PDW AS AN İNFLAMMATION MARKER IN PRIMARY HYPERPARATHYROİDİSM

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Abstract

Aims Primary hyperparathyroidism (PHPT) is common disorder in which parathyroid hormone (PTH) is excessively secreted from one or more of four parathyroid glands. Primary hyperparathyroidism (PHPT) is an endocrinological disorder associated with increased systemic inflammation, endothelial dysfunction. The systemic inflammation may cause subclinical decrease in cardiac function. Our aim in our study is to compare the markers of systemic inflammation in preoperative, postoperative period with PHPT, to show that PDW (platelet distribution width) value may be a predictive value for the development of cardiovascular (CVO), thromboembolic events (TBO) in patients with primary hyperparathyroidism. Results In this study, patients who underwent parathyroidectomy for primary hyperparathyroidism between 2014 - 2021 were retrospectively screened. A total of 56 patients who underwent parathyroidectomy for PHPT were included in the study. In addition to demographic and clinical information; PTH, corrected calcium, phosphate, white blood cell (WBC) count, platelet counts and PDW of the patients were recorded before and three months after parathyroidectomy. Systemic inflammatory index (SII) was calculated according to appropriate formula. Discussion The preoperative PDW value of the patients was found to be significantly higher when compared with the postoperative period and control groups. Preoperative platelet value, on the other hand, was statistically significantly higher when compared with control group. PDW values were found to be statistically significantly decreased in the postoperative period compared to the preoperative period in patients. Conclusion Increased PDW value before parathyroidectomy may be a predictive value of inflammation and the development of CVO ,TBO. Keywords: primary hyperparathyroidism, PDW (platelet distribution width), platelets, parathyroidectomy It is known to cause subclinical inflammation and subclinical cardiac dysfunction in primary hyperparathyroidism. There are conflicting studies on inflammation markers. Our article is the first to study PDW in primary hyperparathyroidism. High preoperative PDW indicates that PHPT may be a risk factor for cardiovascular events.

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Primary hyperparathyroidism (PHPT) is common disorder in which parathyroid hormone

(PTH) is excessively secreted from one or more of four parathyroid glands. Primary hyperparathyroidism (PHPT) is an endocrinological disorder associated with increased systemic inflammation, endothelial dysfunction. The systemic inflammation may cause subclinical decrease in cardiac function. Our aim in our study is to compare the markers of systemic inflammation in preoperative, postoperative period with PHPT, to show that PDW (platelet distribution width) value may be a predictive value for the development of cardiovascular (CVO), thromboembolic events (TBO) in patients with primary hyperparathyroidism.

Results

In this study, patients who underwent parathyroidectomy for primary hyperparathyroidism between 2014 - 2021 were retrospectively screened. A total of 56 patients who underwent parathyroidectomy for PHPT were included in the study. In addition to demographic and clinical information; PTH, corrected calcium, phosphate, white blood cell (WBC) count, platelet counts and PDW of the patients were recorded before and three months after parathyroidectomy. Systemic inflammatory index (SII) was calculated according to appropriate formula.

Discussion

The preoperative PDW value of the patients was found to be significantly higher when compared with the postoperative period and control groups. Preoperative platelet value, on the other hand, was statistically significantly higher when compared with control group.

PDW values were found to be statistically significantly decreased in the postoperative period compared to the preoperative period in patients.

Conclusion

Increased PDW value before parathyroidectomy may be a predictive value of inflammation and the development of CVO ,TBO.

Keywords: primary hyperparathyroidism, PDW, platelets, parathyroidectomy

What is already known about this topic?

It is known to cause subclinical inflammation and subclinical cardiac dysfunction in primary hyperparathyroidism. There are conflicting studies on inflammation markers.

What does this article add?

Our article is the first to study PDW in primary hyperparathyroidism. High preoperative PDW indicates that PHPT may be a risk factor for cardiovascular events.

Introduction

Primary hyperparathyroidism (PHPT) is a disease caused by excessive synthesis of parathormone (PTH) from one or more parathyroid glands. It is caused by a single parathyroid adenoma in most people [1]. It is often associated with hypercalcemia and elevated PTH levels. Sometimes PTH levels can be within normal levels [1].

Serum calcium levels are frequently measured in health centers. Patients with PHPT have moderate to high levels of calcium along with unsuppressed or elevated PTH levels. In the United States, 66 women and 25 men were found to have PTH elevation per 100,000 people in 1 year [2].

The clinical presentations of PHTP are asymptomatic (often detected by routine biochemical testing) or symptomatic (with skeletal and renal complications). PHPT does not require surgical treatment when asymptomatic. However, surgery is required in symptomatic cases.

PHPT causes subclinical inflammation and endothelial dysfunction. Studies have shown that increased levels of highly sensitive C-reactive protein (CRP), interleukin-6 (IL-6) and inflammatory markers increase the risk of cardiovascular disease [3]. It has been shown that patients with PHPT have a decrease in inflammation markers and a subclinical increase in cardiac function after the operation [3].

