Blood Viscosity and Blood Pressure: Role of Temperature and Hyperglycemia

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We planned a study to research the relations among blood pressure (BP), viscosity, and temperature in healthy subjects and among BP, viscosity, and glucose in diabetics. With simple random sampling method, 53 healthy and 29 diabetes mellitus (DM) type II subjects were selected. Parameters were determined with capillary viscometer and glucometer at 22°C, 36.5°C, and 39.5°C in healthy subjects, and at 22°C on diabetic patients during OGTT with 75 g of glucose. Statistical evaluations of the data were made with regression analysis, Student *t* test, Spearman's correlation, and analysis of variance. When temperature decreased from 36.5°C to 22°C, blood viscosity increased 26.13%. This increase resulted in a 20.72% decrease in blood flow rate. According to the Hagen-Poiseuille equation, the required BP increase for compensation of the resulting tissue ischemia was 20.72%. Also, a 34.73% decrease in erythrocyte deformability and 18.71% increase in plasma viscosity were seen. When temperature increased from 36.5° to 39.5°C, blood viscosity decreased 10.38%. This caused 11.15% decrease in blood flow rate, and 11.15% decrease in BP, according to the equation. Erythrocyte deformability increase of 9.92% and plasma viscosity decrease of 4.99% arose from the temperature rise. There is a correlation between total data for temperatures and viscosities ($r = -0.84$, $P < .001$). When the mean value of blood glucose increased from 100 to 400 mg/dL, viscosity increased 25% ($r = 0.59$, $P = .002$). In this state, blood flow rate decrease was 20% and BP increase for physiological compensation was 25%. Consequently, temperature, glucose and viscosity levels of blood are important factors for BP. Am J Hypertens 2001;14:433–438 © 2001 American Journal of Hypertension, Ltd.

Key Words: Viscosity, hyperglycemia, circulatory load, blood pressure, temperature.

The aim of our study is to research the relationships among temperature, glucose concentration, and viscosity of blood and plasma, and to calculate their effects on blood pressure (BP) according to Hagen-Poiseuille's hydrodynamics equation.

If the human circulatory system is considered as a closed system, hemodynamic equilibrium can be determined according to Poiseuille's equation through the pressure, viscosity, flow rate, velocity of blood, and vessel diameter. Viscosity can be defined as the resistance of fluids against flow. The resistance for blood circulation includes friction between the blood elements and between the vessel lumen and blood. To make a fluid flow, the application of energy is required. Therefore, the energy of the circulatory system is spent in correlation with the viscosity level of blood. Energy forms of the circulatory system are BP and blood flow velocity. The velocity (v) and pressure of blood flow can be determined with Poiseuille's equation as $v = 1/4\eta L\,(F_1 - F_2)\,(a^2 - r^2)$, and also BP rate (Q) can be expressed from the above equation as $Q = \pi a^4/8\ \eta L\ (F_1 - F_2)$, where η is the viscosity of the fluid, F_1 and F_2 are the initial and the final cross sectional pressures of blood, L is the length, a is the radius of vessel, and r is the distance from the center of the vessel for a flowing particle.[1,2] Thus, to keep the equilibrium of the equation constant in the circulatory system, BP will increase when viscosity increases.

It has been shown that between 25.32% and 60.16% values of hematocrit, every 11% increase in hematocrit increases blood viscosity by 20%. In this state, according to Poiseuille's equation, blood flow rate decreases by 16.67%, which may lead to tissue ischemia. To keep the circulatory system in equilibrium (that is, keeping the flow rate sufficient and preventing tissue ischemia), a 20% increase in BP or 4.66% vasodilation is needed.[3] However, the human circulatory system is not an exact closed system, because blood viscosity can be altered with the absorption of food or drugs.[4–8] Additionally, the effects of

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dietary fat and of some drugs on blood viscosity and hemodynamics such as BP have been reported. Because atherosclerotic vessels cannot dilate sufficiently as a response to vasodilator drugs, it has been suggested that increased blood viscosity can only be compensated with a BP increase in such circumstances.[9–12] Also, the relationships among BP, headache, coagulation, blood flow velocity, and blood viscosity have been described via the principles of hemodynamics.[13,14]

The study consisted of two groups. For the first group, our aim was to measure the possible alterations in blood and plasma viscosity and erythrocyte deformability due to temperature changes on healthy subjects, and also to determine the changes of BP by using calculations based upon the law of hemodynamics. As diameters of erythrocytes are larger than those of capillaries, they can only pass through capillaries by deforming. Such a shape alteration capacity of erythrocytes can be measured and defined with the concept of deformability. The free flow time of erythrocyte mass through the viscometer is inversely proportional to erythrocyte deformability.[15] Relationships among blood viscosity, erythrocyte deformability, temperature, and BP have not yet been reported.

