ORIGINAL ARTICLE

Eastern Journal of Medicine
East J Med 23(4): 264-268, 2018
DOI: 10.5505/ejm.2018.02703

A retrospective analysis of haemotologic parameters in patients with bilateral tinnitus

Ufuk Düzenli[1*], Nazım Bozan[1], Mehmet Aslan[2], Hüseyin Özkan[1], Mahfuz Turan[1], Ahmet Faruk Kıroğlu[1]

[1]Van Yüzüncü Yıl University, Faculty of Medicine, Department of Otorhinolaryngology
[2]Van Yüzüncü Yıl University, Faculty of Medicine, Department of Internal Medicine

ABSTRACT

Tinnitus is a perception disorder of sound. In addition to otologic diseases; mood disorders, inflammatory diseases, thromboembolic pathologies may lead to tinnitus. Mean platelet volume (MPV), Platelet Distribution Width (PDW) and Neutrophil-to-Lymphocyte Ratio (NLR) were investigated as biomarkers in tinnitus patients. In this study, we aimed to find whether there is any association between these biomarkers and bilateral tinnitus patients.

Fifty eight with tinnitus and 58 healthy subjects were included to the study. The distribution of age and sex in each group were equal. Hearing thresholds of tinnitus patients were obtained with pure-tone audiometry. Hematologic values were evaluated in each group and correlation between these values and audiometric data were investigated in tinnitus patients.

PDW values of the tinnitus group were found statistically significantly higher than those in control group **(p=0.041)**. NLR was found lower in tinnitus patients and it was statistically significant **(p=0.001).** MPV values were found similar in each group. In tinnitus group there were no correlation between hematologic values and audiometric data.

In this study, we found blood marker value alterations in bilateral tinnitus patients, but there was no correlation with audiologic data. And so we need larger studies to obtain more significant results.

Key Words: Tinnitus, Mean Platelet Volume, Platelet Distribution Width, Neutrophil to Lymphocyte ratio, Hematologic Biomarker

Introduction

Tinnitus is a symptom which can be mentioned as perception disorder of sound with no hearing impulse. It is a very common otology complaint that leads to worsening quality of life. There are 2 types of tinnitus: Objective tinnitus and subjective tinnitus. Objective tinnitus can be evaluated with auditory tests, measuring turbulence of blood flow or hearing of extra sounds by a clinician. Subjective tinnitus is the clinical type which the perception of sound is detected by the patient only.

Many aetiological factors can lead to tinnitus like symptoms; cranial trauma, using ototoxic agents, acoustic trauma, sudden sensorineural hearing loss, otosclerosis, presbiacusis and functional disorder of temporomandibular joint (1). Also, vascular diseases can play role in hearing pathologic sounds. Blood flow distortion of inner ear leads to cochlear cell death and impairing their auditory functions easily. It may be shown as tinnitus without hearing loss.

Hematologic samples get importance for predictive analysis for many diseases (2-4). Red blood cell distribution width (RDW) and neutrophil to lymphocyte ratio (NLR) were used for predicting prognosis of Bell Palsy and sudden hearing loss (5-7). Mean platelet volume (MPV), platelet count (PLT)and platelet distribution width (PDW) were found as candidate markers for subjective tinnitus (8-11). The MPV is a value, related to the average size of platelet cells and bigger MPV values may lead more haemostasis (3). PDW is an indicator related to platelet sizes and platelet activation (12).

In this study, we investigated correlation between hematologic values and tinnitus patients and their audiometric data, whether there is an association with inflammatory or thrombotic process.

Materials and Methods

This is a retrospective study. Fifty-eight patients with tinnitus and 58 healthy subjects who referred to the clinic between January 2013 and July 2017 were involved to the study. Twenty-nine of them were female and 29 were male in each group. All data were obtained from the registry system of hospital. Patients were collected according to these criteria: normal ear nose throat examination; having bilateral tinnitus at least since 6 months; without any chronic ear disease such as chronic otitis media, otosclerosis and presbiacusis; without any chronic systemic disease such as diabetes mellitus, hypercholesterolaemia,

***Corresponding Author:** Ufuk Düzenli, Yüzüncü Yıl University, Faculty of Medicine, Department of Otorhinolaryngology
E-mail: drufukd35@hotmail.com, Phone: 09 (0546) 696 86 09
Received: 17.04.2018, **Accepted:** 04.07.2018

Table 1. Demographic parameters of the patients

Parameter	Patients (n=58)	Control (n=58)	value
Age	38.8 ± 9.41	38.8 ± 9.41	
Sex (Female / Male)	29/ 29	29/ 29	

