Effect of Haemaccel on C. V. P. In the Treatment of Burns

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Introduction

THE immediate danger to life in burns is the development of hypovolaemic shock. The damaged capillaries allow the leakage of plasma not only outside, but into the tissue spaces also.

Observing the efficiency of treatment in cholera as advocated by Latta in 1830 and Cantarani in 1850, Buhl (1850) suggested a similar line of treatment in burns also. This was the beginning of the understanding of the value of replacement therapy in burns.

Since then a wide variety of replacement solutions were advocated by research workers each claiming success with their mode of treatment.

When Evans published his formula for replacement fluid it was mainly empirical. Human physiology is a dynamic one and no arithmetical formula can meet the individual needs.

The time honoured parameters for monitoring the adequacy of fluid replacement in oligaemic shock have been

(1) determination of arterial blood pressure,
(2) serial haematocrit readings,
(3) urine output, and
(4) clinical signs, which can easily be elicited at the bed side.

Thirst,restlessness,vomiting are all symptoms of dehydration. But these are not without pit-falls which may mislead the unwary physician.

Recently it has been found that indirect arterial blood pressure does not reflect the adequecy of the microcirculation and at times is even misleading. It is said that this is a way of merely treating the sphygmomanometer and not the shocked patient. The arterial blood pressure does not fall until the volume deficit exceeds 30%. (Rusoff & Berne, 1968). Before this point the arterial blood pressure is maintained by peripheral vasoconstriction. There is also some element of renal ischaemia resulting in oliguria. Thus oliguria occurs much before the fall in arterial pressure. However, when hypovolaemia exceeds 30%, the fluid replacement up to a point where arterial blood pressure comes to normal will still leave a volume deficit of 30% and fail to correct renal ischaemia (Rusoff & Berne, 1968).

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Serial haemoglobin and haematocrit determinations have been used to follow the patient's progress and treatment but it must be remembered that these tests measure the concentration of red cell mass and are dependent on the principle of dilution and concentration. Haematocrit can be totally misleading as a guide to treatment, when there is co-existing kidney, heart or liver disease or when acute blood loss involves tissue trauma and mixed fluid treatment (Maxwell Borow, 1959).

In conditions of sever blood loss or other extracellular fluid loss, there is a marked reduction in the glomerular filtration rate due in part to the fall in B. P., and in part to the vasoconstrictive changes in the renal vasculature. As a result there is a decrease in the filtration of plasma through the glomeruli and a diminished urine output. Thus the hourly urine output is an excellent guide for following oligaemic patients. However, there is necessarily a lag period concomitant upon the production of urine, transportation to bladder and the all important requirement of an indwelling catheter and its resulting complications.

Blood volume studies using radio-active material or dye dilution techniques approximate more accurately the existing fluid volume state at the time of the procedure but can become obsolete quickly in the unstable patient whose heamodynamics are changing constantly from continued depletion or replacement. Repeated blood volume could be performed but these are limited by practical and economic considerations.

An ideal parameter which will depict not only the the fluid volume but also the patient's entire cardiovascular dynamics is therefore very necessary.

Traditionally the venous circulation has been a secondary factor in the evaluation of haemodynamic function. Recently however, more attention has been given to this part of the circulation which contains 60%-70% blood volume. Use of venous pressure measurement in managing acute circulatory failure and in monitoring blood volume has been advocated by Wilson and others. Monitoring right arterial venous pressure during and after whole body perfusion demonstrated that this measurement is fundamental in evaluating the adequancy of the circulation.

C. V. P. has been defined as the pressure in the great veins which represents the diastolic filling pressure of the right atrium (Sykes, 1963). However, contradictory reports regarding, the value of C. V. P. in monitoring blood volume have appeared in the literature. (Artz. 1970, and Rubin & Bongiovi, 1970). C. V. P. is not a direct index of blood volume but is intimately related to it (Wilson 1963). It reflects the degree of cardiac competence in relation to a given blood volume (Wilson, 1965).

If it is assumed that cardiac efficiency is excellent, the C. V. P. is the most valuable guide to the state of blood volume (Keddia, Provan & Austen, 1956) and a low C. V. P. indicates definite hypovolaemia (Barrow, 1963) and the fall in C. V. P. is observed before there is fall in arterial pressure (Brooks, 1967).

