Current Topics in Biophysics 2004, 28(1), 3-8

THE EFFECT OF ACETYLSALICYLIC ACID AND ACENOCOUMARIN ON RHEOLOGICAL PROPERTIES OF BLOOD STUDIED ON PATIENTS AFTER MYOCARDIAL INFARCTION

ANNA MARCINKOWSKA-GAPIŃSKA[1], FELIKS JAROSZYK[2], WALDEMAR ELIKOWSKI[3], LESZEK KUBISZ[2]

[1]Department of Neurology, Karol Marcinkowski University of Medical Sciences in Poznan, Przybyszewskiego 49, 60-355 Poznan, Poland
[2]Department of Biophysics, Karol Marcinkowski University of Medical Sciences in Poznan, Fredry 10, 61-701, Poznan,
[3]Internal Ward Municipal Hospital Poznan-Nowe Miasto, Szwajcarska 3, 61-285 Poznan

It has been established that blood flow in the cardiovascular system is determined not only by physico-chemical properties of blood but also depends on the phenomena resulting from the structure and properties of cardiovascular system. The shear rate-dependent viscosity of blood depends on the hematocrit value, erythrocyte ability to aggregate, deform along with orientation and on the viscosity of blood plasma. Studies on blood and plasma viscosity described in this paper were performed by means of rotary-oscillatory rheometer Contraves LS 40. The measurements were performed for blood collected from patients who experienced myocardial infarction 0.5 to 10 years ago. Patients were treated with acetylsalicylic acid and acenocoumarin. Application of the acetylsalicylic acid in the derivative prevention of myocardial infarction does not exert any influence on the rheological properties of blood. The results suggest that rheological parameters of blood can be used in the diagnosis and evaluation of the effect of the treatment. Application of the MS DIN 412 measuring system and carrying out rheological measurements with duration of 5 minutes and with decreasing shear rate made results the most reliable and repeatable.

INTRODUCTION

A description of blood flow is very complex. This is the reason for including in this description all the accompanying phenomena. The blood flow is influenced both by the properties of the cardiovascular system and physicochemical properties of blood. From the rheological point of view, blood is a non-homogenous suspension of blood cells in plasma, characterized by a non-Newtonian behavior (Chien, 1972). Sometimes blood can be considered as emulsion. Blood cells similarly as drops of emulsion contain fluid enclosed in a lipid membrane, whose shape can be deformed by shearing (Lerche, Bäumler, Kucera, Meier & Paulitschke, 1991).

Studies on rheological properties of blood are based mainly on the measurements of apparent viscosity of the whole blood and plasma. Because the internal friction depends on the shear rate, the viscosity of the whole blood as a function of the shear rate should be determined. Rheological and viscous properties of blood depend on the shear rate while the viscosity of plasma does not depend on the shear rate. The ability of erythrocytes to aggregate and to deform influences the blood viscosity (Copley, 1987). The viscosity of blood depends also on the hematocrit (Copley, 1987, Lerche, Koch & Vlastos, 1993a). Relationships among aggregability, deformability, shear stress, hematocrit and blood flow are well known and described elsewhere (Dintenfass, 1990; Lerche *et al.* 1991, Lerche *et al.* 1993a; Merrill 1969; Sandhagen, 1988; Stuart & Kenny 1980).

The aim of the present study was to estimate the rheological properties of blood from subjects after the myocardial infarction.

MATERIAL AND METHODS

The measurements were performed for blood collected from one hundred persons (all male) aged 37-56. All examined patients were 0.5 to 10 years after the myocardial infarction and they were experiencing the period of clinical stability of the disease. The choice of the patients was also determined by other factors potentially influencing the

