local ethics board of our hospital. The data were obtained from electronic records of the patients. Eighty-nine patients with idiopathic tinnitus diagnosed on an outpatient basis between March 2015 and June 2016 and 87 healthy individuals who presented to our hospital for a routine health examination and had normal audiometry and otoscopy results were included in the study. We included patients without chronic diseases, without chronic medication use, without hearing loss on audiometry, with normal magnetic resonance imaging (MRI), with the tinnitus handicap index (THI) of 2 or higher, and patients who reported subjective tinnitus. Patients with objective tinnitus, tinnitus with a known etiology, unilateral tinnitus, and patients with a THI of 1 (mild tinnitus/no tinnitus) were excluded from the study. Blood samples were obtained during the first examination. The MHR values were obtained by dividing the monocyte count by the HDL level.

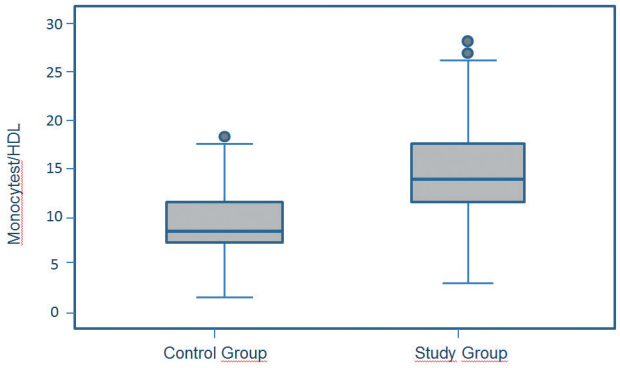

Fig. 1. Graphical display of MHR ratios in the control and study groups

In statistical analyses, means, standard deviations, medians, minimums, maximums, frequencies, and ratios were used for descriptive analysis. Distribution of the variables was assessed using the Kolmogorov-Smirnov test. The Mann-Whitney U-test was used for analyzing quantitative data. Qualitative data were analyzed using the chi-squared test. The effect level and the cut-off value were evaluated using ROC curve analysis. SPSS 22.0 was used for all analyses.

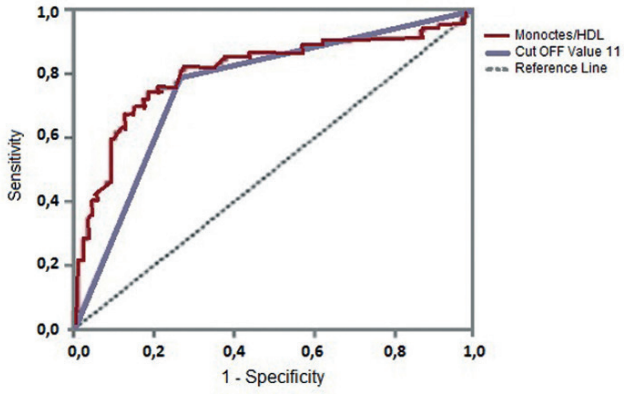

Fig. 2. Graphical display of the MHR cut-off value

RESULTS

A total of 176 individuals were included in the study, 89 in the study group and 87 in the control group. The male-to-female ratio was 52/37 and 39/48 in the study group and control group, respectively. The mean age was 32.5±7.9 years and

Tab. I. Demographic characteristics and laboratory findings in the control and study groups

		CONTROL GROUP							STUDY GROUP							P	
		MEAN±SD/N-%			MED(MIN-MAX)				MEAN±SD /N-%			MED(MIN-MAX)					
Age		31,1	±	7,1	32	16	-	47	32,5	±	7,9	34	16	-	49	0,173	m
Gender	Female	39		44,8%					52		58,4%					0,071	X2
	Male	48		55,2%					37		41,6%						
Monocytes		447,2	±	157,8	405	100	-	1320	634,3	±	213,8	620	155	-	1250	0,000	m
HDL		49,5	±	7,6	49	33	-	69	45,4	±	10,2	44	28	-	79	0,000	m
Monocytes/HDL		9,3	±	3,5	8,5	1,6	-	25,9	14,5	±	5,5	13,7	3,3	-	27,8	0,000	m

