FRUSEMIDE IN BLOOD TRANSFUSION FOR SEVERE ANAEMIA IN PREGNANCY

by

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Severe anaemia of pregnancy is associated with certain cardiovascular changes which make its treatment, direct blood transfusion, hazardous. Sharpey Schafer (1945) considered that heart is abnormal in many respects in severe anaemia. Harrison (1969) showed that rise of venous pressure as a result of direct blood transfusion in patients below 4 Gm.% may lead to pulmonary oedema and fall in cardiac output. Even though the circulating blood volume in severely anaemic pregnant patients may be reduced because of fall in red cell volume, hypervolaemia due to direct transfusion is not well tolerated. Hence attempt should be made to raise the haemoglobin mass without increasing the circulating blood volume.

Partial exchange transfusion (Fullerton and Turner 1962) has solved the problem very effectively but this method needs elaborate arrangement, large amount of packed cells and team of trained personnel, a requirement that is usually not met with in hospitals of outlying areas.

Short acting diuretics before or during transfusion have been tried by various workers like Harrison (1966 & 1968), Krishnakutty (1967) and the results have been satisfactory. But these reports deal with parenteral administration of these diuretics aimed at activating a very rapid and intense diuresis within a very short time. However, we in Tata Main Hospital, considered that such rapid diuresis may not always be desirable and we decided upon giving these drugs by oral route before direct transfusion with whole blood.

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Patients

Nineteen pregnant anaemic patients admitted to the obstetric unit of Tata Main Hospital were selected for this study. The minimum age was 18 years and maximum 32. There were 4 primigravidae and 15 multigravidae. The severity and type of anaemia in relationship to the week of gestation is indicated in Table I.

The patients who did not have the PCV done were those admitted at night and blood transfusion had to be started only after a haemoglobin estimation. As can be seen from Table I at least 3 of these patients were admitted with already established heart failure. The minimum Hb. level was 2 gm.% and maximum 6 Gm.%. The minimum PCV was 9 and maximum 21, average being 12.5 in 10 patients. Four of 19 patients had megaloblastic anaemia.

TABLE I

The severity and type of anaemia in relationship to week of gestation

Case No.	Week of gestation	Hb. Gm.%	P.C.V.	Heart failure
1.	14	4.5	18	Dyspnoea
2.	24	3	10	Nil
3.	20	3.5	10	Oedema
4.	24	5.5	21	Oedema
5.	30	5	—	—
6.	30	3.5	—	—
7.	32	2	—	—
8.	28	3	—	Pulm. oedema
9.	28	2	8	Oedema
10.	24	5	18	Hypertension
11.	34	4	13.5	—
12.	Puerperium 15 days	3	—	Cong. cardiac failure.
13.	38	6	—	Oedema
14.	38	3	9.5	Oedema, hypertension, accidental haemorrhage
15.	Puerperium 25 days	2	8.5	Pulm. oedema
16.	Puerperium 5 days	4	—	—
17.	30	2.5	—	Oedema three plus
18.	32	4	—	—
19.	40	2	9	Oedema one plus

Methods

Each patient was given 80 mgm. of Frusemide (Lasix) orally and fluids were restricted. This was followed within half an hour by whole blood transfusion in 18 cases and packed cells in 1 case. Serum electrolyte estimation was done in 12 cases before and after transfusion. Urine samples were collected before and after transfusion. The electrolyte status of pre-transfusion samples and quantity with electrolyte level of samples collected after transfusion were determined. The quantity of blood transfused varied between 300 to 500 c.c. The transfusion was given slowly over a period between 5 and 14 hours. The heart rate and blood pressure were recorded before and during transfusion. In those patients that required long hours of transfusion, the treatment had to be interrupted several times because of reactions.

Results

Table II gives the details regarding the pattern of diuresis along with serum and urinary electrolyte level.

It can be seen from Table II, the rate of urine secretion varied between 30 c.c. to 260 c.c. per hour. The average was 150 c.c./hour compared to Harrison's figure of 277 c.c./hour (1968). The average sodium level in serum of 12 patients was 135 m.eq/

TABLE II

Details regarding the behaviour and electrolyte changes in patients while receiving the blood transfusion following oral frusemide administration

No.	Amount of blood	Hours of transfusion	Quantity of urine	Rate of urine secretion hour	Serum electrolyte Ma eq/litre Na B*	Na A*	K B	K A	Urine electrolyte Na/K ratio B	A
1.	c.c. 300	10	c.c. 300	30/hr.	130	125	4	4.7	1.5/1	4/3
2.	400	5	840	168	—	—	—	—	2.5/1	3.5/1
3.	400	7	1500	214	139	130	3.7	4	6/1	8/1
4.	300	5½	840	150	136	138.5	4.7	5.1	2/1	2/1
										1.75/1
5.	300	8	1140	142.5	126	141	4.3	5.3	5.2/1	5/1
6.	400	10	2220	222	130	146	3.9	3.9	—	—
7.	400	5	840	168						
8.	400	10	1500	150	133	120	4.4	3.8	20/1	16/1
9.	350	8	1680	210	124	139	4.2	4.78	1.1/1	5/1
10.	350	11	1500	136	138.8	138.8	4	5	10/1	20/1
11.	350	10	840	84	142	143	4.2	4.5	11/1	8/1
12.	350	12	1410	117.5	130	139	4.9	5.2	17/1	3.5/1
13.	350	11	1200	109	—	—	—	—	9/1	6/1
14.	350	14	1020	72	—	—	—	—	—	—
15.	350	10	2280	228	149	140	5.3	5.2	12/1	9/1
16.	(Packed cell) 500	8	900	112.5	—	—	—	—	—	—
17.	500	10	2040	204	—	—	—	—	—	—
18.	500	6	480	80	144	140	4.5	4.7	12/1	15/1
19.	400	6	1560	260	—	—	—	—	—	7/1