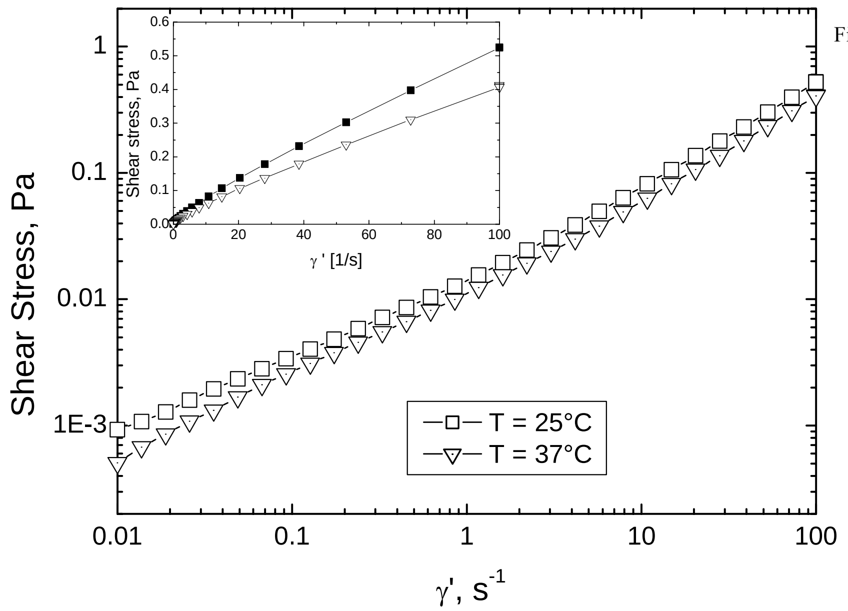

Fig. 1. The relationship between the measured shear stress and shear rate.

blood flow: arterial hypertension, manifest diabetes, atherosclerosis, overweight, age, localisation of the myocardial infarction and lipid profile. The patients were divided into three groups: those treated with the acetylsalicylic acid with the dose of 150 mg per day (group A), those treated with the acenocoumarin with the dose depending on the actual prothrombin indicator value, (group B), and into the control group (C) formed from some patients of groups A and B but after at least seven day interruption in the treatment. The groups A, B and C numbered 38, 20 and 42 persons, respectively. Blood was taken early in the morning on empty stomach. Prior to taking blood samples the patients had rested in the horizontal position for 30 minutes. Blood was collected into special syringes (Saarstedt, Z-Monovette®, 9 ml; 1.6 mg of K-EDTA per 1 ml of blood, sterile; catalogue No. 02.267.001). For all blood samples hematocrit was measured by means of the standard method. Rheological studies included measurements of the whole blood and plasma viscosity by means of rotary-oscillatory rheometer Contraves LS 40. The measurements were performed as a function of shear rate in the range of 100 - 0.01-s^{-1}, in descending order. A special plastic transparent shield protected the measuring bob from the influence of air moving in the room, which is indispensable for the low shear rate measurements. Measuring system MS DIN 412 was used throughout. Studies were performed at two temperatures: 25 and 37°C. Plasma viscosity was calculated from the dependence of shear stress on the shear rate using the method of linear regression. Because the measurements were performed at two different temperatures, the apparent viscosity of blood was normalized with the plasma viscosity to avoid the simple effect of water viscosity temperature dependence. The statistical analysis included calculation of the mean values of rheological parameters, their standard deviations, Student's significance test of the differences in mean values between the pairs and the ANOVA procedure for testing the significance of differences in average values in several groups.

RESULTS

The average value of hematocrit was equal to 0.44±0.01. In Figure 1 the exemplary flow curve and in Figure 2 the dependence of apparent viscosity on shear rate are presented, respectively. The relative viscosity of blood obtained by normalizing full blood viscosity with plasma viscosity is presented in Figure 3. The values of plasma viscosity at the temperatures of 25 and 37°C are shown in Table 1. The average relative blood viscosity values for four chosen shear rates of all measurement sub-ranges are collected in Table 2.

For 27 patients in the group A, measurements were performed twice. First time, when the patients were treated with the acetylsalicylic acid and second time, after one-week interval in the treatment. The results are shown in Table 3.

