RESTORATION OF PLASMA VOLUME UNDER HYPOTHERMIA IN DOGS

By

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Deliberate lowering of the body temperature in order to facilitate surgical intervention is now practiced in many centres. Hypothermia had been introduced into surgical practice primarily to protect tissues from the effect of temporary deprivation of their circulation. The idea, though simple in theory, is beset with many difficulties in practice because of the other physiological events which accompany body cooling (1). At low temperature homeostatic adjustments are poor. Asynchrony in the vascular tone between the organs and the regions could lead to an inadequacy in the tissue perfusion and consequently it would hinder the prolongation of hypothermic state. Alteration of the nervous tone of the Folkow's (7) vascular circuits would change the pattern of distribution of the plasma in the vessels. Agreement exists among various workers (3, 5, 12, 13 and 14) concerning the alteration in the actively circulating plasma volume in the animals under hypothermia, but basic mechanism of such change remained ill-understood. Previous study in our laboratory (17) had suggested that the reduction of plasma volume under hypothermia could probably occur only due to locking up of plasma in the uncirculated intravascular spaces; since a shift of the fluids between various body fluid compartments could not be demonstrated in our studies (17) and by Farrand *et al* (6). The present study had been planned to mobilize the locked up plasma from flow ceased spaces by acutely loading the circulation with the isotonic fluids.

Materials and Methods

Healthy mongrel dogs of either sex, weighing from nine to sixteen kilograms were taken for the experimental study. The dogs were anaesthetized with chloralose 100 *mg./kg.* body weight. This dose of chloralose could also suppress the shivering during the induction of hypothermia in contrast to the normally used dose of 80*mg.* per *Kg.* for anaesthesia in the dogs. All the infusions in the dog were made in its femoral vein, whereas the blood samples were withdrawn from femoral artery. The plasma volume of the dogs was estimated by the dye dilution technique as described by F. P Chanard (4). The dye used for the dilution was Evan's blue (T.1824). Hypothermia was induced by covering the body of animal with crushed ice. The body core temperature was recorded throughout the experiment with the help of a thermocouple in the oesophagus near the cardiac end. The temperature of the body was reduced to 25°C and it remained at 25°C±2 for rest of the time during experiment. The arterial blood pressure was recorded by the direct cannulation method of the femoral artery throughout the experiment. The heart rate was recorded by counting the systolic fluctuations in the pressure recording manometer.

The isotonic and isothermic saline and the plasma of other dog was used for the tra fusions. The transufsion of saline was done in the following stages of the experiment; in the normothermic (control study) animal, (b) in the animal at body temperature of 2 whereas the transfuising of other dogs plasma was done only at 25°C. The amount of tran sion of saline in cooled dogs was graded to 30%, 20% and 10% of their volume of plasma normothermic control temperature in three groups of dogs respectively. The control st of the transfusion in dogs was done only with transfusion of saline amounting 30% of their control palsma volume. As this amount of transfusion in dogs normal temperature could not alter the haemodynamic parameter recorded in the pre study, the other amount e..g, 20% and 10% were not used for the control study. Furthe another group of cooled dogs, the delayed effect of 30% transfusion was also obser for 2 hours. These observations of delayed effects of transfusion were sup mented with control observation of the changes in the plasma volume in the cooled dogs 2 hours.

Results

The induction of hypothermia in all the dogs had produced a reduction of the acti circulating plasma volume (Table 1). The arterial blood pressure (Table III) and the heart decreased in all these dogs during cooling. The plasma mobilizing effect of the saline tr fusion varied with the amount of infusion in the cooled dogs (Table I) and (Fig. 1).

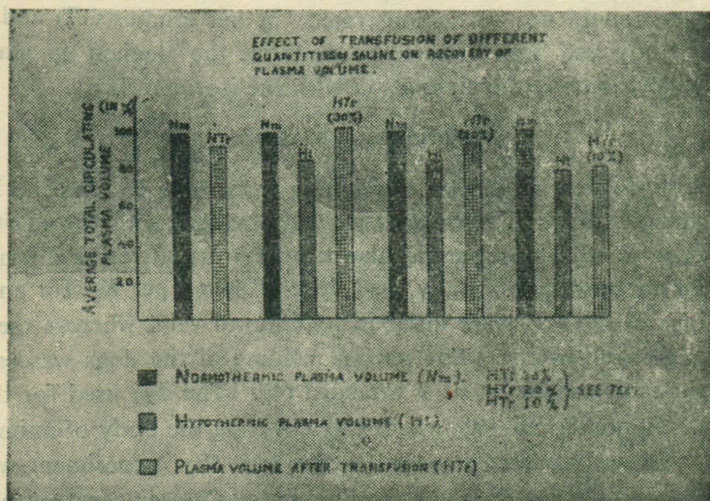

Fig. 1

Showing the effect of transfusion of different quantities of Saline on the pla volume under hypothermia.