When the cardiac efficiency is impaired as in a failing heart, a high C. V. P. will be recorded due to the failure of the heart to cope with the given load. In hypovolaemic shock, cardiac insufficiency may mask hypovolaemia, recording a normal or border line C. V. P , which may give rise to difficulties in estimating adequate fluid replacement.

The outstanding value of the C. V. P. is that it is a dynamic measurement that can be used continuously in a repidly changing situation (Wilson & Owens, 1961; Wilson, Grow and Denong, 1962; Sykes, 1963; Wilson, 1963). The effects of C. V. P. monitoring in burns has been reported by Tarachand (1967) and Sharma (1969).

Thus, the importance of replacement therapy, in burns to combat the initial shock was recognised, various solutions are advocated and are being used presently.

Though the best replacement is blood in shock, situations will arise when delay in procurement of blood will threaten life. It has long been recognised that death in the initial shock period results from a fall in the circulating-intravascular fluid and not from the deficiency of blood cells. Replacement of lost blood by blood or pooled plasma has its own hazards, the latter especially carrying the risk of serum hepatitis. These deficiencies led to a search for an effective blood or plasma substitute, which was spurred by World War I, and which continues to this day. The word "substitute" is used in the place of "expander" because of its more accurate connotation in the circumstances that demand its use.

The more important qualities of an ideal plasma substitute are freedom from toxic, pyrogenic and antigenic reactions, stability at wide temperature ranges, cheapness of manufacture and ease of sterilisation. Its viscosity and osmotic pressure should approximate that of plasma; affecting a durable increase in blood volume with its ultimate metabolisation and excretion when the need for its use has passed.

Gelatin was the earliest plasma substitute put into clinical use by Hogan in 1945, but it fell into disrepute because of its antigenicity and difficulty in sterilisation and a tendency to gel at room temperature.

In 1917, Gum acasia as a 6% solution was introduced into clinical practice by Baylis (1916). A palysaccharide obtained from the natural gum of acacia thorn, it has wide industrial applications, but few clinical uses because of its slow break-down in the body.

The two substances that have enjoyed a long and undisputed period of popularity as plasma expanders have been polyvinyl pyrollidone (PVP) introduced by Hecht & Weese and the dextrans introduced by Gronwall & Inglemann and popularised by Gelin and his co-workers. The dextrans which were derivatives of sucrose have been widely used after world War II. The higher molecular weight dextran—Dextraven with a mean molecular weight of 150,000 and Macrodex with mean molecular weight of 70,000 gave way to dextrans of lower molecular weight—Rheomacrodex and Lomodex having a mean molecular weight of 40,000. The latter had the advantage of

inducing considerable increase in capillary circulation and counteracting the tendency to intravascular sludging. The duration of effective blood volume expansion induced by Lomodex is however limited to about 2 hours as compared with the higher molecular weight dextrans which maintain an increased blood volume for nearly 24 hours.

The recent addition to the surgeons armamentarium in this field is an amino-acid polymer derived from the degradation of gelatin.

Gelatin Substitute (Haemaccel)

A gelatin solution was used as a plasma volume substitutes as early as 1915 by Hogan, but had to be given up as it was difficult to sterilize, caused allergic reactions and had a tendency to gel at room temperature. In 1951, Campbell, et al. developed a technique of degrading and repolymerising gelatin to produce a derivative more suitable to technical and clinical handling.

HAEMACCEL is a plasma volume substitute having a molecular weight of of 30,000 to 35,000. Its composition is :—

Each 100 ml. of Haemaccel contains :

Polymer from degraded gelatin (equivalent to a nitrogen content of 0.63 g.)	...	3.5 g.
Electrolytes and sterile distilled water (pyrogen-free) to	...	100 ml.
Electrolytes in mEq/litre :		
Na^+ ...	...	145.0
K^+ ...	...	5.1
Ca^{++} ...	...	12.5
Cl^- ...	...	145.0

PO_4^{---}, So_4^{--}, in trace. The composition is made isoionic with polypeptides.

HAEMACCEL is predominantly excreted unchanged through the kidney. Between 63-88% is thus eliminated; some of it is possibly excreted via the intestines. A small amount is catabolised since HAEMACCEL is susceptible to enzymatic breakdown by tissue enzymes. The half-life of HAEMACCEL is 4-5 hours. After 12 hours, 27% of HAEMACCEL is still demonstrable in circulating blood, but after 24 hours only small amounts are present. 48 hours following infusion of HAEMACCEL, it completely disappears from the blood.

