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MAIN ARTICLE

Investigation of neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio and mean platelet volume in patients with tinnitus

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Abstract

Objective: This study aimed to evaluate patients with tinnitus in terms of mean platelet volume and platelet distribution width, and to explore neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio, recently reported in the literature as being possible inflammation markers.

Methods: This study comprised 64 tinnitus patients and 64 age-matched healthy controls. Statistical significance level was accepted as $p < 0.05$.

Results: Mean platelet volume ($t = 3.245$, $p = 0.002$) and platelet distribution width ($Z = 3.945$, $p < 0.001$) were significantly higher in the patient group than the control group.

Conclusion: The results suggest that a prothrombotic condition might play a role in the pathophysiology of tinnitus.

Key words: Mean Platelet Volume; Tinnitus; Clinical Marker; Inflammation; Thrombosis

Introduction

Tinnitus is usually defined as sound perception without the external acoustic stimulus. It affects about 12–15 per cent of adults and seriously impacts the life quality of 1–2 per cent of patients.[1–3]

Although many hypotheses have been proposed regarding its aetiology, the mechanism of tinnitus has not yet been fully elucidated. Sound without an external stimulus is thought to arise from aberrant neural activity from any point along the auditory pathway, from the cochlear apparatus to the auditory cortex. Other theories on tinnitus include: damaged hairy cells with unregulated discharge and over-stimulated auditory nerves, hyperactive auditory synovial fibres, excessive stimulation of the auditory nerve, and lack of peripheral auditory nerve activity suppression in the auditory cortex.[3]

Noise exposure, ototoxic drug use, presbycusis, otosclerosis, otitis, cerumen, Ménière's disease and sensorineural hearing loss are the most common causes of tinnitus. The infectious causes of tinnitus include otitis, meningitis and other auditory inflammatory conditions. It has been reported that genetic factors may affect the formation of tinnitus. Tinnitus was first presumed to be due to hearing loss or cochlear damage. However, the relationship between tinnitus and hearing loss has not been fully elucidated. Not everyone with hearing loss develops tinnitus, and hearing loss does not occur in every patient with tinnitus.[1,3]

This study aimed to evaluate patients with tinnitus in terms of mean platelet volume and platelet distribution width,[4–6] and to explore neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio, recently reported in the literature as being possible inflammation markers.[7,8]

Materials and methods

This prospective study comprised 64 consecutive tinnitus patients aged 18–65 years, and 64 age-matched healthy controls.

Routine ENT and audiological examinations, complete blood count and blood lipid profile measurements, and thyroid function tests, were performed to determine the aetiology. Temporal bone magnetic resonance imaging with gadolinium contrast medium was requested in those with unilateral tinnitus or asymmetric sensorineural hearing loss. Patients who had no pathology detected during these examinations were included in this study. Only complete blood count examination was requested in the control group.

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Patients who had established aetiological reasons for the tinnitus, including objective tinnitus, chronic inflammatory disease, acute infection, acute or chronic kidney disease, chronic obstructive pulmonary disease, coronary artery disease, connective tissue disease, allergic rhinitis, liver disease, and otological diseases (such as otosclerosis, chronic otitis media and meningitis), were excluded from the study.

Haematological examination

Neutrophil-to-lymphocyte ratio was calculated as a simple ratio between the absolute neutrophil count and the absolute lymphocyte count in the complete blood count measurements. Platelet-to-lymphocyte ratio was calculated as a simple ratio between the absolute platelet count and the absolute lymphocyte count. Mean platelet volume and platelet distribution width were also obtained from the complete blood count measurements. Neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, mean platelet volume and platelet distribution width were calculated in the control group in a similar manner. An automated blood cell counter (model XE-2100; Sysmex, Kobe, Japan) was used for the analyses.

Audiological examination

Audiometry tests of the patients were performed using an Orbiter 922 version 2 audiometry device (model EN60645-1; Madsen, Taastrup, Denmark) in the hospital audiology centre. Pure tone air-conduction thresholds were 0.25, 0.5, 1, 2, 4 and 8 kHz. Bone-conduction thresholds were 0.25, 0.5, 1, 2 and 4 kHz.

Ethics approval

The study was carried out with the approval of the Clinical Research Ethics Committee (number 26379996/13) at Ankara Yıldırım Beyazıt University.

Population size and power

The sample size and power calculations required for the study were determined using the software program G*Power, version 3.1.9.2.[9] The effect size was calculated as $d = 0.55$ to determine a 10 per cent change in platelet-to-lymphocyte ratio (the primary variable), with a 15 per cent standard deviation. It was estimated that 58 participants were required for the control and patient groups (116 subjects in total) in this study to achieve $\alpha = 0.05$ type I error, $\beta = 0.10$ type II error and 90 per cent power. This study was conducted with 10 per cent more volunteers, with 64 participants in the control and patient groups (a total of 128 volunteers), to compensate for possible data loss.

