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Research Article

Comparative Evaluation of Fibrinolytic System Parameters in Newly Diagnosed Polycythemia Vera and Essential Thrombocythemia Patients

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Abstract

Objectives: Thrombotic complications are major determinants of morbidity and mortality in polycythemia vera (PV) and essential thrombocythemia (ET), yet the role of fibrinolytic dysfunction remains unclear. This study evaluated tissue plasminogen activator (tPA), plasminogen activator inhibitor-1 (PAI-1), and thrombin-activatable fibrinolysis inhibitor (TAFI) in newly diagnosed patients with PV and ET.

Methods: In this prospective, single-center, comparative cross-sectional study, 46 newly diagnosed patients with myeloproliferative neoplasms, including 17 with PV and 29 with ET, and 36 healthy controls were included. Serum tPA, PAI-1, and TAFI levels were measured by enzyme-linked immunosorbent assay and compared between groups.

Results: Among the fibrinolytic parameters, tPA levels differed significantly between groups (p=0.015). Both patients with PV and those with ET had lower tPA levels than healthy controls. No significant differences were observed in PAI-1 or TAFI levels.

Conclusion: Newly diagnosed patients with PV and ET showed reduced tPA levels, suggesting impaired fibrinolytic activation. These findings support a possible contribution of hypofibrinolysis to the prothrombotic tendency of myeloproliferative neoplasms.

Keywords: Essential thrombocythemia, fibrinolytic system, polycythemia vera

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Myeloproliferative neoplasms (MPNs) occur when a multipotential stem cell undergoes neoplastic transformation. According to the World Health Organization (WHO), MPNs are classified as chronic myeloid leukemia (CML), polycythemia vera (PV), primary myelofibrosis, essential thrombocythemia (ET), and other less common entities.[1]

Hemostatic disorders are an important cause of mortality and morbidity in patients with PV and ET.[2] The percentage of patients with thrombosis varies from 40% to 60% in PV and ET. In addition to thrombosis, bleeding is also frequently seen in such diseases. Thrombosis can occur at the arterial, venous, or microcirculatory levels, and hemorrhage is

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predominantly mucocutaneous. The pathophysiological mechanisms of thrombosis and hemorrhage in MPNs are not fully understood.[3] It is known that factors such as being over 60 years old, hypertension, diabetes, and smoking increase the risk of thromboembolic events.[4] It has been shown that erythrocytosis and thrombocythemia contribute to the increased risk of thrombosis by increasing blood viscosity. It has also been shown that platelets have not only numerical but also structural defects in MPNs. Especially in patients with ET, changes in von Willebrand factor (vWF) and FVIII levels have been detected.[5]

The fibrinolytic system is a physiological stabilizing mechanism within the coagulation process. The most crucial activator of plasminogen, the main enzyme of the fibrinolytic system, is tissue plasminogen activator (tPA). The two most important enzymes that reduce fibrinolytic activity by acting on the plasminogen-plasmin system are thrombin-activated fibrinolytic inhibitor (TAFI) and plasminogen activator inhibitor type 1 (PAI-1)[2].

We aimed to comparatively evaluate the parameters of the fibrinolytic system, including tPA, PAI-1, and TAFI, in newly diagnosed patients with PV, ET, and healthy controls. Therefore, we aimed to find potential differences between patients with PV and those with ET through subgroup analyses. Since the pathogenesis of PV and ET is quite different, it was planned to evaluate these diseases separately.

Methods

Study Design and Patient Selection

Our study was conducted as a prospective, single-center, comparative cross-sectional study. The first group of patients was admitted to the Bakırköy Dr. Sadi Konuk Training and Research Hospital Hematology outpatient clinic between January and October 2015 and was newly diagnosed with PV and ET. The second group consisted of healthy volunteers without hematologic disease, serving as the control group. The patient and control groups were similar in terms of age and gender. Participants were 18–80 years old and diagnosed with PV and ET according to the WHO 2008 criteria. Patients who met the following criteria were excluded: 1) use of drugs that affect the coagulation and fibrinolytic system, 2) use of drugs that affect platelet functions, 3) history of arterial or venous thrombosis, 4) presence of heart failure, 5) presence of different hematological diseases, and 6) presence of active malignancy.

