Technical Article

Whole blood viscosity extrapolation formula: Note on appropriateness of units

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Abstract

Background: A series has recently been done on whole blood viscosity. The first on the series proposed extrapolation chart with conventional reference range. Since the publication, two concerns have been received in personal communications. The first expressed concern over the use of serum proteins values in 'g/L' instead of 'g/dL' that was contained in the referenced material. The second enquired on suitability of the formula for determination of blood viscosity at low shear rate. **Aim**: This work sets out to compare different units-converted-modifications of the extrapolation with a view to develop a statement of comparison and suitability of units. **Materials and Methods**: The values of haematocrit and serum proteins were used in different unit-conversions on the mathematical formula to derive four modifications, which were compared. Five clinical cases that were specifically tested for whole blood viscosity, and had results for haematocrit and serum proteins were evaluated. The appropriateness of modifications for determination of viscosity at low shear rate was reviewed. **Results**: Except as modified and used in the series, determination of whole blood viscosity at low shear rate using other unit conversions on the formula yields negative values for all five cases. **Conclusion**: Given that it is unexpected for blood viscosity level to be zero let alone less, it is logical that negative values are invalid. A formula that gives the least invalid results may be most appropriate. Therefore, extrapolation modification used in the series is most appropriate.

Keywords: Blood viscosity at low shear rate, conversion of units, invalid levels.

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Introduction

Whole blood viscosity (WBV) Issue no. 1 proposed an extrapolation chart [1], which was based on a referenced mathematical formula [2]. Since the publication, two comments or concerns have been received in personal communications. The first was on the units (Proteins g/L; HCT %) used in developing the proposed chart. The colleague expressed concern that the working of the reference range had used the value of serum proteins in 'g/L'[1], while the reference articled indicated 'g/dL'[2]. A second person emailed to express delight on the work, and enquired whether the formula has been reviewed for suitability to determine WBV at low shear rate.

In response to the two concerns, this work sets out to compare the outcomes of using different units-converted-modifications of the extrapolation and their suitability for determination of WBV at high and low shear rate. It is known that low WBV, which is anaemia related, complicates low shear rate and constitutes part of abnormalities that are associated with decreased vasodilating response to endothelial mechanical stimulation [3]. Changes in WBV are measured at high and low shear rates and there has been interest in determining percentage increase in both, especially after haemodialysis [4]. Therefore, it would be logical that any formula that provides the values of WBV at both high and low shear rates, regardless of anaemia is appropriate.

The primary intension here is not to modify the formula

per se. The objective is to develop a position statement regarding the combination of units of haematocrit and serum proteins that are most appropriate to be employed on the mathematical extrapolation formula. To our knowledge, the actual fractional contribution of haematocrit or serum proteins to WBV by this extrapolation method has yet to be reviewed. It may provide additional basis to discern a most appropriate combination of units for the formula.

Materials and Methods

This work is part of a Translational Biomedical Science Research initiative. It was supported materially by the Albury South West Pathology – a unit of Western Pathology Cluster of NSW Health Australia. Ten years of de-identified archived clinical pathology data for the period of January 1999 to December 2008 constitute the research database. In a 10-year period, the Pathology referred only ten cases for WBV determination, of which five cases that were selected for this evaluation. Selection criteria are as recently published [5].

The pair of haematocrit (HCT) and serum total protein (TP) values was used in various units to derive four units-converted-extrapolations of the same formulae for:

High shear rate: WBV (208 Sec^{-1}) = (0.12 x HCT) + 0.17(TP – 2.07)

Low shear rate: WBV (0.5 Sec^{-1}) = (1.89 x HCT) + 3.76(TP – 78.42)

- Extrapolation 1: According to the units employed in developing the chart, which converted the units for serum total protein only:
  Where HCT = haematocrit (%) and TP = Serum total proteins (g/L)
- Extrapolation 2: based on units (TP g/dL; HCT %) in referenced material [2].
- Extrapolation 3: based on 'Prot g/dL' and 'HCT fraction'. That is, both units of HCT and TP from the referenced formula were converted.
- Extrapolation 4: WBV 208 Sec^{1} based on 'Prot g/L' and 'HCT fraction'. That is, only the HCT has been modified.

The fractional contribution of haematocrit or serum proteins to WBV were worked out, in percentages, according to the following formulae

- Haematocrit (HCT %) contribution = (0.12 x HCT)/((0.12 x HCT) + 0.17(Prot – 2.07))
- Protein (TP %) contribution = 0.17(Prot – 2.07)/((0.12 x HCT) + 0.17(Prot – 2.07))

Results

The outcomes of the modifications for WBV at high shear rate are presented (Table 1).

Table 1 Numeric values of results from all 4-modifications for all cases

	HCT*	TP*	WBV ext-1	WBV ext-2	WBV ext-3	WBV ext-4
Case 1	0.29	99	19.96	4.81	1.37	16.51
Case 2	0.47	70	17.07	6.36	0.89	11.60
Case 3	0.41	76	17.48	5.85	0.99	12.62
Case 4	0.41	63	15.40	5.76	0.77	10.41
Case 5	0.44	62	15.42	5.93	0.75	10.24

*Reported diagnostic result, HCT: haematocrit, TP: serum total protein, WBV: whole blood viscosity level (CPs) at high shear rate (208 Sec^{-1}), ext: extrapolation formula, 1: based on units (TP g/L; HCT %) – converted TP only, as used in the series; 2: based on units (TP g/dL; HCT %) used in referenced paper, 3: based on units (TP g/dL; HCT fraction) - converted HCT only, 4: based on units (TP g/L; HCT fraction) - converted both units.

