

BLOOD ELECTRICAL IMPEDANCE CLOSELY MATCHES WHOLE BLOOD VISCOSITY AS PARAMETER OF HEMORHEOLOGY AND INFLAMMATION

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ABSTRACT:

Red blood cell aggregation (RBCa) is a sensitive inflammation marker. RBCa determination from erythrocyte sedimentation rate, *ESR*, is used since long, but is unspecific unless corrected for hematocrit, *Ht*. Whole blood viscosity measurement at low shear rate is also sensitive to RBCa but is cumbersome to apply. To investigate whether electrical blood impedance, being sensitive to spatial red cell distribution, can be a good alternative to determine RBCa in low shear conditions. Blood was collected from 7 healthy volunteers. From each 16 different samples were prepared with 4 different *Ht*'s and with 4 different fibrinogen concentrations. Viscosity was measured at low shear rate (4.04 s^{-1}) with a rotational viscometer at 37°C . Electrical blood impedance was measured during similar shear conditions and temperature in a specially designed cuvette. *ESR* was determined according to Westergren. A logarithmic increase of viscosity as well as of capacitance, C_m , is seen when fibrinogen rises and an exponential increase when *Ht* rises. However, *ESR* shows a logarithmic decrease with increasing *Ht* and an exponential increase when fibrinogen rises. The viscosity could be accurately described using an exponential model. Under similar low shear conditions and temperature in-vitro, either whole blood viscosity or electrical blood capacitance reflect red blood cell aggregation due to fibrinogen and *Ht* variation in a similar way.

ZUSAMMENFASSUNG:

Die Aggregation roter Blutkörperchen (RBCa) ist ein aufschlussreicher Test für Entzündungen. RBCa-Bestimmung aus der Sedimentationsrate der Erythrozyten, *ESR*, wird seit langem verwendet, aber ist unspezifisch so lange er nicht mit dem Hämatokritwert, *Ht*, korrigiert wird. Die Messung der Blutviskosität bei kleinen Scherraten ist ebenfalls RBCa-sensitiv jedoch schwierig in der Anwendung. Es wurde hier untersucht, ob die Messung der elektrischen Impedanz, welche ebenfalls sensitiv auf die räumliche Verteilung der roten Blutkörperchen reagiert, eine gute Alternative zu Bestimmung der RBCa bei kleinen Scherraten ist. Blutproben von sieben gesunden Probanden wurden so präpariert, dass 16 verschiedene Proben mit vier verschiedenen *Ht* und vier verschiedenen Fibrinogenkonzentrationen vorlagen. Die Scherviskositäten wurden bei kleinen Scherraten (4.04 s^{-1}) mit einem Rotationsrheometer bei 37°C gemessen. Die elektrische Impedanz des Blutes wurde unter ähnlichen Scherraten und Temperaturen in einer speziell konzipierten Küvette gemessen, sowie die *ESR* nach dem Verfahren von Westergren bestimmt. Ein logarithmischer Anstieg der Viskosität als auch der Kapazität, C_m , wurde für einen ansteigenden Fibrinogenanteil, und ein exponentieller Anstieg für einen Hämatokritwertanstieg beobachtet. Die *ESR* zeigt jedoch eine logarithmische Abnahme mit ansteigendem Hämatokritwert und einen exponentiellen Anstieg für einen Fibrinogenanstieg. Die Viskosität konnte mit Hilfe eines exponentiellen Modells genau beschrieben werden. Unter vergleichbaren Bedingungen bei kleinen Scherraten und in-vitro-Temperaturen zeigen die Messungen der Blutviskosität und der elektrischen Impedanzmessungen eine ähnliche Aggregation der roten Blutkörperchen auf Grund von Fibrinogen und *Ht*-Veränderung.

RÉSUMÉ:

L'agrégation de cellules sanguines rouges (RBCa) est un indicateur très réceptif de l'inflammation. La détermination de la RBCa à partir de la vitesse de sédimentation de l'érythrocyte, *ESR*, est employée depuis longtemps, mais n'est pas spécifique si elle n'est pas corrigée en tenant compte de l'hématocrite, *Ht*. Les mesures de viscosité à faible vitesse de cisaillement de sang non traité sont elles aussi sensibles à la RBCa, mais sont délicates à appliquer. Nous avons cherché à savoir si la mesure de l'impédance électrique du sang, qui est sensible à la distribution spatiale en cellules rouges, peut être une bonne alternative à la détermination de la RBCa dans des conditions de faible cisaillement. Les échantillons de sang ont été collectés sur 7 volontaires sains. A partir de ces 7 échantillons, 16 échantillons différents ont été préparés avec 4 *Ht* différents et avec 4 concentrations en fibrinogène différentes. La viscosité a été mesurée à faible vitesse de cisaillement (4.04 s^{-1}) à l'aide d'un visco-