Before the study, informed consent was obtained from the volunteers in the patient and control groups. The study was performed in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. The protocol was approved by the Ethics Committee of Bakırköy Dr. Sadi Konuk Training and Research Hospital with decision number 2014/15/12, dated 10.11.2014.

Data Collection and Procedures

Demographic and clinical characteristics of eligible patients were collected. Hematological, biochemical, and hemostasis tests were performed and recorded. In addition, the presence of diabetes mellitus, hypertension, and dyslipidemia, which may increase thrombotic risk, was noted.

A total of 5 mL of blood was collected from the patient and control groups between 08:00 and 10:00 in the morning, after a 10–12-hour overnight fast, in a sitting position, into a vacuum gel tube. After the collected blood was kept at room temperature for about 30 minutes, it was centrifuged at 3000 rpm for 15 minutes, and the separated serum was stored at -80 °C until the day of analysis. Serum TAFI, tPA, and PAI-1 levels were analyzed by ELISA using YH Biosearch Laboratory, China, kits (Cat. Nos. YHB2957Hu, YHB3009Hu, and YHB2361Hu, respectively). The intra-assay CV values of the methods were 10%, and the inter-assay CV values were 12%.

PAI-1, TAFI, and tPA measurements were made using ELISA and biotin-labeled sandwich methods. After the serum samples were pipetted, the reaction was completed by incubation and washing steps, and the measurements were performed.

Statistical Analysis

The demographic features of the study population were stratified and recorded. SPSS version 23 (IBM Corp., Armonk, NY, USA) was used to analyze the patient groups' numerical data and generate statistics. Whether the distribution was normal was determined using the Kolmogorov-Smirnov test. The independent t-test was used to evaluate parameters with normal distribution, and the Mann-Whitney U test was used to evaluate parameters that did not show normal distribution. The ANOVA (Tukey) method was used to compare differences among the three normally distributed groups (PV, ET, and healthy controls), and the Kruskal-Wallis test was used to compare differences among the non-normally distributed groups. The chi-square test or Fisher's exact test was used to analyze categorical variables. A two-tailed p-value <0.05 was considered statistically significant.

Results

A total of 82 participants, 46 in the MPN group and 36 in the control group, were included. Among the MPN group, 17 (37%) patients were diagnosed with PV and 29 (63%) with ET. The clinical and laboratory findings of the participants are presented in Table 1. Parameters with abnormal distribution were described using the median, upper, and

Table 1. Clinical data of patients

Parameter (unit)	ET n=29	PV n=17	Control n=36	p
Age	53 (21- 81)	51 (26- 71)	52 (27-81)	0.395
Gender (F/M)	18/11	9/8	21/15	0.832
Hemogram Parameters				
WBC (mm^3)	9300 (3510- 15800)	8700 (5070-23100)	7700(5200-16850)	0.151
HGB (g/dl)	13.25±2.54	18.28±1.71	13.72±1.48	<0.01
HCT	39.6 (24.6-49.2)	52.8 (49.8-64.7)	41.3(23.5-48)	<0.001
PLT (mm^3)	748 (484-2092)	328 (176-2650)	252 (153-540)	<0.001
NEU	5490 (1680-10320)	5870 (3250-17700)	4327.5(2500-10000)	0.011
Biochemical & Lipid profiles				
LDH	248 (163-396)	218 (182-454)	190.5 (148-326)	<0.001
Erythropoietin	5.88 (1.6-48.5)	2.41 (0.76-16)	11.3 (1.89-30.7)	<0.001
Uric Acid	4.94±1.67	6.17±1.09	5.4±1.63	0.060
CRP	0.35 (0.02-9.2)	0.34 (0.07-1.4)	0.245 (0.05-1)	0.080
Vitamin B12	282 (100-1500)	258 (122-942)	301 (37-544)	0.666
Total Cholesterol	189.03±52.44	179.62±33.71	203.22±40.64	0.174
LDL	103 (41.6-208)	103 (24.6-160)	114 (63-255)	0.213
HDL	45.5 (13-76)	40.5 (29-55)	48 (28-97)	0.091
Triglyceride	129 (53-722)	167 (57-274)	133 (61-319)	0.088