Statistical analyses

The distribution of each variable in the study, including age, platelet-to-lymphocyte ratio, neutrophil-to-lymphocyte ratio, platelet counts, platelet distribution width, white blood cell (WBC) count and mean platelet volume, was graphically assessed using the Shapiro–Wilk test. Although mean platelet volume showed a normal distribution, other variables did not fit the normal distribution.

Descriptive statistics were presented as number and percentage for gender, and mean ± standard deviation for mean platelet volume (variables with normal distribution); median (and interquartile range) values were used for the other variables, which were not normally distributed.

The Mann–Whitney U test was used to examine differences in age, platelet-to-lymphocyte ratio, neutrophil-to-lymphocyte ratio, platelet count, platelet distribution width and WBC count between the patient group and the control group. The independent-samples *t*-test (student's *t*-test) was used to compare the mean platelet volume variables according to the groups. A chi-square test was performed to test the similarity of gender distribution between the groups.

For the statistical analyses and calculations, SPSS Statistics version 21.0 (IBM, New York, USA) and Microsoft Excel® 2007 software were used. Statistical significance level was accepted as $p < 0.05$.

Results

This study comprised 64 patients and 64 healthy volunteers. The median age was 41.0 years (interquartile range = 17.8) in the control group and 45.0 years (interquartile range = 17.8) in the patient group. No statistically significant difference in age was found between the patient group and the control group ($Z = 0.923$, $p > 0.05$) (Table I). In addition, no statistically significant difference was observed between the groups in terms of gender ($\chi 2 = 0.791$, $p > 0.05$). The female:male ratio was 26:38 (40.6 per cent females) in the control group, and 31:33 (48.4 per cent females) in the patient group.

The mean platelet volume was 10.8 ± 0.9 fl in the patient group and 10.3 ± 0.6 fl in the control group (Figure 1). Mean platelet volume was significantly higher in the patient group than the control group ($t = 3.245$, $p = 0.002$). The median platelet distribution width was 13.1 fl (interquartile range = 2.3) in the patient group and 12.2 fl (interquartile range = 1.7) in the control group (Figure 2). Median platelet distribution width was significantly higher in the patient group than the control group ($Z = 3.945$, $p < 0.001$) (Table I).

The neutrophil-to-lymphocyte ratio was 1.7 (interquartile range = 0.7) in the patient group and 1.8 (interquartile range = 0.7) in the control group, with no significant difference between the groups ($Z = 1.222$, $p > 0.05$). The platelet-to-lymphocyte ratio was 107.1 (interquartile range = 36.3) in the patient group and 104.7 (interquartile range = 33.7) in the control group, with no significant difference between the groups ($Z = 0.548$, $p > 0.05$) (Table I).

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TABLE I
BETWEEN-GROUP COMPARISON OF DESCRIPTIVE STATISTICS OF VARIABLES

Variable	Patient group	Control group	Test statistics*	
			Z (or *t*)	*p*
Patient age (years)	45.0 (17.8)	41.0 (17.8)	0.923	0.356
Platelet-to-lymphocyte ratio	107.1 (36.3)	104.7 (33.7)	0.548	0.584
Neutrophil-to-lymphocyte ratio	1.7 (0.7)	1.8 (0.7)	1.222	0.222
Platelet distribution width (fl)	13.1 (2.3)	12.2 (1.7)	3.945	<0.001
WBC count ($\times 10^9$/l)	6.9 (1.6)	7.4 (1.8)	1.737	0.082
Mean platelet volume (mean ± SD; fl)	10.8 ± 0.9	10.3 ± 0.6	$t = 3.245$ (independent sample *t*-test)	0.002
Platelet count ($\times 10^9$/l)	234.5 (87.3)	254.0 (72.8)	1.599	0.110

Data represent medians (and interquartile ranges), unless indicated otherwise. *Mann–Whitney U test statistics were conducted, with data representing *Z* values, unless indicated otherwise. WBC = white blood cell; SD = standard deviation

Discussion

Although many theories have been proposed about the aetiology and pathophysiology of tinnitus, the mechanisms have not been fully elucidated.[3] The most significant finding of this study was that mean platelet volume and platelet distribution width were higher in the patients with tinnitus.

