Plasma viscosity in inflammatory bowel disease

A J Lobo, S C Jones, L D Juby, A T R Axon

Abstract

**Aims:** To assess the relation of plasma viscosity to disease activity in patients with inflammatory bowel disease.

**Methods:** Crohn's disease ($n = 60$) and ulcerative colitis ($n = 71$) were diagnosed on the basis of typical histological or radiological features. Active Crohn's disease was defined as a Crohn's disease activity index of 150 or over. Active ulcerative colitis was defined as a liquid stool passed three times a day or more with blood. Blood samples were assessed for haemoglobin concentration, total white cell count, platelets, plasma viscosity, erythrocyte sedimentation rate, serum albumin, and C-reactive protein.

**Results:** Plasma viscosity was higher in those with active Crohn's disease compared with those with inactive Crohn's disease or active ulcerative colitis. Plasma viscosity correlated significantly with erythrocyte sedimentation rate, C-reactive protein, and platelet count in patients with Crohn's disease. In ulcerative colitis plasma viscosity correlated only with serum C-reactive protein. Plasma viscosity showed a low sensitivity for detecting active Crohn's disease, with 48% of those with active disease having a plasma viscosity within the laboratory reference range.

**Conclusions:** Plasma viscosity is related to disease activity in Crohn's disease, but is insufficiently sensitive for it to replace erythrocyte sedimentation rate as a measure of the acute phase response in Crohn's disease.

The advantages of plasma viscosity are that, unlike the ESR, its value is independent of packed cell volume, sex, and for practical purposes, age. Viscosity is lower in neonates and rises slightly in the elderly due to changes in the plasma fibrinogen concentration. The use of automated systems reduces the biohazard risks and produces reproducible, precise results and these can be subjected to quality assurance. Plasma must be separated as soon as possible and never more than six hours after venesection, but once separated, its viscosity may remain stable for several days if kept at 15–20°C.

The initial capital cost of an automated viscometer is currently about £7500 with very low running costs. Measurement of ESR requires a very low initial outlay, but the subsequent running costs are higher. If the annual running costs are said to include laboratory disposables, appropriate venesection containers, a maintenance contract for the viscometer cost, interest repayments on the initial outlay for the viscometer and a sum to contribute to its eventual replacement, the approximate respective costs for performing 32 000 (the annual number performed at this institution in 1990) measurements of ESR and plasma viscosity would be £10 848 and £6464, respectively (P Day, personal communication). The initial capital outlay would therefore be recouped within two years and more rapidly if plasma viscosity was measured from the same blood container as the blood count.

There are few data on the use of plasma viscosity in clinical practice. In unselected patients attending a general medical and rheumatological clinic plasma viscosity was a more reliable measure of changes in acute phase reactants. In rheumatoid arthritis plasma viscosity was said to be at least as reliable as ESR and C-reactive protein (CRP) in terms of diagnosis, and as an index of improvement. More recently, however, plasma viscosity was found to compare less well than ESR with a battery of other measures of inflammation in rheumatoid arthritis.

There are no previous reports of the use of plasma viscosity in inflammatory bowel disease. This paper reports the prospective evaluation of plasma viscosity measurement in a large series of patients with inflammatory bowel disease.

**Methods**

One hundred and thirty one patients with inflammatory bowel disease attending the gas-
Plasma viscosity in inflammatory bowel disease

Laboratory assessment of disease activity

All patients had blood drawn for haemoglobin concentration, total white cell count, platelet count (Coulter counter; Coulter electronics, Luton), plasma viscosity (Coulter viscometer), ESR (Westergren method), C-reactive protein (CRP) (Boehringer nephelometer; Hoechst UK, Hounslow), and serum albumin (sequential multiple autoanalyzer with computer; Technicon, Basingstoke). The laboratory reference range for plasma viscosity was 1.5–1.72 millipascal seconds (mPa.s), and for C-reactive protein, the lower limit of detection of the assay is 5 mg/l and the reference range is 5–10 mg/l.

Differences between plasma viscosity in active and inactive disease and between Crohn’s disease and ulcerative colitis were assessed by the Mann–Whitney U-test. The correlation between plasma viscosity and the CDAI, ulcerative colitis disease severity and laboratory variables was performed using the Spearman rank order correlation coefficient.