Normal distribution parameters were presented as mean and standard deviation (X) ± (SD). Non-normal distributed parameters were presented as median values (M) and smallest (S). largest (L). (M)-(S-L). ET: Essential thrombocythemia; PV: Polycythemia vera; WBC: White blood cell; HGB: Hemoglobin; HCT: Hematocrit; PLT: Platelet count; NEU: Neutrophil count; LDH: Lactate dehydrogenase; CRP: C-reactive protein; LDL: Low-density lipoprotein; HDL: High-density lipoprotein.

lower values, and parameters with normal distribution were described using the mean and standard deviation values. Patient ages were similar across groups, and ET was more common in women.

Compared with the control group, hemoglobin was significantly higher in patients with PV, and the platelet count was significantly higher in patients with ET. Neutrophil counts and LDH values were higher in all patients with MPN compared with the healthy group. As expected, the erythropoietin (EPO) value was lower in the MPN group. These differences were statistically significant ($p<0.05$). Although the number of white blood cells was numerically higher in the MPN group, no statistical difference was observed. In addition, there was no significant difference between the groups in uric acid, C-reactive protein, and vitamin B12 values. Similarly, no difference was found in lipid profiles. However, in the subgroup analysis, high-density lipoprotein (HDL) values were found to be significantly lower in patients with PV compared with healthy subjects ($p=0.008$).

The evaluation and comparison of hemostasis parameters are summarized in Table 2. PT and aPTT durations were longer, and fibrinogen was lower in patients with MPN ($p<0.05$). There were no significant differences in factor VIII (FVIII), von Willebrand factor antigen (vWF), and ristocetin cofactor activity (vWF-Ris) values between the three groups.

In evaluating the fibrinolytic system, the tPA value was statistically significant among the three groups ($p=0.015$) (Table 2). tPA values were 10.261 (2.666–51.494) in the PV group, 9.517 (0.179–59.802) in the ET group, and 19.357 (6.125–67.1) in the control group. When the groups were evaluated separately, the PV and ET groups had lower values than the control group. The differences were statistically significant, respectively ($p=0.015$, $p=0.018$). The distributions of tPA levels are shown in Figure 1. However, there was no significant difference between the PAI-1 and TAFI values.

Discussion

In MPNs, thrombosis and hemorrhage are complications that are important in mortality and morbidity. In our study, tPA, the main activator of the fibrinolytic system, was significantly lower in MPNs compared with the control group. There was no significant difference in the other anti-fibrinolytic system parameters, PAI-1 and TAFI. When patients diagnosed with PV and ET were compared with a separate

Table 2. Comparison of hemostasis parameters

Parameter (Unit)	ET n=29	PV n=17	Control n=36	p
PT	12.5 (11.3-15.9)	12.9 (11.1-38.2)	11.9 (10.5-14.9)	0.02
aPTT	28.2 (21.5-39.6)	29.2 (23.2-43.5)	26.25 (21.4-29.8)	<0.001
Fibrinogen	266 (191-705)	229 (108-435)	292 (197-412)	0.043
FVIII	62.1 (20.7-164.1)	57.35 (11.6-112)	68.8 (19-210)	0.251
vWF	73.8 (17.4-294.7)	81.95 (15-172.5)	96.85 (18.3-229)	0.412
vWF Ris	57.6 (15-165.9)	61.25 (15-161.3)	73 (15-228)	0.200
PAI-1 (ng/ml)	15.762 (0.591-86.654)	11.348 (2.751-83.875)	18.7335 (3.674-93.812)	0.234
TAFI (%)	56.41 (15.262-558.166)	70.072 (10.831-532.181)	79.88 (7.647-611.961)	0.833
t-PA (ng/ml)	9.517 (0.179-59.802)	10.261 (2.666-51.494)	19.357 (6.125-67.1)	0.015