DISCUSSION

The results of the hemorheological studies presented in this paper support the choice of the

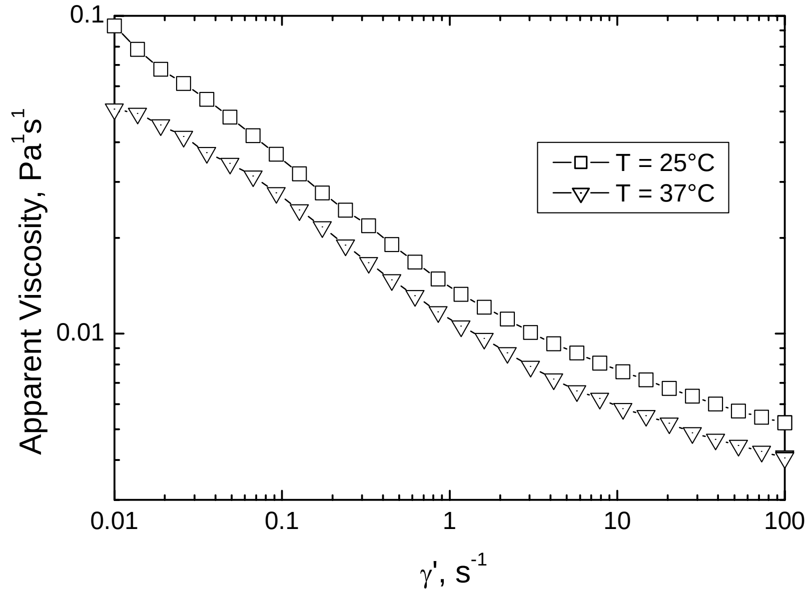

Fig. 2. The relationship between apparent viscosity and shear rate. Data from Figuue 1.

applied methodology established on the basis of other authors' reports (Lerche, Vlastos, Koch, Pohl & Affeld, 1993b; Merrill, 1969; Vlastos, Koch, Lerche & Pohl, 1992) and own experience (Marcinkowska-Gapińska, Jaroszyk & Górski, 1998). The selection of the group of patients was based on the observations, which suggested that the disturbances in the rheological properties of blood could cause heart and cardiovascular diseases (Berent, Kochmański, Kuczyńska, Wocial, Ignatowska-Świtalska, Łapiński, Januszewicz & Januszewicz, 1995; Chmiel, 1979; Dodds, Boyd, Allen, Bennett, Flute & Dormandy, 1980; Kochmański & Żochowski, 1990; Sandhagen, 1988; Stuart & Kenny, 1980; Turczyński *et al.*, 1987a; Wysocki & Grajek, 1985). The results of blood viscosity measurements confirmed the complexity of the analysis and interpretation of the phenomena occurring during blood flow (Lerche *et al.*, 1993a). The values of the rheological parameters of blood depend not only on the applied method and the type of apparatus but also on the patient's illness, his mode of life and medicines that he takes (Lerche *et al.*, 1993a; Turczyński, Sroczyński, Nałogowska, Szczęsny & Młynarski, 1989; Turczyński, Sroczyński, Tawrdowska-Saucha, Szczęsny & Grzegorczyn, 1988; Turczyński, Znamirowska & Szczęsny, 1987b). The data for the viscosity of blood plasma collected in Table 1 shows that the elevated viscosity of blood plasma was observed only for the patients treated with acenocoumarin (ANOVA, $p<0.08$). No