TABLE. I

Changes in the plasma volume in the dogs under hypothermia after the transufision of saline

Groups;	Control Normothermic plasma volume	Plasma volume at 25°C	Percent from their control;	HYPOTHERMIA; Volume of saline transfused	Percent from their control plasma volume	Rate of Plasma volume transufsion immediately	after transfusion plasma volume immediately	Percent from their control	Plasma volume after one hour —	Percent from their control	Plasma volume after two hours —	Percent from their control	No. of dogs from used in their each group control and remarks
	Ml.	Ml.	%	Ml.		Ml./Min	Ml.	%	Ml.	%	Ml.		
Normothermic 30% Group	Mean 627	..	..	150	30%	14.75	706.25	97.5	..	..	...	..	4 dogs
	SD ±87.95	..	..	..	..		±64.59	±5.36	..	..	...	..	Control transfusion at normthermic temperature.
Hypothermia 30% Group	Mean 641	559.3	86.5	184.8	30%	16.9	884.5	101.9	..	..	...	..	
	±80.2	±122	±9.8	±30.6		±1.6	±116.7	±10.3	..	..	...	..	9 dogs
Hypothermia 20% Group	Mean 552	419	84.2	106.7	20%	10.7	617.7	92.3	..	..	..	..	4 dogs.;
	SD±48.7	±73	±5.8	±7.7		±1.7	±63.7	±5.7	..	..	..	..	...
Hypothermia 10% Group	Mean 699	531.8	78.2	69.4	10%	6.6	690.6	79.8	..	..	..	..	5 dogs
	SD±130	±81.4	±17	±12.9		±1.2	±130.5	±12	..	..	..	..	...
Hypothermic control delayed group	Mean 688.6	583	84.4	No	No	No	No	No.	546	79.4	579	82.7	5 dogs
	SD±51.3	±56.3	±3.3						±65.9	±7.7	±46.5	±4.7	Transfusion not given.
Hypothermic 3 % delayed; group	Mean 741.2	583.8	79.6	232.8	30%	18.8	990.4	101.4	575.8	72.8	606	82.3	5 dogs
	SD±155.2	±131.2	±6.6	±53.2		±2.15	±212.4	±15.2	±156.5	±7.5	±212.6	±7.7	

Effect of the Transfusion of Saline on the Plasma Volume

A control study was conducted on four normothermic dogs (Normothermic 30% Gro[...] Table I). These dogs received a transfusion of saline amounting to 30% of their pretransfus[...] plasma volume at normal temperature. The infused saline quickly disappeared from act[...] circulation. The actively circulating plasma volume showed an insignificant change immedi[...]ly after transfusion. The recovery of transfusate was incomplete in all the dogs. The he[...] rate and the arterial blood pressure remained unchanged during and after transfusion [...] each dog.

Similarly the transfusion of saline amounting to 30% of the volume of plasma at co[...]trol normothermic temperature was made in nine cooled dogs (Hypothermic 30% Grou[...] Table 1). In contrast to the transfusion in the normothermic 30% group the recovery [...] transfusate was complete in all the dogs after transfusion. The reduced plasma volume [...] these cooled dogs was also restored to their control normothermic values after infusion [...] saline.

In another group of four cooled dogs (Hypothermic 20% Group, Table I), the amount [...] transfusion of saline was decreased to 20% of the volume of plasma at control normotherm[...] temperature. This amount of transfusion was approximately equal to the mean loss of t[...] plasma from active circulation during cooling. After transfusion, the actively circulati[...] plasma volume in these cooled dogs was restored to their control normothermic values. B[...] the recovery of transfused saline was incomplete in the dogs of this group in contrast to t[...] hypothermic 30% group.

A further reduction of the amount of transfusion in the five cooled dogs to 10% [...] the volume of plasma at normal temperature was practically ineffective (Hypothermic 10[...] Groups, Table I). In the dogs of this group the actively circulating plasma volume was n[...] restored to the control value in contrast to other two hypothermic groups. The infused sali[...] completely disappeared from active circulation during transfusion.