Mean platelet volume and platelet distribution width are markers of platelet activation, with mean platelet volume being the most frequent marker used.[4–6] Mean platelet volume indicates the size of platelets and platelet distribution width is used to assess variations in platelet size. An increase in these parameters suggests that bone marrow has released larger-volume platelets into blood circulation. Platelets with a large volume have been reported to be metabolically and enzymatically more active and more prone to aggregation compared with the small ones.[5,6,10]

It has been reported that the concurrent use of mean platelet volume and platelet distribution width is more meaningful for the evaluation of coagulation tendency.[6,10]

Yilmaz *et al*. reported that myocardial infarction and ischaemic complications were more frequent in acute coronary syndrome patients with elevated mean platelet volume levels and without ST-segment elevation.[11] Another study reported that platelet microparticles and mean platelet volume levels were higher in acute ischaemic stroke patients than in healthy subjects.[4] In another study, mean platelet volume and platelet distribution width were high in patients with cerebral venous sinus thrombosis.[12] It has been suggested that auditory system perfusion may be impaired in tinnitus patients.[13,14] Sarıkaya *et al*. reported that mean platelet volume was significantly increased in patients with tinnitus.[13]

Tinnitus characteristics, including duration, frequency, episode length, intermittency and noise description, have been evaluated using mean platelet volume. However, no relationship has been reported between mean platelet volume and tinnitus characteristics such as duration, frequency, episode length and sound identification.[13]

In a retrospective study by Kemal *et al*., mean platelet volume was higher in patients with tinnitus.[14] Both mean platelet volume and platelet distribution width were higher in the tinnitus patients in the present study, in line with the literature. These results suggest

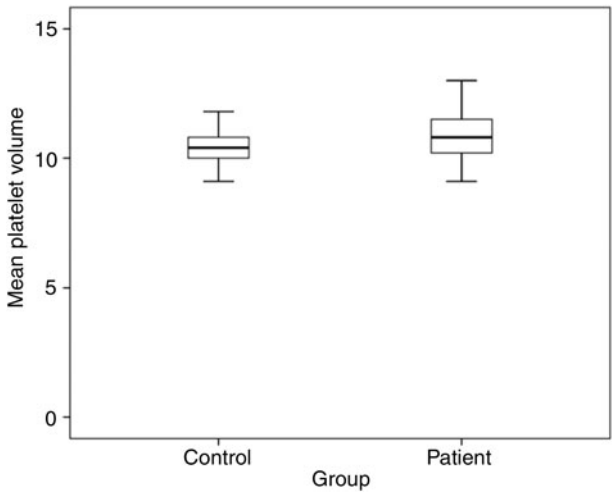

FIG. 1
Mean platelet volume in the control group and patient group.

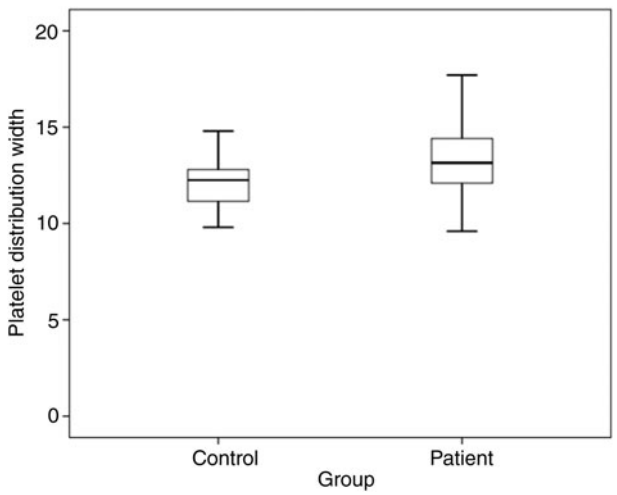

FIG. 2
Platelet distribution width in the control group and patient group.

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that a prothrombotic condition might exist in patients with tinnitus. Previous studies have also reported that mean platelet volume is lower in patients with tinnitus,[15] with no significant difference compared with healthy subjects.[16]

- **The aetiology of tinnitus has not yet been fully elucidated**
- **This prospective study evaluated tinnitus patients in terms of mean platelet volume and platelet distribution width**
- **Mean platelet volume and platelet distribution width were significantly increased in tinnitus patients**
- **Mean platelet volume and platelet distribution width are markers of platelet activation**
- **Large volume platelets are metabolically and enzymatically more active and more prone to aggregation than small ones**
- **Prothrombotic condition might play a role in the pathophysiology of tinnitus**

Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio have been used frequently as indicators of inflammation in recent publications.[7,8] Özbay *et al*. reported that neutrophil-to-lymphocyte ratio was higher in patients with severe tinnitus compared with healthy subjects, but they reported no significant difference in mean platelet volume.[17] However, Bayram *et al*. reported no significant increase in neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in patients with tinnitus.[16] In the present study, no significant differences were found between patients with tinnitus and healthy participants in terms of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio.

Conclusion

The results of this study suggest that a prothrombotic condition might play a role in the pathophysiology of tinnitus. However, further studies are required to confirm these results.

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