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Does Suppression of Tsh Affect The Mean Platelet Volume? Retrospective Case Control Study

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ABSTRACT

There have been reports that the mean platelet volume changes in the way of increasing or decreasing in inflammatory diseases. We also wanted to investigate whether there is such a change in the mean platelet volume in thyroid diseases.

The data of 1410 patients admitted to the endocrine outpatient clinic were reviewed retrospectively. Age, sex, thyroid disease diagnoses, TSH(µIU/ml), fT3(pg/ml), fT4(ng/dl), MPV(fl) values were recorded. The patients were divided into three groups according to TSH levels and their diagnosis

This study included 1410 patients who were admitted to our endocrine outpatient clinic with a preliminary diagnosis of thyroid. 75.2% of the patients were female and 24.8% were male. The mean age of all patients was 47.87. The mean and standard deviation value of MPV(fl) was 7.49±1.25. We divided the patients into 3 according to their TSH levels: those with TSH values less than 0.35 µIU/ml, those with TSH values 0.35-4.94 µIU/ml and TSH values 4.94 µIU/ml ' greater than. There was no significant correlation between MPV and TSH (p=0.19).

At the subgroups according to the diagnosis; (subacute thyroiditis, Graves disease, toxic adenoma, toxic multinodular goiter, hypothyroidism, tsh suppression in pregnancy, thyroid cancer, euthyroidism, suppressed TSH due to excessive drug use) there was no significant correlation between MPV and TSH (p=0.11, p=0.56, p=0.50, p=0.06, p=0.14, p=0.53, p=0.33, p=0.30, p=0.91 respectively).

Is MPV a biomarker or can it play a role in thyroid diseases? According to our study, MPV is not considered as a suitable biomarker for thyroid diseases.

Key Words: Suppression, TSH, affect, MPV

Introduction

Every organ in the body needs thyroid hormone (1). The most important hormones produced by the thyroid gland are thyroxine (T4), triiodothyronine (T3) and reverse triiodothyronine (rT3)(1). Thyroid stimulating hormone (TSH), secreted from the anterior pituitary gland, controls thyroid hormones (1). Since most thyroid diseases indicate an inflammatory condition on the genetic background, we investigated whether there was a relationship with the mean platelet volume (MPV). Measuring MPV can inform us about the course and outcome of some inflammatory diseases (2). MPV indicates platelet activation (3). It is a useful inflammatory biomarker used in many diseases (3).

Materials and Methods

This study received permission from Karatay University, Faculty of Medicine Ethics Committee. Patient data were collected retrospectively.

Selection of cases for the study: We retrospectively reviewed the files of 1410 patients who were admitted to the endocrine outpatient clinic with a pre-diagnosis of thyroid disease in the last 5 years. We recorded age, gender, thyroid disease diagnosis, TSH, MPV. In the study, we examined the relationship between TSH and MPV in two ways: First, is there a change in MPV value between patients with TSH suppression and patients with normal or high TSH; Second, we looked at whether there was a change between the diagnosis of thyroid disease and MPV. We divided the patients into 3 according to TSH levels. TSH value less than 0.35µIU/ml, TSH value 0.35-4.94 µIU/ml and TSH value greater than 4.94 µIU/ml. These values were the reference values given in our laboratory. Normal and high values of tsh were evaluated as control groups in the study. When grouping thyroid diseases; we considered TSH, fT3, fT4, scintigraphy, thyroid USG, thyroid autoantibodies. Apart from the TSH value, we divided the cases according to their diagnosis for further investigation; subacute thyroiditis, Graves disease, toxic adenoma, toxic multinodular goiter, hypothyroidism, TSH

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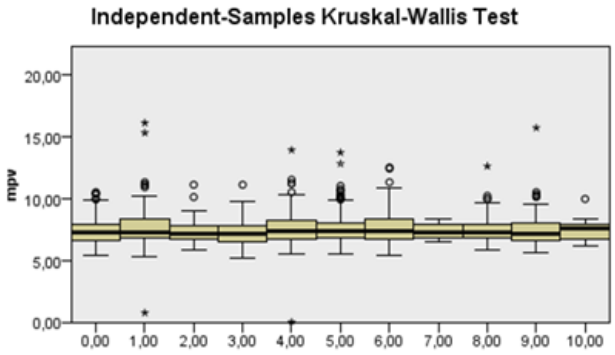

Fig. 1. Histogram of the Relationship Between TSH and MPV in Thyroid Diseases
MPV: Unit value:fl
0: Subacute thyroiditis
1: Graves
2: Toxic adenoma
3: TSH suppressed, normal scintigraphy
4: Toxic multinodular goiter
5: Euthyroidism (antibody positivity, nodule and/or heterogeneity on ultrasonography)
6: Hypothyroidism
7: Tsh suppression in pregnancy
8: Euthyroidism(all values normal)
9: Thyroid cancer
10: Suppressed TSH due to excessive drug use

suppression in pregnancy, thyroid cancer, euthyroidism (all values normal), suppressed TSH due to excessive drug use etc.

