

Platelet function in euthyroid patients undergoing thyroidectomy in women

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Abstract. – BACKGROUND: Several studies have reported several platelet abnormalities in patients with sub-clinical or overt thyroid dysfunctions. The primary mechanism that affects the hemostatic balance is excess or deficiency of thyroid hormones. The different ways of thyroid gland to the platelet function are not yet clearly understood. The relationship between in the thyroid gland and platelet activation without thyroid hormones has not been studied yet.

AIM: The aim of our study is to determine the platelet function in euthyroid patients undergoing thyroidectomy in females.

PATIENTS AND METHODS: The study group includes 52 female euthyroid patients undergoing thyroidectomy. The control group consisted with 21 healthy euthyroid female. Platelet count (PC), platelet mass (PM), mean platelet volume (MPV), and platelet distribution width (PDW) were measured. PM was calculated by multiplying MPV and PLT.

RESULTS: MPV (8.4 ± 1.3 versus 7.9 ± 0.8) and PDW (17.8 ± 1 versus 17.6 ± 0.8) values were similar between the two groups.

CONCLUSIONS: Thyroid gland does not directly affect platelet activation. Accordingly, platelet abnormalities of thyroid disease can be considered to be independent of the underlying thyroid tissue. This finding suggests that association between thyroid diseases and platelet function is dependent on the status of thyroid hormones.

Key Words:

Platelets, Thyroid gland, Thyroidectomy.

fibrinolytic system, such as decreased synthesis or reduced activity of clotting factors, including von Willebrand factor (VWF) and factor VIII (FVIII: C), decreased response to adrenergic stimulation (enhanced VWF release from endothelial cells), and alteration in the coagulation-fibrinolytic balance^{4,7}. Previous reports suggested that hyperthyroidism and hypothyroidism were associated with increased risks for thrombosis and bleeding, respectively^{4,6}. Some studies demonstrated that thyroid hormone deficiency is tending to be the main cause of coagulation disorders in thyroid disease^{4,5,8,9}. Their findings showed that association between changes in coagulation factors and thyroid functions are mainly mediated by T4 and not by TSH (increasing levels of factor (F) FVIII, FIX, VWF, fibrinogen and T4). Also some authors showed that the thyroid gland of healthy subjects possess thromboplastin, antithrombin, anticoagulant substances, antiheparin and fibrinolytic properties and contain plasminogen, plasminogen activators and antiplasmins^{10,11}. The function of the external hemocoagulation system was reduced due to diminished thromboplastin and antiheparin activity of the gland tissue, reduction of aggregation and increase of disaggregation properties of the gland tissue. The relationship between platelet activation and direct effect of thyroid gland without T3, T4 and TSH has not been studied yet. The aim of this investigation is to compare the platelet count and other platelet parameters in euthyroid patients undergoing thyroidectomy and euthyroid healthy control group.

Introduction

Thyroid diseases are extremely common, particularly among women¹. Thyroid hormone receptors play an important role in whole body systems. The coagulation-fibrinolytic system is also sensitive to the thyroid hormones^{2,3}. Thyroid hormone alterations are related with various changes in this system. There are many regulatory effects of thyroid hormones associated with coagulation-

Patients and Methods

Patients

52 female euthyroid patients undergoing thyroidectomy for multinodular goiter and Graves'

disease were retrospectively included in our case series (Group 1, mean age = 46.7 ± 8.9). These patients' followed up at the Outpatient Clinic of Internal Medicine Clinic of Duzce Ataturk State Hospital. All patients in this group were on levothyroxine therapy. The control group consisted of 21 healthy euthyroid female subjects (Group 2, mean age = 40.9 ± 9.9). None of the patients had a history of blood coagulation disorders and none of them was on treatment with anticoagulants. Also patients with sub/overt hyperthyroidism, sub/overt hypothyroidism, severe hypertension, i.e. (present or past antihypertensive drug use or detection of systolic pressure > 140 mmHg and/or diastolic pressure > 90 mmHg on three separate occasions), diabetes mellitus, alcohol consumption, dyslipidemia, cardiac, renal, hepatic, and other systemic diseases, and patients on drugs affect platelet and thyroid function (e.g. diuretics, beta-blockers, anti-hyperlipidemic agents, anticoagulant drugs, anti-histamines, or corticosteroids), pregnancy and malignancy were excluded. Dyslipidemia was defined in the presence of at least one of the following conditions: raised plasma triglycerides (> 140 mg/dl), total cholesterol (> 200 mg/dl), LDL cholesterol (LDL-C > 130 mg/dl), or HDL cholesterol (HDL-C < 45 mg/dl). The study was approved by the local Ethics Committee of Abant Izzet Baysal University School of Medicine.

