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Hemodynamic Influences of Chronic Post-Hemorrhagic Anemic Blood Transfused into Normal Men*

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The increased cardiac output both in acute and chronic anemia was reported by many investigators.[1,2,3] The mechanism responsible for the increased cardiac output, however, is not satisfactorily settled. The postulation that a humoral agent is delivered to the blood stream in an anemic subject and the action of this humoral principle is to increase the cardiac output has been claimed in dog[4].

This paper reports an experiment designed to confirm the possibility of the presence of such humoral agent in chronic post hemorrhagic anemic human blood.

Subjects and Methods

Two normal and seven anemic men served as blood donors. The anemic donors were in severe chronic post-hemorrhagic anemia as a result of frequent blood donation which ranged on average 2 times a week well over 3 years period. The hematological values of them are listed in table 2. The high cardiac output of them is also shown. The last donation by the anemic men was at least within one week before experimentation. Four hundred and fifty cc. of blood with 150 cc. of anticoagulant were withdrawn in a vacuum bottle and were transfused immediately into the recipient subjects. The blood types of donors and recipients were cross-matched in each case. The recipients were normal subjects and pre-medicated with pentobarbital and were studied recumbent in the post absorptive state and after resting for 30 minutes. The volume of transfusion was 10% of the total blood volume estimated as 8.1%[5] of body weight. Period of transfusion ranged between 20 and 30 minutes. On average the rate of transfusion was 0.35 ml/min/kg.

Cardiac output measurements were made before and 20-30 minutes after the end of blood transfusion. Cardiac output was determined by means of dye dilution method of Stewart-Hamilton[6,7], and the modified formula[8,9] using T-1824. The multiple sampling procedure was employed with sampling device modified from the Newman's apparatus[10]. Arterial sampling was performed through an indwelling needle inserted into the femoral artery. Femoral arterial pressure was recorded through a Statham pressure transducer.

Dye concentration in plasma was read upon an Evelyn electrophotometer using a 620 mμ filter. Measurements of time and concentration components in the T-1824 dilution curve were carried out as defined by Wood and Swan[11,12].

Plasma CO_2 was determined by Van Slyke's manometric apparatus. Plasma pH was measured by a Beckman Model-G pH meter.

Two control experiments were carried out in which normal subjects were infused with normal blood through the same procedures in two subjects.

Results

Control results. The results of two control experiments are summarized in Table 1. At an infusion rate of about 0.35 ml/min/kg of normal blood into normal recipient there was an elevation of blood pressure. In both cases the mean arterial pressure showed a steady increase during the period of infusion. After cessation of infusion the blood pressure returned to the pre-infusion level. Total peripheral resistance increased after infusion in both cases.

Anemic blood infusion. Results are summarized

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Table 1. Hematologic and Hemodynamic Indices of Recipient Subjects. Subject Number of Donor (Table 2) and Recipient Corresponds Each Other.

