EFFECT OF HEMATOCRIT AND VISCOSITY ON CORONARY CIRCULATION AND MYOCARDIAL OXYGEN UTILIZATION

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The elevation of hematocrit is known to provoke myocardial ischemia in various clinical conditions. In order to clarify the effect of hematocrit and blood viscosity on coronary hemodynamics and oxygen utilization, isovolemic exchanges of blood with plasma or packed red cell were performed in ten open chest anesthetized dogs. Hematocrit was varied in the range of 20 to 60%. Coronary blood flow and cardiac output changed inversely with hematocrit. Coronary vascular resistance and blood viscosity elevated in logarithmic relation to hematocrit. Coronary vascular resistance and blood viscosity revealed linear relationship, the coronary vascular hindrance (resistance/viscosity) remaining constant for the hematocrit range of 20 to 60%.

The arterial oxygen content increased linearly with the elevation of hematocrit, and the myocardial oxygen extraction rate was unchanged. The systemic oxygen transport rate increased with hematocrit. However, the left ventricular oxygen transport rate varied little, although the left ventricular oxygen transport at medium hematocrit was slightly higher than at low or high hematocrit. The myocardial oxygen consumption remained constant at each hematocrit, and the efficiency was high at low hematocrit in the face of the elevated cardiac output.

The increase in hematocrit elevated the blood viscosity and played a significant role in determining the coronary vascular resistance. This could induce a disturbance in coronary microcirculation especially in pathological conditions.

THE disturbance of the coronary circulation is known to be induced not only by the pathological or functional coronary stenoses, but also by rheological changes, such as blood viscosity or hematocrit. The major factors of the hyperviscosity syndrome¹ are the elevation of

hematocrit and plasma fibrinogen, decrease in red cell deformability, aggregation and low shear rate. In patients with angina pectoris or myocardial ischemia the elevation of hematocrit or blood viscosity was noted to be an important causative factor.²⁻⁴ We also found the elevation of hematocrit after blood transfusion to induce the reversible myocardial infarction or ischemic changes in the electrocardiogram.⁵⁻⁶

In order to evaluate the effect of hematocrit and blood viscosity on the coronary circulation and the myocardial oxygen transport, experiments were performed in thoracotomized

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dogs at various hematocrit levels between 20 and 60%.

METHODS

Ten mongrel dogs weighing 10 to 12 kg were anesthetized with intravenous sodium pentobarbital, 30 mg/kg and small supplemental doses. They were ventilated via endotracheal tube by a constant volume respirator with room air, and bilateral thoractomy was performed. After intravenous injection of heparin (1000 units/kg), a modified Gregg cannula with convoluted tip was inserted into the left main coronary artery via the right subclavian artery. The left coronary artery was perfused with own blood led from the left subclavian artery, and coronary blood flow was measured with an electromagnetic flowmeter inserted in the perfusion circuit. Aortic flow was measured with a flow probe placed at the thoracic aorta, and both carotid arteries were perfused from femoral artery in order to include the cephalic flow into the thoracic aortic flow. Aortic and left atrial pressure were measured with the use of transducers. Oxygen contents of arterial and coronary sinus samples were analysed by the Lex-O₂-Con (Lexington Instrument Corp).

Measurements of hemodynamics and oxygen utilization were made at various levels of hematocrit in each of 10 dogs. In order to vary the hematocrit level while maintaining the blood volume constant, fresh heparinized blood was obtained from two donor dogs and the plasma and packed cells were separated. For each step of hemato-

Fig.1. Representative responses in hemodynamic parameters and oxygen contents to the hematocrit changes. The substituted blood volume was shown at the top of the figure.

crit change, 50 ml of blood was withdrawn from the femoral vein, and either plasma or packed

TABLE I HEMODYNAMIC AND OXYGEN UTILIZATION STUDIES AT LOW, MEDIUM AND HIGH HEMATOCRIT

		Low		Medium		High	
		mean	SE	mean	SE	mean	SE
Hematocrit	%	22.6	1.3	37.6	1.3	57.7	2.0
Viscosity 0.0459 sec ⁻¹	CP	40.9	8.7	143.3	22.2	331.8	12.3
Heart Rate	/min	167.3	7.6	162.5	8.6	160.3	5.5
Blood Pressure	mmHg	81.3	3.8	75.6	4.3	81.4	4.5
Coronary Blood Flow	ml/min	88.6	3.5	55.1	5.6	36.4	3.8
Cardiac Output	ml/min	1257	109	905	126	718	93
O ₂ Content Artery	ml/dl	9.2	0.8	15.3	0.7	22.4	1.4
Coronary Sinus		2.3	0.5	3.7	0.7	5.4	0.6
O ₂ Extraction Rate	%	76.0	4.3	76.1	3.9	75.0	4.3
Myocardial O ₂ Consumption	ml/min	6.2	0.6	6.9	0.5	6.2	0.8
Efficiency	g.m/ml	247.9	26.9	139.7	16.0	159.2	34.2
LVO ₂ Transport	ml/min/100g	12.3	1.2	13.9	1.1	12.1	1.2
Systemic O ₂ Transport	ml/min/kg	9.0	1.4	13.2	2.2	15.4	1.5