Biochemical tests: After 8 h fasting, morning blood samples were taken to measure thyroid stimulating hormone (TSH), free triiodothyronine (fT3) and free thyroxine (fT4) on the ARCHITECT *i*2000SR immunoassay analyzer (Abbott Diagnostics). The patient and control groups had MPV levels measured in venous blood samples placed in EDTA-standard tubes using Abbott Cell-Dyn 3700 Hematology Analyzer with the flow cytometry method.

Statistical Analysis: Statistical analysis was carried out using the SPSS for Windows version 22.0 program and $p < 0.05$ was accepted as statistically significant. The suitability of TSH and MPV variables to normal distribution was examined by Kolmogorov-Smirnov test. Since TSH and MPV variables are not normally distributed, descriptive statistics should be given in the median (25% -75%) percentile. Mann-Whitney U test and Kruskal-Wallis ANOVA tests were used for comparison by groups. The relationship between TSH and MPV was investigated by Spearman Correlation coefficient.

Results

This study included 1410 patients who were admitted to our endocrine outpatient clinic with a pre-diagnosis of thyroid disease. 75.2% of the patients were female

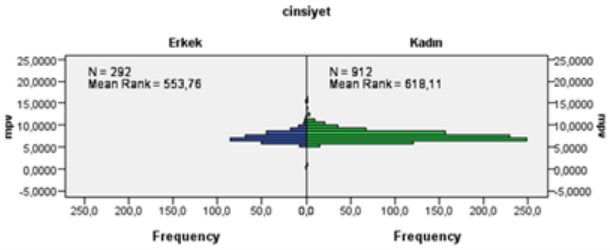

Fig. 2. Distribution of MPV by sex

and 24.8% were male. The mean age of all patients was 47.87, the mean age of female patients 46.31, the mean age of male patients 52.54. The mean and standard deviation value of MPV(fl) was 7.49±1.25. In women and men, the mean and standard deviation value of MPV(fl) was 7.55±1.26, 7.32±1.23 respectively.

We divided the patients into 3 according to their TSH levels (Table 1, Figure 1): those with TSH values less than 0.35 µIU/ml (n = 756, 53.76%, p=0.14), those with TSH values 0.35-4.94 µIU/ml(n = 542, 38.54%, p=0.51) and TSH values 4.94 µIU/ml greater than (n = 108, 7.68%, p=0.85). Normal and high values of TSH were evaluated as a control group in the study.

There was no significant correlation between MPV and TSH in TSH suppressed, normal and high patients (p=0.19); There was no correlation between age and MPV (p = 0.20).

There was a significant relationship between age (p = 0.00) and sex (p = 0.00) in TSH suppressed, normal and high patients. There was a correlation between age and TSH. As age increased, tsh level increased (p = 0.00). TSH levels were lower in men than in women (p = 0.00).

When we look at subgroups; in subacute thyroiditis patients (n=146) there was a minimal relationship between age and TSH (p = 0.05) (As age increased, TSH level increased), there was no significant correlation between age and MPV (p = 0.72), and between TSH and MPV (p = 0.11).

Although there was a significant correlation between age and TSH (p=0.00) (As age increased, TSH level increased); There was no significant correlation between age and MPV (p=0.83), and between TSH and MPV (p=0.56) in patients diagnosed with Graves disease (n=170).

There was significant correlation between age and TSH (p=0.03) (As age increased, TSH level increased); There was no significant correlation between age and MPV (p=0.36) and between TSH and MPV (p=0.06) in patients with toxic multinodular goiter (n=115).