simètre rotationnel à 37°C. L'impédance électrique sanguine a été mesurée sous des conditions de cisaillement et de température similaires dans une cuvette spécialement élaborée. L'ESR a été déterminée suivant la méthode de Westergren. Un accroissement logarithmique de la viscosité ainsi que de la capacitance, C_m , est noté lorsque le fibrinogène augmente, alors que un accroissement exponentiel est mesuré lorsque la Ht augmente. Cependant, l'ESR montre une diminution logarithmique quand la Ht croît, alors que une diminution exponentielle est observée lorsque le fibrinogène augmente. La viscosité a pu être précisément décrite avec un modèle exponentiel. Sous des conditions similaires de cisaillement et de température in vitro, la viscosité de même que la capacitance électrique du sang non traité rendent compte de l'agrégation des cellules rouges sanguine due à la variation correspondante en Ht et fibrinogène.

KEY WORDS: blood viscosity, electrical impedance of blood, red blood cell aggregation, inflammation

1 INTRODUCTION

Whole blood viscosity is highly dependent on shear rate and therefore blood is called a non-Newtonian fluid. At low shear rate, blood viscosity is an important parameter in vascular medicine for two main reasons. First the viscosity-mediated resistance to blood flow increases at low shear rate, due to the occurrence of red blood cell aggregation [1 - 3]. Low shear rate not only exists at the venous side of the circulation, but is present also in the center of the flow in arteries [4]. The other important aspect of whole blood viscosity at low shear is that it also reflects inflammatory activity [5, 6] as this is also strongly correlated with the aggregation tendency of red blood cells [7, 8]. Therefore, in patients with chronic inflammatory diseases and hence enhanced RBC aggregation, whole blood viscosity at low shear rate is increased.

Red blood cell aggregation is mainly determined by the hematocrit and by the presence of macromolecules in the medium, of which fibrinogen is the most important [9, 10]. Most inflammatory 'acute-phase' proteins, of which especially C-reactive protein (CRP) and fibrinogen are determined in clinical practice, are present also during chronic inflammation.

The most widespread method in clinical medicine to measure the red blood cell aggregation tendency as a marker of inflammation has been the determination of the erythrocyte sedimentation rate, *ESR* [11, 12]. However, the *ESR* is

measured in stagnant blood. Another method, recently introduced for determination of red blood cell aggregation, is the electrical impedance technique [13 - 15]. This method can be used also during flow of blood.

Aim of our study was to investigate in low shear rate conditions in-vitro, whether the electrical impedance of blood reflects adequately whole blood viscosity over a wide range of hematocrit (Ht) levels and fibrinogen concentrations. Using electrical blood impedance in vascular medicine might open the possibility of on-line estimation of the two afore-mentioned aspects of whole blood viscosity at low shear: its hemodynamic consequences and its capacity to reflect inflammatory activity.

2 MATERIALS AND METHODS

2.1 STUDY PARTICIPANTS

7 healthy volunteers (5 males, 2 females) participated in this study after informed consent was obtained. Age varied between 25 and 50 years with a mean of 35. Two were smokers and 5 non-smokers. No history of infection was present in the weeks before blood donation.

2.2 BLOOD SAMPLING

Two hundred ml of blood was collected from each individual and heparinized (25 IU/ml blood).

An amount of 0.1 ml of blood was used for measuring hematocrit, *Ht*, (in duplo) by using a micro-hematocrit centrifuge at 15000 g for 5 min. In the remaining blood sample, plasma and cells were separated by centrifugation at 800 g during 10 minutes. Using these constituents, we made 7 ml solutions of blood which after addition of a 1 ml fibrinogen solution (see below), had *Ht* values of 30, 37, 44 and 51%. For the *Ht* of 44% we prepared 5 samples, for the others 4.