The second group consisted of diabetes mellitus (DM) type II patients without diabetic complications. Our aim was to determine the relationship between blood glucose and viscosity during an oral glucose tolerance test (OGTT), and to calculate the effects of these factors on BP with the law of hydrodynamics. Diabetic patients were chosen to research the relationship between glucose and viscosity in a wide range of blood glucose concentrations. Although the relationship between blood glucose and viscosity has been shown, the relationship between blood glucose and BP has not yet been reported.[16,17]

Materials and Methods

Case Selection

For the first group of the study, a total of 53 healthy subjects were chosen by a simple random sampling method. The study population was selected from the visitors of our clinic's patients, who had no complaints and had not used any medications for the last week. The group was made up of 36 men and 17 women with a mean age of 26.5 $\pm$ 6.5 years. For the second group, a total of 29 subjects who had uncomplicated DM and had not taken any medications were selected by a simple random sampling method from newly diagnosed DM type II patients at our department's diabetes mellitus outpatient clinic. Informed consent was obtained from all individuals participating in the study.

Preparation of Blood Samples

After an overnight fasting period, a 9.9 mL blood sample was collected from the brachial vein of every subject over 0.1 mL (500 IU) of heparin sodium. Each sample was centrifuged at 3000 rpm for 5 min by a centrifuge with a 9.5 cm radius. The plasma was obtained as a supernatant and the buff-coat was thrown away. To separate the remaining erythrocyte sediment from leucocytes, it was mixed with 5 mL of 0.9% NaCl solution and centrifuged twice by the same method.

Measurement of Viscosity and Deformability

Measurements were made by using the simple capillary tube viscometer method that has been used in our department since 1990.[3,11,12,18] The viscometer had a reservoir at the upper part with a volume of 2 mL. It was filled in the vertical position with fluid sample to the upper line of the reservoir, and then the free flow time of the sample to the lower line of the reservoir was measured in seconds (sec).

If the free flow time of distilled water is accepted as 1, the value achieved by comparison to the free flow time of a sample may be termed as "relative viscosity".

The viscometer was used at the selected constant laboratory conditions in the same vertical position and without exposure to direct sunlight or airflow. We used free flow time instead of relative viscosity value as data, to make the statistical and graphic estimates more accurate and to prevent rounding of the calculations.

The free flow times of blood, plasma, and erythrocyte mass were determined at 22°, 36.5°, and 39.5°C. To prevent protein precipitation, the viscometer was used after it was washed with 0.9% sodium chloride solution, rinsed with distilled water, and dried with acetone. For study at different temperatures, the viscometer was placed in a transparent, plastic enclosed bath system, in which the two ends of the viscometer stood vertically and heat-controlled water was circulated continuously with a high output peristaltic pump in the bath system.

Erythrocyte deformability is the shape-changing capacity of an erythrocyte. One of the methods to measure deformability is determination of erythrocyte passing time through a filter that has standard sized pores. Because of the difference in erythrocyte diameter and volume between individuals, the specificity and the sensitivity of this method may be insufficient.[15] Because free flow time of pure erythrocyte mass represents erythrocyte deformability, fluidity, and internal viscosity, and because using the viscometer to determine the erythrocyte free flow time was more inexpensive and easier, we preferred this method and its data for the study.