There was no significant correlation between age and TSH (p=0.52), and between age and MPV (p=0.62),

Table 1. Relationship Between TSH and MPV According to TSH Levels and Diagnosis of Thyroid Disease

Groups	N	TSH (µIU/ml) Mean± standard deviation	MPV(fl) Mean± standard deviation	CC	P
TSH<0.35(µIU/ml)	761	0,09±0.01	7.36±1.45	0.05	0.14
TSH=0.35-4.94(µIU/ml)	539	1,63±1.00	7.56±1.27	0.02	0.51
TSH>4.94(µIU/ml)	97	16,36±25.48	7.40±1.28	-0.02	0.85
Subacute thyroiditis	146	0.70±3.71	7.37±1.10	0.13	0.11
Graves disease	170	0.22±0.48	7.60±1.56	-0.04	0.56
Toxic adenoma	68	0.22±0.47	7.38±0.98	-0.08	0.50
Toxic multinodular goiter	115	0.22±0.63	7.59±1.54	0.17	0.06
Tsh suppression in pregnancy	9	0.10±0.10	7.30±0.66	0.23	0.53
Suppressed TSH due to excessive drug use	14	0.09±0.10	7.49±0.95	0.03	0.91
Thyroid cancer	115	4.95±17.04	7.41±1.29	0.09	0.33
a-RAI +	87	4.78±18.54	7.41±1.33	0.09	0.40
b-RAI-	28	4.70±8.44	7.38±1.21	0.04	0.83
TSH was suppressed, normal scintigraphy	86	0.40±1.17	7.19±0.97	0.01	0.88
Euthyroidism, (antibody positivity, nodule/heterogeneity on ultrasonography).	232	1.66±1.06	7.57±1.15	0.12	0.05
Hypothyroidism	169	4.61±8.55	7.59±1.23	-0.11	0,14
Control(all thyroid values normal)	71	1.50±1.02	7.48±1.15	0.12	0.30

CC: Correlation coefficient
N: Number of cases

and between TSH and MPV (p=0.50) in patients with toxic adenoma (n=68).

Although TSH was suppressed in patients with normal scintigraphy (n=86); there was no significant correlation between age and TSH (p=0.09), and between age and MPV(p=0.35), and between TSH and MPV(p=0.88).

There was no significant correlation between TSH and age (p=0.73) and between age and MPV(p=0.39), there was significant correlation between TSH and MPV (p=0.05), in patients with normal TSH (n=232) (however, there is antibody positivity, nodule and / or heterogeneity on ultrasonography).

There was no significant correlation between age and TSH (p=0.17), and between age and MPV (p=0.40), and between TSH and MPV (p=0.14) in patients with hypothyroidism (n=169).

There was no significant correlation between age and TSH (p=0.35), and between age and MPV (p=0.93), and between TSH and MPV (p=0.53) in patients diagnosed with pregnancy and who had TSH suppression (n=9).

There was no significant correlation between age and TSH(p=0.14), age and MPV(p=0.26), and TSH and MPV(p=0.33) in patients with thyroid cancer (n=115). There was no significant correlation between age and TSH, age and MPV, TSH and MPV in patients with thyroid cancer who had received radioactive iodine (p =0.11, p=0.09, p=0.40 respectively). There was no significant correlation between age and TSH, age and MPV, TSH and MPV in patients with thyroid cancer who did not receive radioactive iodine (p =0.30, p=0.34, p=0.83 respectively).

There was no significant correlation between age and TSH (p=0.65), and between TSH and MPV (p=0.91); There was significant correlation between age and MPV (p=0.05) in patients with hypothyroidism but who had suppressed TSH due to excessive drug use (n=14).

There was no significant correlation between age and TSH (p=0.21), between age and MPV(p=0.39), and between TSH and MPV(p=0.30) in patients with a pre-diagnosis of thyroid disease and all values (thyroid ultrasonography, TSH, fT3, fT4, antibodies) were normal (n=71).

When we look at gender (Figure 2); although there was a significant correlation between age and TSH (p=0.00) in female patients(n=1056), there was no significant correlation between age and MPV (p=0.20) and between TSH and MPV (p=0.37). Although there was a significant correlation between age and TSH (p=0.00) in male patients (n=354) , there was no significant correlation between age and MPV (p=0.83) and between TSH and MPV (p=0.83) .

Discussion

Thrombocytes are extremely reactive blood morphotic components (2). Increased IL-6, IL-1 and TNF-α in inflammation, stimulates precursor blood cells (2). In this case, the blood platelet count increases significantly (2). Platelets have very important roles in inflammatory reactions and immune response (4). MPV, the parameter that shows this best, is widely used (4). MPV increases as activated platelets increase (4). The mean platelet volume (MPV) is probably the most extensively studied platelet activation marker (5).