Delayed ffEects of the Transfusion on the Plasma Volume

In a group of 5 cooled dogs again the transfusion of saline, amounting to 30% of t[...] volume of plasma at normal temperature, was made to watch the delayed effect of the tran[...]fusion (Hypothermic 30% delayed Group, Table I). The plasma volume was measured [...] one hour and two hours interval after transfusion. The reduced plasma volume during coolin[...] was restored to the control normothermic value as it was observed in the hypothermic 30[...] group. The transfused saline was also fully recovered immediately after transfusion. Th[...] plasma volume fell back to the pretransfusion value after one hour and it remained unchange[...] after two hours (Table I and Fig. 2). However, the first hour value of plasma volume showe[...] an insignificant decrease from the pretransfusion value. The second hour value of the plasm[...] volume showed an insignificant increase from its pretransfusion value.

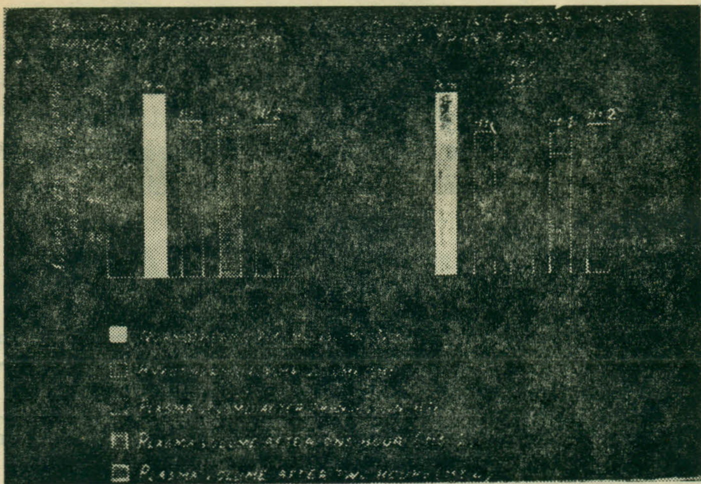

Fig. 2

Showing the delayed effect of transfusion of saline in cooled dogs for two hours.

For a control study the changes in the plasma volume were observed for 2 hours in the 5 cooled dogs without transfusion. The plasma volume remained unchanged during two hours in dogs under hypothermia. However, an insignificant decrease was observed in the plasma volume after one hour from the initial value and an insignificant increase in the plasma volume was observed after 2 hours from intial value.

Effect of the Transfusion of Plasma

The transfusion of saline in the dogs would give rise to a diuretic response. Hence, a plasma transfusion was made to confirm the observation made with saline. Isothermic plasma of the other dog was transfused in two cooled dogs amounting to 30% of their control plasma volume at normal temperature (Table II).

TABLE II

Change in the plasma voluma in the cooled dogs after infusion of isothermic plasma amounting to 30% of their control normothermic plasma volume

S. No.	Dog No.	Control	HYPOTHERMIA					
		Normothermic plasma volume ml	Plasma volume at 25 C.	Percentage from their control; % ml.	Volume of plasma transfused ml.	Rate of; transusion ml./min.	Plasma volume immediately after trsnsfusion ml.	Percent from their control% %
1.	76	590	529	89	177	18	1109	157
2.	77	532	482	90	159	16	719	104

These plasma transfusions in cooled dogs had produced complete restoration of reduced plasma volume to their control values. Further, the transfusate was fully recov after transfusion. Moreover, the plasma volume immediately after transfusion was m than the sum of the control plasma volume and the transfused plasma. This indicated t the actively circulated areas in the cooled dogs increased beyond the normothermic limits

Effect of the Transfusion of Saline on the Arterial Blood Pressure and on the Heart Rate

The induction of hypothermia had produced a marked fall of the arterial blood p sure (Table III) and the heart rate. But the heart rate had not shown any change during and a transfusion.

