Whole blood viscosity assessment in arterial hypertension: a mathematical approach

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Abstract

Three mathematical models for calculation of whole blood viscosity (\textit{WBV}) based on data for hematocrit (\textit{Hct}), plasma viscosity (\textit{PV}) or alternatively total plasma protein (\textit{TP}) were tested for healthy subjects and drafts with different forms of hypertension. The equation of J. P. A. Weaver and coauthors was found to give the best statistical significance in observing alterations in \textit{WBV} at particular shear rate (208 s\textsuperscript{-1}) from patient with arterial hypertension of all types studied, including the most common type of hypertension – the essential hypertension.

The mathematical approach is an alternative to the expensive and arduous experimental estimation of \textit{WBV} recommended worldwide as very important in evaluation of the total peripheral resistance of the ongoing systemic atherosclerosis in arterial hypertension.

Keywords: Arterial hypertension, whole blood viscosity, mathematical approach, expedient alternative

1. Introduction

Communications on hypertension exist since more than two centuries. Most studies have focused on cardiac and/or vascular factors. Increasing interest in the association between hemorheological parameters and hypertension occurs just in the last three decades [3, 4]. The hemodynamic role of whole blood viscosity (\textit{WBV}) in determining the total peripheral resistance is the incentive to studying the possible relation between \textit{WBV} and hypertension [2, 7, 10]. Unfortunately the expensive \textit{in vitro} measurement techniques for \textit{WBV} set limitations in their use. Epidemiological hemorheological investigations surmount these hurdles by mathematical models describing the relations of hematocrit (\textit{Hct}) and plasma viscosity (\textit{PV}) or its substitute - the total plasma protein concentration (\textit{TP}) to \textit{WBV} validated by comparison with direct viscosity measurements [6, 9, 10].

The aim of the study was to test three mathematical models in calculations of \textit{WBV} at high shear rate (208 s\textsuperscript{-1}) for healthy subjects and patient drafts with different forms of arterial hypertension (AH): J. P. A. Weaver and coauthors (\textit{WBV}_{\text{W}}) [12], G. de Simone and coauthors (\textit{WBV}_{\text{S}}) [9, 10], and N. Kametas and coauthors (\textit{WBV}_{\text{k}}) [6]. The objective of the study design is the achievement of statistically significant changes of the \textit{WBV} values in AH compared with those of healthy subjects.

2. Methods

Recruitment with assessment of the cardiovascular system (standardized questionnaire and blood pressure (BP) measurement) and other mandatory clinical performances were accomplished for healthy subjects (HS, male - n=16 and female - n=53), healthy pregnant women (HP, - n=53) and pregnant women with preeclampsia (PP, - n=40), symptomatic hypertension (SH, male - n=10 and non-pregnant female -
n=26) as well as essential hypertension (EH, male - n=8 and non-pregnant female - n=21). Blood collection, the PV-test and Hct measurements were done after ICSH [5]. Hct was determined by centrifugation. Hematological indices (erythrocyte count (EC), hemoglobin (Hb)) and TP were measured by routine clinical laboratory tests in auto analyzers.

Whole blood viscosity was calculated in mPa.s at a shear rate 208 s⁻¹ using the equations:

1. \[ \log WBV_w = \log WBV_0 + k \times Hct(\%) \] (J. P. A. Weaver and coauthors),
where \( \log WBV_0 \) is the intercept when \( Hct \rightarrow 0 \) and \( k = 0.03 - 0.0076 \times \log \gamma \), i.e. \( k \) introduces the shear rate (\( \gamma \)) dependence;

2. \[ WBV_s = 0.12 \times Hct(\%) + 0.17 \times TP(g/dL) - 2.07 \] (G. de Simone and coauthors);

3. \[ WBV_K = PV \left( \frac{4.7}{1.34} \right)^{\frac{Hct}{45}} \] (N. Kametas and coauthors),
where 4.7 and 1.34 are respectively the mean values of WBV and the PV in mPa.s for healthy subjects with mean Hct of 45% and likewise is the Hct-unit for the patient’s value. All calculations are made for 37°C.

All acquired data were processed by statistical comparison (t-test) and regression analyses. As a nominal level of significance the value 0.05 was chosen.

3. Results

A significant increase of Hct in PP vs. HP was found as plausible suggestion for likelihood of increased blood viscosity in an evolution of hypertension during pregnancy [11]. A real salient plethora show the hematological indices (erythrocyte count, hematocrit and hemoglobin) of EH (Table 1).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Hematological indices</th>
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<tbody>
<tr>
<td>Index</td>
<td>HS (♀, ♂)</td>
</tr>
<tr>
<td>EC (10¹²/l)</td>
<td>4.4 ± 0.4, 5.1 ± 0.3</td>
</tr>
<tr>
<td>Hct (l/l)</td>
<td>0.408 ± 0.02, 0.446 ± 0.03</td>
</tr>
<tr>
<td>Hb (g/l)</td>
<td>131.3 ± 12, 152.6 ± 8.7</td>
</tr>
</tbody>
</table>

Data are presented as: Mean value ± SD. Indices: EC - erythrocyte count; Hct - Hematocrit, Hb - Hemoglobin. *:P<0.05, **:P<0.01, ***:P<0.001- level of significance vs. HS.