Aim of the Study

The present study was undertaken to evaluate the therapeutic efficacy of this solution in the treatment of hypovolaemic shock in burn cases.

Methods and Materials

The study was carried out in phases. In the first phase 15 normal individuals admitted to the Plastic Surgery Department with various complaints, but nothing pertaining to C.V.S. which might have affected the central venous pressure were included. The C.V.P. was recorded by taking the average value of three consecutive readings taken at an interval of 5 minutes. The result are tabulated in Table I.

The second phase was carried out in 20 cases of acute burn admitted into the Department of Plastic Surgery, Patna Medical

cal College Hospital. The efficacy of volume restoration was observed by the effect on Central Venous Pressure, monitored by placing a polythene tube in the superior vena cava and connecting it to a saline manometer. Blood pressure was not recorded as this may remain at normal levels even when the patient has lost 30% of his blood volume. Urine output which is the important parameter in monitoring the volume replaced was charted out by placing a Foley's catheter into the bladder. Blood was taken before and after influsion for grouping and cross matching. Burns above 50% were infused with 1000 ml. of HAEMACCEL solution. Those cases below 50% were given 500 ml. of HAEMACCEL.

Excepting for one case in which it was infused during the eschar removal, HAEMACCEL was administered immediately after admission into the hospital.

Observations :

Effect on Central Venous Pressure

C.V.P. was found below normal in 18 cases studied. There was an average rise of 1.5—3 cm. of saline after infusion of 500-1000 ml. of HAEMACCEL. This was maintained in the absence of other solutions for 2-3 hours depending upon the severity of burns. Pulse was imperceptible in the majority of cases which became perceptible after infusion of 500 ml.

Effect on diuresis

None of the patients had passe durine after the burn accident and before admission into hospital. Urine formation started with $\frac{1}{2}$ hour of HAEMACCEL infusion and was maintained on an average in 24 hours, the diuretic effect was good.

HAEMACCEL did not interfere with blood grouping and cross matching and there was not a single case of bleeding after infusion.

In two cases, patients developed a paralytic ileus after 48 hours.

Discussion

The C.V.P. in our series is compared with the range obtained by other workers.

Name	*Year*	*C.V.P. in cm. of water*
Wilson	1962	8-13
Hallin	1963	5-12
Johnson	1964	9-11
Barrow	1965	5-11
Tarachand	1967	5-11.5
Barrow & Escaro	1968	6.12
Present series	1972	4.8-12 8 cm.

It is seen that the average C.V.P. tend to be a little lower in our Indian patients.

The volume expanding capacity of HAEMACCEL could be sufficiently explained by its oncotic activity and molecular size. The solution stays in vascular bed for 4-5 hours and is mainly excreted through the kidney.

HAEMACCEL seem to behave in a manner similar to buffered lactated Ringer's solution. The configuration of the molecule is globular; this alters the behaviour and mechanics of the molecule for crossing the capillary membrane and seems to explain its property

Table I

S. No.	Sex	Age in years	Blood Pressure in mm of Hg.	Central Venous Pressure in cms. of saline
1.	M	13	120/80	10.0
2.	M	23	112/78	11.4
3.	M	22	126/84	11.0
4.	F	18	116/76	6.8
5.	F	60	140/84	7.4
6.	M	28	120/80	10.5
7.	F	35	132/80	5.8
8.	M	38	122/82	6.8
9.	M	20	114/82	4.6
10.	M	26	120/78	8.8
11.	F	23	116/86	8.6
12.	F	32	130/84	10.8
13.	M	38	132/88	12.8
14.	F	35	118/86	7.6
15.	F	18	126/78	9.2
				Range 4.8 to 12.8 cm. Average 8.4 cms.