2.3 FIBRINOGEN ADDITION, SAMPLE PREPARATION

A dialysis of purified human fibrinogen (Enzyme Research Laboratories) was performed during 24 hours in 0.9% NaCl solution to obtain an isotonic and iso-osmotic solution. The Na-citrate buffer in which the human fibrinogen was delivered was diluted until 10%, resulting in a pH of 7.4 - 7.5. To each initial 7 ml blood sample, 1 ml 0.9% NaCl/Na-citrate buffer with no fibrinogen or one of 3 increasing levels of fibrinogen were added. This resulted in 16 samples of 8 ml with 4 different *Ht* values (30, 37, 44 and 51%) and 4 different fibrinogen levels varying between 2 and 12 g/l. The extra 44% *Ht* sample received 30 mg addition of fibrinogen (3.75 g/l) and was used as control to check stability of the impedance and viscosity measurements over time. We placed all tubes in a temperature-controlled incubator (37°C) on a rocking platform to ensure permanent mixing of the blood. We performed all measurements within 5 hours after blood collection; the sample identical to the control sample was tested first and the control sample was tested as the last one. Measurements of the different mixtures were performed in random order. From each tube we took 0.1 ml to determine again *Ht* (in duplo).

2.4 IONS AND PH

The levels of sodium Na = 142 ± 0.95 mmol/l, potassium K = 3.3 ± 0.45 mmol/l, and pH = 7.45 ± 0.07 remained constant in all samples during the experiments.

2.5 VISCOSITY MEASUREMENTS

One ml of blood was used for the determination of viscosity using a rotational viscometer (Contraves LS 30, proRheo, Althengstett, Ger-

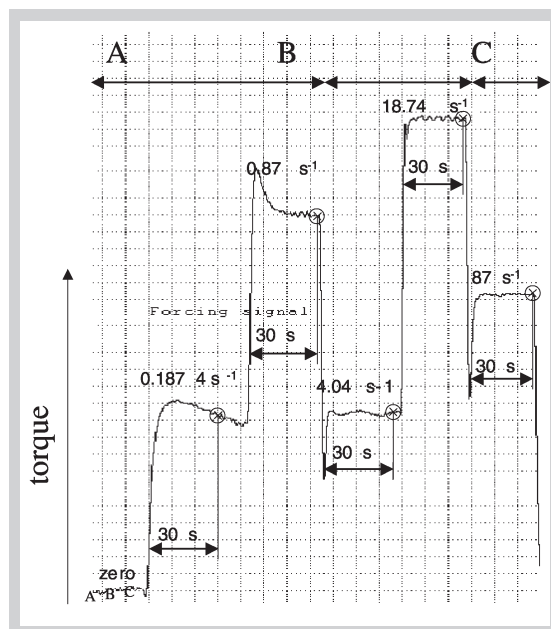


Figure 1: Example of a viscosity recording with the Contraves LS 30 at 5 consecutive shear rates (0.1874, 0.87, 4.04, 18.74 and 87 s⁻¹). The torque was read out always 30 sec after starting a new shear rate (A = first sensitivity range, B = second sensitivity range, C = third sensitivity range).

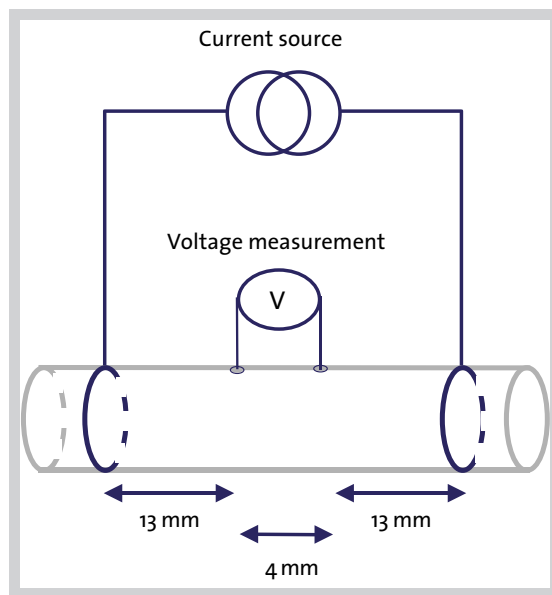
many). Viscosity measurements were performed at 5 consecutive shear rates: 0.1874, 0.87, 4.04, 18.74 and 87 s⁻¹ always at a temperature of 37°C. The viscosity was continuously recorded in a PC based data acquisition instrument (Dataq Instruments, Akron, Ohio, USA). Considering the time dependency of low shear whole blood viscometry [9], we measured according to a fixed time protocol, depicted in Fig. 1. After an equilibration phase of the blood sample in the cup of the Contraves LS 3 during 1 minute, shearing was started and torque was determined at the indicated moments in Fig. 1. From the torque read out and the applied sensitivity range the viscosity was calculated. The entire viscosity measurement for each sample took always less than 5 minutes.

