Technical Article

Whole blood viscosity issue VIII: Comparison of extrapolation method with diagnostic digital viscometer

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Abstract

Background: The first issue of this series proposed extrapolation chart with conventional reference range and suggested comparison of results with other methods. **Aim**: This work sets out to compare interpretative results from the extrapolation method with those from a digital viscometer method. **Materials and Methods**: Five cases in our archived clinical pathology database that were specifically tested for whole blood viscosity by the digital method, and had results for haematocrit and serum proteins were pooled. The values of haematocrit and serum proteins were used to derive extrapolated values. The interpretative results of the extrapolation method were compared with those of digital viscometer-based clinical reports. Non-Newtonian fluids such as whole blood have different viscosities at different shear rates. Comparative statement can only be based on interpreted outcome. **Results**: Two-fifth absolute concordance and one-fifth discordance is observed between extrapolation and viscometer-based clinical reports. The discordance is a case of hyperviscosity in the presence of neither hyperproteinaemia nor polycythemia. **Conclusion**: The extrapolation method may underestimate whole blood viscosity in some patients when compared with digital viscometer, which in turn may suggest hyperviscosity that cannot be explained by hyperproteinaemia or polycythemia concepts. The impact of oxidative stress is highlighted.

Keywords: Digital viscometer, extrapolation chart, whole blood viscosity.

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Introduction

Whole blood viscosity (WBV) issue no. 1 on this series proposed an extrapolation chart with reference ranges [1], based on a validated mathematical formula [2]; and upon which issues No. 2-7 were developed. Given that different analytical methods have different reference values and buoyed by the fact that whole blood is a non-Newtonian fluid, which has different viscosities at different shear rates, it was recommended to investigate how the proposed reference ranges compare with the reference ranges of other blood viscosity methods [1].

Several methods exist for the assessment of WBV, but not every pathology unit has equipment for any of the diverse methods. The implication is that not many clinicians are able to assess WBV when they want to. Among the many different methods for the assessment of WBV is Brookfield's digital viscometer (Model LVDV-I+), which is being used at the Royal Prince Alfred hospital. The objective of this study is to review archived pathology case reports of WBV in order to determine level of concordance and/or discordance in interpretative abnormal or normal result between the extrapolation and Brookfield viscometer methods.

Materials and Methods

This study is part of the ongoing WBV series. In a 10-year period of January 1999 to December 2008, Albury South West Pathology has referred only ten cases to the Royal Prince Alfred hospital laboratory at Sydney, of which five cases were selected for this comparative evaluation. Among the excluded five cases: four do not have complete

data (haematocrit (HCT) and/or serum total proteins (TP)) to enable mathematical extrapolation method, while one was reported as 'insufficient sample' for WBV assessment.

The pair of haematocrit and serum protein values was used to extrapolate level of WBV at high shear stress (208 Sec^{-1}) as per the 'WBV Issue no. 1' on this series[1], according to the following formula:

WBV (208 Sec^{-1}) = 0.12 x HCT + 0.17(Prot – 2.07)
Where HCT = haematocrit (%) and Prot = Serum total proteins (g/L)

It was previously advised that the suggested reference range (15.01–19.01 centipoises (CPs) for the extrapolation method is based on conventional reference range for haematocrit 37–54%, and serum total protein 60–78g/L; stressing that the concept of individualized reference may need to be employed [1, 3]. Therefore, for the purpose of this case review, Albury's South West Pathology reference range for haematocrit being 0.36–0.49 for men and 0.32–0.46 for women, as well as serum total protein being 60–80 g/L for both men and women, were used to determine confidence intervals and laboratory specific reference range for females and males.

Enquiry into the shear rate and viscometer used at Royal Prince Alfred indicated that WBV was determined by the Brookfield viscometer (Model LVDV-I+) method at 12rpm, and reference range given as 'Normal 7.0–10.0 CPs'. In order to determine whether the extrapolation method at shear rate of '208 sec^{1}' can produce results with interpretations comparable with those from Brookfield digital method, the diagnostic results were then put side-by-side with their corresponding extrapolation results (Table 1). The review for concordance or discordance was then performed on the basis of interpretation outcomes of (i) laboratory specific reference range for extrapolation method vs. (ii) reference range of 7-10cP for reported result.