Table 2. Value of haematologic blood parameter and statistical analysis (Values are mean ± SD; *p* value accepted significant at < 0.05

Parameters	Patients (n=58)	Controls (n=58)	p
Platelet count (x103/mm3)	259.4±61.5	248.5±57.0	0.469
Mean platelet volume (fL)	8.66±1.02	8.34±1.08	0.323
Hemoglobine (g/dL)	5.14±0.52	5.23±0.46	0.467
Haematocrit (%)	44.5 ± 5.49	45.2 ± 4.78	0.564
NLR	1.87 ± 0.51	2.68 ± 1.20	0.001
Red Cell Distribution Width (%)	14.1 ± 1.34	13.6 ± 1.07	0.104
Platelet Distribution Width (%)	16.6 ± 0.34	16.2 ± 1.03	0.041

hypertension; no chronic drug consumption; without infection disease. The exclusion criteria for the control group was determined as: cardiovascular disease, diabetes mellitus, hypercholesterolaemia, hypertension, drug consumption, presence of infection disease, smoking cigarette and presence of ear diseases such as chronic otitis media, otosclerosis, presbiacusis. Blood samples of the control group were obtained from the individuals who admitted to hospital for routine control. The subjects in the control group that had increased or decreased hematologic sample values were not included to study. All patients have no psychiatry record and the patients that were referred to psychiatry clinic were not included to the study.

Routine blood sample analysis and audiometric evaluation were performed for every patient who was admitted to the clinic. Also, the same number of blood analysis was obtained from healthy patients that were admitted to the clinic for routine control. The ages and genders were equal in each group.

Complete blood count was assessed by means of an automatic blood counter (*Beckman-Coulter, LH 780, USA*). The white blood cell, red blood cell, neutrophil, lymphocyte and platelet counts, RDW, Hemoglobin (Hgb), Haematocrit (Htc), MPV and PDW values were measured. And NLR calculated for each patient one by one.

Pure-tone audiogram was performed by evaluating hearing levels at 250, 500, 1000, 2000, 4000, 6000 and 8000 Hz with an audiometer (Interacoustic Clinical Audiometer; model AC 40; Assens, Denmark). Audiometric analysis was not applied to healthy patients.

Statistical Analysis: Haemogram count values were evaluated and compared for each group. In study group, blood sample value and audiometric value correlations were evaluated. All results were evaluated as mean±standard deviation. The comparison of continuous variables was performed with independent-samples *t* test. The correlation between hematologic parameters and audiometric data were done with Pearson correlation analysis. Categorical variables of the study were compared by chi-square test. The results were considered statistically significant when the *p* value was less than 0.05. The data were analyzed using Statistical Package for Social Sciences program version 23.0 (*SPSS Inc., Chicago, IL, USA*).

Results

There were 29 female and 29 male subjects in each group (Table 1). The mean age was found 38.8±9.4 in two groups (Table1). All values of haemogram were found at normal levels (Table 1). Red blood cell, haemoglobin and haematocrit count were similar for 2 groups and there was no statistical difference (Table 2). Platelet count of tinnitus patients was found higher than those in healthy group, but there was also no statistical difference (Table 2). MPV values of tinnitus patients were higher than healthy subjects, but it was not statistically significant (p= 0.323). PDW was counted higher in tinnitus group and this difference was statistically significant (p= 0.041). Neutrophil to lymphocyte ratio was statistically lower in tinnitus group (p= .001).

The averages of the hearing thresholds were determined in all frequencies (Table 3). The correlation analysis was performed to elucidate

Table 3. Pure tone audiogram means of patient with tinnitus

Frequencies	250 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz	6000 Hz	8000 Hz
Hearing Levels (dB)	27.3±13.4	23.9± 12.9	21.0±13.8	20.7± 18.4	33.2± 24.4	37.0± 26.6	43.5± 27.5

whether there was any association between MPV, RDW, NLR levels and hearing thresholds of the patients with tinnitus. There was no correlation between MPV, RDW, NLR levels and hearing thresholds at any frequency except for one example (p> 0.05). Positive correlation was observed between haemoglobin level and hearing levels at 6000 Hz in tinnitus patients (r=0.389; p=0.028).

Discussion

Tinnitus is an otolaryngologic disorder characterized with perception sound without hearing impulse. It may affect 15% of all population (13). Many aetiologic factors and mechanisms of pathology were hypothesized (14). However, there are not any certain pathophysiological explanations about tinnitus (15-17). This clinical problem can occur at older ages and decrease hearing caused by any ear diseases like otosclerosis, Meniere etc. noise, decreased blood flow or blood vessel occlusion might lead to outer hair cell damage of cochlea (18). In addition, functional disorder of outer hair cell can lead to tinnitus if there is a pathology effecting cochlear homeostasis (14). It was observed that ischemic and inflammatory reactions of cochlear microcirculation may cause tinnitus (18). Also emotional stress disorders can go with subjective tinnitus (19).