2.6 IMPEDANCE MEASUREMENTS

Electrical resistivity of blood, R_p , and its capacitance, C_m , were measured in 3.8 ml of blood placed in a so called Rho-cuvette (4 ml) leaving space for a small 0.2 ml bubble (CD-Leycom, Zoetermeer, The Netherlands). Measurements were performed by applying alternating current of $100 \mu A_{rms}$ at 20 kHz, 800 kHz and 1200 kHz using a recently developed impedance measuring instrument [16]. The Rho-cuvette consists of a perspex cylinder containing a four-electrode impedance measuring configuration [17]. Two outer cylindrical electrodes administer current to the sample and the two inner electrodes measure the resulting voltage drop (Fig. 2). During measurement, mixing of blood and constant temperature (37°C) are maintained by placing the Rho-cuvette on a rocking platform in a temperature controlled (0.1°C stability) water basin. The rocking frequency was 0.25 Hz, which resulted in a directional change in flow each 2 seconds.

Figure 2 (left): Schematic design of the Rho-cuvette, and the four-electrode positioning (Cd-Leycom, Zoetermeer, The Netherlands).

Figure 3 (right): Non-linear regression analysis between predicted whole blood viscosity according to the equation of Walburn and measured viscosity determined at different shear rates (0.19, 0.87, 4.04, 18.74, 87 1/s), different hematocrits (between 30 and 51%), and increasing levels of fibrinogen (between 1.5 and 12.9 g/l; $r^2 = 0.95$)



All measurements were recorded using the above mentioned data recording system.

The impedance registration at the 3 different frequencies (20, 800 and 1200 kHz) started after a conditioning rocking period of 3 minutes. Data, averaged over a 50 ms period, were obtained when the cuvette had reached its most upwards position, which was always 1 s after noticing a short (200 ms) impedance rise due to bubble passage. The average was taken of 3 successive measurements. R_p and C_m were calculated from the impedance-value at 20, 800 and 1200 kHz according to the formula described by Zhao et al. [18]. In order to calculate the specific resistivity of blood, the cuvette was calibrated by using different saline concentrations of which the specific resistivities were determined in a calibration instrument of CD-Leycom.

2.7 ERYTHROCYTE SEDIMENTATION RATE (ESR)

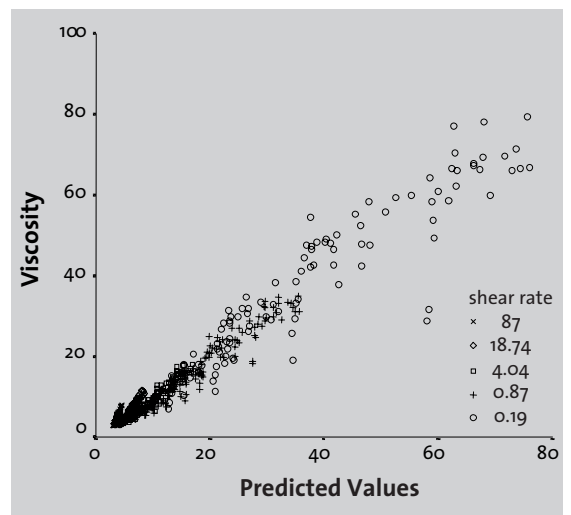
The erythrocyte sedimentation rate was determined according to the classical Westergren method [12].

2.8 FIBRINOGEN AND HEMATOCRIT

After the impedance measurement, the blood from the cuvette was utilized for a control measurement of the fibrinogen concentration (von Clauss method). Fibrinogen data reported in this study are derived from this measurement. Furthermore, a control determination of the Ht was derived automatically with a Radiometer (Copenhagen, Denmark) instrument.

2.9 STATISTICAL ANALYSIS

We analyzed the relation between viscosity and the variables impedance, Ht and fibrinogen levels by means of non-linear regression using the shear stress model, described by Walburn et al.



[19], being modified to express viscosity and also adding a constant term A :

$$\eta = A + c_1 e^{c_2 H} \left[e^{c_4 \left(\frac{TPMA}{H^2} \right)} \right] \dot{\gamma}^{-c_3 H} \quad (1)$$

where η is the viscosity, H is Ht (0.00-1.00), $TPMA$ is the total protein minus albumin (for which we substituted Fibrinogen) and $\dot{\gamma}$ is the shear rate. Because the Walburn formula was based on viscosity measurements mainly determined at high shear rate, we developed also a more appropriate model for low shear rate conditions. This model was used to relate impedance parameters to the measured variables and to predict viscosity from impedance measurements (SPSS version 9.0 for Windows, Microsoft). Unless otherwise stated, data are expressed as mean $\pm$ SD. A p-value of < 0.05 was considered to be statistically significant.