The calculated \( WBV \) by the equation of J. P.A. Weaver and coauthors are close to the reference values for normal adults obtained by measurements [1, 2, 6, 7, 9] and/or calculated by the other equations of G. de Simone and coauthors, N. Kametas and coauthors (Table 2). The equation of J. P. A. Weaver shows best discriminative ability of disease because it indicates significant changes of \( WBV \) in all forms of hypertension compared with HS (Table 2). The equation of J. P. A. Weaver was found to be best fit for \( WBV \) calculations at particular shear rate (Table 3). The comparison of \( WBV \) in AH in relation to the values of HS at native Hct
demonstrates that: it is decreased for HP ($P<0.0001$), PP ($P<0.05$) and SH ($P=0.05$) and increased for EH ($P<0.01$).

### Table 2

Whole blood viscosity in different forms of hypertension calculated after JPA Weaver and coauthors ($WBV_w$), G. de Simone and coauthors ($WBV_s$) and H. Kametas and coauthors ($WBV_k$) ($\gamma = 208$ s$^{-1}$ at 37$^\circ$C).

<table>
<thead>
<tr>
<th></th>
<th>HS</th>
<th>HP</th>
<th>PP</th>
<th>SH</th>
<th>EH</th>
</tr>
</thead>
<tbody>
<tr>
<td>$WBV_w$</td>
<td>♀</td>
<td>4.08±0.4</td>
<td>3.56±0.4</td>
<td>3.79±0.6$^*$</td>
<td>3.78±0.71$^{*\text{ns}}$</td>
</tr>
<tr>
<td></td>
<td>♂</td>
<td>4.52±0.59</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$WBV_s$</td>
<td>♀</td>
<td>4.11±0.31</td>
<td>3.46±0.33</td>
<td>3.44±0.54$^{*\text{ns}}$</td>
<td>3.56±0.74$^{*\text{ns}}$</td>
</tr>
<tr>
<td></td>
<td>♂</td>
<td>4.54±0.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$WBV_k$</td>
<td>♀</td>
<td>4.29±0.58</td>
<td>3.62±0.5</td>
<td>3.95±0.84</td>
<td>3.92±0.87</td>
</tr>
<tr>
<td></td>
<td>♂</td>
<td>4.87±0.84</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Values are expressed as means ± SD.

$^*P<0.05$, $^{*\text{ns}}P=0.05$- level of significance vs. HS.

The same comparison for $WBV$ in men demonstrates that: it is decreased for SH ($P<0.01$) and increased for EH ($P<0.01$). The $WBV$ corrected for 45% Hct is significantly elevated only for EH ($P<0.001$). This is associated with elevated $PV$ ($P<0.001$) as represented in Table 3.

### Table 3

Whole blood viscosity and plasma viscosity in different forms of hypertension

<table>
<thead>
<tr>
<th></th>
<th>HS</th>
<th>HP</th>
<th>PP</th>
<th>SH</th>
<th>EH</th>
</tr>
</thead>
<tbody>
<tr>
<td>$WBV$</td>
<td>♀</td>
<td>4.08±0.4</td>
<td>3.56±0.4$^{*\text{ns}}$</td>
<td>3.79±0.6$^{*\text{ns}}$</td>
<td>3.78±0.71$^{*\text{ns}}$</td>
</tr>
<tr>
<td></td>
<td>♂</td>
<td>4.52±0.59</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$WBV_{Hct}$</td>
<td>♀ and ♂</td>
<td>4.57±0.26</td>
<td>4.52±0.28</td>
<td>4.63±0.28$^{*\text{ns}}$</td>
<td>4.58±0.46</td>
</tr>
<tr>
<td>$PV$</td>
<td>♀ and ♂</td>
<td>1.266±0.07</td>
<td>1.252±0.08</td>
<td>1.285±0.08$^{*\text{ns}}$</td>
<td>1.27±0.13</td>
</tr>
<tr>
<td>$WBV_{rel}$</td>
<td>♀ and ♂</td>
<td>3.61</td>
<td>3.61</td>
<td>3.6</td>
<td>3.6</td>
</tr>
</tbody>
</table>

$WBV_{Hct}$: whole blood viscosity corrected for Hct = 45%; $WBV_{rel} = WBV_{Hct}/PV$.

$^*P<0.05$, $^{*\text{ns}}P=0.05$- level of significance vs. HS.

4. Discussion

Our attempt at applying mathematical approach in order to assess the $WBV$ in arterial hypertension is successful for many reasons. We were able to detect a statistically significant increase of $WBV$ in EH - the most common type of hypertension. This result is in difference to data obtained from Devereux and coauthors [2]. Our finding is accompanied with statistically significant elevation of Hct and $PV$ in EH, which was also found by T. Linde and coauthors [7] but it was not explored in the before mentioned study [2]. Hematocrit
and plasma viscosity are two of the major factors determining whole blood viscosity therefore our observations are not surprising. They may serve as explanation for the obtained results, especially having in mind, that these two parameters are the basis for the calculation of the whole blood viscosity. The mathematical approach for easier assessment of WBV offers many perspectives in further extension of EH studies especially for the possible influence of enhanced erythrocyte aggregation [10] and impaired erythrocyte deformability [8].

By virtue of our presented results it is not entirely unjustified in saying that the mathematical approach of WBV seems appropriate to arterial hypertension research. Reliable conclusions would be possible after a proper extended patient excerpt. Most important for successful future investigations stays the problem with workable draft design of patients for certain race population-based differences and/or burdensome hypertension with metabolic syndrome constellations including abnormalities of lipid metabolism, obesity, impaired glucose tolerance [10, 13].

References