Table II

S. No.	Sex	Age in yrs.	Time elapsed before admission	%Age of burnt area	Amount of HAEMACCEL infused in ml.	Central Venous Pressure in cm. (Saline)		Pulse/ Minute		Urine output in ml.				Remarks
										During infusion		After infusion		
						Before infusion	After infusion	Before infusion	After infusion	½ hr.	1 hr.	2 hrs.	4 hrs	
1.	M	11	14 days (during Eschar excision,	40	500	7	11	140	118	15	20	65	50	Good.
2.	F	22	2½ hrs.	44	500	0	3	I	138	12	15	28	32	Satisfactory
3.	F	25	8 hrs.	36	500	16	18.1	I	—	—	—	15	—	Patient died within 48 hrs. irreversible shock.
4.	F	20	2 hrs.	38	500	11	13	124	98	20	28	38	40	Good.
5.	M	16	2½ hrs.	42	500	0	4.8	I	132	18	20	41	38	Satisfactory.
6.	F	25	6½ hrs.	40	500	0	4.6	I	150	20	30	38	28	
7.	F	50	5 hrs.	45	500	0	3.8	I	138	—	39	28	22	
8.	F	70	2½ hrs.	80	1000	14	18	I	I	—	—	—	—	Patient died within 48 hrs. irreversible shock.
9.	F	20	2 hrs.	40	500	0	3.5	126	94	—	30	48	52	Developed ileus and abdominal distention.
10.	F	30	3 hrs.	34	500	0	2	I	I	—	22	42	48	Urine output persistently low
11.	F	35	2 hrs.	73	1000	0	4.3	I	162	—	15	28	22	Developed ileus and vomiting
*12.	F	60	14 hrs.	40	500	0	4	I	140	28	22	60	58	Satisfactory.
**13.	F	22	2 hrs.	78	1000	3	6.4	I	120	—	28	62	56	Satisfactory.
14.	F	10	2½ hrs.	58	1000	CVP could not be done due to extensive burn of both arms		I	86	20	28	72	68	Good.
15.	F	12	4½ hrs.	34	500	0	2.8	I	120	18	24	75	64	Satisfactory.
16.	F	7½	6 hrs.	50	500	0	3.6	I	92	20	22	64	58	Good.
17.	F	70	4 hrs.	40	500	0	12.8	I	I	—	10	—	22	Pt died within 48 hrs. developed pulmonary oedema.
18.	F	30	1½ hrs.	54	1000	0	4.8	I	88	NR	38	62	68	Developed pain in the arm thrombophlebitis.
19.	F	40	7½ hrs.	62	1000	1.5	2.8	I	136	15	30	28	68	Satisfactory.
20.	F	25	2½ hrs.	38	500	2.6	5.2	138	86	20	80	61	58	Satisfactory.

*Patient already received 6 pints of crystalloids and 1 pint of colloid

**Patient received some resusitative measures in another Hospital

I = Imperceptible

of retaining fluid and the distribution of fluid between the IVF and ISF compartments. With this solution, both plasma volume and ISF volume are increased. (Fukuda, 1965).

HAEMACCEL may be administered alone in patients having a blood loss up to 30% of the normal blood volume. If a larger volume of blood is lost, blood will have to be administered to the patient in the proportion of one bottle of HAEMACCEL to one bottle of blood. In every severe degrees of blood loss, it has been recommended that HAEMACCEL and blood be given in the ratio of 1:2 (Lundsgaard-Hansen, 1969). He concludes that the risk of producing the dangerous combination of haemodilution and circulatory overload is less with gelatins than with dextrans. Higher doses of low molecular weight dextran may produce kidney damage, and high molecular weight dextran: a bleeding diathesis. The gelatins have no such side effects. The therapeutic safety margin of the gelatins is therefore larger, permitting a more flexible handling of volume replacement therapy in shock.

The diuretic effect of HAEMACCEL observed is in confirmity with the findings of Lutz and Hallwacha. Studying the effects of various plasma substitutes in anaemic dogs, they found a strongly pronounced diuresis during the whole period of observation after HAEMACCEL infusion and reduced urinary excretion during the period after replacement with Rheomacrodex.

The complete freedom of HAEMACCEL from producing any clinical manifestations of increased bleeding tendency have been confirmed by many investigators (Eichler & Stephan, Bergentz, et al.; Gelin, et al.; Jacobaeas, et al.).

Summary and Conclusion

1. HAEMACCEL does not cause pyrogenic or allergic reaction after infusion.
2. All patients tolerated the solution well.
3. The volume replacing capacity of HAEMACCEL was good.
4. HAEMACCEL evoked a diuresis, the effect of which seemed to last for two hours. The diuretic action of HAEMACCEL was more pronounced than that of other plasma volume expanders.
5. HAEMACCEL does not interfere with blood grouping and cross matching and no clinical evidence of interference with clotting mechanism was observed.

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