Laboratory Analysis

We assessed Complete Blood Count (CBC) by an automatic hematologic analyzer (Beckman Coulter LH780, Fullerton, CA, USA). 0.5 ml citrate for 2 ml blood sample was applied as an anticoagulant for each blood sample. Automated chemiluminescent immunoassays performed by the Dxl system (Beckman Coulter, Inc., Brea, CA, USA) were to measure FT4 (free thyroxine, normal range 0.6-1.7 ng/dl), FT3 (free triiodothyronine, normal range: 1.8-4.4 pg/ml) and TSH (normal range 0.27-4.2 mU/ml). The platelet count (PC), platelet mass (PM), mean platelet volume (MPV), and platelet distribution width (PDW) were evaluated. PM was calculated by multiplying MPV and PLT. Reference values for our laboratory are 150-450 U 10/L, 6.8-10.8 fL, for PC, MPV, respectively.

Statistical Methods

Statistical analyses were performed by SPSS software, Version 16 (SPSS Inc, Chicago, IL, USA) packet programme. We compared the groups by Student's paired two-tailed *t*-test for normally

distributed variables, and by Wilcoxon signed-rank test for non-normally distributed parameters. Between-group differences were evaluated using the one-way ANOVA test or the non-parametric Mann-Whitney U test. Data were described as mean values \pm standard deviation (SD). A *p* value less than 0.05 was considered significant.

Results

Table I shows the main characteristics of study and control groups. No significant difference was found between two groups, with the exception of age, which was significantly higher in group 1 than in group 2 ($p < 0.05$). Also there was no significant difference between two groups in terms of hemoglobin, hematocrit, aminotransferases (ALT, AST), fasting blood glucose, creatinine, and cholesterol levels ($p > 0.05$).

Platelet parameters and thyroid function tests were not significantly different between two groups. (MPV: 8.4 ± 1.3 vs 7.9 ± 0.8 fl, $p = 0.083$; PDW: 17.8 ± 1 vs 17.6 ± 0.8 , $p = 0.383$; PC: 320.4 ± 98.4 vs $307.2 \pm 96.4 \times 10^9/l$, $p = 0.286$; PM: 2190.80, 134.20-4042.60 vs 2256.75, 1013.70-5046.6, $p = 0.139$; fT3: 2.6 ± 0.6 vs 2.8 ± 0.6 ng/dl, $p = 0.180$; fT4: 1.0 ± 0.2 vs 0.9 ± 0.2 ng/dl, $p = 0.240$; TSH: 1.6 ± 0.4 vs 1.9 ± 0.5 mIU/ml, $p = 0.750$) (Table II).

Discussion

The major finding of this study is that there are no differences in the platelet function between euthyroid patients undergoing thyroidectomy and healthy euthyroid individuals.

Thyroid hormones are mandatory for various processes that are essential for human metabolism, such as growth and normal development. Therefore, thyroid hormone deficiency is not compatible with normal health^{12,13}. All cells in the body are targets for thyroid hormones. Thyroid hormone has been reported to have a number of actions on platelet functions^{5,6}. Both thyroid dysfunction and thyroid autoimmunity may cause thrombosis or hemorrhage affecting primary and secondary physiologic hemostasis. Whereas the patients with hypothyroidism are under the risk of bleeding, patients with hyperthyroidism show a tendency toward thromboembolic complications, including major emboli which account for 18% of deaths associated with

Table I. Clinical characteristics of patients.

Parameters	Group 1 (n = 52)	Group 2 (n = 21)	p value
Age (years)	46.7 ± 8.9	40.9 ± 9.9	0.01
SBP (mmHg)	125 ± 13	128 ± 14	0.76
DBP (mm/Hg)	76 ± 9	78 ± 11	0.75
Current smoker	5/52	2/21	0.18
Fasting glucose (mg/dl)	89.6 ± 67.4	90.3 ± 66.5	0.21
Creatinine (mg/dl)	0.76 ± 0.31	0.75 ± 0.35	0.56
AST (U/l)	28.45 ± 8.7	27.57 ± 9.5	0.65
ALT (U/l)	26.86 ± 4.7	26.66 ± 4.6	0.54
Total cholesterol (mg/dl)	177.46 ± 21.3	176.56 ± 20.9	0.21
LDL cholesterol (mg/dl)	101.46 ± 32.5	100.96 ± 31.4	0.11
HDL cholesterol (mg/dl)	48.46 ± 12.7	49.16 ± 12.9	0.41
Triglyceride (mg/dl)	123.54 ± 31.8	122.96 ± 32.3	0.31
Hemoglobin (g/dL)	12.8 ± 0.8	12.7 ± 0.9	0.65
Hematocrit (%)	37.9 ± 2.8	38.1 ± 3.1	0.76
WBC (×10 ³ /mm ³)	7.4 ± 1.7	7.1 ± 2.1	0.15

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; AST: aspartate aminotransferase; ALT: alanine aminotransferase; BMI: body mass index; HDL: high-density lipoprotein; LDL: low-density lipoprotein; WBC: White blood count; Results are given as either mean ± SD: or number (n).

thyrotoxicosis^{7,9}.

