Viscosimetric effect of fibrinogen

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Abstract

Aims—To investigate the correlation between fibrinogen concentration and plasma and serum viscosity.

Methods—Measurements of paired plasma viscosity and serum viscosity were compared in 45 subjects with a considerable range of fibrinogen concentrations and serum viscosity.

Results—Plasma and serum viscosity correlated well with plasma fibrinogen in cases of normal serum viscosity, but not in cases of myeloma or macroglobulinaemia. When an exponential correlation between plasma and serum viscosity was used, fibrinogen showed a good correlation in both normal and abnormal conditions.

Conclusions—There is an exponential correlation between plasma and serum viscosity which depends on the plasma fibrinogen concentration. This is in accordance with Arrhenius's formula for solutions of varying concentrations.

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Plasma fibrinogen is a major plasma protein that is required for normal coagulation of blood. It is increased in chronic or acute disorders—the haematological stress syndrome¹—and is of clinical importance and prognostic value in intermittent claudication.^{2,3} An increase has been noted in sickle cell anaemia⁴ and ischaemic heart disease,⁵ with the risk of stroke, coronary heart disease, and total cardiovascular disease being in proportion to the fibrinogen concentration.⁶ The specific viscosity of fibrinogen is greater than the other plasma proteins⁷⁻⁹ and therefore has a considerable effect on blood fluidity.¹⁰

When plasma is coagulated and serum is produced, only the fibrinogen is removed, so it should be possible to assess the plasma fibrinogen concentration from a comparison of the viscosity of plasma and serum.

In early rheumatoid disease the use of paired plasma and serum viscosity measurements was shown to be a useful predictor for differentiating between acute or chronic conditions.¹¹ An approximate evaluation of the plasma fibrinogen concentration could also be calculated by subtracting the result of serum viscosity from the plasma viscosity.^{12,13} However, although this formula worked in normal cases, it was unsuitable for the high values of serum viscosity found in myeloma and macroglobulinaemia.^{14,15}

Methods

Samples were collected from normal subjects and from patients with a variety of disorders, including rheumatoid conditions, myeloma, and macroglobulinaemia. Samples for plasma viscosity were collected into potassium-EDTA 1.5 mg/dl. For serum viscosity, a clotted sample was taken and allowed to stand for one hour before analysis, and for the plasma fibrinogen assay, a sample was taken into 3.8% tri-sodium citrate.

The study was conducted in two parts: in the first the plasma and serum viscosity was measured using the Coulter Harkness viscometer at 25°C¹⁶; and in the second using the automated Coulter viscometer mark II at ambient temperature and corrected to 25°C by the inbuilt programme.¹⁷ Plasma fibrinogen was measured using a modification of the clot opacity method.¹⁸

Results

The plasma viscosity result obtained with the Coulter Harkness viscometer was compared with that obtained on the Coulter automated viscometer mark II. The results showed a close linear association ($r = 0.998$, gradient = 0.999, intercept = 0.007) illustrating the comparability of the two viscometers. Results obtained in the two parts of the study^{19,20} were so close that they were amalgamated to give an overall correlation and remove any single instrument bias. The results of plasma and serum viscosity and fibrinogen measurements varied widely.

The use of the simple arithmetic difference between the plasma viscosity and the serum viscosity (PV – SV) showed an acceptable and significant correlation when the serum viscosity was not abnormally raised.

When samples with increased serum viscosity, as found in myeloma and macroglobulinaemia, were included, the results did not reach significance, confirming the observations of previous authors.^{14,15}

Several other correlations were examined as possible solutions. The relative viscosity (PV/SV) and log relative viscosity (log

Table 1 Assayed and reference ranges of fibrinogen, plasma, and serum viscosity

	Assayed range	Reference range
Fibrinogen g/dl	1.8–13.0	1.5–4.5
Plasma viscosity mPas	1.47–11.0	1.50–1.72
Serum viscosity mPas	1.32–6.8	1.40–1.60

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Table 2 Correlation values and significance of plasma and serum viscosity ratios analysed against fibrinogen concentration

Ratio	Samples	r =	p
PV – SV	Normal subjects only	0.961	<0.001
PV – SV	Paraproteins included	0.117	NS
PV/SV	Paraproteins included	0.381	NS
Log (PV/SV)	Paraproteins included	0.404	NS
Log PV/Log SV	Paraproteins included	0.924	<0.001

(PV/SV)) were also found to be non-significant, but the relative log viscosity (log PV/log SV) was a suitable correlation which encompassed all samples including high serum viscosity.

Regression formula:

$$\text{Fibrinogen} = 13.579 \times (\log \text{PV}/\log \text{SV}) - 14.0273$$

By simple manipulation of the formula it can be shown that:

$$\log \text{PV} = \log \text{SV} \times (\text{fibrinogen} + 14.023)/13.579$$

$$\log \text{PV} = \log \text{SV} \times f$$

$$\text{PV} = \text{SV}^f$$

where f is the fibrinogen coefficient of:

$$\text{either } f = (\text{fibrinogen} + 14.023)/13.579$$

$$\text{or } f = (\text{fibrinogen} \times 0.0736) + 1.033.$$

Discussion

The results show that the difference between the plasma viscosity and the serum viscosity is a useful, rapid, quantitative indication of the fibrinogen concentration,^{11–14} when abnormal samples are excluded.

In samples with high concentrations of plasma proteins, as found in myeloma and macroglobulinaemia, the simple correlation is inaccurate. This deviation of myeloma samples from the simple arithmetic line of plasma viscosity–serum viscosity has been shown before,^{14,15} with many varied interpretations. It was suggested that in cases of myeloma the methods of analysis of the plasma and serum viscosity,¹⁴ or of fibrinogen¹⁵ were inaccurate, perhaps due to fibrin degradation products.¹² A further suggestion was that the fibrinogen of patients with myeloma was either chemically or functionally abnormal.^{12,14} The possibility that the correlation was not a simple arithmetic one was not considered.

This study has shown an exponential correlation²¹ which is applicable to both normal and abnormal samples. The results obtained are in accordance with the formula of Arrhenius of 1887²²:

$$\text{Viscosity} = \text{viscosity of solvent}^{(K/C)}$$

where K is a constant and C is the concentration of solute (fibrinogen) in the solvent (serum):

$$\text{Plasma viscosity} = \text{serum viscosity}^{(\text{Fibrinogen} \cdot \text{constant})}$$

This is identical with the formula obtained in this study, thus confirming the theory with the results obtained.

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