Measurement of Blood Glucose Concentration

The blood glucose concentration measurements were made with an Accutrend GC glucometer (Boehringer Mannheim, Mannheim, Germany). At least four measurements of blood glucose and simultaneous measurements of

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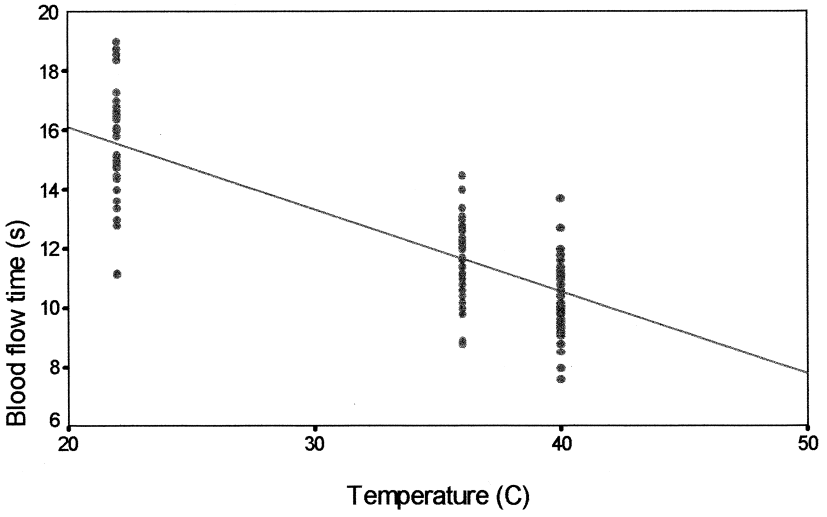

FIG. 1. Effect of temperature on blood viscosity. When blood temperature decreases from 36.5° to 22°C, blood viscosity increases 26.13%. If temperature increases from 36.5° to 39.5°C, blood viscosity decreases 10.38%. To make a more accurate presentation in the graphic representation and statistics, instead of the "relative viscosity" value, blood free flow time in seconds (s) was used as data. When all of the differences at three temperatures are evaluated together, a negative correlation is seen between blood temperature and viscosity ($r = -0.84$, $P < .001$).

blood and plasma viscosity were made for all of the 29 cases at 0, 30, 60, and 120 min at 22°C, after ingestion of 75 g of glucose.

Statistical Evaluation

Results of the first group were evaluated statistically with the Student *t* test and Spearman correlation test. The relationship between blood glucose concentration and viscosity was evaluated statistically by using the Student *t* test, analysis of variance, and regression analysis.

Results

Relationship of Blood Temperature, Viscosity, and Pressure

When the blood temperature decreased from 36.5° to 22°C, the mean blood free flow time increased from 11.62 to 15.55 sec (26.13%). According to Poiseuille's equation, the blood flow rate decreases 20.72%, and for the compensation of this ischemic state, a 26.13% BP increase or 5.9% vasodilation is needed. If viscosity (η in the denominator of the equation) changes from 100 to 126.13 (26.13%), the flow rate Q would decrease 100/126.13 = 20.72%. If viscosity increases 26.13%, the pressure ($F_1 - F_2$) value (multiplier in the equation) must be increased with the same percentage to keep the equation constant. When the viscosity increases 26.13%, to keep the flow rate constant, the radius of vessel (initial) a^4, must increase 26.13%. The calculation of this increased radius (final) is $a^4_{\text{final}} = 1.2613 \times a^4_{\text{initial}}$. From this calculation, $\alpha_{final} = \sqrt[4]{1.2613} x a_{initial} = 1.0597$ and so, 5.97% vasodilation can be estimated.

When the temperature increased from 36.5° to 39.5°C, the blood free flow time decreased from 11.59 to 10.58 sec (10.38%). In this state, the blood flow rate increased 11.15%; according to Poiseuille's equation, a 10.38% decrease in BP or 2.71% vasoconstriction was needed to keep the hemodynamic equilibrium constant.

The correlation between temperature and blood viscosity is $r = -0.84$, $P < .001$ when all the differences at the three temperatures are evaluated together (Fig. 1). When all of the blood free flow time data for the three temperatures were evaluated together according to age, there was a negative correlation ($r = -0.1381$ and $P < .05$); when the data were evaluated according to sex, it was found that the mean blood free flow time in women was 12.97% less than that in men ($r = 0.3408$, $P < .001$).

When the temperature decreased from 36.5° to 22°C, plasma free flow time rose from 4.81 to 5.71 sec (18.71%); with a temperature increase from 36.5° to 39.5°C, it decreased from 4.78 to 4.57 sec (4.99%). A negative correlation was seen ($r = -0.9342$, $P < .001$) when the plasma flow times at the three temperatures were evaluated together. With a temperature decrease from 36.5° to 22°C, erythrocyte free flow time increased from 27.03 to 36.42 sec (34.73%). When the temperature increased from 36.5° to 39.5°C, erythrocyte free flow time decreased from 27.02 to 24.35 sec (9.92%). There was a negative correlation between temperature and erythrocyte free flow time ($r = -0.62$, $P < .001$). All of the blood, plasma viscosity, and erythrocyte deformability differences due to temperature were statistically significant ($P < .001$).