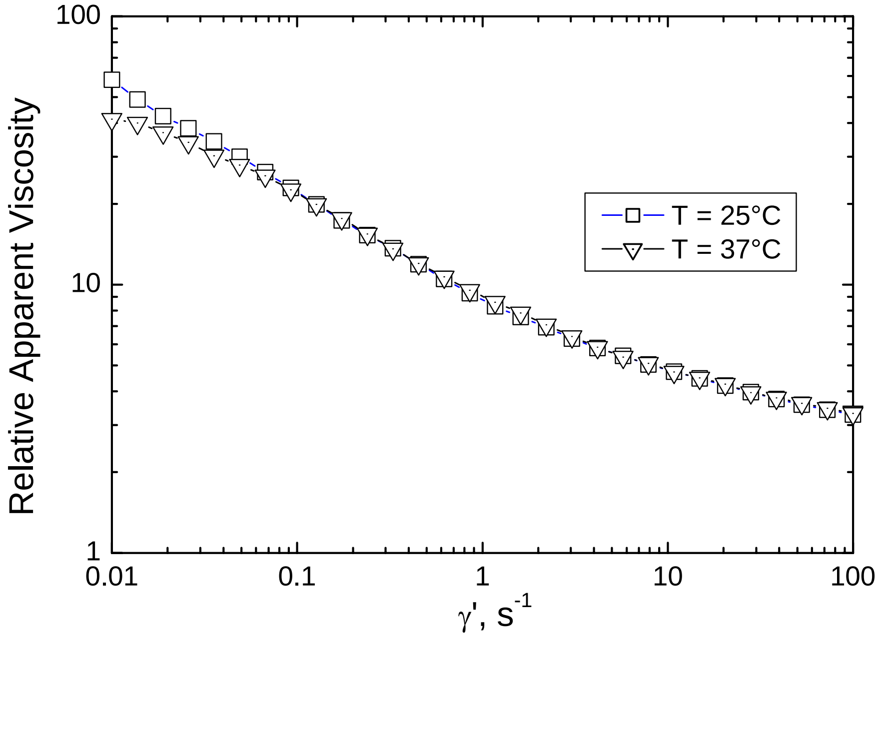

Fig. 3. Relative apparent viscosity (apparent viscosity of blood divided by the viscosity of blood plasma measured at the same temperature)

Table 1. Viscosity of blood plasma for patients after myocardial infarction (average values and their standard deviations).

Group of patients	Apparent viscosity η_p mPa s		Ratio of apparent viscosity $\frac{\eta_p(25°C)}{\eta_p(37°C)}$
	T = 25°C	T = 37°C	
A Acetylsalicylic acid	1.65±0.02	1.26±0.01	1.31
B Acenocoumarin	1.71±0.02	1.31±0.02	1.30
C Controls	1.65±0.01	1.28±0.01	1.29

Table 2. Relative apparent viscosity of blood measures at the temperatures of 25 and 37 °C for the shear rate of 0.1, 1, 10 and 100 s^1; A, B and C group of patients (average values and their standard deviations).

Shear rate, s^{-1}	Relative Apparent Viscosity at T=25°C			Relative Apparent Viscosity at T=37°C		
	A	B	C	A	B	C
100	3.42±0.05	3.45±0.06	3.46±0.04	3.48±0.04	3.49±0.07	3.52±0.05
10	5.4±0.1	5.6±0.02	5.5±0.1	5.5±0.1	5.7±0.2	5.6±0.1
1	11.5±0.4	12.6±0.5	11.8±0.4	11.9±0.4	12.9±0.6	12.2±0.4
0.1	28±1	29±2	29±1	25±1	23±2	26±1

Table 3. Relative apparent viscosity of blood measured for the shear rate of .100,10,1 and 0.1 s^{-1}, for patient treated with acetylsalicylic (A) acid and during one-week interval in the treatment (A_I) measured (averaged values and their standard deviations).

Shear rate, s^{-1}	Relative Apparent Viscosity at T=25°C		Relative Apparent Viscosity at T=37°C	
	A	A_I	A	A_I
100	3.46±0.06	3.50±0.05	3.53±0.04	3.52±0.05
10	5.5 ± 0.2	5.6 ± 0.2	5.6±0.1	5.6±0.1
1	11.8 ± 0.5	12.2 ± 0.5	12.2±0.3	12.4±0.4
0.1	28 ± 2	30 ± 2	25±1	26±1