It is also believed that non-skeletal diseases such as insulin sensitivity, arterial hypertension, and cardiovascular diseases also increase in patients with PHPT. In the study, some gene expression was examined in the adipose tissue taken from the neck of patients with PHPT, and as a result, inflammatory and metabolic changes were observed. Pro-inflammatory stimuli are thought to initiate the early stages of atherosclerosis by altering the expression of adhesion molecules in the endothelium, mediating endothelial attachment of circulating lymphocytes, monocytes. [4].

Various biochemical, hematological markers are used to evaluate and document systemic inflammation. Some parameters are quite expensive and therefore cheap parameters are needed. Neutrophil-lymphocyte ratio (NLR) is found by dividing the neutrophil count by the lymphocyte count, and this result is accepted as an inflammatory marker and is a very inexpensive method. NLR has been studied in various types of inflammation and cancer [5]. There are very few studies in which these inflammation markers are studied in primary hyperparathyroidism. The results of a small number of studies have been found to be inconsistent. In some studies, CRP and IL-6 levels were found to be similar in the patient and control groups, and in some studies, the effects of parathyroidectomy on subclinical inflammation were found to be reduced, similar or increased [6].

Platelet and neutrophil lymphocyte ratio have been studied in some cancer types, and it was found to be a marker of prediktor on the survey [7]. At the same time, the systemic inflammatory index (SII) has also been studied in some cancer types [8], but this parameter has not yet been studied in primary hyperparthyroidism. Our aim in our study is to compare the markers of systemic inflammation in the preoperative and postoperative period in primary hyperparathyroidism and to show that the PDW value may be a predictive value for the development of cardiovascular events (CVO) and thromboembolic events (TBO).

Materials and Methods

In this study, patients who underwent parathyroidectomy for primary hyperparathyroidism between 2014 - 2021 were retrospectively screened. Patients with missing information, those who were operated for tertiary hyperparathyroidism due to chronic renal failure, those with liver or rheumatological disease diagnosis, those with high CRP and sedimentation levels, those with thyroid cancer in their pathology, and those with active infection were not included in the study. A total of 56 patients who underwent parathyroidectomy for PHPT were included in the study. In addition to demographic and clinical information, PTH, corrected calcium, phosphorus, white blood cell (WBC) count, platelet counts and PDW of the patients were recorded before and three months after parathyroidectomy. This information was also recorded for the control group similar to age and gender, which did not have active infection and inflammation. Systemic inflammatory index (SII; absolute platelet count multiplied by absolute neutrophil count divided by absolute lymphocyte count) was calculated according to the appropriate formula.

Statistical analysis

Continuous variables were expressed as mean \pm standard deviation and median (min-max). Categorical data were expressed as numbers and percentages. In the intergroup analysis of continuous variables, normality analyzes were performed with the Kolmogorov-Smirnov Goodness of Fit Test. Student's T-Test was used for comparisons of data with normal distribution, and Mann-Whitney U-Test was used for those that did not. Comparisons of categorical data were made with the Chi-Square Test. T-Test for Dependent Groups was used to compare data with normal distribution in within-group analyses, and Wilcoxon Ordered Signs Test was used for those that did not. Analyzes were performed with IBM SPSS (Statistics Package Program for Social Sciences) version 24.0 (IBM Corporation, Armonk, NY, USA). A power analysis was not necessary for this retrospective study. Values of P < 0.05 were considered to be significant.

Results

No statistically significant difference found between the groups in terms of age and sex ratios. The presence of additional disease was found to be significantly higher in the patient group (44.6%) than in the control group (22.0%) (p=0.014) (Table 1).

In patients, preoperative phosphorus values were significantly lower than in the control group, while preoperative eGFR and calcium values were significantly higher (p < 0.05). In the postoperative period, EGFR, calcium and phosphorus values between the groups were found to be similar to the control group (p>0.05).

In the postoperative period, eGFR and calcium values were found to be statistically significantly decreased (p<0.05), while phosphorus values were significantly increased (p<0.05) in the postoperative period compared to the preoperative period (Table 2). In patients, preoperative 25 OH Vit D values were significantly lower than in the control group, while PTH values were significantly higher (p<0.05). Postop PTH values were significantly higher in patients than in the control group (p<0.05).

It was determined that the PTH values of the patients decreased significantly in the postoperative period compared to the preoperative period (p<0.05), and the 25 OH Vit D values were significantly increased (p<0.05) (Table 2).

There is a decrease in patient (PLT*NEU/LYM) rates in the preoperative and postoperative periods, and this decrease was not found to be statistically significant (Table 3).

Discussions

Many studies in patients with symptomatic or asymptomatic PHPT have shown that postmenopausal women are affected more frequently than men [1]. In our study, the mean age in women was consistent with postmenopausal age. The most common finding in classical PHPT is hypercalcemia [1]. It may be accompanied by hypophosphatemia [9]. In our study, calcium and phosphorus levels in the preoperative period were found similar to the literature.

