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TREATMENT OF SEVERE ANAEMIA IN PREGNANCY WITH EXCHANGE TRANSFUSION

by

M. K. KRISHNA MENON*, B.A., M.D., F.R.C.O.G.,

and

MARY WILLMOTT**, M.D.,

The commonest complication met with in pregnancy in India is anaemia. It is so severe that in Madras it accounts for nearly 20 per cent of all maternal deaths and in another 20 per cent it is an associated factor.

During a five year period (1957-1961), there were 80 maternal deaths from anaemia alone in this hospital. The haemoglobin levels in these fatal cases ranged from a maximum of 5.8 g.% to less than 2.5 g.%. Eighty per cent had levels below 3.5 g.%. Equally low was the packed cell volume in these cases — the range being 16% to 7%. Seventeen patients died in the antenatal period, 18 in labour and within the first 24 hours of delivery and the rest within 3 weeks of delivery. Of these 80 deaths 55 patients had established signs and symptoms of congestive failure — massive oedema, severe dyspnoea, oliguria and pulmonary congestion.

It is not proposed to enter into a controversy regarding the aetiology of the severe anaemia in pregnancy except to state that the common varieties met with here are: (i) microcytic hypochromic anaemia due to iron deficiency, (ii) dimorphic anaemia due to a deficiency of iron and folic acid or B_{12} or all three. Whatever be the aetiology of the anaemia its onset is very insidious and this gradual deterioration may cause the patient to seek treatment only when the condition is very advanced.

These neglected cases come into hospital usually at a late stage in

* *Director and Professor.*

** *Research Assistant, Institute of Obstetrics & Gynaecology, Government Hospital for Women & Children, Egmore, Madras-8.*

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pregnancy and often in premature labour. Some come in also after premature delivery at home when failure has set in. In a series of 250 cases of anaemia it was observed that 5.6% were between 12 — 24 weeks, 34.4% were 24 — 32 weeks and 60% over 32 weeks at the time of admission to hospital. Established congestive failure was evident in all the severely anaemic. In our experience congestive failure is usually in evidence when the haemoglobin level is less than 4 g.%; more so, if the packed cell volume is less than 12%. In some cases congestive failure has been present with packed cell volume at 16%.

The usual treatment of this anaemia in pregnancy has been oral iron with or without folic acid (depending on the type of anaemia) in those with haemoglobin levels more than 7.2 g.%, and parenteral iron with or without folic acid in those who are advanced in pregnancy and haemoglobin less than 7.2 g.%. In the very severely anaemic, with congestive failure, oral therapy is of little value and parenteral iron, especially intravenous iron, is in our opinion contraindicated as it is risky. The aim of treatment should be and is to obtain a maximum haematological response in the minimum possible time to tide over the crisis. For this purpose the conventional forms of therapy are of very limited value. Further, there is the ever present dread of premature labour setting in which is usually lethal in these cases. Obviously, therefore, blood transfusion suggests itself as the choice method of treatment.

The role of anaemia in producing cardiac failure in those who are not pregnant is well known. When severe anaemia complicates pregnancy, the anoxic heart has to raise its output which is a feature of normal pregnancy. To add to this there is the increased blood volume in pregnancy. Simple blood transfusion, though it increases the oxygen carrying capacity of the blood, also increases the blood volume. If the patient is in failure the transfusion will be lethal; if she is not it might precipitate her into failure. The expenditure of energy involved in labour and circulatory changes attending delivery impose an intolerable burden on a heart already failing or working at maximum capacity. Blood transfusion can at this stage be dangerous.

These facts demonstrate that ordinary blood transfusion is contraindicated when there is cardiac failure and could be dangerous even in those not in failure. Hence a means has to be found of rapidly increasing the red cell mass without augmenting the total blood volume.

Packed cell transfusions, 150 ml. — 200 ml., have been employed in these severely anaemic cases. Our experience with such small packed cell transfusions has not been very encouraging. The amounts so given, do not seem to improve the oxygenation sufficiently and rapidly to be of help in tiding over a crisis. In fact during 1961, of 23 deaths from anaemia, 18 died of congestive failure. This method while better than the conventional therapy with drugs is not effective enough to help in reducing significantly the maternal mortality.

A partial exchange transfusion has

been used in modern times in the adult for the treatment of poisonings, (Bessis and Bernard 1948), acute haemolytic anaemia (Kuhns and Bauerlein 1953) in severe anaemia (Ward 1952) and in a case of severe pregnancy anaemia (Walshe 1954). Since with the previous methods of treatment the results obtained were unsatisfactory it was decided to try exchange transfusion in these desperately ill cases.

Material and Method

Only patients with established congestive failure or those who are so severely anaemic that congestive failure is anticipated to set in are taken up for this treatment. As stated previously, congestive failure was almost always present with packed cell volume less than 12% and haemoglobin below 4 gm.% and it is to be anticipated in patients with packed cell volume not more than 16% and haemoglobin less than 4 gm.%.