*A = After transfusion. *B = Before transfusion.

litre before transfusion and 136 m.eq/litre after. The mean serum potassium level was 4.3 before and 4.5 m.eq/litre after transfusion. These were not statistically significant. The urinary sodium potassium ratio varied widely between 1.5 to 20.

The mean reduction of heart rate was 20/min. Blood pressure did not record any fluctuation. The patients with hypertension showed some fall. All patients admitted with heart failure improved considerably. Subsequent repetition of blood transfusion proved to be very safe even without frusemide.

There was no maternal death in our series.

Discussion

Dollry, *et al* (1964) observed intense diuresis and reduction of plasma volume after ingestion of oral Ethacrynic acid. Harrison & Lawson (1966) used parenteral Ethacrynic acid during blood transfusion in pregnant patients with severe anaemia. David Lewis (1966) reported on the use of 40 mg. of intravenous frusemide at the outset of blood transfusion and believed that this procedure would effectively prevent pul-

monary oedema. He also thought that this method will cause preferential loss of fluid components and corresponding gain in packed cell volume in patient's blood. Krishnakutty (1967) obtained better diuretic response by use of intravenous frusemide 20 mgm. half an hour before starting blood transfusion. In this series whole blood was used. Fisher *et al* (1967) found no instance of pulmonary oedema or increasing congestive cardiac failure in thirteen anaemic patients receiving blood transfusion. But he mentioned about convulsion "in two patients who were in chronic renal failure". Harrison (1968) made a detailed study of the use of parenteral Ethacrynic acid in 20 patients with severe pregnancy anaemia and obtained excellent results. In our series of 19 patients also the results have been extremely good. Thus it can be categorically stated that short acting diuretics have a definite place in the management of severe anaemia of pregnancy requiring blood transfusion.

Mode of action

Harrison (1968) has shown definite reduction of plasma volume in 18 out of 20 patients after use of Ethacrynic acid parenterally. Whether this point is of definite importance is doubtful. Vyas *et al* (1969) failed to detect proportionate rise of plasma volume in anaemic pregnant patients. On the other hand, two of Harrison's cases did show actual rise of plasma volume after blood transfusion, preceded by intravenous Ethacrynic acid.

Samet and Barnstein quoted by Harrison (1968) observed reduction in pulmonary blood volume after I.V. Ethacrynic acid. Bhatia *et al* (1969) observed reduction of blood volume by 23%, cardiac output by 33%, and central blood volume by 11% after intra-cardiac injection of 40 mgm. of Frusemide. In their series of cases filling pressure and work index of both ventricles decreased while the pulmonary and systemic vascular resistance increased. It is quite possible that the improvement noted may be due to combined effect of reduction of plasma volume and improvement of cardiac function due to reduction of pulmonary blood volume.

Rationale of using oral Frusemide: Very rapid shrinkage of extracellular fluid compartment along with marked decrease in cardiac output (Bhatia *et al* 1969) may lead to alarming hypotension and death. One of our patients, before this trial, collapsed and died soon after intravenous administration of Frusemide 20 mgm. before blood transfusion for severe anaemia in puerperium. (Hb. 2 gm.%). Moreover, there are dangers of unpredictable sodium or potassium loss even though Harrison maintains that these are of no significance. These considerations influenced our decision to administer the drug orally instead of by parenteral route.

Our trial of oral Frusemide as short acting diuretic before direct blood transfusion in severe anaemia of pregnancy appears to make the problem of transfusion still simpler in the moribund patients admitted to outlying hospitals.

References

1. Bhatia, N. L., Inder Singh, Manchanda, S. C., Khanna, P. K. and

Roy, S. B.: Brit. Med. J., 2: 551, 1969.
2. David Lewis: Lancet, August 13, 1966, Letters to Editor.
3. Dollry, C. T., Parry, E. H.O. and Young, D. S.: Lancet, 1: 947, 1964.
4. Fisher et al: J. Irish Med. Ass., 60: October 1967 (Communication from Hoechst Pharm. Ltd.)
5. Fullerton, W. T. and Turner, A. G.: Lancet, 1: 75, 1962.
6. Harrison, K. A. and Lawson, J. B.: Lancet, 2: 905, 1966.
7. Harrison, K. A.: Brit. Med. J., 4: 84, 1968.
8. Harrison, K. A.: International Seminar, Bombay, 1969.
9. Krishnakutty, P. K.: Lancet, 2: 465, 1967.
10. Sharpey Schafer, E. P.: Lancet, 2: 296, 1945.
11. Vyas, R. B., Patel, V. R., Patel, V. G. and Jaiswal, S. C.: J. Obst. & Gynec. India, 19: 174, 1969.