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Does anisocytosis play a role in benign paroxysmal positioning vertigo (BPPV) pathogenesis?

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ABSTRACT

Aim: To investigate whether anisocytosis in circulating blood plays a role in benign paroxysmal positioning vertigo (BPPV) pathology or not.

Methods: This study is retrospectively and enrolled with 32 patients and 32 control group. Patients with chronic ear disease and systemic disease that affect red cell distribution width (RDW) value excluded from the study. Mean platelet volume (MPV), RDW, platelet distribution width (PDW), Neutrophil-Lymphocyte ratio and Platelet- Lymphocyte ratio were compared between study and control group.

Results: RDW is significantly higher than in control group (p<0,001). The platelet/lymphocyte ratio (PLR) was statistically higher in BPPV patients than in control group (p=0,044). There were no statistically differences between MPV, PDW and neutrophil/lymphocyte ratio.

Conclusion: RDW is a quantitative parameter of anisocytosis and can be considered as subclinical systemic inflammation marker. RDW value was higher than control group. BPPV may cause systemic inflammation or BPPV may occur as a result of systemic inflammation. This is the first study about whether anisocytosis in circulating blood plays a role in BPPV pathology or not.

Key words: BPPV, anisocytosis, RDW, platelet/lymphocyte ratio.

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Introduction

Benign paroxysmal positioning vertigo (BPPV) occurred due to changes of head position, is one of the most common causes of the vestibular disorder [1]. Head trauma, vestibular neuritis and other inner ear pathologies can cause BPPV. Its lifetime prevalence is 2,4% [2]. The vast majority of BPPV is idiopathic and presumably occurs as a result of the degeneration of the macula. There are two theories about the pathophysiology of the BPPV, cupulolithiasis and canalolithiasis [3, 4]. Although majority of BPPV is idiopathic and the exact mechanism is unclear, vascular risk factors could play role in labyrinth ischemia that causes detachment of otoconia from the otolith membrane [1]. Characteristic nistagmus with Dix-Hallpike and head roll test is important to diagnosis [5]. BPPV is treated with canalith repositioning maneuvers [5]. BPPV is also associated with increased inflammatory markers such as platelet (PLT), neutrophil to lymphocyte ratio (NLR), mean platelet volume (MPV), and platelet distribution width (PDW) [1, 6, 7].

Hemogram parameters derived indices are suggested as novel inflammatory markers recently. These indices include NLR, MPV,

platelet distribution width (PDW), red cell distribution width (RDW), and platelet to lymphocyte ratio (PLR) [8-11]. The inflammatory role of PDW, NLR, and MPV has been shown in hepatitis, sepsis, vitamin D deficiency, diabetes mellitus, thyroid conditions and tuberculosis [6, 8-11]. The red cell distribution width (RDW), generally calculated by automated cell counters routine complete blood count analysis, refers to variability of erythrocyte volume. It is a quantitative parameter of the anisocytosis. Studies in literature confirmed relation between RDW and sepsis, diabetes mellitus, cancer, and coronary heart disease. Its upper limit is approximately is 15% and an elevated RDW is used as a prognostic factor in benign (especially cardiovascular disease) and malignant conditions and is recognized as a marker of subclinical systemic inflammation [12].

Considering limited information about the etiology of BPPV, I hypothesized that BPPV is a response to subclinical systemic inflammation. This is a preliminary study and aims to investigate (inflammatory changes during BPPV attack) whether anisocytosis in circulating blood plays a role in BPPV pathology or not.

Materials and metods

This retrospectively study enrolled with 32 BPPV patients and 32 control subjects between 2018-2019 in Medicana International Samsun Hospital. Medicana International Samsun Hospital ethics committee approved this study (Date and decision number: 2019/2081). All data were obtained from hospital's database records. Inclusion criteria were normal otolaryngological examination and bilateral normal audiometric findings; positive examination findings on Dix-Hall Pike and head roll test, first BPPV attack and had no infectious disease within 30 days. Patients with chronic otitis media, Eustachian tube dysfunction, Meniere disease, tinnitus, otosclerosis, hearing loss, diabetes mellitus, hypertension, atherosclerosis, malignant disease and other chronicle disease are excluded from the study. Patients' hemogram evaluation at the time of BPPV attack was obtained from database records. White blood cell, platelet, mean platelet volume (MPV), Platelet Distribution Width (PDW), red cell distribution width (RDW), neutrophil, lymphocyte values on hemogram analyze were recorded for statistical evaluation. MPW, PDW, RDW, neutrophil/ lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR) were compared between two groups. Control group data obtained from hospital stuff screening program at hospital's data records according to study inclusion and exclusion criteria. Cases with confusing complete blood count analysis (study and control group) was consulted to a hematologist to decide whether include to study or not and all suspicious patient data was excluded from the study. Complete blood count (CBC) was analyzed by an automated blood counter and venous blood sample was collected with potassium EDTA tubes.

