RELATIVE PLASMA VISCOSITY: A SIMPLE TEST FOR THE BED SIDE DIAGNOSIS OF MULTIPLE MYELOMA

Falih S. Sarhan *FIBMS*

Abstract

Background: The measurement of plasma viscosity (PV) has long been recognized to be important for the diagnosis of paraproteinemia and it is widely used recently for the assessment of peripheral vascular disorders, diabetes mellitus and malignant diseases. The WHO recommended method for measuring PV is the electronic Harkness viscometer, but it is expensive and not widely available.

Objective: A simplified, cheaper and accurate technique using the red cell pipette is worth trying as a rapid bedside test.

Methods: The relative plasma viscosity (RPV) was measured in 30 patients with multiple myeloma and 150 healthy adults. The method applied was that of Wright and Jenkins in which a comparison of the vertical flow of plasma to distilled water using the red cell pipette is used to measure the relative viscosity of plasma. The erythrocyte sedimentation rate for both the patients and control was performed for comparison.

Results: The mean RPV in multiple myeloma patients was highly raised compared to normal and that increment is highly significant statistically ($p<0.001$). These results are considered highly supportive of the diagnosis of myeloma. In the other hand, although the results of ESR were statistically significant, it cannot be differentiated from those due to other disorders.

Conclusion: The measurement of RPV has proved to be simple and reliable and may be used at the bed side to detect the activity and to assess the diagnosis of multiple myeloma.

Key words: Plasma viscosity, multiple myeloma.

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Introduction

The viscosity of a bulk liquid is its intrinsic resistance to flow, which arises because of the internal friction between its molecular and particulate components[1]. For protein solutions, this resistance to flow is influenced by both concentration and intrinsic viscosity of individual proteins, and the intrinsic viscosity, in tern, is affected by the molecular size and shape of that protein[2].

The plasma viscosity (PV) is directly correlated with the concentration of large sized plasma proteins namely fibrinogen and some immunoglobulins (secretary IgA and IgM)[3].

The prompt recognition of the potentially fatal hyperviscosity syndrome in Waldenström's macroglobulinemia and multiple myeloma is of great clinical importance since dramatic relief of symptoms may result from the lowering of viscosity by plasmapheresis[4].

The usual technique for measuring PV i.e. The Harkness viscometer is relatively simple but require equipment frequently not available in clinical laboratories[4]. Therefore the present study was undertaken to prove that the measurement of relative plasma viscosity (RPV) can serve as a rapid and accurate screening test, adaptable even to the hospital ward.

Patients and Methods

RPV and erythrocyte sedimentation rate (ESR) were measured for 30 patients with multiple myeloma (proved by bone marrow study and protein electrophoresis), attending Al-Kadhimiya Teaching Hospital for the period of five years (2000-2004).

A hundred and fifty health adults were selected as control, half of these are

Dept. Pathology, College of Medicine, Al-Nahrain University
Address correspondence to Dr. Falih D S. Sarhan
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males and the other is females. All healthy adults are 20-40 years of age. Venous blood was collected with minimal stasis and anticoagulated with di potassium EDTA for RPV or sodium citrate for ESR. The ESR is measured immediately in Westergren tubes for one hour.

For RPV testing, plasma is immediately separated by centrifugation (3000g for 5 minutes) then kept in stoppered plastic tubes were it could be stored in room temperature (not the refrigerator) for one week without change in viscosity[4]. The method applied was that described by Wright and Jenkins[4] and modified by Falih et al[5], using the red cell pipette (Figure 1).

Student's t-test was utilized for statistics with p value less than 0.05 was considered statistically significant.

Results

The mean RPV for the healthy (control) subjects was 1.81±0.19 with a range of 1.58-2.1 as it shown in table 1.

Table 1: Mean ±SD of RPV and ESR values in healthy subjects.

Control group	No. of cases	Mean RPV±SD	Mean ESR±SD
Males	75	**1.79**±0.11 (1.58-1.98)	**6**±3.9 (2-13)
Females	75	**1.83**±0.16 (1.61-2.1)	**10**±6.2 (2-18)
Total	150	**1.81**±0.19 (1.58-2.1)`	**8**±6.6 (2-18)

Table 2: The RPV results of the thirty multiple myeloma patients with their corresponding ESR values.

Patient number	RPV	ESR
1	2.09	80
2	2.17	105
3	2.48	95
4	2.52	100
5	2.59	90
6	2.61	93
7	2.65	110
8	3.00	104
9	3.09	105
10	3.10	115
11	3.11	100
12	3.15	120
13	3.21	137
14	3.28	125
15	3.32	166
16	3.40	145
17	3.46	119
18	3.50	132
19	3.69	125
20	3.75	136
21	3.77	171
22	3.86	105
23	3.88	129
24	3.94	144
25	4.00	118
26	4.2	142
27	4.37	180
28	4.43	146
29	4.51	170
30	4.84	175
Mean	3.399	126.06
Range	2.09-4.84	80-180
SD	0.710	27.31

A comparison of the results of RPV and ESR of normal and multiple myeloma patients is shown in table 3.