3 RESULTS

3.1 HEMATOCRIT

The obtained values of Ht (measured in duplo) were $30 \pm 0.1\%$, $37 \pm 0.2\%$, $44 \pm 0.1\%$ and $51 \pm 0.2\%$ (centrifugation method) and $29.6 \pm 0.6\%$, $36.1 \pm 0.8\%$, $42.7 \pm 1.0\%$, and $49.6 \pm 1.2\%$ according to the automatic analysis (OSM2hemoximeter, Radiometer).

3.2 FIBRINOGEN

The obtained 4 fibrinogen levels slightly varied because the basal level was not equal in the 7 volunteers and some variation was applied in the added amounts. The basal fibrinogen level did not exceed 3.1 g/l, demonstrating that no signs of inflammation were present. The respective mean obtained fibrinogen levels in the preparations were 2.2 ± 0.5 g/l, 4.3 ± 0.5 g/l, 7.1 ± 1.1 g/l, and 10.8 ± 1.6 g/l.

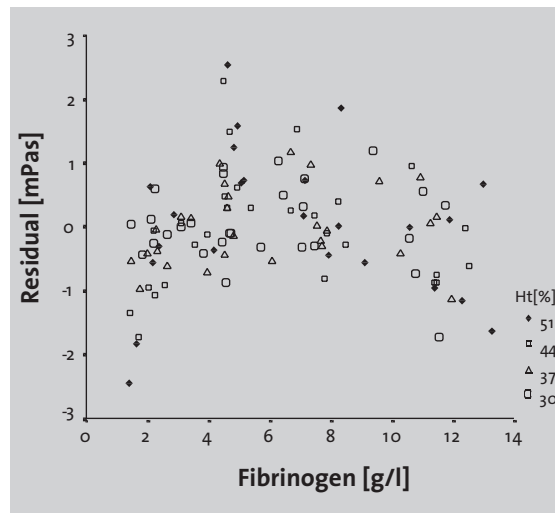
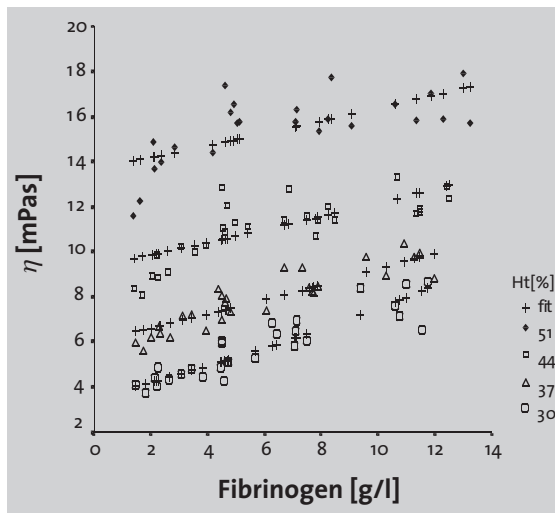


Figure 4:
a (left above): Relation between measured whole blood viscosity at the single shear rate 4.04 sec^{-1} versus fibrinogen level [g/l] for 4 different hematocrits [%]. The fitted values according to the equation of Walburn for each hematocrit are depicted by "+".

b (right above): Residuals from the Walburn equation showing that the model fits too high values for low and for high fibrinogen levels.

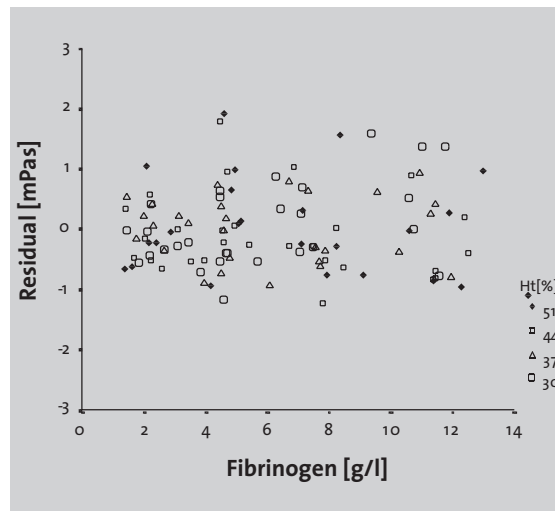
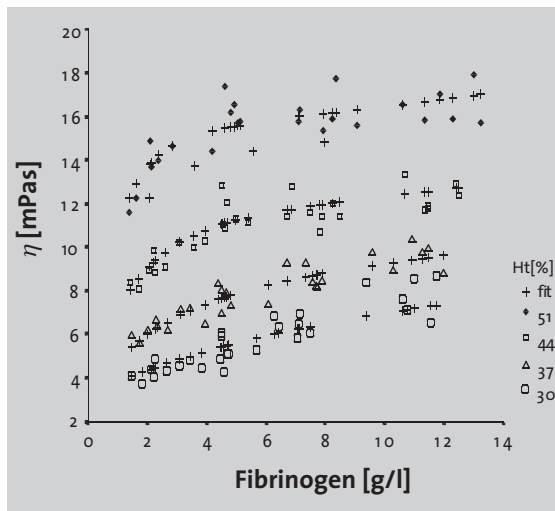