Any change in blood cell function, homeostasis or blood flow may lead to cochlear damage easily. In this study we aimed to detect any correlation between blood counts and audiometric results in tinnitus patients. In this study, we found statistical difference between 2 groups about PDW values. Also, NLR was observed lower in the tinnitus group.

As a blood marker MPV shows platelet volume and gives information about platelet function. Highly MPV values were associated with more platelet aggregation and increased risk of ischemic injury (4-20,21). There are many studies on MPV and tinnitus relationship. In two studies, it was evaluated that tinnitus patients had higher MPV levels according to healthy group (8,9). The study with 86 tinnitus patients mentioned that increased MPV levels could be related to increased platelet aggregation and lead to impairment of cochlear blood flow (8). However, no correlation was found between MPV levels and severity of tinnitus (8). On the other hand, a study with 100 tinnitus patients introduced that MPV had been found statistically significant lower in the tinnitus patients` blood samples (10). In this study while tinnitus had negative correlation with MPV, had positive correlation with platelet count and PDW (10). And they mentioned that tinnitus might occur as a result of the inflammatory process. There was no significant difference between healthy subjects and tinnitus patients concerning MPV values in our study with patients of bilateral tinnitus. Similar to our study, MPV values were found higher in tinnitus patients, but the results were not statistically significant in two different studies (11,22).

Platelet distribution width is a marker which measures platelet sizes and increased values are related to increased platelet activation (12). Higher PDW levels were observed in tinnitus group than those in control group, but there was not any correlation between PDW values and hearing levels. Yuksel et al. observed similar to our results about PDW values in tinnitus patients (10).

Neutrophil-to-lymphocyte ratio was investigated in several studies as, predictive or prognostic marker of inflammatory processes, malignancies and cardiac diseases (2-23). It was also studied for otorhinolaryngologic diseases such as Bell Palsy, sudden hearing loss and nasal polyposis (5-7,24). This marker was also studied in tinnitus patients. It was sentenced that tinnitus patients had higher NLR levels and they mentioned that increased NLR could be related to inflammatory diseases and cardiovascular disorders (11). Bayram et al. found no relationship between NLR and tinnitus (22). In our study, NLR had decreased in tinnitus patients when compared to the control group. These different results may be related to the number of patients, unknown systemic pathologies or personal differences.

In our study, there were no correlation between hearing levels and haemogram parameters in tinnitus group. Hearing levels were calculated and average high frequency levels of the patients were revealed. The patients who had levels better than 30 dB was evaluated separately, but there was no correlation between normal hearing levels and blood levels. Platelet contributes to aggregation and it may have different haemostasis potential (8). Yuksel et al. did not find any correlation between hematologic parameters and audiometric data except for platelet count(10). They mentioned negative correlation between platelet count and hearing loss (10).

Tinnitus is a perception disorder of sound without an acoustic impulse from outside. It can have broad spectrum from slight to severe, which can affect quality of life seriously. Many studies had been performed to find a mechanism of tinnitus and to provide certain treatment. Blood sample count studies related to tinnitus were aimed to investigate predictive markers. In our study, we found PDW and NLR have statistically significant relationship with tinnitus patients. In different studies, different markers were investigated as biomarkers and were statistically significant.

We included patients who had bilateral tinnitus to study and the number of subjects was limited. There are contradictory results of different studies and it can be useful to make multicentre large numbered study which will also investigate pathophysiological pathways.

In this study, we found that the increased PDW and the decreased NLR can be related to tinnitus and there was no correlation between hearing levels and haemogram values. These blood parameters may be guide for an etiologic investigation. Also, these parameters are easily available and cost-effective. However, in order to get more accurate information we need more comprehensive studies about the pathophysiology and possible predictive markers.

Funding: No sources of support/funding were obtained for this study

Conflict of interest: All Authors declared no conflict of interest.

Ethical approval: Our study is in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments.