Fig. 2. Effect of hematocrit variations on blood viscosity at the shear rate of 0.0459 sec^{-1} . The thick line indicated the mean change.

Fig. 3. Effect of hematocrit variations on coronary vascular resistance. The thick line indicated the mean change.

cells of equal amount were infused. Variations in hematocrit over a range of 20 to 60% were achieved.

The hematocrit was determined by centrifugation at 15000 g for 5 min with a microcentrifuge. The blood viscosity was measured at 37°C at shear rates of 4.59, 0.0459, and $0.000624 \text{ sec}^{-1}$ with coaxial cylinder viscometer (Low Shear-100, Contraves).

Coronary vascular resistance (mmHg/ml/min) was calculated by dividing the aortic pressure by coronary blood flow. The vascular hindrance was expressed by dividing the vascular resistance by blood viscosity. The left ventricular oxygen transport (ml/min/100 g) was the product of coronary blood flow and arterial oxygen content, and systemic oxygen transport (ml/min/kg) was the product of cardiac output and arterial oxygen content.

RESULTS

1. Hematocrit, blood viscosity and coronary circulation

The representative responses to the hematocrit variation are shown in Fig. 1. The substitu-

tion of 300 ml of blood with plasma lowered hematocrit to 20.5%, and increased cardiac output and coronary blood flow. The replacement of blood with packed red cells by 100, 100 and 150 ml increased the hematocrit to 37.0, 47.0 and 60.5%, with an elevation of blood viscosity and arterial oxygen content. Cardiac output and coronary blood flow declined with an elevation of hematocrit, while heart rate, blood pressure and left atrial pressure remained fairly constant.

The hemodynamic variations in heart rate, blood pressure, coronary blood flow and cardiac output at low, medium and high hematocrit are shown in Table I. The coronary blood flow increased from 55.1 to 88.6 ml/min in an average with a hematocrit change from 37.6 to 22.6%, and decreased to 36.4 ml/min with an elevation of hematocrit to 57.7%. The cardiac output also declined from 1257 to 905 and 718 ml/min at the low, medium and high hematocrit. The heart rate and blood pressure changed little for a hematocrit range of 20 to 60%.

An increase in hematocrit resulted in a curvilinear elevation of blood viscosity. Values of blood viscosity measured at a shear rate of

Fig.4. The hematocrit is plotted against the logarithm of coronary vascular resistance (upper panel) and blood viscosity (lower panel).

0.0459 sec⁻¹ are illustrated in Fig. 2. The semi-logarithmic plot revealed linear relationship indi-

cating the exponential function between the hematocrit and blood viscosity (Fig. 4).

The elevation of hematocrit increased coronary vascular resistance in a similar fashion (Fig. 3), and the semilogarithmic plot also revealed the linear relationship (Fig. 4). The relationship between the coronary vascular resistance and blood viscosity is shown in Fig. 5. The linear relationship was observed in each experiment indicating the constant vascular hindrance, the resistance divided by the blood viscosity, in the hematocrit range of 20 to 60%.

2. Hematocrit and myocardial oxygen utilization

Systemic and myocardial oxygen transports, myocardial oxygen consumption, oxygen contents in arterial and coronary sinus blood at low, medium and high hematocrit are shown in Table I. The systemic arterial oxygen content increased linearly with the elevation of hematocrit. The coronary sinus oxygen content rose with hematocrit by lesser amount and the myocardial oxygen extraction rate remained constant for the hematocrit range of 20 to 60%. The systemic oxygen transport rate increased with hematocrit. The left ventricular oxygen transport rate was almost constant over the hematocrit range of 20 to 60%, although it was slightly lower in low or high hematocrit than medium hematocrit. The myocardial oxygen consumption remained essentially constant for a hematocrit range of 20 to 60%.

Fig.5. Relationship between blood viscosity and coronary vascular resistance at various hematocrit levels. The thick line indicated the mean change.

This constancy of myocardial oxygen consumption in the face of marked elevated cardiac output at low hematocrit indicated an increase in efficiency for myocardial oxygen utilization.