Hematological analyzers calculate MPV based on volume measurement during routine blood testing (2). 2-5% of all platelets are composed of enlarged platelets (2). The normal range of MPV is 7.5-12.0 fl (2). In physiological events, such as maintaining hemostasis and maintaining a fixed platelet mass, MPV varies inversely with the number of platelets (2).

Measuring MPV can inform us about the course and outcome of some inflammatory diseases (2). MPV increases in peripheral (4), cardiovascular, respiratory, intestinal and rheumatological diseases, as well as in cerebral stroke, chronic kidney failure, diabetes (4,2) and some cancers (2). MPV decreases in acute exacerbation of tuberculosis, ulcerative colitis, adult SLE, and various neoplastic illnesses (2).

One of the most important components of routine blood tests is MPV (3). MPV is associated with increased platelet activation with the pathophysiology of inflammatory diseases (3). In addition, MPV changes due to platelet activation pose a great risk for cardiovascular disease. In studies conducted before us, MPV has been accepted as an inflammatory biomarker in diabetes mellitus, cerebrovascular disease and rheumatic diseases (3). In many inflammatory diseases, there was a correlation between inflammatory markers such as MPV, CRP and erythrocyte sedimentation rate (3). For this reason, MPV shows platelet activation in inflammatory diseases (3).

Kisacık et al., showed that MPV value is a clue in acute exacerbation in patients with ankylosing spondylitis and rheumatoid arthritis (3).

Wang et al., demonstrated that MPV decreased in patients with acute periodontitis, as connection with the severity of periodontal inflammation (3). Moreover, MPV has indicated an inflammatory burden in diabetes mellitus and obese patients (3).

In a study of Conversion disorder patients MPV was shown to reflect inflammation (6).

In contrast, another study has suggested that MPV is not a biomarker that indicates acute exacerbation of chronic obstructive pulmonary disease (3).

There were few studies investigating the association between MPV and thyroid diseases. These studies were limited to thyroid cancer and nodules.

Since most thyroid diseases indicate an inflammatory condition on the genetic background, we investigated whether there was a relationship with MPV.

Fırat et al. found an increase in MPV in patients with RAI in patients with papillary thyroid cancer, but did not see this relationship in patients without RAI (7). In our study, there was no correlation between MPV levels in all patients with thyroid cancer (with or without RAI).

In a study comparing thyroid cancer patients with the control group, MPV levels were significantly lower in cancer patients (8). However, in our study we did not see such a change in MPV.

In a study of elderly patients with papillary thyroid cancer, MPV was significantly reduced in patients with hashimatone on the ground (9).

Thrombocyte indexes were examined in patients with papillary thyroid cancer, no significant MPV changes were observed (10).

In another study, there was no significant difference between benign nodular goiter and papillary thyroid cancer in terms of MPV level (11).

In addition, in another study, there was no relationship between the presence-size of thyroid nodules and MPV (12).

Accordingly, we also examined the level of MPV in thyroid diseases. Can MPV be used as a biomarker in thyroid diseases; we examined it. We investigated whether MPV decreased or increased in cases of hyperthyroidism, hypothyroidism and euthyroidism.

Lippi et al. found a significant relationship between tsh values and MPV in euthyroid elderly patients (13). In our study, we did not find a significant relationship between TSV and MPV whether patients were hyperthyroid, euthyroid or hypothyroid. A Previous study found that MPV increased in Graves' patients

(14). Bagir et al. compared recurrent Graves' disease with remission and found MPV significantly higher in the recurrent group and attributed this state to hypermetabolism (15). On the contrary we did not find a relationship between Graves' disease and MVP in our study.

In our study, we thought that MPV may change because most thyroid diseases are chronic, triggering inflammation (with autoantibodies) and genetic predisposition. However, we could not obtain such data. Even in patients with subacute thyroiditis triggered by acute inflammation, we did not see any change in MPV values. In our study, MPV is not considered as a suitable biomarker for thyroid diseases.

Study Limitations: MPV showing platelet activation can be affected by many factors that trigger inflammation. When evaluating MPV, it would be better to evaluate it with other inflammatory biomarkers such as CRP. In addition, it is necessary to rule out conditions such as smoking, hypertension, diabetes mellitus, hyperlipidemia.

Conclusion: Is MPV a biomarker or can it play a role in thyroid diseases? Further and comprehensive studies are needed.

Ethics: This study received permission from Karatay University, Faculty of Medicine Ethics Committee.
Conflict of Interest: There is no conflict of interest.

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