M Mann-Whitney U-test / X2 chi-squared test/ nSample size / %Percent

31.1±7.1 years in the study group and control group, respectively. No statistically significant differences were seen between the groups with respect to gender and age (*p=0.173 and p=0.071, respectively).* The mean monocyte count was 634.3±213.8 and 447.2±157.8 in the study group and control group, respectively. The HDL level was 45.4±10.2 and 49.5±7.6 in the study group and control group, respectively. The mean MHR was 14.5±5.5 and 9.3±3.5 in the study group and control group, respectively. The monocyte count and the MHR were higher and the HDL level was lower in the study group compared to the control group (*p<0.05)* (*Table 1, Figure 1*). The MHR cut-off value was 11 for diagnosing tinnitus in this present study (Figure *2*)

DISCUSSION

Monocytes and macrophages develop into foamy cells after phagocytosis of oxidized LDL molecules in atherosclerosis plaques, which destabilizes the plaques [14]. The monocyte count has been demonstrated to be an independent and important factor implicated in the development and progression of atherosclerotic plaques [14]. HDL cholesterol plays a vasoprotective role by exerting anti-inflammatory, anti-thrombotic, and antioxidant effects by inhibiting LDL oxidation in the vessel wall, which balances the atherosclerotic properties of monocytes [15]. Murphy et al. [16] demonstrated in their experimental study that the anti-inflammatory effects of HDL and its major protein, apolipoprotein A1, on monocytes are mediated by CD11b inhibition. Ganda[17] detected an increased monocyte count and a decreased HDL level in the blood of patients with renal failure, and reported that this condition might be associated with diffuse atherosclerosis. The MHR has been defined as a new cardiovascular prognostic marker related to oxidative stress and development of atherosclerosis [7-10].

High oxidative stress and low nitric oxide (NO) levels have been reported to play a role in the etiology of idiopathic tinnitus by increasing low-density lipoprotein (LDL) oxidation and monocyte v-chemoattractant activity [18]. It was reported in the same study that increased concentrations of oxidants may cause dysfunctional changes in the microcirculation of the inner ear [18]. Tuzuner [19] reported that decreased HDL levels together with an increased monocyte level could be associated with tinnitus. Atherosclerotic plaques may cause tinnitus by narrowing vessel wall and causing turbulent flow. Moreover, a vessel that is narrowed due to atherosclerosis may cause increased blood flow in carotid arteries, thereby leading to tinnitus[20]. Brenstetter[21] reported that atherosclerotic plaques located at any level from the internal carotid artery to the intracranial carotid siphon might cause tinnitus, and managing such changes can ameliorate tinnitus. Sutbas[22] reported that low cholesterol diet was associated with favorable auditory results in hyperlipidemic patients exposed to acoustic trauma. In an experimental model of hyperlipidemia, Gratton[23] demonstrated that lipid particles accumulate in the cochleae of chinchillas. Hyperlipidemia may cause obstruction of cochlear vessels by increasing blood viscosity, and tinnitus might develop as a result of turbulent flow [24,25]. All of the above-mentioned studies clearly demonstrate that a low HDL level and hyperlipidemia are closely associated with tinnitus.

The monocyte count and the MHR were significantly higher in patients with tinnitus compared to the control group. Moreover, HDL values of patients with tinnitus were lower compared to controls. A combination of an increased monocyte count and decreased HDL may lead to the development of tinnitus by augmenting the oxidative and inflammatory processes.

Canpolat et al. [9] reported that the MHR was associated with diffuse atherosclerosis, inflammation, and microvascular dysfunction that are considered to cause decreased coronary flow in cardiovascular diseases. An elevated MHR reflects increased oxidative stress and an increased the risk of atherosclerosis[7].

Kanbay[11] reported that the MHR was associated with a poor cardiovascular profile, and that it can be used as an independent marker of future cardiovascular events. Kundi[12] found that elevated MHR values are associated with high syntax scores and poor prognosis in coronary artery disease, and reported that the MHR could be a parameter that can be used in future daily practice. The cut-off value for MHR was 11 in our study. The risk of tinnitus is increased with MHR ratios greater than 11. An increased MHR is an expected finding in idiopathic tinnitus considering the role of both oxidative stress and atherosclerotic disease in the etiology of tinnitus.

CONCLUSIONS

The MHR was elevated in patients with idiopathic tinnitus, which supports the role of atherosclerotic events and oxidative stress in the etiology of tinnitus.

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