A complete clinical and haematological examination was made. X-ray of the heart and electro-cardiogram were also done whenever possible while compatible blood was got ready. A sample of the patient's blood was also taken for serum electrolyte determinations. One hour prior to transfusion, the patient was given 100 mgms. of pethidine and 25 mgms. of chlorpromazine intramuscularly along with an antihistamine; 500 ml. of concentrated cells from compatible blood was run in under pressure either by the closed method or by a cut down on the anterior tibial vein while simultaneously 600 ml. of the patient's blood was withdrawn from the anterior cubital vein or, at times, from the femoral vein on the opposite side. The rate of transfusion was so adjusted as to be a little slower than the withdrawal. The average time taken for the whole process was about ten to fifteen minutes. Prior to and at the end of the transfusion, the pulse, blood pressure, general condition of the patient and any reactions were all noted. These observations were made every half hour for four hours. In all cases after the acute crisis, conventional therapy with iron and with or without folic acid was continued.

Haematological examination and serum electrolyte studies were repeated at weekly intervals and then every fortnight till delivery or discharge. An X-ray of the chest to visualise the cardiac shadow was also taken at the end of 3 weeks and prior to delivery.

Observations and Results

This report is based on the first 50 cases treated. The type of case and duration of pregnancy is shown in Table I.

All of them had congestive failure as manifested by gross oedema, dyspnoea and X-ray evidence. The type of anaemia was microcytic in 12, dimorphic in 38 of which 8 had megaloblastic bone marrow. The average haemoglobin level in the 50 patients was 2.5 g.% and packed cell volume 12%. In 32 patients the haemoglobin level was too low for estimation with the photo-electric colorimeter. Fifteen patients had in addition severe pre-eclamptic toxaemia with blood pressure range of 140 — 180 mm. of Hg systolic and 90 —

TABLE I

Duration of pregnancy	14-20 weeks	20-28 weeks	28-36 weeks	Over 36 weeks	Total
Antenatal	1	11	26	2	40
Abortion or in labour	2	—	6	1	9
Puerperium	—	—	1	—	1
Total	3	11	33	3	50

130 mm. of Hg diastolic with moderate to heavy albuminuria and oedema. Table II below shows the haemoglobin levels, and packed cell volume percentage levels prior to transfusion and the results at the end of 6 weeks.

matous patients who were so severely dyspnoeic that they could hardly lie flat in bed, were within a few hours of transfusion almost completely relieved of their dyspnoea and were able to sleep soundly lying in bed. Within 24 hours there also was a

TABLE II

	Initial		48 hours		1st week		2nd week		4th week		6th week	
	Hb G%	PCV %	Hb	PCV	Hb	PCV	Hb	PCV	Hb	PCV	Hb	PCV
Average	2.5	12	4.4	18	5.2	22	6.5	26	8.8	32	9.7	34
Minimum	Below 2.5	8	2.5	13	2.8	15	4.2	19	5.7	25	7.2	27
Maximum	3.6	16	7.6	29	8.3	31	9.0	33	10.4	41	10.8	41

There was within 48 hours an average increase of haemoglobin level by 2 g.%, the maximum rise observed being 3.7 g.%. The packed cell volume showed an average increase of 6% in 48 hours with a maximum of 11%. Once the acute critical stage was got over, with the usual treatment satisfactory improvement was very noticeable. At the end of six weeks on an average the haemoglobin level had reached 9.7 g.% and packed cell volume 34%. This is a very satisfactory response considering the severity of the cases.

Apart from the improvement in the haematological status of the patients, striking improvement was visible in their general condition. These oedemarked diuresis with the result that at the end of 48 hours it was often difficult to recognise the patients as the oedema had subsided markedly and the colour also had improved. X-rays taken three weeks after transfusion and prior to delivery showed in all cases very marked reductions in the size of the cardiac shadow.

No serious reactions were observed in the series. At the end of transfusion in all cases the patients' condition remained satisfactory. In 14 patients a transient rise in blood pressure was noticeable. The average pre-transfusion blood pressure in these cases was on an average 120/70 mm. of Hg the range being 100-130 mm. of Hg systolic and 50-90 mm. of

diastolic. The systolic blood pressure rose on an average by 20 mm. of Hg and the diastolic by 14 mm. of Hg. Similar rises were also observed in 6 of 15 patients with pre-eclamptic toxaemia. In the toxaemic patients the average pretransfusion blood pressure was 154/110 mm. of Hg the range being 140-180 mm. of Hg systolic and 90-130 mm. of Hg diastolic. In one patient the systolic blood pressure rose to 220 mm. of Hg but settled down to 150/110 within two hours and no untoward results were noticed.