Subj. No.		HR (per min)	RBC (million/mm³)	Hct (%)	Hb (gm/dl)	CI (l/min/M²)	SVI (ml/M²)	TPR $\left(\frac{\text{dyne·sec}}{\text{cm}^5}\right)$	CO_2 (mM/l)	plasma pH
Control										
10	B	75	515	44.0	14.5	7.40	98.8	714	21.5	7.40
	A	90	523	45.1	14.7	6.00	66.7	1090	20.3	7.40
11	B	65	536	44.3	14.5	6.47	100.2	764	22.8	7.38
	A	60	547	44.5	15.3	4.85	81.4	1224	23.2	7.38
Anemic Blood Infusion										
1	B	66	485	40.0	15.0	3.73	56.6	1382	24.0	7.38
	A	54	480	38.8	14.1	4.85	89.7	1026	23.8	7.10
2	B	64	485	43.1	16.3	4.87	76.1	1088	23.4	7.32
	A	66	463	41.8	14.4	4.34	65.8	1447	24.1	7.35
3	B	67	491	34.5	12.5	4.40	65.6	1042	21.8	7.40
	A	65	401	32.0	12.2	4.46	68.6	926	22.8	7.35
4	B	81	456	40.5	14.6	6.27	77.4	652	21.9	7.34
	A	72	417	38.0	13.3	5.84	81.1	777	19.3	7.32
5	B	84	498	42.0	15.5	5.83	69.4	852	21.0	7.35
	A	85	421	40.9	13.5	5.51	64.8	977	22.3	7.32
6	B	55	492	47.6	16.3	4.59	83.4	1016	23.0	7.37
	A	55	431	41.6	14.4	4.21	76.6	1182	21.8	7.37
7	B	65	515	46.4	16.4	5.05	77.6	812	21.4	7.35
	A	72	495	47.3	15.4	5.26	73.0	977	22.1	7.35
Mean	B	67.0	488	42.0	15.2	4.96	72.3	978		
SD		9.4	16.4	10.80	1.29	0.797	8.38	217		
Mean	A	68.8	443	41.3	13.9	5.15	78.5	995		
SD		9.94	32.5	4.29	0.94	0.581	8.32	198		

HR: Heart rate, RBC: Red blood cell count: Hct: Hematocrit, Hb: Hemoglobin concenration, CI: Cardiac index, SVI: Stroke volume index, TPR: Total peripheral resistance, B: Before infusion, A: After infusion.

Table 2. Hematologic Indices of Chronic Post-Hemorrhagic Anemic Donor Subjects. Subject Number of Donor and Recipient (Table 1) Corresponds Each Other

Subj No.	RBC (million/mm³)	Hct (%)	Hb (gm/dl)	CI (ml/min/M²)
1	3.25	23.1	7.0	6,150
2	2.24	22.9	5.6	6,500
3	3.20	23.0	6.0	5,910
4	2.06	16.2	5.7	7,830
5	3.24	22.5	7.0	4,070
6	3.05	19.5	6.2	7,470
7	2.50	25.0	7.5	4,900
10	5.26	4.6	15.5	3,200
11	5.62	4.8	16	3,750

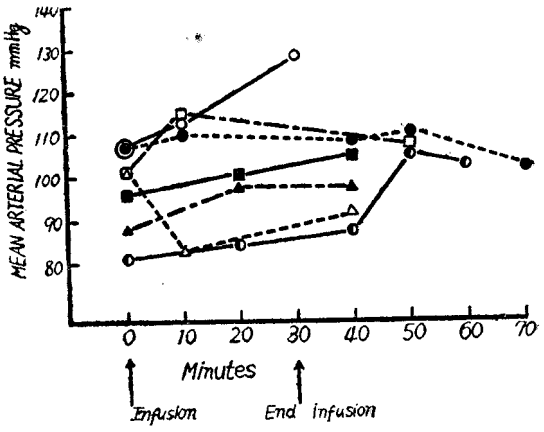

Fig. 1. Time Course of Changes in mean Arterial Pressure Following Infusion of Anemic High Cardiac output Blood at Zero Time.

in Table 1.

Blood pressure. Mean arterial pressure before infusion period averaged 97±8.7(mean±S.D.) mmHg. The temporal sequence of changes in individual subjects during and after infusion period is shown in Fig. 1. There was a steady rise in mean arterial pressure during the infusion period except subject No. 3 in whom there was a sharp drop from 101

mmHg to 82 mmHg. Up to 10 minutes after transfusion period the mean arterial pressure remained at the same level. After 20 minutes there was a decline of mean arterial pressure to the preinfusion level.

Cardiac output. There were no changes in cardiac output measured 20 or 30 minutes after the end of anemic blood infusion. Cardiac index before infusion averaged 4.96±0.80 l/min/M^2 in 7 subjects and the value after infusion was 4.92±0.58 l/min/M^2. Stroke volume index showed also no changes, namely the value was 72 before and 74ml/M^2 after the infusion.