Relationship of Blood Glucose, Viscosity, and Pressure

The correlation coefficient of blood glucose versus blood free flow time and plasma free flow time ranged from 0.59 to 0.49 and from 0.55 to 0.53, respectively. Regression

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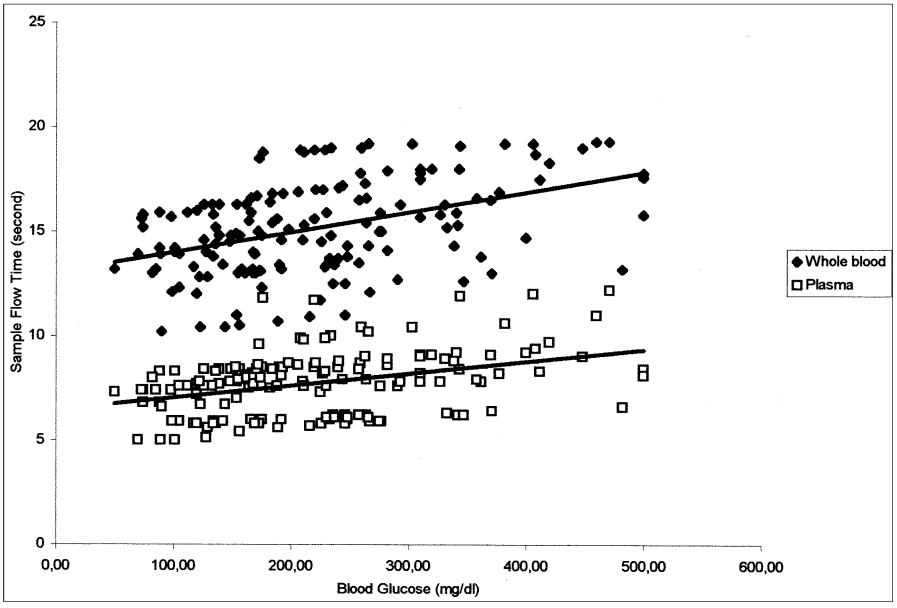

FIG. 2. Representation of the role of blood glucose on blood viscosity on scatter diagram with regression lines. Changes in the values of the blood free flow time and the plasma free flow time were measured with the capillary viscometer in seconds and used as the data against blood glucose concentrations of oral glucose tolerance test (in mg/dL). Correlation coefficient of blood glucose versus blood viscosity and plasma viscosity levels ranged from 0.59 to 0.49 ($P = .002$) and from 0.55 to 0.53 ($P = .0007$), respectively.

lines were drawn for free flow time of blood and plasma versus blood glucose concentrations, and their slopes did not show any significant difference. Thus, the below formulas were derived from the equation $y = ax + b$: blood free flow time = (0.011)(blood glucose) + 12.10; plasma free flow time = (0.008)(blood glucose) + 5.4.

From these formulae, the calculated blood free flow time for a 100 mg/dL blood glucose concentration was 13.2 sec, and plasma free flow time was 6.2 sec. For each 100 mg/dL increase in blood glucose concentration, there was a 1.1 sec increase in blood free flow time and 0.8 sec increase in plasma free flow time. At 400 mg/dL blood glucose concentration, blood free flow time increased from 13.2 to 16.5 sec (25%).

In the regression analysis, the following values were calculated: $F = 11.59$, $P = .002$ ($P < .05$) for blood free flow time and $F = 14.6$, $P = .0007$ ($P < .05$) for plasma free flow time. The squared multiple correlation coefficient (R^2) value was 0.35, meaning that there was a 35% effect of the blood glucose on the blood free flow time.

The relationship between the blood and the plasma viscosity values versus glucose concentrations are represented on scatterplots with regression lines in Fig. 2. Significant increases in glucose concentration and viscosity values (free flow time) of blood and plasma were observed ($P < .05$). According to Poiseuille's equation, a 25% increase in viscosity results in a 20% decrease in blood flow rate. For the physiological compensation of this ischemic state, a 25% increase in BP or a 5.7% vasodilatation was required.