Figure 5:
a (left below): Relation between measured whole blood viscosity at the single shear rate 4.04 s^{-1} versus fibrinogen level [g/l] for 4 different hematocrits [%]. The fitted values according to Eq. 2 for each hematocrit are depicted by "+".

b (right below): Residuals from our formula show that the model fits good for low as well as for high fibrinogen levels.

3.3 VISCOSITY MEASUREMENTS

The viscosity data over the whole range of shear rates were evaluated according to the equation of Walburn, which showed a highly significant correlation ($r^2 = 0.95$, Fig. 3). The coefficients of Eq. 1 with the corresponding standard errors, SE, confidence intervals were: $A = 1.09$ (SE 0.41), $C_1 = 0.99$ (SE 0.10), $C_2 = 0.06$ (SE 0.0017), $C_3 = -0.01$ (SE 0.0003) and $C_4 = 60.4$ (SE 3.9). In a subsequent analysis we focused on modeling the viscosity measurements at a low shear rate of 4.04 s^{-1} in relation to the applied variables. This shear rate was selected because aggregation phenomena dominate at low shear rate and because this shear rate is of the same order of magnitude as applied in our impedance measuring device. Using the Walburn equation for this shear rate the obtained fit did not describe with sufficient detail the viscosity data of our experiments (Fig. 4). Especially at the lower (physiological) levels of fibrinogen this equation did not describe the important increase of viscosity with increasing fibrinogen, nor the tendency of reaching a plateau phase at highest fibrinogen and highest Ht . Therefore, we developed another model to describe the low shear viscosity data for

the different Ht and fibrinogen levels, which was expressed as

$$\eta = A + B \cdot \text{Fib} + C \cdot Ht^D \cdot \left(1 - e^{(E \cdot \text{Fib} \cdot Ht^D)}\right) \quad (2)$$

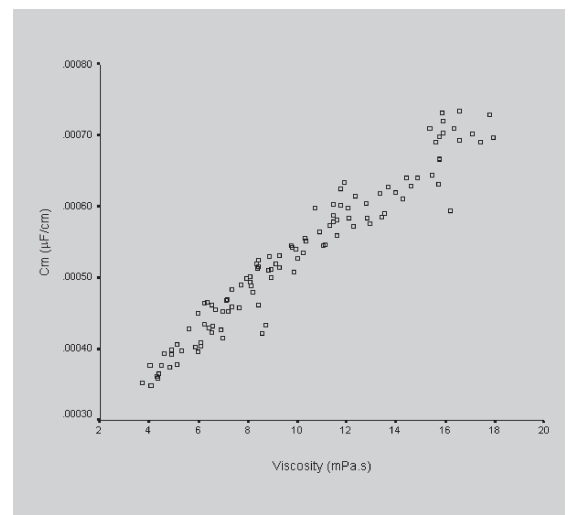
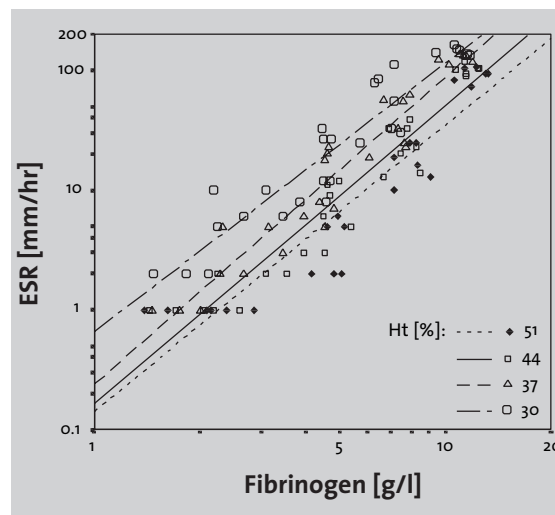
where η is the blood viscosity, Fib the fibrinogen level, Ht the hematocrit (0–1), and A, B, C, D, E are constant coefficients. Figure 5 shows the predicted data according to Eq. 2 versus our experimental data. A highly significant correlation ($r^2 = 0.97$) between our experimental data and the predicted values was obtained. The values for the coefficients and the corresponding standard errors are $A = 3.19$ (SE 0.38), $B = 0.16$ (SE 0.03), $C = 85.8$ (SE 9.5), $D = 2.97$ (SE 0.2), and $E = 7.6$ (SE 1.5).