Results

The results from extrapolated and *in vitro diagnostic use* digital method for the five cases are indicated in the table, along with reference ranges. Based on the normal reference that is employed in the coverage area of the pathology and available large pool of data, 95% confidence interval for HCT and TP were determined, and in turn the reference ranges for WBV were worked out (Table 1).

Case reviews: comparison between 'extrapolation' and Brookfield results

Case 1 presents WBV determined 14th December 2000 on a 59yo male. Diagnostic hyperviscosity result is concordant with the extrapolation method. The subject has abnormally low haematocrit and is a classical possibility of hyperviscosity in the presence of anaemia [4]. Cases 2 and 3 are those who had WBV determined 13th January 2003 on a 74yo male, and 25th September 2003 on a 49yo female respectively. Diagnostic results indicated 'slightly higher than normal' viscosity; but extrapolation method indicates normal. Case 4 presents WBV determined 4th November 2003 on a 76yo male. Diagnostic normoviscosity is concordant with the extrapolation method. Lastly, Case 5 presents WBV tested 10th April 2004 on a 75yo male. Diagnostic hyperviscosity result is discordant with normoviscosity by the extrapolation method.

Table 1 Numeric values of results from digital and extrapolations methods

	*HCT**	*TP**	*WBV‡*	*WBV†**
Case 1	0.29	99	20.0	20.5
Case 2	0.47	70	17.1	11.5
Case 3	0.41	76	17.5	12.0
Case 4	0.41	63	15.4	9.0
Case 5	0.44	62	15.4	15.5
Female ref top limit	0.46	80	18.8	11.0
Female ref bottom limit	0.32	60	13.7	7.0
Male ref top limit	0.49	80	19.1	11.0
Male ref bottom limit	0.36	60	14.2	7.0

*As per reported diagnostic laboratory result, ‡Extrapolated WBV at high shear rate 208 Sec-1 based on units (Prot g/L; HCT %), †Brookfield's digital method, HCT: haematocrit; TP: serum total protein; WBV: whole blood viscosity in centipoise.

A critical evaluation of the Table shows that both methods have reference ranges with almost the same standard deviation (digital = 1; extrapolation = 1.3).

Discussion

In comparing the results from extrapolation method with diagnostic Brookfield viscometer, it is observed that numeric values of results from the both method are close. This calls for caution. Non-Newtonian fluids such as whole blood have different viscosities at different shear rates. The digital and extrapolation methods measure WBV at different shear rates. Therefore, comparative statement cannot be based on numeric values, but only on interpreted outcome.

However, one positive observation is that standard deviation is about equal in both reference ranges. From the case reviews, it is observed that the interpretative results from extrapolation model are in absolute concordance with the diagnostic report for two of the five (#1 & #4) cases. Of importance is case 1, which is a classical possibility of hyperviscosity in the presence of anaemia [5].

Cases 2 and 3 presented slight (within +4 standard deviation) hyperviscosity by the digital method, but not very concordant with the extrapolation model where they are on upper standard deviation of the normal range. Case 5 also presented hyperviscosity result by the digital method that is not corroborated by the extrapolation formula. This seems to indicate that the extrapolation method may underestimate the value of WBV. It is pertinent to note that all three subjects have normal haematocrit and serum protein levels. Perhaps a poser could be: '*what is the*

possible explanation of hyperviscosity report in a patient with laboratory evidence of neither hyperproteinaemia nor polycythemia?'

Underestimation of hyperviscosity could be due to the factor of unaccounted contribution of oxidative stress. The understanding that oxidative stress contributes to blood viscosity dates back to more than four decades [5-7]. The understanding explains why aspirin therapy has as yet no clinical evidence-base, but with additional intervention of the underlying oxidative stress, reduces blood viscosity in diabetes [8, 9].

Upon audit of laboratory record, case 5 had result of low 'Albumin' level, which is an index of oxidative stress. Further, the patient was tested for coagulation profile, which means there could have been a blood flow issue requiring anticoagulant. Thus, oxidative stress can be inferred to be *the possible explanation of hyperviscosity report in a patient with laboratory evidence of neither hyperproteinaemia nor polycythemia*. The implication is that there is a limitation of the extrapolation method, which may not identify hyperviscosity without hyperproteinaemia or polycythemia.

Conclusion

The summary 'comparative statement' is that WBV may be underestimated in some cases by the extrapolation method. This is due to oxidative stress factor, which contributes to blood viscosity but not incorporated in the extrapolating mathematical formula.

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