Statistical analyses

Statistically analyses were performed by SPSS for MAC version 23. Shapiro-Wilks' test was used for to assess the data normality. Arithmetic mean values and median values between two groups compared with Mann Whitney U and Student T test and $p<0,05$ value considered as statistically significant.

Results

There were 12 male and 20 female patients' age between 23 to 73 ages. Mean age was 46,4 years. 16 right and 16 left ears were affected. In control group there were 13 male and 19 female

patients. Mean age was 38,4 (19-74) years (Table1).

RDW is significantly higher (13,8 ± 1,04) than in control group (12,94 ± 0,44; p<0,001) with Student T test. The platelet/lymphocyte ratio (PLR) was statistically higher in BPPV patients (8,49 ± 3,21) than in control group (7,14 ± 1,85; p=0,044) with Student T test.

There were no statistically differences between MPV, PDW and neutrophil/lymphocyte ratio (p=0,123, p=0,083, and p=0,320, respectively) (Table 1, Figure 1).

Table 1. Comparison of demographic characteristics and laboratory results of the study and control group.

Parameters	**BPPV**		**Control**		
	Mean	SD	Mean	SD	*P* value
Gender Male Female	12 (37.5%) 20 (62.5%)		13 (40.6%) 19 (59.4%)		0,875
Age	43,03	8,46	41,25	7,84	0,386
WBC	7,17	1,57	6,93	0,99	0,477
Neu	4,13	1,22	3,59	0,64	**0,030**$^{\beta}$
Lymp	2,33	0,66	2,17	0,48	0,351
Plt	241,93	64,71	236,43	48,44	0,799
PDW	12,34	1,80	11,65	1,25	0,083
MPV	10,19	0,85	9,88	0,68	0,123
RDW	13,80	1,03	12,93	1,25	**0,001**$^{\delta}$
PLR	8,49	3,21	7,14	1,85	**0,044**$^{\beta}$
N/L Ratio	1,88	0,71	1,71	0,41	0,320

WBC: White blood cell; Neu: neutrophil, Lymp: lymphocyte, Plt: platelet, PDW: platelet distribution width, MPV: mean platelet volume, RDW: red cell distribution width, N/L ratio: neutrophil to lymphocyte ratio, β: Independent sample t-test, δ: Mann-Whitney U test, Statistically significant results marked as bold.

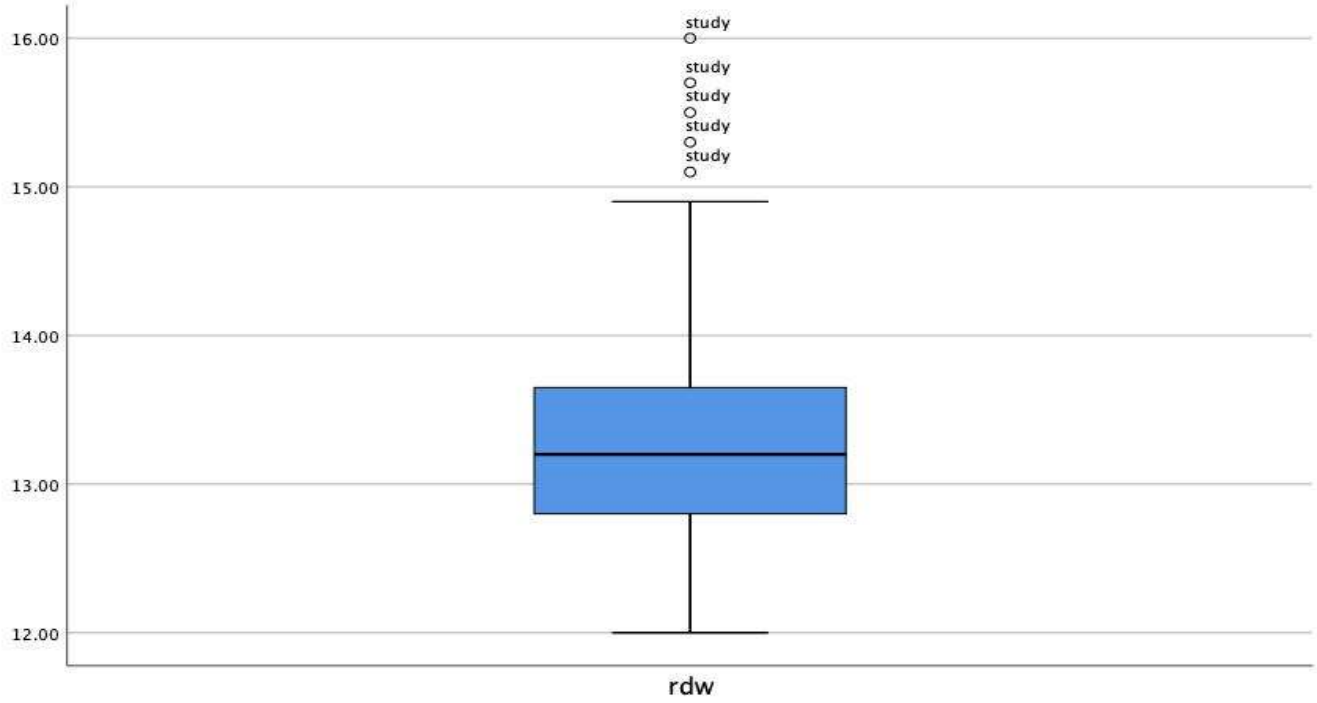

Figure 1. The distribution of RDW values in BPPV patients. Extreme values belong to 5 patients were indicated by circle.