Table 3: Comparison of RPV and ESR results of control and myeloma group

Group	No. of cases	RPV	ESR
Control group	150	**1.81**±0.19 (1.58-2.1)	**8**±6.6 (2-18)
Myeloma patients	30	**3.39**±0.71 (2.09-4.84)	**126.06**±27.31 (80-180)
P value		< 0.001	< 0.001

Discussion

The ESR and plasma viscosity usually increase in parallel, and therefore has long been used as acute phase reactant[6,7]. Plasma viscosity is, however, primarily dependant on the concentration of plasma proteins, especially fibrinogen, and it is not affected by anemia[6]. Changes of viscosity seem to reflect the clinical severity of disease more closely than does the ESR[8]. Furthermore changes in ESR may lag behind those of viscosity by 24-48 hours[6]. Unlike the ESR, the test in RPV could be delayed for one week without change in viscosity[6,11].

The results of plasma viscosity are highly reproducible, and there are no significant differences in plasma viscosity between men and women, or in pregnancy[6,9]. It is remarkably constant in health, with little or no diurnal variation, and it is not affected by exercise, therefore a change of only 0.03-0.05 mPa/s is likely to be clinically significant[6].

This study assesses the use of a simple instrument i.e. the red cell pipette which is usually available in every laboratory to aid in the diagnosis of multiple myeloma at the bed side.

Falih et al (2000)[5] confirmed the work of previous authors[4,8] that the results of plasma viscosity could be classified into three zones, a control, chronic, and a myeloma zone.

According to Falih et al the control zone was 1.56-1.95, and the myeloma zone is 2.09-4.43. Both of these ranges are comparable to ours[5]. The control zone in our study was 1.58-2.1 relative units with no male to female differences. The normal range for the ESR was 2-18 mm/hr.

The RPV values of the myeloma patients ranged from 2.09-4.84 relative units which is highly statistically significant ($p<0.001$). The results of the ESR for these patients ranged from 80-180 mm/hr with a p- value <0.001.

More than 86% of patients showed ESR values more than 100 mm/hr (26 patients); however these results cannot be differentiated from the high ESR seen in a wide range of acute and chronic disorders[5,6,11].

In contrast to the results of the ESR, myeloma patients showed very high results of RPV with 23 out of the 30 cases (76.67 %) had RPV more than 3 relative units consistent with the myeloma zone described by previous authors[4,5,8]. In 1984, the international committee for standardization in hematology (ICSH) recommended that an RPV value greater than 3 relative units should be considered diagnostic of paraproteinemia and requires further establishment of its cause[1,2,10].

In addition to the above mentioned advantages of RPV measurement, the technique of using the red cell pipette has only few limitations including the need of thorough cleansing after each test since dried proteins may impede the flow of fluids thus resulting in false high RPV. Another cause of false high results is the use of red cell pipettes with cylindrical; type of beads which may occlude the opening and reduce the flow of plasma, therefore it is recommended to use pipettes with star shaped beads for more accurate results. The

non verticality of the apparatus may adversely affect the results and should be avoided.

Conclusion and Recommendations

Technically, the measurement of RPV by this method appears to be easy, accessible, cheap and rapid and can be used at the bed side to test for the presence of paraproteins.

The test may yield values which are diagnostic of myeloma unlike ESR in which the high values could be seen in a variety of disorders, therefore cannot be considered diagnostic of myeloma[3,5,10].

A much simpler device to measure RPV can be tried by using a technique which do not require cleaning, possibly using a disposable apparatus is recommended to be used which may prove to be more helpful for the rapid and bed side diagnosis of paraproteinemia.

References

1. ICSH: Recommendation for a selected method for the measurement of plasma viscosity. J Clin Pathol, 1984; 37: 1147-52.
2. Leonard RC: Simple technique for the measuring serum viscosity with disposable apparatus. BMJ, 1981; 283: 31.
3. Hutchinson RM, and Eastham RD: A comparison of the ESR and plasma viscosity in detecting changes in plasma proteins. J Clin Pathol, 1977; 30: 345-49.
4. Wright DJ, and Jenkins DE: Simplified method for estimation of serum or plasma viscosity in multiple myeloma and related disorders. Blood, 1970; 36: 516-21.
5. Falih SS: Simple technique for the measurement of plasma viscosity in multiple myeloma and various other clinical disorders.
6. Lewis SM: Miscellaneous tests. In: Lewis, S.M., Bain, B.J., Bates, I. (ed.), Dacie and Lewis Practical Haematology. Ninth edition, Churchill Livingstone (London), 2001; p.p. 531-32.
7. ICSH: Guidelines on the selection of laboratory tests for monitoring the acute phase response. J Clin Pathol, 1988; 41: 1203-12.
8. Harkness J: The viscosity of human plasma; its measurement in health and disease. Biorheology, 1971; 8: 171-93.
9. Inglis TC, Stuart J, George AJ, and Davies AJ: Haemostatic and rheologic changes in normal pregnancy and pre-eclampsia. Br J Haematol, 1982; 50: 461-65.
10. Lowe GDO: Blood rheology and hyperviscosity syndrome. In Lowe GDO (ed.) Bailliéres Clinical Hematology; International Practice and Research. Bailliéres Tindall, 1987; 1: 3.
11. ICSH: Reference method for the erythrocyte sedimentation rate (ESR) test on human blood. Br J Haematol, 1973; 24: 671-73.