Total peripheral resistance. There was an increase in total peripheral resistance after infusion of anemic high cardiac output blood. Total peripheral resistance averaged 978±217 before infusion and 1044±198 dynes.sec.cm^{-5} after infusion.

Discussion

The transfusion of anemic high cardiac output blood into normal recipient showed no significant hemodynamic influences except the change in arterial pressure. The increase in arterial pressure after infusion of anemic blood in normal recipient subject was not particularly related to the anemic high cardiac output blood. The recipient of normal blood also showed an increase in mean arterial pressure.

When assumptions are made that there is some humoral agent in anemic blood and causes an increase in cardiac output of recipient subject, there are several possibilities. First, the humoral agent is inactivated rapidly in the recipient's body. In the present study, the cardiac output measurement was done 20 or 30 minutes later than the cessation of infusion. Thus the possibility of rapid inactivation could not be neglected. Second, the infusion rate of 0.35 ml/min/kg is too small to elicite any action by the agent. In dog, however, a rise in cardiac output at an infusion rate of 0.5 ml/min/kg was most frequently observed[4]. Consequently, the low rate of infusion could be omitted as a cause of the negative result of this study. Third, in chronic post-hemorrhagic subject the agent is not produced at all. The high cardiac output seen in them would be an adaptation of heart to a chronic decrease in oxygen transporting capacity. In them, such humoral agent as hemopoietin is produced no more than normal subject as seen from the Fe^{59} uptake by the rat red blood cell[13]. Fourth, the cardiac output of normal recipient before infusion was elevated and there was no room to increase the cardiac output after infusion of humoral agent. The pre-infusion value of cardiac index was an average of 4.96 l/min/M^2 and is greater than the normal value using the same procedure[4]. The average value of cardiac index in the anemic donor subjects was 6.12 l/min/M^2 and is far greater than the pre-infusion value of normal recipient subjects. Comparing these two figures, 4.96 and 6.12, it can be said that there should be a cardiac reserve in normal recipient subject to increase its output in response to the humoral agent if this existed in the incoming anemic blood.

So far, it seems that a humoral agent which gives rise an increased cardiac output is not confirmed in the chronic post-hemorrhagic anemic human blood.

Summary

The anemic blood of chronic post-hemorrhagic man whose cardiac output was much elevated was infused into normal recipient. Seven anemic bloods were infused into seven recipients, respectively. No significant hemodynamic influences were observed excetp a transitional rise of arterial blood pressure. The possibility of the presence of a cardiac output increasing humoral agent was not confirmed.

국 문 초 록

정상인에 수혈된 만성 실혈성 빈혈자 혈액의 혈류 역학적 영향

서 울 대 학 교 의 과 대 학
생 리 학 및 외 과 학 교 실
남 기 용 · 박 길 수 · 신 동 훈

혈액 은행에 피를 파는 만성 실혈성 빈혈자의 심장 박출량은 정상인에 비하여 훨씬 증가되어 있다. 이 사람의 혈액내에 어떠한 액성인 작용 물질이 포함되어 있어서 심장 박출량의 증가를 일으키는 것일가 하는 가능성을 보고저 본 실험을 했다. 채혈 직후의 빈혈자 혈액을 체중의 10% 만큼 0.35ml/min/kg의 속도로 정상인에 수혈하고 피를 받는 사람에서 여러 혈류 역학적 지수들을 검색했다. 수혈은 20~30분 동안 걸렸다.

심장 박동수, 심장 박출량등에는 수혈 전후에 아무런

차이를 찾을 수 없었고, 다만 평균 동맥 혈압이 수혈 도중에 증가하였다가 수혈이 끝난 후 20~30분에 다시 수혈전 값으로 회복되는 변화를 보았다. 말초 혈관의 혈류저항의 총계도 혈압의 변동에 맞추어서 변동하였는바, 수혈 후에 증가함을 보았다.

위와같은 관찰로서 만성 빈혈자의 혈액내에 어떤 액성인 작용 물질이 있어서 심장 박출량을 증가시킬 것이라는 가능성은 찾을 수 없었다.

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