PLASMA β-THROMBOGLOBULIN AND PLATELET FACTOR 4 LEVELS IN ESSENTIAL HYPERTENSION

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Abstract

To affect an increased platelet activation is nowadays an attractive therapeutic objective in the treatment of arterial hypertension with an aim to stop the progression of atherosclerotic process, enable its regression and prevent a rise of secondary complications of hypertension.

In the article, we evaluate a relevance of platelet function measurement using platelet markers in patients with essential hypertension (EH). The β-thromboglobulin (BTG) plasma level was significantly increased in patients with EH. BTG level was increasing according to the EH stage. Also other factors can participate in the increased plasma BTG level in patients with EH, e.g. impaired BTG elimination in patients with renal dysfunction. The increased level of platelet factor 4 (PF4) in relation to the stage of hypertension was less expressed. A considerable elevation of the PF4 plasma level was detected only in patients with EH stage III. On the basis of these results, we can assume an increased platelet activation in patients with EH. The effect of essential hypertension on the platelet activation can be evaluated by measuring the increased release of both BTG and PF4 from platelet a granules.

Key words: Essential hypertension (EH), platelet markers, β-thromboglobulin (BTG), platelet factor 4 (PF4)

INTRODUCTION

Cardiovascular diseases are currently one of the most serious health care problems, since they participate in a great extent in a temporary and permanent invalidity and overall mortality as well (1). High blood pressure plays an important role in pathogenesis of vascular cerebral episodes and contributes to the complications of ischemic heart disease (2). Nowadays, it is well known that the majority of cardiovascular diseases is connected with an increased platelet activity (3, 4, 5).

Platelet markers are molecules, mostly proteins, that are released into the circulation during platelet activation and they belong to the so called molecular markers of hemostasis. They are detected by enzyme-linked immunoassay (ELISA). Introduction of the molecular markers of hemostasis among examination methods represents an important progress in the knowledge of physiology and pathophysiology of hemostasis. At the same time, it enables to evaluate the activation of platelets in different diseases (6, 7).

In our article we evaluate the activity of platelets using the platelet markers in patients with arterial hypertension. The objective is to point out their diagnostic significance and bring an interpretation of the results toward to the clinical practice.

MATERIAL AND METHODS

Venous blood samples were drawn in resting and fasting conditions into DIATUBE H, containing 0.109 M solution of sodium citrate, citric acid and mixture of platelet aggregation

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inhibitors (dipyridamol, adenosine, theophylline). The samples were centrifuged (5 minutes at 3000 G) and tested immediately or stored at -70°C until assayed. All platelet markers were measured by ELISA using commercial kits (Asserachrom, Asnieres, Diagnostica Stago). All study activities performed were in consistency with ethical norms and Helsinki Declaration (1975, revision 1983).

Statistical analysis: Medians and the 25th and 75th percentiles were calculated for all the measurements in each group. The non-parametric Mann-Whitney test was used for comparisons between the two groups. Analysis of variance (ANOVA) was used to compare more than two groups of data. Significance was defined as p<0.05.

RESULTS

Tab. 1. Platelet markers in controls and patients with essential hypertension

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet markers (BTG, PF4) in a control group of healthy individuals</td>
<td></td>
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<tr>
<td><strong>BTG (ng/ml)</strong></td>
<td>20</td>
<td>37.6</td>
<td>(28.3-49.5)</td>
</tr>
<tr>
<td><strong>PF4 (ng/ml)</strong></td>
<td>20</td>
<td>4.5</td>
<td>(3.2-6.3)</td>
</tr>
</tbody>
</table>

Platelet markers (BTG a PF4) in patients with EH WHO I.

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Median</th>
<th>Range</th>
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</thead>
<tbody>
<tr>
<td><strong>BTG (ng/ml)</strong></td>
<td>20</td>
<td>83.4</td>
<td>(31.2-139.0)</td>
</tr>
<tr>
<td><strong>PF4 (ng/ml)</strong></td>
<td>20</td>
<td>29.3</td>
<td>(8.7-51.8)</td>
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</tbody>
</table>

Platelet markers (BTG a PF4) in patients with EH WHO II.

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BTG (ng/ml)</strong></td>
<td>29</td>
<td>101.8</td>
<td>(60.2-143.6)</td>
</tr>
<tr>
<td><strong>PF4 (ng/ml)</strong></td>
<td>29</td>
<td>41.5</td>
<td>(17.3-95.1)</td>
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Platelet markers (BTG a PF4) in patients with EH WHO III.

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<tr>
<th></th>
<th>N</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BTG (ng/ml)</strong></td>
<td>51</td>
<td>157.2</td>
<td>(91.4-223.8)</td>
</tr>
<tr>
<td><strong>PF4 (ng/ml)</strong></td>
<td>51</td>
<td>84.0</td>
<td>(26.8-172.6)</td>
</tr>
</tbody>
</table>

Abbreviations: N – number of patients, BTG – β (beta) thromboglobulin, PF4 – platelet factor 4; Range = values between 25th and 75th percentiles

Notes: Analysis of the platelet markers values (BTG a PF4) in patients with EH WHO I, II, III and in a control group of healthy individuals:

1. Significantly increased BTG values in patients with EH WHO I compared to a control group (p < 0.05).
2. Significantly increased BTG level in patients with EH WHO II compared to a control group (p < 0.01).
3. Significantly increased BTG values in patients with EH WHO III EH compared to WHO II patients (p < 0.01), also compared to EH WHO I patients (p < 0.005) and mainly in comparison with a control group (p < 0.00001).
4. Significantly increased PF4 values in patients with EH WHO III compared to EH WHO I patients (p < 0.05) and in comparison with a control group (p < 0.001).
DISCUSSION

Platelet activity is a result of stimulation and inhibition by active substances, occurring in blood circulation or produced locally by a vascular endothelium (8, 9, 10).

In the last 20 years were gathered many pieces of information that point to the key role of platelets in the origine and development of atherosclerosis (3, 7). This is the reason for our present increased interest in platelet dysfunction as one of the possible causes of cardiovascular morbidity in hypertensive individuals.

BTG and PF4 are proteins of platelet a granules, released into the surroundings during the platelet activation. BTG and PF4 plasma levels measurement is hence a suitable indicator of the platelet activity assessment in vivo. BTG together with PF4 are considered as the most specific markers of an intravascular activation and release reaction of platelets (3, 9, 11).

Increased BTG and PF4 levels in hypertensives depend on the stage of hypertension (12). Elevated platelet activity can be related to an increased sympathoadrenal activity. It is possible that the sympathetic nervous system activation in hyperadrenergic hypertensive individuals results in high levels of endogenous catecholamines and may lead to the increased platelet activation and more profound release reaction (12). Elevated activation of platelets already in early stages of hypertension was sustained by several authors (5, 12, 13).

The above mentioned facts were also confirmed by the results of examined levels of the platelet markers in our patient groups. We proved increased BTG levels in all groups of patients with EH, classified according to WHO into patients with EH WHO I, II, III. The elevation of BTG levels was closely related to the stage of hypertension. BTG level increased simultaneously with an increasing stage of hypertension. Differences in PF4 levels in patients with essential hypertension were less expressed. We detected a considerable increase of PF4 levels only in patients with essential hypertension WHO III.

REFERENCES