Discussion

The Effect of Temperature on Blood Pressure

The observed BP increase of 26.13% related to decreased temperature and increased viscosity must be clinically important. As the main goal of the control system of blood circulation is keeping the blood flow volume at a constant and sufficient rate, some of the high BP measured in patients may be due to physiological compensation of decreased blood flow rate.

The temperature of the lower extremities in normal conditions is approximately 25°C,[19] and the temperatures of the extremities, face, lungs, and other parts of the body can decrease in cold weather. This situation can lead to decreased blood flow rate due to increased blood viscosity, and can explain the coronary angina and exertion difficulty observed in a cold environment. A similar state is medical hibernation, in which blood temperature falls to 22°C. Because atherosclerotic vessels cannot dilate and sufficiently respond to vasodilator drugs, BP increase may be the main mechanism for prevention of ischemia in some patients.[20–24] The risk for ischemia can be increased in a cold environment if patients are hypertensive and have no reserve capacity of BP increase to compensate the circulatory load. In these patients, decreasing viscosity by using appropriate drugs should gain importance.[11,12]

The pressure decrease of 10.38% due to a temperature increase to 39.5°C must be clinically important. This information can explain some clinical situations such as hypotension attacks observed in hot environments, and

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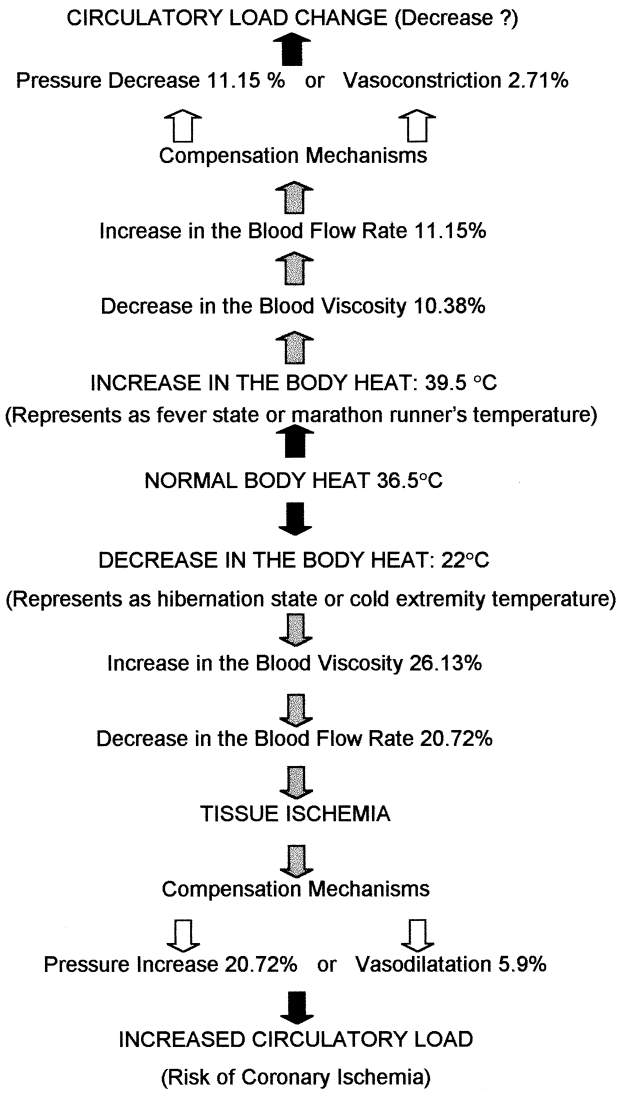

FIG. 3. Presentation in a flow chart of the stoichiometric relations of the changes in the blood viscosity, flow rate, pressure, and vessel diameter with the changing blood temperature.

fever-related tachycardia, which is the early physiological compensatory reflex for decreased BP.[19] Additionally, keeping the body temperature at about 39.5°C during a marathon run may bring a circulatory advantage to an athlete by increasing the blood flow rate via decreased viscosity. The power gain of athletes before competition by warm-up exercises can be considered as an example supporting this point. As decreasing blood viscosity has an effect similar to decreasing the peripheral resistance of circulation, blood temperature becomes an important factor for peripheral resistance and BP. The flow chart in Fig. 3 shows the relationships among BP, viscosity, and temperature.