3.4 ERYTHROCYTE SEDIMENTATION RATE, ESR

In contrast to whole blood viscosity, which increases with fibrinogen and Ht , ESR shows that for all fibrinogen levels a higher Ht decreases ESR (Fig. 6). Univariate analysis of variance showed the ESR relations versus fibrinogen to be different ($p < 0.001$) for the varying Ht levels.

Figure 6 (left):
For each different hematocrit a linear relation is obtained between erythrocyte sedimentation rate and fibrinogen. An increase in hematocrit appears to decrease sedimentation rate.

Figure 7 (right):
Comparison between whole blood viscosity measured at shear rate 4.04 s^{-1} and the impedance parameter C_m , measured in similar low shear conditions.



3.5 IMPEDANCE MEASUREMENTS

A high correlation ($r^2 = 0.97$) was found between the whole blood viscosity at shear rate 4.04 s^{-1} and the impedance parameter C_m (Fig. 7). Comparing C_m with the viscosity measurements at the other shear rates of 0.1874 , 0.87 , 18.74 and 87 s^{-1} showed correlations of respectively 0.95 , 0.96 , 0.96 and 0.93 . Using the developed model (see Eq. 1) also for C_m , a highly significant correlation ($r^2 = 0.96$) was found between the predicted C_m and the experimental data.

Interestingly, in contrast to C_m the R_p was much less sensitive to fibrinogen. In the levels of fibrinogen below 6 g/l , which are most relevant for clinical medicine, R_p was almost independent of fibrinogen. R_p only showed some sensitivity to fibrinogen with increasing Ht . This can be illustrated by comparing R_p and C_m at lowest and highest Ht for two different fibrinogen values in the clinical range ($< 6 \text{ g/l}$). For $Ht = 37\%$ and fibrinogen 2 and 5 g/l , R_p was respectively 123.8 ($SE 2.2$) and 124.5 ($SE 1.3$) Ohmcm (0.6% difference). C_m was respectively 451.9 ($SE 5.9$) and 492.4 ($SE 12.3$) pF/cm (9.0% difference). For $Ht = 51\%$ the same fibrinogen variation showed R_p to be respectively 173.2 ($SE 3.4$) and 176.2 ($SE 3.4$) Ohmcm (1.7% difference) and C_m 605.5 ($SE 13.3$) and 656.2 ($SE 23.9$) pF/cm respectively (8.4% difference). Therefore, for this clinical range of fibrinogen and Ht it appears that using the mere 2 impedance parameters C_m and R_p it is possible to predict rather accurately ($r^2 = 0.82$) whether a change in R_p and C_m is due to a variation in Ht and/or in fibrinogen. The measured and predicted level in fibrinogen on base of R_p and C_m can be described according to the expression

$$\text{fibrinogen}_{\text{predicted}} = A + B \cdot R_p + C \cdot C_m \quad (3)$$

while slope and intercept were allowed to vary from case to case [1-7].

4 DISCUSSION

Nowadays atherosclerosis is considered to have a major chronic inflammatory component [20, 21]. Accordingly the determination of 'acute-phase' proteins has improved cardiovascular risk assessment in the short and long term in individuals with known coronary disease [22, 23], as well as in apparently healthy populations [24]. The common characteristic of most 'acute-phase' proteins is that they increase RBC aggregation [7, 8]. In the determination of blood sedimentation rate, RBC aggregation has been used since many years as a marker of systemic inflammation [9]. Similarly, assessment of blood echogenicity, which is also importantly influenced by RBC aggregation, has been proposed as an alternative method to monitor acute phase reactions [25]. As is well known from previous studies, whole blood viscosity at low shear rate, being predominantly influenced by RBC aggregation, also reflects adequately the inflammatory activity while blood is flowing. However, determination of whole blood viscosity is rather cumbersome and therefore new approaches like measuring electrical impedance of blood, possibly applicable in an online set up, are worthwhile to investigate.

