Plasma viscosity: A forgotten variable

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Abstract. Evaluation of plasma viscosity has been underutilized in the clinical practice. Plasma viscosity is determined by water-content and macromolecular components. Plasma is a highly concentrated protein solution, therefore weak protein–protein interactions can play a role that is not characterized by electrophoresis. The effect of a protein on plasma viscosity depends on its molecular weight and structure. The less spheroid shape, the higher molecular weight, the higher aggregating capacity, and the higher temperature or pH sensitivity a protein has, the higher plasma viscosity results. Plasma is a Newtonian fluid, its viscosity does not depend on flow characteristics, therefore it is simple to measure, especially in capillary viscosimeters. Its normal value is 1.10–1.30 mPa s at 37°C and independent of age and gender. The measurement has high stability and accuracy, thus little alterations may be pathologically important. Inflammations, tissue injuries resulting in plasma protein changes can increase its value with high sensitivity, though low specificity. It can increase in parallel with erythrocyte sedimentation rate (ESR), but it is not influenced by hematocrit (anemia, polycytemia), or time to analysis. Based on these favorable features, in 1942 plasma viscosity was recommended to substitute ESR. In hyperviscosity syndromes plasma viscosity is better in follow-up than ESR. In rheumatoid arthritis, its sensitivity and specificity are better than that of ESR or C-reactive protein. Plasma fibrinogen concentration and plasma viscosity are elevated in unstable angina pectoris and stroke and their higher values are associated with higher rate of major adverse clinical events. Elevation of plasma viscosity correlates to the progression of coronary and peripheral artery diseases. In conclusion, plasma viscosity should be measured routinely in medical practice.

Keywords: Plasma viscosity, erythrocyte sedimentation rate, C-reactive protein, hyperviscosity syndromes, ischemic heart disease, acute phase response

1. Introduction

Evaluation of plasma viscosity has been underutilized in the clinical practice. Plasma is a Newtonian fluid; its viscosity is independent of blood flow characteristics, but is determined basically by water-content and macromolecular components of blood. Plasma is a highly concentrated protein solution, therefore weak protein–protein interactions can play a role that is not characterized by electrophoresis. Plasma viscosity is simple to measure, capillary viscosimeters are preferred in its measurement. The procedure has high stability and accuracy and can be rapidly performed. Even little alterations may be pathologically important [1–3].

The range of normal viscosity is narrow, 1.10–1.30 mPAs at 37°C and independent of age and gender. It can increase in parallel with erythrocyte sedimentation rate (ESR), but it is not influenced by hematocrit (anemia, polycytemia), red blood cell aggregation, hemoglobinopathias, or time to analysis. Based on these favorable features, in 1942 plasma viscosity was recommended to substitute ESR [1–3].

Inflammations, tissue injuries resulting in plasma protein changes can increase its value with high sensitivity, though low specificity. In certain pathological conditions (e.g., paraproteinemias), the ranges of plasma viscosity are considerably wider. The effect of a protein on plasma viscosity depends on...
its molecular weight and structure. Plasma viscosity is higher when a protein has more asymmetrical molecular shape, high molecular weight, high aggregating capacity, and sensitivity to temperature or pH alterations [1,2].

2. Plasma hyperviscosity syndromes

Plasma hyperviscosity syndromes have been reported both in monoclonal and polyclonal immunoglobulin disorders such as Waldenström’s macroglobulinemia, multiple myeloma and certain autoimmune diseases [1,2].

Plasma hyperviscosity syndromes may be caused by the following mechanisms: (1) extreme levels of paraprotein, usually more than 120–130 g/l, especially in IgG1 myeloma; (2) stable IgA, IgG aggregates by formation of disulfide bridges (dimer, tetramer), at relatively low paraprotein concentration (40 g/l); (3) unstable (concentration and temperature dependent) non-covalently bound paraprotein (IgG2) complexes, at moderate concentration (40–60 g/l); (4) rare paraproteins with extraordinary molecular characteristics; (5) complex formation of interacting paraproteins and other plasma proteins (e.g., in IgA myeloma, polyclonal diseases, autoimmune diseases) [1].

Common laboratory findings in hyperviscosity syndromes are the followings: anemia, increased erythrocyte sedimentation rate, red blood cell aggregates in smear, bone marrow infiltration, marked paraproteinemia, elevated serum and plasma viscosity, elevated whole blood viscosity, cryoglobulinemia, increased plasma and blood volume, increased bleeding time, decreased platelet adhesion, renal disturbances. Plasma viscosity was found to be better in follow-up of patients with hyperviscosity syndromes [1].

