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Evaluation on Thrombotic Events Frequency in JAK2 V617F Positive Patients

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Abstract

The Polycythemia Vera is a myeloproliferative neoplasia whose overall incidence is 0.7-2.6 cases per 100.000 inhabitants/year; 92.3% of the patients were positive to the JAK2 V617F mutation (exon 14) and 7.7% were negative also to the mutations on the exon 12. Around 29.16% of the JAK2 V617F positive patients had arterial or venous thrombosis. The percentage of patients with the JAK2 V617F mutation and the frequency of thrombosis in PV JAK2 positive patients demonstrated in our study are according to the data presented in the literature.

Keywords: Polycythemia vera; JAK2 V617F; Thrombotic events

Introduction

The Polycythemia Vera (PV) is a myeloproliferative neoplasia which comes from a change in the multipotent hematopoietic stem cells that causes the accumulation of erythrocytes, leukocytes and morphologically normal platelets independent of erythropoietin. It can bring about leukocytosis, thrombocytosis, splenomegaly and an increased risk of thrombotic events. Around 95% of the patients diagnosed with PV have the JAK2 V617Fmutation [1]. Even in the absence of thrombotic events, the patients with a type of myeloproliferative neoplasia (MPN) present a hypercoagulable state which can be identified for an increasing in the concentration of several plasmatic markers on the system of haemostatic activation [2].

Besides this studies suggest that these patients with MPN who have the JAK2 V617Fmutation are exposed to an increasing risk of thrombotic complications possibly because of the increased platelet and the leukocyte activation [3].

Material and Methods

There were 31 patients with PV diagnoses were selected according to the established criteria by WHO (2008) between March and September, 2013. Considering this total number five patients refused to participate in the research. The project was approved by the Human Research Ethics Committee of University Hospital. The PCR-AE technique was performed according to standard conditions and the product of PCR was visualized on 2% Agarose gel [4]. On the negative samples to the presence of the JAK2 V617F mutation automatic sequencing was done with the aim of identifying possible changes in the exon 12 in the *JAK2* gene. All the DNA samples were genotyped for the JAK2 V617F mutation situated in exon 14. The mutations were determined by comparison with the normal JAK2 sequence (accession NM-004972) and with a normal control that was included in each run.

Results

Considering the 26 collected samples 24 (92.3%) were positive for the JAK2 V617F mutation and two (7.7%) were negative also for the mutations in exon 12. The automatic sequencing of these samples did not reveal alteration. The negative patients for the mutations in exons 14 and 12 did not present different clinical signs from the other ones and also did not have a history of thrombotic events between the patients identified as JAK2 V617F positive; 7 of them (29.16%) presented thrombosis history. All the patients with thrombosis were positive to the JAK2 V617F mutation.

Discussion

The frequency of thrombosis in patients with PV varies from 19% to 39% as we can see in Table 1. With this data, we emphasize the role of the research about this mutation on the investigation about the causes of thrombotic events especially in unusual site highlighting the MPN as a cause of thrombophilia. This probably occurs due to correlation of the mutation presence and the increase of platelets and leukocytes and with the hypercoagulable state [3].

Publications	Patients with PV	Occurrence of thrombotic events (%)	Arterial Thrombosis (%)	Venous Thrombosis (%)
Passamonti et al.	163	34%	64%	36%
Barbui and Finazzi	1638	38.60%	75%	25%

Passamonti et al.	70	24.30%	70.60%	29.40%
Marchiolli	1638	38.60%	-	-
Coucelo et al.	31	39%	75%	25%
Alvarez-Larrán et al.	163	23%	-	-
Edahiro et al.	66	19%	-	-

Table 1: Scientific data about the relation between the number of patients with PV and the occurrence of thrombotic events associated with the disease.

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