In this study the blood viscosity data at 5 different shear rates could be fitted well with the shear stress adapted model of Walburn. Obviously the highest viscosity values, derived at the lowest shear rates, dominate this evaluation and it can be observed that viscosity at the lowest shear rates increase by a steeper slope than the prediction (Fig. 3). However, applying the equation for viscosity data at a fixed low shear rate (4.04 sec^{-1}) with only variation of Ht and fibrinogen, the Walburn equation appears to fail (Fig. 4). Reason is that this equation was developed to cover viscosity variations at high shear rates. At low shear rate and at higher levels of fibrinogen, especially at higher Ht , a plateau-phase

occurs as has been described in earlier studies of viscometry [26] and photometry [27]. Both characteristics could be described very accurately by a newly developed formula, which was based on our own blood viscosity data at shear rate 4.04 sec^{-1} (Fig. 5). Extension of these findings to other shear rates may deliver a very accurate viscosity description based on Ht and fibrinogen content, which will be highly useful in the modeling of blood in computational fluid dynamics as applied in many patient studies.

In the last century the erythrocyte sedimentation rate, *ESR*, introduced by Fahraeus and Westergren in 1928 has been the most widely used clinical tool to measure the red cell aggregation. One of the important pitfalls of the *ESR* is its lack of specificity and sensitivity due to the influence of Ht [28] although a linear correction for Ht has increased its diagnostic value [29]. Our *ESR* data also show the influence of Ht , and from our data it appears that a non-linear correction should be made (Fig. 6). Indeed, whole blood viscosity at low shear is also strongly influenced by the Ht and this should be taken into account, when viscosity is used as inflammation marker. However, in contrast with *ESR*, viscosity is rightly positively correlated with Ht and therefore an increase in Ht cannot obscure an increase in fibrinogen.

Our experiments show a highly significant correlation between whole blood viscosity at low shear and the impedance parameter C_m measured in similar flow conditions (Fig. 7). In addition, the model developed for blood viscosity and its major variables Ht and fibrinogen could adequately describe the capacitance C_m as well. Although it is well known, that R_p may be used to estimate Ht [30] and therefore viscosity, the more specific fibrinogen dependency of C_m , as demonstrated in this study, may make the latter parameter more useful for determining inflammation marker proteins. Previously, the sensitivity of C_m to aggregation was described also in another set up, which however applied standstill of blood to reach an aggregation time up to 45 s [18]. In the current study we focused to measure C_m in a more physiological set up, applying flow reversal in the measuring set up each 2 seconds. Eventually, it is our goal to develop a catheter based impedance measuring set up, allowing recording of impedance changes as useful markers to predict changes in hemorheology. Using

both impedance parameters, C_m and R_p it appeared possible to predict from these whether a clinically relevant variation occurred in Ht and/or fibrinogen at the same time. In the clinical setting hemorheology plays an important role in vascular hemodynamics and in the occurrence of thrombosis, in an acute as well as in a chronic situation. If hemorheology may be determined adequately by electrical impedance technique, on-line measurement might help to improve hemodynamic deterioration or to prevent thrombosis in patients and might help to evaluate medical therapy.

4.1 LIMITATIONS OF THE STUDY

A limitation of our study is that we were not able to measure the electrical parameters at exactly identical shear rate conditions as applied for whole blood viscosity determination. Therefore, instruments need to be developed to make this possible. Fibrinogen is not the only acute-phase protein that increases aggregation in a chronic inflammatory disease like atherosclerosis. C-reactive protein (CRP) and other acute-phase proteins have shown to have also effects on RBC aggregation [7]. But as RBC aggregation is the pivotal factor in this process and as C_m increases with the area of contacting cell membranes [31], the current results probably also reflect the effects when studying the addition of other acute-phase proteins.

CONCLUSION

Whole blood viscosity at low shear rate can be described accurately by a mathematical model, with hematocrit and fibrinogen as variables. This model adequately incorporates the non-linear effects of hematocrit and fibrinogen on viscosity. The combined electrical impedance parameters of blood, i.e. resistivity and capacitance, also accurately reflect changes in hematocrit and fibrinogen concentration and can thus be used to predict changes in whole blood viscosity. Consequently, the blood impedance measuring technique offers potential as detector of inflammation and is useful for estimation of changes in blood viscosity over time.

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