Figure 1 shows the differences in fractional or percentage contribution of haematocrit and serum proteins to the WBV value due to the different four units-converted-extrapolations.

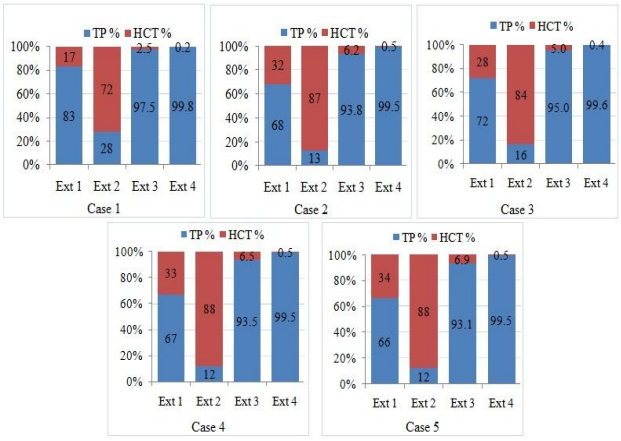

Fig. 1 Disparity in contributions of HCT and TP to WBV in different units-converted-extrapolations. HCT: haematocrit, TP: serum total protein, WBV: whole blood viscosity level (CPs) at high shear rate (208 Sec^{-1}), Ext 1: extrapolation formula 1, Ext 2: extrapolation formula 2, Ext 3: extrapolation formula 3, and Ext 4: extrapolation formula 4.

Table 2 Results from Extrapolations 1 – 4 for WBV at low shear rate (0.5 Sec^{-1})

	Ext-1	Ext-2	Ext-3	Ext-4
Case 1	132.19	-202.83	-257.09	77.93
Case 2	55.28	-181.60	-267.67	-30.79
Case 3	68.20	-188.98	-265.51	-8.33
Case 4	21.40	-191.79	-270.38	-57.19
Case 5	20.66	-189.14	-270.72	-60.92

WBV: whole blood viscosity, Ext: extrapolation formula, 1: based on units (TP g/L; HCT %) – converted TP only, as used in the series, 2: based on units (TP g/dL; HCT %) used in referenced paper, 3: based on units (TP g/dL; HCT fraction) - converted HCT only, and 4: based on units (TP g/L; HCT fraction) - converted both units.

Determination of WBV at low shear rate (0.5 Sec^{-1}) using the formula to derive four units-converted-extrapolations yielded negative values, except in 'extrapolation 1' modification (Table 2).

Discussion

In comparing the outcomes of the different units-converted-modifications of the extrapolation formula, attempt has been made to consider the impact of haematocrit and serum proteins to the WBV value. On one hand, it is determined that extrapolation 2 model attributes more to haematocrit than serum proteins. For instance, in Case 1 who has anaemia and hyperproteinaemia (Table 1), serum total proteins have contributed less than 30% to hyperviscosity (Fig. 1). In our opinion, this is not in agreement with current scientific understanding, whereby the impact of total proteins to viscosity in certain diseases associated with hyperproteinaemia underpins the concept of assessing plasma viscosity in place of WBV.

On the other hand, it is determined that extrapolations 3 modification attribute only about 5% effect to haematocrit in WBV of a healthy individual who has HCT at the upper normal range; and much less by 'ext-4' modification. This raises concern on the 'hyperviscosity versus polycythemia' theory. That is, a question of *where is the essence of managing or monitoring polycythemia with WBV measurement if the impact of haematocrit is ignorable?* It also raises the question of potential difference in reference values based on gender differences in haematocrit. This is an issue that has actually being deliberated for more than four decades [6-8]. In our opinion, attribution of insignificant contribution to haematocrit tantamount to no gender differences, and contradicts its inclusion in the formula. Therefore, we submit that the combination of units employed on extrapolation 'ext-1' as used in developing the chart is most appropriate.

From the comparison of different units-converted-modifications of the extrapolation formula for the assessment of WBV at low shear rate (Table 2), it is observed that the contribution by haematocrit is grossly infinitesimal, while that of total proteins default to 'negative' at any value below 78.42 g/L. In our opinion, this is unthinkable; especially as it would mean that only people with hyperproteinaemia have measurable blood viscosity. Tamariz et al. might have missed this observation since they excluded extreme haematocrit and total protein values in their study protocol [2]. Indeed, assuming normoproteinaemia, blood viscosity level may not be zero even when the haemoglobin concentration is very low [9].

Perhaps at this juncture, it is pertinent to acknowledge the notion of a critical haematocrit level below which measurement of whole blood viscosity may be invalid [6]. That is, WBV may be too low to be measureable or valid for man or woman who has concomitant anaemia and hypoproteinaemia. The cases reviewed in this study do not include any concomitant anaemia and hypoproteinaemia to enable such observation (Table 1). Nevertheless, results in Table 2 does show that only by extrapolation 1 modification can WBV at low shear rate be determined. This observation supports the preceding discuss to suffice that using 'haematocrit (%) and Serum total proteins (g/L)' is most appropriate in the formula.

Conclusion

The summary 'comparative statement' is that extrapolation formula using units of haematocrit in [%] and serum total proteins in [g/L] is most appropriate. Use of other units may render the method not able to assess WBV at low shear rates or at protein levels below 78 g/L.

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