The above calculations and interpretations can be made for the observed relationships among temperature, plasma viscosity, and erythrocyte deformability.

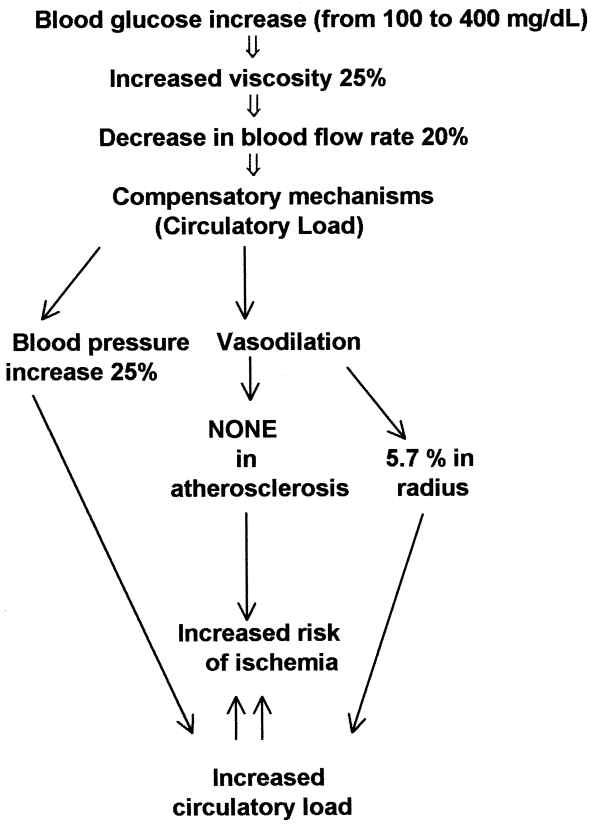

FIG. 4. According to Hagen-Poiseuille Hydrodynamics Law and our study results, stoichiometric relations between BP, viscosity, glucose, flow rate, and vessel diameter can be shown as a biological system analysis in a flow chart.

The Effect of Glucose on Blood Pressure

We showed that BP must increase 25% to compensate the decreased blood flow rate due to hyperviscosity seen with hyperglycemia at 400 mg/dL, and this finding must be clinically important.

After an insulin-resistant state had been shown in essential hypertension,[25] Resnick et al reported that in normal and hypertensive patients, increasing glucose concentrations raised intracellular calcium ion concentrations in erythrocytes.[26] Then, Barbagallo et al demonstrated that hyperglycemia may underlie the predisposition to hypertension and vascular diseases among diabetic subjects by increasing the intracellular free calcium concentrations in vascular smooth muscle cells.[27]

Because vascular complications and atherosclerosis are more common in DM, these results can be applied in some clinical situations.[28,29] For diabetics and for diabetics with atherosclerosis, BP increase may be the only possible or dominant compensation mechanism of decreased blood flow rate due to hyperglycemic hyperviscosity, because of insufficient vasodilation led by increased intracellular calcium concentration and atherosclerosis. High BP in a patient who is admitted to the emergency service with hyperglycemic coma can in fact be a physiological response to compensate the ischemia. A rapid and uncon-

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trolled decrease in BP in such a patient before treatment of hyperglycemia can lead to a sudden fall in blood flow rate, which means acute tissue ischemia. Hyperglycemic hyperviscosity can be one explanation for the postprandial exertion difficulty. For the adjustment of antihypertensive drugs, BP measurements under normoglycemic conditions should not be ignored.

These relationships among blood flow rate, glucose, viscosity, pressure, and vasodilatation capacities are shown as a system analysis on a flow chart in Fig. 4.

Conclusion

In this study, we stoichiometrically showed that temperature and hyperglycemia have an important effect on blood viscosity and BP. According to this information, the mechanism of cold weather angina, peripheric resistance, tachycardia, and hypotension in hot weather, postprandial exertion difficulty, and physiological gain with warm-up exercises and with temperature increase can be explained on a new basis. The information in our study increases the number of hemodynamic parameters and should be considered in the treatment and follow-up of patients with hypertension and analysis of the circulatory system.

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