difference was observed between patients treated with acetylsalicylic acid and the controls. This can be explained by the fact that acenocoumarin was relatively often administered to patients with essential hemodynamic and biochemical disturbances, contrary to the controls along with patients treated with acetylsalicylic acid. Blood plasma viscosity is determined mainly by the concentration of fibrinogen and γ-globulins, which are simultaneously responsible for red blood cells aggregation (Chien, Usami, Dellenback & Gregersen, 1970). Viscosity of blood plasma depends also on the concentration of its lipid components (Turczyński *et al.* 1987a). In order to eliminate the effect of plasma viscosity on the whole blood viscosity, the relative viscosity was calculated by normalising the blood viscosity with the viscosity of plasma measured at this same temperature. The average relative viscosity of blood measured for chosen shear rates (Table 2) showed the difference only for the shear rate of $1s^{-1}$ ($p<0.1$). The viscosity of blood was higher for patients treated with acenocoumarin than for the two other groups. The elevated values of the viscosity of blood cannot be explained by the higher hematocrit, because the average hematocrit was identical for all three groups of patients. Moreover, in case of higher hematocrit, observed changes should occur in the whole range of the shear rate. The increase in the viscosity at the shear rate of $1s^{-1}$ was probably due to the increased trend of erythrocytes to form reversible aggregates. It has been found that erythrocytes in the aggregates are linked by bridges formed by fibrinogen and γ-globulin molecules (Chien & Jan, 1973; Skalak, Zarda, Jan & Chien, 1981). The raised susceptibility to aggregate should correlate with the concentration of the plasma proteins and hence, plasma viscosity, as it was observed in the experiment.

The apparent viscosity of blood taken from the patients treated with acetylsalicylic acid and from patients experiencing one-week interval in the treatment was measured for the chosen shear rates (Table 3). The acetylsalicylic acid did not influence the apparent viscosity of blood.

To summarise, we found no difference in the shape of the rheogram and the values of viscosity of blood and blood plasma for the group pf patients treated with acetylsalicylic acid and the control group. It suggests that the acetylsalicylic acid did not influence the rheological properties of blood and blood plasma.

CONCLUSION

On the basis of analysis of the data obtained by means of the rotary-oscillatory rheometer Contraves LS 40, we have drawn the following conclusions concerning rheological properties of blood of patients who had experienced myocardial infarction:

The most reliable and repeatable results of the measurements of rheological properties of blood were given by the following method: duration of measurement: 5 minutes, decreasing shear rate and application of the measuring system MS DIN 412.

Application of the acetylsalicylic acid in the derivative prevention of myocardial infarction does not exert any influence on the rheological properties of blood.

The obtained results of studies on rheological parameters of blood for three different groups of patients made it is possible to suppose that rheological parameters of blood can be used in the diagnosis and evaluation of the effect of the treatment.

REFERENCES

Berent H., Kochmański M., Kuczyńska K., Wocial B., Ignatowska-Świtalska H., Łapiński M., Januszewicz A. & Januszewicz W. (1995). Rola czynników reologicznych w patogenezie nadciśnienia tętniczego. *Kardiol. Pol.* **42**, 463-468.

Chien S. & Jan K-M. (1973). Ultrastructural basis of the mechanism of rouleaux formation, *Microvascular Research*, **5**, 155-166.

Chien S., Usami S., Dellenback R.J. & Gregersen M.I. (1970). Shear dependent interaction of plasma proteins with erythrocytes in blood rheology, *American Journal of Physiology* **219**, 143-153.

Chien, S. (1972). The present state of blood rheology. In: Hemodilution. Theoretical basis and clinical application, (ed.) K. Messmer, H. Schmid-Schönbein, Karger, Basel, 1-45.

Chmiel H. (1979). Determination of blood rheological parameters and clinical application, *Advances in Cardiovascular Physics* **3**, 1-44.

Copley A.L. (1987). On erythrocyte aggregation and dissagregation. *Clin. Hemorheol.* **7**, 3-14.

Dintenfass L. (1990). Blood as a near-"ideal" emulsion: a retrospective on the concept of the red cell as a fluid drop, its implications for the structure of the red cell membrane. *Biorheology* **27**, 149-161.