TABLE III

Change in the arterial blood presssure during transfusion of isotonic and isothermic saline under hypotherm

S. No.	Dog No.	Control normothermic arterial blood pressure *mm.* of *Hg*	HYPOTHEERMIA: Arterial blood pressure at 25°C *mm.* of Hg	Arterial blood pressure during transfusion *mm.* of Hg.	Rate of transfusion *ml/min.*	Arterial bl pressure minutes a transfus *mm.* of
1	36	100	53	62	..	66
2	37	160	76	66	..	80
3	38	112	62	83	..	80
4	39	130	80	90	.	80
5	62	130	80	84	18	76
6	63	140	40	50	18	50
7	64	160	70	86	17	60
8	65	130	40	50	18	52
9	71	134	66	94	10	86
10	72	126	80	92	10	90
11	75	110	60	68	8	60

The arterial blood pressure rose with all grades of the transfusion in cooled dogs contrast to normothermic transfusion which were ineffective. The rise of arterial blood pro ssure was directly proportional to the amount of saline transfusion (Table III).

Discussion

Since Blair *et al* (2) and Sealy *et al* (15) had observed a marked depression of the para sympathetic and the sympathetic activity at a lower body temperature of 28°C. a decrea in the fullness of blood stream could be due to an increase in the diameter of the vessel due t

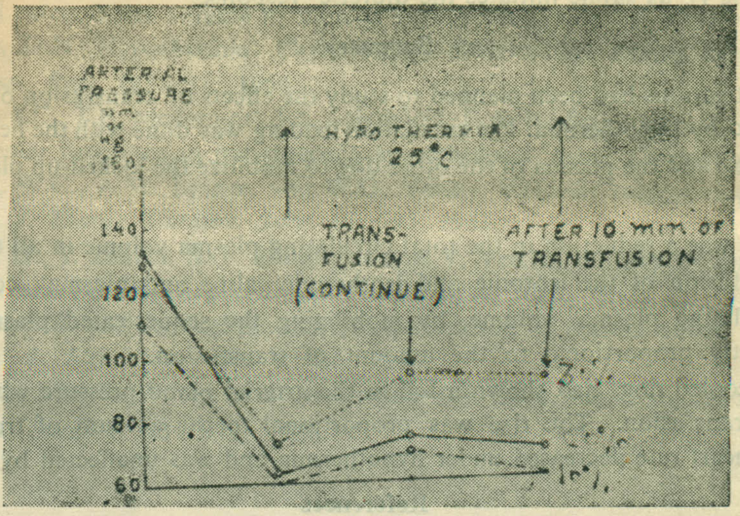

Fig. 3

Showing the effect of transfusion on the arterial blood pressure.

depre-ssion of nervous tone. The marked reduction of arterial blood pressure (16) during cooling could be also due to such changes in the vascular calibre. However, marked bradycardia (17) in the cooled animals could equally share the production of hypotension. Moreover, the fall of arterial blood pressure beyond a critical level could induce a cessation of flow in the small vessels like capillaries and the veins (8, 9, 18). Further the decrease of nervous tone at subnormal temperature could open the A-V shunts (8). Such cessation of flow in the vessels would certainly reduce the actively circulating plasma volume (17) and induce haemoconcentration (3, 17). At low temperature. the sludging of red blood cells (9, 11) prevented the entry of blood cells into capillary circulation.

The reduction of actively circulating plasma volume in all the cooled dogs in the present study was possibly due to cold induced vascular failure. The rapid mobilization of sequestrated plasma (Table I) by saline, in the acute experiments, supports the concept of intra-vascular locking of plasma at subnormal temperature. The observations in the present study conform to the observation of Chang *et al* (3) that there was no reduction of the plasma volume in one of their cooled dogs, when they transfused one litre of normal saline. D'Amato *et al* (5) had also observed an increase in the arterial blood pressure, cardiac output, and minute work after the infusion of normal saline in one dog at 35°C. Blood pressure changes, after the saline infusion were probably also due to Starling effect of increased venous return in response to transfusion. Thus the present study suggests that the lack of driving force in the vessels was probably the most important cause of the sequestration of plasma in the cooled dogs. Therefore, the plasma transfusion (Table II) could produce a better effect than the saline transfusion (Table I), as saline initiates the diuretic response.

Summary

The investigations had been planned to study the effects of transfusion on blood vc changes produced by hypothermia. The circulation loading was done with the help of isoth and isotonic saline and the plasma of the other dog to mobilize the locked-up plasma. The vations made are :—

(1) There was a reduction in the total circulating plasma volume in all the cooled

(2) Transfusion of the isotonic and isothermic saline and plasma could restor circulating plasma volume, by mobilizing the sequestrated plasma. This directly proportional to the amount of transfusion.

(3) The cooled dogs had shown a fall in the arterial blood pressure which was r on transfusion. This rise was proportional to the amount of transfusion.

(4) The heart rate decreased under hypothermia and was unaffected by the transfu

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