DISCUSSION

Hematocrit, viscosity and coronary flow

The increase in hematocrit in the present study elevated the blood viscosity and coronary vascular resistance in exponential relationship. Jan et al.⁷ reported that flow resistance relationship in coronary, systemic and pulmonary circulations at various hematocrit showed non linear functions, and the decrease in resistance with hemodilution was greater in the coronary than in the systemic and pulmonary circulations, while the increases in resistance following hemoconcentration were relatively similar in these three circulations. Surjadhana et al.⁸ found that the slopes relating the logarithm of resistance to hematocrit for pulmonary and coronary circulation were not significantly different indicating the role of viscosity to vascular resistances. Similar decrease in coronary blood flow after red cell transfusion was observed in patients with blood loss anemia.⁹

The relationship of hematocrit and blood viscosity at relatively low shear rates was curvilinear, and the logarithmic plot of viscosity to hematocrit showed a linear function in the present study. Burch and DePasquale¹⁰ emphasized the effect of shear rates on the blood viscosity, and calculated the phasic changes of shear rates in coronary circulation, although the effective shear rate in the coronary circulation was yet to be determined. The viscosity revealed the linear relationship to the coronary vascular resistance (Fig. 5), indicating the constant vascular hindrance for the hematocrit range of 20 to 60%. Jan et al.⁷ also found the coronary vascular hindrance index to be constant over a hematocrit range of 20 to 60%, but to decrease beyond this range in either direction. This suggested that changes in coronary flow resistance was attributable to the alteration in blood viscosity.

Myocardial oxygen utilization

The arterial oxygen content increased as hematocrit rose, and this balanced the decrease in coronary flow. The myocardial oxygen extraction did not change with hematocrit. The left ventricular oxygen transport changed little for the hematocrit range of 20 to 60%, and the myocardial oxygen supply was well maintained (Table I). However, the oxygen transport in the coronary

circulation was noted to decline over the hematocrit of 68%⁸ or beyond the range of 20 to 60%.⁷ The effect of lower hematocrit of less than 20% to the left ventricular oxygen transport was controversial; Murray and Rapaport¹¹ observed the increase, and von Restorff et al.¹² found no decrease. The oxygen transport in the systemic circulation increased with the elevation of hematocrit (Table I), but the systemic oxygen transport declined over the hematocrit of 60%.⁷ Thus, the oxygen transport showed bell shaped relations with hematocrit, but the range of optimal hematocrit for oxygen transport was wider in the coronary circulation than in the systemic circulation.⁷

The myocardial oxygen consumption remained constant for the hematocrit range studied. Jan et al.⁷ also observed the constant myocardial oxygen consumption for a hematocrit range of 20 to 60%. As hematocrit deviated from this range in either direction, the oxygen consumption decreased. This constancy of myocardial oxygen consumption was achieved by regulating the rate of oxygen transport, and the coronary dilatation might occur in extreme anemia or polycythemia by metabolic autoregulation.

Clinical implications

The extension of the present data to the clinical situations needed some consideration, since the study was performed in acutely induced normovolemic anemia and polycythemia in normal dogs. Surjadhana et al.⁸ found that the polycythemia per se did not alter the even distribution of flow across the left ventricular wall, but subendocardial underperfusion began at higher perfusion pressure in polycythemic than in normocythemic dogs. Hagl et al.¹³ observed that lowering the hematocrit to 15% under the stenosed coronary artery increased endodiastolic length and decreased the contraction amplitude, while non ischemic segments showed compensatory rise in contraction. The effect of hematocrit or blood viscosity on coronary flow could be different in the coronary stenosis where the maximal coronary dilatation was reached. The increased blood viscosity due to polycythemia could decrease the coronary flow enough to outweigh the high arterial oxygen content, and myocardial hypoxia could occur in the subendocardial layer.

In clinical studies patients with polycythemia vera accompanied hyperlipidemia in 38.8%, and myocardial infarction was found in 30.4% in the hyperlipidemic group, but infarction was

found in 23.4% even in the non-hyperlipidemic group.¹⁴ The effect of hematocrit on cerebral blood flow was also demonstrated by Thomas et al.^{15,16} Cerebral blood flow in patients with hematocrit in the range of 47 to 53% was found to be significantly lower than in the hematocrit range of 36 to 46%, and the venesection increased the flow by a mean of 50%. We also found the elevation of hematocrit after blood transfusion in gastrointestinal bleeding or surgery to induce the reversible myocardial infarction⁵ or ischemic changes in the electrocardiogram.⁶

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