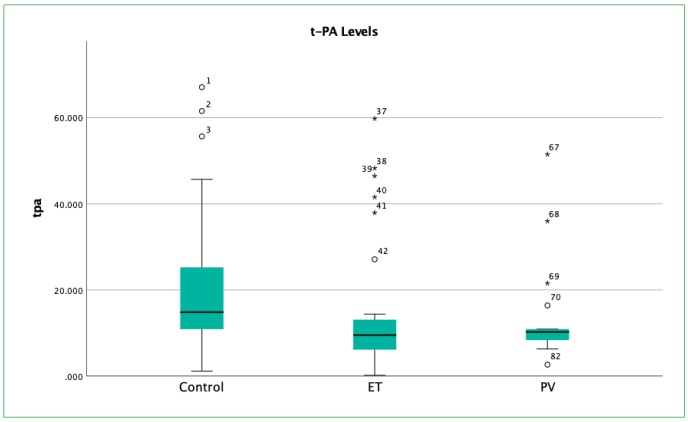

Figure 1. Distribution of tPA levels in ET, PV, and control groups.

control group and with each other, there was no difference in tPA levels among MPNs. Still, tPA levels were significantly decreased compared with the control group.

tPA is the primary activator of the fibrinolytic system; it converts inactive plasminogen to plasmin. PAI-1 limits fibrinolytic activity by inhibiting fibrinogen activators, including tPA and uPA. An increase in PAI-1 inhibits the fibrinolytic system, shifting the equilibrium toward procoagulation.[6] There are conflicting results regarding the fibrinolytic system in MPNs. In the study in which 20 patients diagnosed with ET were included by Bazzan et al.[7], similar to our study, tPA levels were lower in the healthy group compared with the patient group. Nevertheless, contrary to our study, PAI-1 values were significantly higher. As a result of the study, they stated that fibrinolytic imbalance might be a critical factor in thrombosis seen in patients with ET. However, in the study by Rosc et al.[8], in which tPA and PAI-1 values of 20 patients with CML, 17 with ET, and 5 with MF were compared with those of healthy volunteers, no significant difference was found in tPA levels. Nevertheless, in the subgroup analysis of this study, PAI-1 levels increased significantly in patients with ET compared with the control group. It has been suggested that the increase in PAI-1 levels may be due to vascular endothelial damage caused by proteolytic enzymes and cytokines secreted by leukocytes, especially neutrophils, and by granulocyte elastase, which are significantly increased in patients with MPN.[8]

In another study in which a total of 112 patients with MPN, including 63 with ET, 29 with PV, 11 with CML, and 9 with PMF, were included, tPA levels were higher in the MPN group, and statistically significant D-dimer elevation accompanied tPA elevation between the patient and control groups. It has been noted that elevated tPA and D-dimer levels in patients with MPN may be due to secondary activation in the fibrinolytic system. In addition, contrary to our study, PAI-1 levels of patients with ET and PV were higher than those in the control group. It has been suggested that the increase in PAI-1 may be due to increased production of activated platelets and vascular endothelial damage.[2] Similarly, PAI-1 levels of 19 patients with PV and 14 with ET were significantly increased compared with those of healthy volunteers in another study. There was a more significant increase in those with a history of thrombosis than in those who were asymptomatic or had a history of hemorrhage. They also found that PAI-1 levels correlated with platelet count in patients with PV and ET. They emphasized that fibrinolytic activity was significantly reduced in patients with MPN compared with the control group.[9]

TAFI activity has been shown to cause hypofibrinolysis.[10,11] However, our study observed no significant difference in TAFI activity between healthy controls and patients with MPN. Studies evaluating TAFI activity in patients with MPN are very few in the literature. In a study in which TAFI activity and susceptibility to thrombosis were measured in 21 patients diagnosed with ET and 21 healthy controls, TAFI was significantly higher in patients with ET. They emphasized that hypofibrinolysis, caused by increased TAFI activity, better explains the susceptibility to thrombosis in patients with ET.[12]

Our study has limitations. Although the study was designed as a prospective study, it was cross-sectional and lacked follow-up, so the relationships between fibrinolytic system parameters and thrombosis could not be determined. In 2015, the WHO 2008 criteria were still used to diagnose PV and ET. Since it was designed in 2015, patients were included according to the WHO 2008 criteria. However, since bone marrow biopsies were performed on all newly diagnosed patients, they also met the WHO 2016 criteria. Molecular tests such as CALR and MPL status are unknown, as they were not widely used at the time of data collection. The low number of patients has meant that the fibrinolytic system has not been evaluated in larger populations. The lack of standard measurements and cut-off values for tPA, PAI-1, and TAFI, which we evaluated in the study, is another limitation.