Dodds A.J., Boyd M.J., Allen J., Bennett E.D., Flute P.T. & Dormandy J.A. (1980). Changes in red cell deformability and other hemorheological variables after miocardial infarction. *Br. Heart J.* **44**, 508-511

Kochmański M. & Żochowski R.J. (1990). Lepkość krwi a mikrokrążenie w mięśniu serca. *Kardiol. Pol.* **33**, 64-70.

Lerche D., Bäumler H., Kucera W., Meier W. & Paulitschke M. Flow properties of blood and hemoreological methods of quantification, in: Physical Characterization of Biological cells. Basic research and clinic relevance. Ed. W. Scütt, H. Klinkmann, I. Lamprecht, T. Wilson, Verlag Gesundheit GmbH Berlin 1991, 189-214.

Lerche D., Koch B. & Vlastos G. (1993a). Flow behaviour of blood, *Rheology* **93**, 105-112.

Lerche D., Vlastos G., Koch B., Pohl M. & Affeld K. (1993b). Viscoelastic behaviour of human blood and polyacrylamide model fluids for heart valve testing, *J. Phys. III France* **3**, 1283-1289.

Marcinkowska-Gapińska A., Jaroszyk F. & Górski S. (1998). Application of Quemada rheological equation to analysisi of blood flow curves in certain cases. Part I, *Polish Journal of Medical Physics and Engineering* **11**, 38-49.

Merrill E.W. (1969). Rheology of blood, *Physiological Reviews* **49**, 863-888.

Milnor W.R., Hemodynamics, Williams & Wilkins, Baltimore, Maryland USA, 1989, 3-101.

Sandhagen B. Assesment of blood rheology. Methodology and studies in healthy individuals, in patients with certain diseases and during liquid blood preservation, *Acta Universitatis Upsaliensis*, Comprehensive Summaries of Uppsala Dissertation from the Faculty of Medicine, Uppsala 1988, 1-50.

Skalak R., Zarda P.R., Jan K.-M. & Chien S. (1981). Mechanics of rouleau formation, *Biophysical J.* **35**, 771-781.

Stuart J. & Kenny M.. (1980). Blood rheology, *J. Clin. Pathol.* **33**, 417-429.

Turczyński B., Sroczyński J., Nałogowska K., Szczęsny S., Młynarski J. (1989). Submaksymalny wysiłek a lepkość krwi. *Ann. Acad. Med. Siles.* **18-19**, 125-130.

Turczyński B., Sroczyński J., Twardowska-Saucha K., Szczęsny S. & Grzegorczyn S. (1988). Niektóre właściwości reologiczne krwi w niskich szybkościach ścinania u narażonych na działanie pól elektrycznych o częstotliwości przemysłowej w aspekcie wieloletniej obserwacji. *Ann. Acad. Med. Siles.* **16-17**, 141-147.

Turczyński B., Znamirowska D., Szczęsny S. & Grzegorczyn S. (1987). Wybrane składniki biochemiczne osocza a lepkość krwi u chorych na miażdżycę, *Pol. Arch. Med. Wewn.* **77**, 300-305.

Turczyński B., Znamirowska D. & Szczęsny S. (1987). Obwodowy przepływ krwi wyznaczany metodą izotopową a lepkość krwi. *Post. Fiz. Med.* **22**, 35-44.

Vlastos G., Koch B., Lerche D. & Pohl M. Polymer solutions as model fluids for the non-newtonian behaviour of blood, *Theoretical and Applied Rheology*, Ed. P.Moldenaers and R.Keunings. Proc. XI-th Int.

Congr. on Rheology, Brussels, Belgium, August 17-21, 1992. Elsevier Science Publishers B.V. 1992.

Wysocki M. & Grajek S. (1985). Zaburzenia właściwości fizycznych krwi u chorych na nadciśnienie tętnicze pierwotne, *Kard. Pol.*, XXVIII, 690-697.