While the calcium level decreased significantly and the phosphorus level increased significantly after the operation and was found to be similar to the control group.

Preoperative PTH levels were found to be significantly higher compared to the postoperative period. This shows that the operation plays an important role in lowering PTH levels. However, postoperative PTH levels were found to be significantly higher when compared to the control group. This is thought to be due to operation failure or parathyroid hyperplasia in some patients. Vitamin D deficiency is common in Turkey. In our study, vitamin D deficiency was frequently detected in the patient and control groups. 25 OH vit vitamin D deficiency is frequently seen in PHPT. This situation is based on two reasons. The first is that 1 alpha hydroxylase activity is increased in PHPT, and the half-life of 25 OH vit D is shortened. Another reason for the decrease in 25 OH vit D skin synthesis due to the direct stimulatory effect of high 1.25 OH vit D [10]. In our study, 25 OH vit D levels in the preoperative period were found to be lower than the control group, similar to the literature.

It is thought that inflammatory markers such as IL-6, CRP, tumor necrosis factor-? (TNF-alfa) may increase in patients with hyperparathyroidism (HPT). Conflicting results have been encountered in studies. In some studies, it has been shown that inflammatory markers increase in PHPT, and in some studies, CRP, IL-6, leukocyte levels were found to be similar to the control group. The effect of parathyroidectomy on subclinical inflammation was found to be uncertain; it has been shown to decrease in some studies, increase or not change in others [6]. In our article, we studied PDW, platelet count and SII as markers of inflammation.

MPV (mean platelet volume), PDW, and plateletcrit (PCT) are the most important markers of platelet activation [11]. PDW is a more specific marker of platelet activation [12]. In one study, a significant increase in PDW value was found to be associated with coronary artery disease and the severity of the disease in acute coronary syndrome [13, 14]. In another study, PDW and MPV were studied in patients with type 2 diabetes, and these two values were found to be significantly higher than in non-diabetic individuals. In addition, since these two values are well defined for cardiovascular disease risk, it was thought that they may be important in determining treatment options [15]. When we searched the literature, PDW was not studied in PHPT. In our study, preoperative and postoperative 3rd month values were found to be statistically significantly higher in patients with PDW PHPT compared to the control group. In addition, it was determined that this value decreased significantly after parathyroidectomy compared to the preoperative period. This suggests that there may be a significant increase in platelet activation and an increased risk of thromboembolic (TBO) and cardiovascular events (CVO) in PHPT. According to the data in our study, it can be predicted that this situation may decrease with parathyroidectomy, but there may still not be a complete recovery. As shown in our study, RDW in PHPT can be an important, inexpensive and easily accessible parameter in terms of determining the risk of TBO and CVO.

The number of platelets may increase during primary hematological diseases as well as secondary causes such as benign, inflammatory and neoplastic diseases. Therefore, it is necessary to identify potential causes and use molecular tests when necessary to diagnose a particular disease [16]. In our study, an increase in platelet levels was found in the preoperative period of patients with PHPT compared to the control group. It was thought that the increase in platelet count may have occurred after subclinical inflammation with PHPT.

Systemic immune inflammation index (SII); it is calculated by the platelet, neutrophil and lymphocyte counts, showing the patient's inflammatory-immune balance [17]. Along with some markers of inflammation, SII has been associated with some diseases and their surveillance. It is an index that has been mostly studied with some types of cancer. In one study, it was considered to be a prognostic marker of overall survival before treatment in epithelial ovarian cancer patients [17]. One study found a positive correlation between SII and obese smokers [18]. In another study, SII was found to be a potential indicator of clinical outcome in patients with acute myocardial infarction [19].

Subclinical inflammation in PHPT may be a risk factor for early atherosclerosis. Systemic immune inflammation index can give us important information in this respect. When we look at the literature, our study is the first study in PHPT in which SII was studied. At the end of the study, this index was compared in the preoperative and postoperative periods. At the end, there was a decrease in the postoperative period, but it was not found statistically significant. Studies with a larger number of patients may show that SII may be a marker of subclinical inflammation in patients with PHPT.

Conclusions

In studies with PHPT and inflammation markers, increased inflammation was positively correlated with the development of CVO and TBOs. Increased PDW value has been shown to be associated with coronary artery disease and acute coronary syndrome.

Our study is the first to show that the increased PDW value in PHPT in the preoperative and postoperative period may be a predictive value for the development of CVO and TBO. It can be a source of ideas for larger randomized and controlled trials. Larger studies with more patients are needed for SII to be predictive value.

Ethical Approval

This study was performed with the approval of the ethics committee of Medical University of Vienna in accordance with the principles of the Helsinki Declaration of 1964 and its further amendments. All authors had full Access to all of the data in this study and take complete responsibility for the integrity of the data and accuracy of the data analysis.

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