3. Cardiovascular diseases

Plasma viscosity was shown as an independent risk factor in several studies. Its level can change in parallel with fibrinogen, especially in acute phase response (e.g., in acute ischemic events), but can also be influenced by the level of triglycerides. Plasma viscosity was shown to be higher in patients with ischemic heart diseases compared to healthy subjects. A correlation with the severity of coronary heart disease could also be found. In acute coronary syndromes and after percutaneous coronary interventions plasma viscosity elevates as a part of acute phase response. Its higher value can be related to poorer prognosis in ischemic heart disease [4–8].

4. Acute phase markers

Acute phase markers increase due to tissue damage caused by trauma, acute infections, chronic inflammation, myocardial infarction, malignancy and burning. Acute phase response is generally involving the whole organism and not specific. Main direct stimuli are inflammatory cytokins, e.g. interleukin-1, interleukin-6 and tumor necrosis factor. Acute phase proteins include C-reactive protein, fibrinogen, ferritin, haptoglobin, ceruloplasmine, serum amyloid A, etc. Erythrocyte sedimentation rate and plasma viscosity can also reflect changes in acute phase response, because their level depends on the concentration of acute phase proteins. Assays of proteins are usually more sensitive to rapid changes in tissue injury or inflammation; they need sophisticated, expensive laboratory tests. ESR and plasma viscosity –
reflecting a cumulative effect – change more slowly, but can be more informative in chronic processes and methods of their detection are much cheaper [9,10].

C-reactive protein (CRP, Streptococcus pneumoniae C polysaccharide reacting) elevates in connect-
ing tissue diseases, malignancies, bacterial infections and is usually normal in viral infections. CRP
is better in detecting rapid alterations, because it is independent of fibrinogen, immunglobulins, num-
ber and shape of red blood cells. CRP can be useful in screening organic diseases, monitoring disease
activity (e.g., rheumatoid arthritis, infections, malignancies), estimating prognosis (acute pancreatitis),
distinguishing bacterial and viral infections, detecting transplant rejection. It remains normal or slightly
elevated in osteoarthritis, systemic lupus erythematoses, leukemia, anemia, polycytemia, viral infection,
ulcerative colitis, gravidity, estrogen effect, steroid effect. In bacterial meningitis increased serum and
liquor CRP normalizes within 7 days when treated properly. In coronary artery disease and stroke, CRP
was shown to have higher predictive value than LDL cholesterol and it also has an additive value. CRP
can be predictive in the development of type 2 diabetes mellitus [9,10].

Erythrocyte sedimentation rate reflects a cumulative effect of the elevation of acute phase proteins,
especially of those increasing red blood cell aggregation. Therefore its value is increased when fib-
rinogen is elevated in acute phase, but is also above normal due to immunoglobulins in autoimmune
diseases without acute phase response. ESR is influenced by several factors: e.g., age, gender, men-
strual cycle, gravidity, drugs (steroids), hematocrit, red blood cell anomalies and time to analysis (max.
4 hours). Thus it is less reliable comparing to plasma viscosity. Normal ESR value does not exclude
organic impairment and ESR = 30 mm/h does not have much information. High (100 mm/h) values
refer to marked disorders. Inflammations (infectious, autoimmune, arthritic), tuberculosis, myocardial
infarction, anemia, high fibrinogen, paraproteinemias result in high ESR; while polycytemia, hypofibri-
ogenemia, heart failure, spherocytosis, sickle cells cause low ESR. It is more valuable than CRP in
polymyalgia rheumatica, arteritis temporalis (diagnosis, monitoring relapses). It is an independent car-
diovascular risk factor: in 45–64 year-old males, in the highest quintile risk of coronary artery disease is
twice higher than those in lower quintiles [9,10].

Plasma viscosity is also sensitive, but not specific. In several disorders it increases in parallel with
ESR, but is independent of the effects of red blood cells (anemia, polycytemia, red cell aggregation
changes) or time to analysis. It is independent of gender, independent or lower dependent of age. Thus
it is more reliable than ESR. It is influenced by physical activity and gravidity. Having a narrow normal
range, elevated plasma viscosity refers to a disease. In plasma hyperviscosity syndromes, it is better in
monitoring than ESR. Its sensitivity and specificity in rheumatoid arthritis is higher than those of ESR or
CRP. Elevated plasma viscosity and fibrinogen can predict adverse events in unstable angina and stroke,
increase in plasma viscosity can be related to the deterioration of peripheral and coronary artery disease
[3,9,10].

In conclusion of this brief review, plasma viscosity can add useful information in the diagnostics and
treatment of various disorders and should be utilized more frequently in clinical medicine.

References
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