To our knowledge, this is the first study evaluating platelet function in euthyroid patients undergoing thyroidectomy. We showed that PC, PM, PDW and MPV level has been independent of thyroidectomy. We showed also that the rise of MPV levels has been independent from the etiology of thyroid disease. Previous reports have not clarified the direct effects of the thyroid gland to the platelet system without TSH, T3 and T4. Kiruchuk et al¹⁰ reported that the thyroid gland of healthy persons was shown to possess thromboplastin, antithrombin, anticoagulant, antiheparin and fibrinolytic properties and to contain plasminogen, plasminogen activators, antiplasmins. The function of the external hemocoagulation system was reduced due to diminished thromboplastin and antiheparin activity of the gland tissue, reduction of aggregation and increase of disaggregation properties of the gland tissue. Local fibrinolysis was enhanced in patients with diffuse toxic

goiter on account of increase in the thyroid gland of plasminogen activators, reduction of antiplasmin activity and increase of the nonenzymatic fibrinolysis activity. Debeij et al¹⁴ observed the effects of T4 and TSH levels on the coagulation system. Their findings show that changes in coagulation factors associated with thyroid functions are mainly mediated by T4 and not by TSH (increasing levels of FVIII, FIX, VWF and fibrinogen with rising levels of T4). Also Yango et al¹⁵ demonstrated that thyroid hormone deficiency is likely to be the main cause of coagulation disorders in hypothyroidism and high TSH levels in individuals with normal free thyroid hormones have no influence on hemostatic parameters. Our data support these two studies. We believe that platelet functions associated with thyroid functions are mainly mediated by T4 and T3, not by TSH or another way from thyroid gland.

Five English reports with small cohorts have evaluated the platelet parameters in the thyroid

Table I. Platelet and thyroid parameters.

Parameters	Group A (n = 52) mean ± SD	Group B (n = 21) mean ± SD	p value
Platelet counts (×10 ⁹ /l)	307 ± 54.2	319 ± 56.7	0.10
MPV (fl)	8.4 ± 1.3	7.9 ± 0.8	0.12
PDW	17.8 ± 1	17.6 ± 0.8	0.44
TSH (uIU/nL)	1.6 ± 0.4	1.9 ± 0.5	0.75
Free T3 (ng/dl)	2.6 ± 0.6	2.8 ± 0.6	0.18
Free T4 (ng/dl)	1.01 ± 0.26 (median, min-max)	0.96 ± 0.29 (median, min-max)	0.24
PM	2190.80, 134.20-4042.60	2256.75, 1013.70-5046.6	0.139

diseases. Erikci et al¹⁶, Coban et al¹⁷ and Yilmaz et al¹⁸ found that MPV levels increase in subclinical hypothyroidism. Yilmaz et al¹⁸ aimed in their study to compare MPV values of patients between in subclinic hypothyroid period and in euthyroid period after 12 weeks of levothyroxine replacement therapy. MPV values were decreased after subclinical hypothyroid patients became euthyroid. However, post-treatment MPV values were still higher ($p = 0.035$) in the patient group than in the control group. These results suggest that subjects with subclinical hypothyroidism may be susceptible for increased platelet activation and increased MPV values which contribute to increased risk of cardiovascular complications. Panzer et al¹⁹ reported platelet changes such as lower platelet counts and increased MPV in hyperthyroidism. Erem et al²⁰ investigated hemostatic parameters in 41 hyperthyroidic patients and compared them to 20 euthyroidic controls. They found that MPV was correlated with anti-thyroid peroxidase antibodies. The present study is the first, to our knowledge, to evaluate MPV in euthyroid thyroidectomy patients, showing that rise of MPV levels has been independent from etiology of thyroid disease.

According to our data, thyroidectomy in euthyroid female patients does not affect MPV values. Partial rise of platelet count in the surgery group may be associated of those people were older than the control group.

Conclusions

Thyroidectomy does not affect platelet activation in euthyroid subjects. Thus, increased atherothrombotic complications of thyroid disease can be considered to be independent from the underlying thyroid disease. This finding suggests that the association between thyroid diseases and MPV is dependent on the status of thyroid hormones.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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