Discussion

Benign paroxysmal positioning vertigo (BPPV) is one of the most encountered vestibular disorders characterised by episodic vertigo attacks with head movement. BPPV may be primary or secondary and triggered by partition of otoconia from the membrane [1, 3, 5]. The most encountered form of BPPV is the primary type and may be distinguished from the secondary type. The secondary type occurs as a result of Meniere disease, head trauma, hypertension, diabetes and osteoarthritis [3, 13]. On the other hand, hypertension and vascular disease reduces blood flow to inner ear and this situation causes partition of otoconia from the membrane. Besides these diseases, osteoporosis and vitamin D deficiency are associated with recurrence of BBPV attacks [7, 14].

Considering the literature information, BPPV can be interpreted as a pathological process resulting from subclinical systemic inflammation. The distribution of cells in circulating blood is used for the identification of systemic inflammation. For this purpose, the comparison of the parameters of the complete blood count was investigated in many areas and the results were presented to the literature. These parameters are mean platelet volume, neutrophil/lymphocyte ratio and platelet/lymphocyte ratio. Beside these parameters, anisocytosis is one of the other parameter of subclinical systemic information like interleukin-6, hepcidin, C-reactive protein and erythrocyte sedimentation rate [12]. These parameters are commonly used as prognostic factors in cardiovascular and malignant disease [15].

RDW is a quantitative parameter of anisocytosis and is calculated by automated cell counters routine complete blood count analysis. RDW can be affected with various clinical situations. In the literature, different studies have been stated about whether RDW is high or low in some diseases. These situations are iron deficiency anemia, bone narrow disease like primary myelofibrosis, malignant diseases and cardiovascular diseases, etc [12, 15]. Kahveci et al. showed that RDW levels statistically increased in functional bowel disease [16]. Tel et al. found that RDW levels significantly and positively correlated with COVID-19 disease [17]. Ustaoglu et al. showed that RDW levels statistically increased in autoimmune liver diseases [18]. Aktas et al showed that median RDW levels statistically raised in malign thyroid cancer patients [19]. In contrast, Bilgin et al. showed that RDW levels found to be significantly lower in the hypothyroid patients [20]. Lu et al. showed that RDW levels found to be significantly lower in the non-elderly (below 65 ages) Connective Tissue Disease-Associated Interstitial Lung Disease [21]. These clinical conditions may be RDW as a confusing parameter for evaluating systemic inflammation. For preventing these biases about RDW evaluation, patients that had anemia, cardiovascular disease and other chronic diseases were excluded by the author.

The results obtained in this study showed that RDW value during BPPV attack was higher than control group. According to these findings, we can think that BPPV causes systemic inflammation or BPPV occurs as a result of systemic inflammation. There is no data about anisocytosis with BPPV in literature. This is the first study about whether anisocytosis in circulating blood plays a role in BPPV pathology or not. It is clear that the data in this study is not enough to reveal a new mechanism about BPPV pathogenesis but that one of the important findings about BPPV pathogenesis is obtained.

According to the results of this study, some theoretical suggestions about pathophysiological

process of BPPV can be listed as follows; 1. Anisocytosis in circulating blood may cause reducing blood flow rate at semicircular canal. So this may cause hypoxi at semicircular canal membrane and leads to detachment of otoconia from membrane and cause attack. 2. Vascular occlusion in the cochlear and semicircular canal microcirculation like vasooclusive crisis at sickle cell anemia may cause cellular hypoxia or death during attack [22]. 3. Released inflammatory mediators during BPPV attack from semicircular canal membrane may cause systemic subclinical inflammation and this situation may cause anisocytosis in circulating blood therefore anisocytosis can be used as a follow up or prognostic parameter. These theoretical suggestions and hypotheses need to be investigated with further studies. RDW is a quantitative parameter of anisocytosis and easily calculated automated blood count devices and can help investigators for their researches.

In our study, there were some limitations. The major limitations of the study included its retrospective nature and the other is small study population. These limitations make our results difficult to interpret in clinical practice. However, current study is important by showing increased RDW in subjects with BPPV, which may add a lot to the literature knowledge. Since there are not enough studies in the literature, our results are also important in terms of making a contribution.

Conclusions

In conclusion, the relationship between anisocytosis and BPPV attack is a new issue and need to be investigated with further studies. RDW changes in circulating blood can be used as a follow-up parameter. This study is a preliminary study and needs to be supported with large sample groups and multi-central participation.

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