Discussion

Despite the claimed advantages of plasma viscosity over ESR, our data highlight limitations in the use of this test in inflammatory bowel disease. The assessment of disease activity in Crohn’s disease is difficult, and a major clinical problem is to differentiate those with symptoms due to active disease from those with symptoms due to other causes. Laboratory indices may be particularly helpful here, but no laboratory test or clinical assessment has been shown to be without limitations. No gold standard exists for the assessment of disease activity in Crohn’s disease. The most commonly used evaluation for clinical studies, including therapeutic trials, is the CDAI, which is closely related to physicians’ overall assessment of disease severity.

Forty eight percent of those with active Crohn’s disease had plasma viscosity values within the reference range. The presence of symptoms not due to active disease may...
overlap between active Crohn’s disease and both inactive disease and the reference range makes a single normal value a poor predictor for differentiating active from inactive disease. There is also an overlap of values for ESR between active and inactive Crohn’s disease. In contrast, however, this is due to several increased values in patients without symptoms, and in the clinical context does not pose a diagnostic problem.

This can also be expressed in terms of the sensitivity and specificity of the tests. These are, in turn, critically dependent on where the cut-off lines are drawn. The upper limit of the reference range in our laboratory is 1.72 mPa.s. This gives a specificity of 90% but a sensitivity of just 52%. In comparison, using an ESR of 20 as an upper limit, the sensitivity is much improved at 85%, but with a lower specificity of 71%. To obtain similar figures for the plasma viscosity would require the upper limit of the reference range to be dropped to 1.65 mPa.s. At the levels currently used therefore, the ESR is more sensitive at detecting active Crohn’s disease, but the plasma viscosity is more specific.

It has been pointed out that plasma viscosity may be less useful in conditions associated with anaemia and hypoalbuminaemia as both tend to increase the sedimentation rate.² Crohn’s disease is associated with both, although the hypoalbuminaemia may be partly due to the acute phase response. The anaemia of Crohn’s disease may be multifactorial, but is partly related to disease activity, and the effect of an associated anaemia in increasing the sedimentation rate may make the ESR more sensitive. It is therefore of interest that in patients with Crohn’s disease there was only a trend towards correlation between haemoglobin concentration and plasma viscosity. This presumably reflects a balance between the lack of effect of packed cell volume on viscosity and the common effect of disease activity by haemoglobin via the plasma protein concentration. The ESR has also been noted to perform better than plasma viscosity in rheumatoid arthritis, where similar considerations obtain.¹⁰

The higher values of plasma viscosity found in those with active Crohn’s disease compared to active ulcerative colitis again reflect the acknowledged difference in the extent of the acute phase response between the two conditions.¹¹ ¹² Although there was a trend towards increasing plasma viscosity with increasing severity in ulcerative colitis, this was not significant, but may reflect the low number of cases in the severe group, which are now quite uncommon.

Our data cannot support the replacement of ESR by plasma viscosity for the assessment of inflammatory bowel disease, especially Crohn’s disease. We have documented a considerable overlap in plasma viscosity between those with active and those with inactive disease. Although plasma viscosity may provide a greater specificity in the differentiation of active from inactive Crohn’s disease, ESR is more sensitive, and in the clinical context this is more useful.

Sensitivity and specificity of plasma viscosity (PV) and ESR in distinguishing active from inactive Crohn’s disease for different levels of both PV and ESR

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma viscosity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.65 mPa.s</td>
<td>90</td>
<td>67</td>
</tr>
<tr>
<td>1.72 mPa.s</td>
<td>52</td>
<td>90</td>
</tr>
<tr>
<td>ESR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14 mm/h</td>
<td>90</td>
<td>54</td>
</tr>
<tr>
<td>20 mm/h</td>
<td>85</td>
<td>71</td>
</tr>
<tr>
<td>42 mm/h</td>
<td>35</td>
<td>90</td>
</tr>
</tbody>
</table>

Figure (A) Plasma viscosity (○) and erythrocyte sedimentation rate (ESR) (○) in active and inactive Crohn’s disease and ulcerative colitis. (B) Serum C-reactive protein in active and inactive Crohn’s disease and ulcerative colitis.

spuriously increase the CDAI, but eight of 10 patients with a normal plasma viscosity and high CDAI also had increased concentrations of circulating CRP suggesting that the symptoms causing a high CDAI were genuinely due to active inflammation rather than the fibrotic strictures that complicate Crohn’s disease or coexisting irritable bowel symptoms.
Plasma viscosity in inflammatory bowel disease.

A J Lobo, S C Jones, L D Juby and A T Axon

doi: 10.1136/jcp.45.1.54

Updated information and services can be found at:
http://jcp.bmj.com/content/45/1/54

**Email alerting service**

*These include:*

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Notes**

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/