References

1. Michiels S, Naessens S, Van de Heyning P, et al. The Effect of Physical Therapy Treatment in Patients with Subjective Tinnitus: A Systematic Review. Front Neurosci 2016; 10: 545.
2. Jung MR, Park YK, Jeong O, et al. Elevated preoperative neutrophil to lymphocyte ratio predicts poor survival following resection in late stage gastric cancer. J Surg Oncol 2011; 104: 504-510.
3. Vizioli L, Muscari S, Muscari A. The relationship of mean platelet volume with the risk and prognosis of cardiovascular diseases. Int J Clin Pract 2009; 63: 1509-1515.
4. Machin SJ, Briggs C. Mean platelet volume: a quick, easy determinant of thrombotic risk? J Thromb Haemost 2010; 8: 146-147.
5. Bucak A, Ulu S, Oruc S, et al. Neutrophil-to-lymphocyte ratio as a novel-potential marker for predicting prognosis of Bell palsy. The Laryngoscope 2014; 124: 1678-1681.
6. Kilickaya MM, Tuz M, Yariktas M, Yasan H, Aynali G, Bagci O. The Importance of the Neutrophil-Lymphocyte Ratio in Patients with Idiopathic Peripheral Facial Palsy. Int J Otolaryngol 2015; 2015: 981950.
7. Kocak HE, Elbistanli MS, Acipayam H, Alakras WME, Kiral MN, Kayhan FT. Are neutrophil/lymphocyte and platelet/lymphocyte ratios related with formation of sudden hearing loss and its prognosis? Eur Ann Otorhinolaryngol Head Neck Dis 2017; 134: 383-386.
8. Kemal O, Muderris T, Basar F, Kutlar G, Gul F. Prognostic value of mean platelet volume on tinnitus. J Laryngol Otol 2016; 130: 162-165.
9. Sarikaya Y, Bayraktar C, Karatas M, et al. Increased mean platelet volume in patients with idiopathic subjective tinnitus. Eur Arch Otorhinolaryngol 2016; 273: 3533-3536.
10. Yüksel F, Karatas D. Can Platelet Indices Be New Biomarkers for Subjective Tinnitus? Journal of Craniofacial Surgery 2016; 27: 420-424.
11. Ozbay I, Kahraman C, Balikci HH, et al. Neutrophil-to-lymphocyte ratio in patients with severe tinnitus: prospective, controlled clinical study. J Laryngol Otol 2015; 129: 544-547.
12. Mirvakili A, Dadgarnia MH, Baradaranfar MH, Atighechi S, Zand V, Ansari A. Role of Platelet Parameters on Sudden Sensorineural Hearing Loss: A Case-Control Study in Iran. PLoS One 2016; 11: 0148149.
13. Axelsson A, Ringdahl A. Tinnitus--a study of its prevalence and characteristics. Br J Audiol. 1989; 23: 53-62.
14. Baguley DM. Mechanisms of tinnitus. Br Med Bull 2002; 63: 195 - 212.
15. McCormack A, Edmondson-Jones M, Somerset S, Hall D. A systematic review of the reporting of tinnitus prevalence and severity. Hear Res 2016; 337: 70-79.
16. Zenner HP, Delb W, Kroner-Herwig B, et al. A multidisciplinary systematic review of the treatment for chronic idiopathic tinnitus. Eur Arch Otorhinolaryngol 2017; 274: 2079-2091.
17. Phillips JS, McFerran DJ, Hall DA, Hoare DJ. The natural history of subjective tinnitus in adults: A systematic review and meta-analysis of no-intervention periods in controlled trials. Laryngoscope 2018; 128: 217-227.
18. Nondahl DM, Cruickshanks KJ, Huang GH, et al. Tinnitus and its risk factors in the

Beaver Dam offspring study. Int J Audiol 2011; 50: 313-320.

19. Langguth B, Landgrebe M, Kleinjung T, Sand GP, Hajak G. Tinnitus and depression. World J Biol Psychiatry 2011; 12: 489-500.
20. Yilmaz M, Dagli MN, Uku O, et al. Focusing on a complete blood cell parameter: mean platelet volume levels may be a predictor of coronary slow flow. Vasc Health Risk Manag 2017; 13: 255-261.
21. Ozturk S, Gurbuz AS, Efe SC, et al. Association of mean platelet volume with presence of non viable myocardium in ischemic cardiomyopathy. Kardiol Pol 2017; 75: 1013-1019.
22. Bayram A, Yasar M, Dogan M, Güneri E, Özcan I. Assessment of neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio and mean platelet volume in patients with tinnitus. ENT Updates 2015; 5: 103.
23. Torun S, Tunc BD, Suvak B, et al. Assessment of neutrophil-lymphocyte ratio in ulcerative colitis: a promising marker in predicting disease severity. Clin Res Hepatol Gastroenterol 2012; 36: 491-497.
24. Atan D, Ozcan KM, Koseoglu S, et al. New predictive parameters of nasal polyposis: neutrophil to lymphocyte ratio and platelet to lymphocyte ratio. Kulak Burun Bogaz Ihtis Derg 2015; 25: 97-101.