No change in pulse rate after transfusion was noticed in 10 patients who had pulse rates below 100 (80 — 100). There were 40 patients with pulse rate ranging from 100-150 (average 110). In 35 of these, after transfusion, the pulse rate dropped by an average of 23 points within one hour (range 10 — 40). In the remaining five there was no change. On the whole, the pulse rate showed a tendency to slow and settle down remarkably after the transfusion. Rigor with temperature rising to 101°-102°F. was observed in 10 patients. The rigors were short lived and temperature settled to normal in 24 hours. Two cases developed mild jaundice. Three patients went into premature labour within 24 hours of transfusion. As premature labour is so common in these severely anaemic patients it is difficult to prove that transfusion precipitated premature labour.

Serum Electrolytes

Table III below shows the electrolyte changes before and after transfusion (14 cases).

TABLE III

Electrolyte	Serum K in mE/L	Serum Na in mE/L	Serum Ca in mgm%
Initial	4.6 (3.6-5.7)	135.6 (125-143)	8.3 (8.3-8.5)
48 hours	5.6 (4-8.4)	144.6 (138.4-150)	8.6 (7.9-10.4)
1st week	6.4 (5.4-8.3)	133 (141-147)	11.6 (8.2-14.5)
2nd week	4.9 (4.6-5.3)	137.2 (131.5-143)	—

In general there seems to be a small rise in the serum potassium levels which returned to normal by the second week. In 3 cases there was a marked increase of serum potassium —2.6 mE/L — 4 mE/5 at the end of 48 hours. Electro-cardiogram taken at this time did not show any changes characteristic of hyperkalaemia. Similar small increases were noticeable in general in serum sodium levels also. However, at no time did these patients show any evidence of disturbed electrolyte balance. The serum calcium levels remained unchanged.

In this series of 50 patients, with congestive failure treated by exchange transfusion, only one was lost. She was a primigravida with severe pre-eclamptic toxaemia, anaemia and congestive failure. Twenty-four hours after transfusion, she went

into labour with a brow presentation resulting in prolonged labour, craniotomy and death. Her death was not attributable to transfusion. In 1961, prior to the start of this treatment, out of 23 mothers who died from anaemia 18 were due to congestive failure. The value of this line of treatment then becomes obvious.

It is necessary to emphasise the necessity for continuing with the usual lines of treatment of the anaemia after the transfusion. Exchange transfusion is a desperate remedy for a desperately ill patient. It is designed mainly to pull back the patient from the brink of death if one may so call it. It is a life-saving measure and is not a substitute for the conventional forms of therapy.

Discussion

Fullerton and his colleagues (1962) have reported excellent results with exchange transfusion in the treatment of severe anaemia in pregnancy with failure. They used 1000-1500 ml. of concentrated cells and have been able to reduce the maternal mortality from 20% to under 3%. In this series of 50 patients, only one has been lost. The amount of concentrated cells given was only 500 ml. This was because of difficulty in getting sufficient compatible blood in an emergency, as almost all these patients are those coming in for the first time in failure or in labour having had no antenatal care at any time. There is no doubt that the transfusion of 1000 ml. — 1500 ml. of concentrated cells would give better results. Hyperkalaemia has been reported by Miller et al following exchange transfusions of whole blood in erythroblastotic infants. De Gowin also has reported similar findings in adults when whole blood transfusion was given. It is well known that, during storage of blood, potassium passes from the erythrocyte to the plasma and this is more likely to occur if the blood is stored for more than a week. Marked increase of serum potassium was demonstrable in three cases in this series but there has been no clinical manifestation or electro-cardiographic evidence of hyperkalaemia. Levine and others have found that hypocalcaemia potentiates the electrocardiographic manifestation in hyperkalaemia. In this group of cases calcium studies have shown no evidence of hypocalcaemia.

Apart from minor reactions, like rigor and slight elevation in temperature, no serious reactions have been encountered. In some of the grossly oedematous, desperately ill cases the difficulty in getting suitable veins for transfusion and withdrawal often poses very serious technical problems. A cut down may often be necessary as also using the femoral vein. No untoward effects have followed from these procedures. The results have been very gratifying.

Summary and Conclusions

1. Severe anaemia in pregnancy resulting in congestive failure has been responsible for 18 deaths out of 23 deaths in 1961 and for 55 out of 80 deaths from anaemia in the last 5 years. These patients have been treated along the usual conventional lines and also with small transfusions of concentrated cells 150-200 ml. The

results have not been encouraging.

2. As transfusion of large quantities of whole blood is deemed dangerous in such cases, partial exchange-transfusion of 500 ml. of concentrated cells with withdrawal of 600 ml. of patient's blood was tried out in a series of 50 cases. Only one mother was lost.

3. The response to treatment, the reactions encountered, and other observations are discussed.

4. It is concluded that partial exchange transfusion is indeed a life-saving measure in these desperately ill cases and should be more frequently employed if the mortality from severe anaemia in pregnancy is to improve.

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