Conclusion

In conclusion, our study found that tPA levels, the main activator of the fibrinolytic system, were lower in patients with PV and ET than in the healthy control group. These results suggest that fibrinolytic system activity is reduced in patients with PV and ET. The number of studies on fibrinolytic system activity in patients with MPN is limited, and the studies are small in size. Although some studies are contrary to our results, the detection of a decrease in tPA and an increase in PAI-1 in most studies supports our finding that fibrinolytic system activity decreases in patients with PV and ET. We think that a decrease in fibrinolytic system parameters is a condition that predisposes to thrombosis.

Disclosures

Ethics Committee Approval: The protocol was approved by the Ethics Committee of Bakırköy Dr. Sadi Konuk Training and Research Hospital with decision number 2014/15/12, dated 10.11.2014.

Informed Consent: Written informed consent was obtained from all participants.

Conflict of Interest: The authors declare that they have no competing financial or non-financial interests.

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References

1. Barbui T, Thiele J, Gisslinger H, Kvasnicka HM, Vannucchi AM, Guglielmelli P, et al. The 2016 WHO classification and diagnostic criteria for myeloproliferative neoplasms: document summary and in-depth discussion. Blood Cancer J 2018;8(2):15. [CrossRef]
2. Gadomska G, Rość D, Stankowska K, Boinska J, Ruszkowska-Ciastek B, Wieczór R. Selected parameters of hemostasis in patients with myeloproliferative neoplasms. Blood Coagul Fibrinolysis 2014;25(5):464–70. [CrossRef]
3. Reeves BN, Beckman JD. Novel Pathophysiological Mechanisms of Thrombosis in Myeloproliferative Neoplasms. Curr Hematol Malig Rep 2021;16(3):304–13. [CrossRef]
4. Landolfi R, Di Gennaro L. Pathophysiology of thrombosis in myeloproliferative neoplasms. Haematologica 2011;96(2):183–6. [CrossRef]
5. Cervantes F, Arellano-Rodrigo E, Alvarez-Larrán A. Blood cell activation in myeloproliferative neoplasms. Haematologica 2009;94(11):1484–8. [CrossRef]
6. Medcalf RL. Fibrinolysis, inflammation, and regulation of the plasminogen activating system. J Thromb Haemost 2007;5(Suppl 1):132–42. [CrossRef]
7. Bazzan M, Tamponi G, Gallo E, Stella S, Schinco PC, Pannocchia A, Pileri A. Fibrinolytic imbalance in essential thrombocythemia: role of platelets. Haemostasis 1993;23(1):38–44. [CrossRef]
8. Rość D, Kremplewska-Nalezyta E, Gadomska G, Zastawna E, Michalski A, Drewniak W. Plasminogen activators (t-PA and u-PA) and plasminogen activators inhibitors (PAI-1 and PAI-2) in some myeloproliferative syndromes. Med Sci Monit 2000;6(4):684–91.
9. Cancelas JA, García-Avello A, García-Frade LJ. High plasma levels of plasminogen activator inhibitor 1 (PAI-1) in polycythemia vera and essential thrombocythemia are associated with thrombosis. Thromb Res 1994;75(5):513–20. [CrossRef]
10. Minnema MC, Friederich PW, Levi M, von dem Borne PA, Mosnier LO, Meijers JC, et al. Enhancement of rabbit jugular vein thrombolysis by neutralization of factor XI. In vivo evidence for a role of factor XI as an anti-fibrinolytic factor. J Clin Invest. 1998;101(1):10–4. [CrossRef]
11. van Tilburg NH, Rosendaal FR, Bertina RM. Thrombin-activatable fibrinolysis inhibitor and the risk for deep vein thrombosis. Blood 2000;95(9):2855-9. [CrossRef]
12. Kaftan O, Balcik OS, Cipil H, Ozet G, Bavbek N, Koşar A, et al . Plasma levels of thrombin-activatable fibrinolysis inhibitor in primary and secondary thrombocytosis. Clin Appl Thromb Hemost 2005;11(4):449–54. [CrossRef]