Exchange and simple transfusion in sickle-cell diseases in pregnancy

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Summary

The management of sickle-cell crisis in a pregnant patient by exchange transfusion is described, the procedure leading to immediate and dramatic improvement in the condition.

Partial exchange transfusion in three other patients with sickle-cell anaemia, judged by episodes of crisis in previous pregnancies to be at particular risk, is also reported and the value of this method of management discussed.

Introduction

The basic features of sickle-cell anaemia and sickle-cell/haemoglobin C disease are the chronic haemolytic anaemia, with its attendant complications and the tendency towards intravascular thrombosis, leading to crises. Factors which may precipitate crises include diminished oxygen tension, a lowering of blood pH, a lowering of environmental temperature and infections: in the case of SC disease, crises may be manifest for the first time in pregnancy.

When patients with these diseases are pregnant, the hazards appear greater in SC disease (Smith & Conley, 1954; Edington, 1957; Molina & Marks, 1957). Reporting from the West Indies, Anderson et al. (1960) agreed that symptoms in SC disease might be manifest for the first time during pregnancy but felt that, at least in their patients, the hazards appeared less than in other reports. Buckle (1968), reporting from the United Kingdom, reported crises in three of four pregnant patients with sickle-cell anaemia, and in one of three pregnant patients with SC disease.

The increased foetal and maternal mortality rates during pregnancy in patients with these diseases is well known, it being suggested that foetal anoxia from sickling in the maternal venous sinuses in the placenta contributes to the increased perinatal mortality (Curtis, 1959).

An earlier paper (Buckle, 1968) dealt with the general scheme of management in pregnancy and labour, in a total of nine patients with sickle-cell diseases seen through thirteen pregnancies. A further six pregnancies in such patients have since been observed (4 SS; 1 SC and 1 S/Thalassaemia). One patient with sickle-cell anaemia was treated by exchange-transfusion during crisis, and it was subsequently decided to amend clinical management to include limited partial exchange-transfusion on patients who had a reasonable haemoglobin level and simple transfusion on those with a low haemoglobin level, the patients selected for this form of management having a history of crises and being judged to be at particular risk. Brief clinical details from patients so managed follow.

Replacement transfusion in the management of sickle-cell crisis

Case No. D. 60457: West Indian, aged 29; gravida 2. The patient was a known case of sickle-cell anaemia who had attended the sickle-cell anaemia clinic in the University of the West Indies for 3 years. She had a history of joint pains, mainly in the knees, which were usually provoked by cold weather. She had come to the United Kingdom on alkali and supplementary folic acid therapy. Previous history included a cholecystectomy. There had been one previous pregnancy, complicated by intermittent crises, ending in term-delivery of a live male, weight 3·0 kg. In the present pregnancy, the patient was admitted to hospital at 22 weeks with a 3-day history of joint pains, mainly in the knees. The patient said that she had not been taking alkali.

On examination, temperature 37°C; pulse 100/min; blood pressure 130/80 mmHg; no abnormality in the heart or chest. Abdominal examination revealed slight hepatomegaly and the presence of a 22-week pregnant uterus.
**Investigations:** Haemoglobin 7-8 g/100 ml. Serum bilirubin 5-8 mg/100 ml. Alkali was prescribed, initially intravenously, and supplementary folic acid by mouth. Alkalization of the urine was achieved within 24 hr of admission, but the joint pain remained unchanged and required narcotics for relief. There was some improvement over the subsequent 3 days but there was then a recurrence of pain in the knees and back, and 10 days after admission the patient developed a pulmonary infarct associated with a high pyrexia and a fall in haemoglobin level to 4-1 g/100 ml. Because of the continuing crisis and the fall in the haemoglobin level, it was decided to carry out replacement transfusion.

**Technique**

A polythene catheter was inserted, via the right ante-cubital vein, into the superior vena cava to act as the output point. A similar catheter was inserted into the left ante-cubital vein for intake. Heparin was given in a dose of 10,000 units 6-hourly. Over a period of 22 hr, 2-5 litres of blood were removed and an equal volume of fresh heparinized blood given to the patient. The output catheter was removed and a further 500 ml of blood slowly infused. The patient was covered both during and subsequent to the procedure with ampicillin, 250 mg 6-hourly. By the following day the patient had little pain and the temperature had subsided, and within a few days she was pain-free. A further 500 ml of blood was given 10 days later, and a further 500 ml 3 days after this. The effect on the haemoglobin level and the amount of sickle-haemoglobin is shown in Fig. 1.

One month after original admission the patient was transferred to the obstetric unit in total remission, the last reported haemoglobin being 10 g/100 ml and the sickle haemoglobin approximately 52%. She was given oral alkali and supplementary folic acid. It was hoped to maintain the haemoglobin level at the 10 g/100 ml level and the sickle haemoglobin below 75/80%. She was allowed home and attended regularly in the ante-natal clinic. She was readmitted at 37 weeks in view of the rise in sickle haemoglobin level. There was some difficulty with the veins, and it was decided not to exchange transfuse but to give the patient 1 litre of whole blood. Two weeks after the last transfusion the patient was admitted for surgical induction of labour, being given intravenous sodium bicarbonate during labour. The latter proceeded uneventfully until the onset of the second stage when, because of meconium staining of the liquor, delivery was completed by forceps under pudendal block. A liveborn female was delivered, weight 3-12 kg.

**Summary of labour**

1st stage: 7 hr 30 min;
2nd stage: 25 min;
3rd stage: 5 min.

Induction/delivery interval: 16 hr 10 min.

The patient remained well for 5 days, and was then found to be more jaundiced and to have considerable hepatomegaly. It was felt that she had
probably had a further crisis despite adequate alkalinization, but that the hepatomegaly merely reflected the difficulty in feeling the liver at an earlier stage due to the encroachment on the abdomen by the pregnant uterus. Her symptoms subsided and she was subsequently discharged from hospital, being maintained on the supplementary alkali and folic acid regime already mentioned. (This patient subsequently had a further replacement transfusion prior to operative surgery on her hip.)

**Limited exchange transfusion: history of crises during previous pregnancies**

Case No. D.13410: Nigerian, aged 29; gravida 4. The patient was a known case of sickle-cell anaemia and had had two previous pregnancies observed in this hospital. The first one, 3 years earlier, had been complicated by a severe pulmonary infarct at 32 weeks, the patient going into premature labour following this and delivering herself of a stillborn male infant. She became pregnant a year later and had crises during this pregnancy despite management by standard regime. She eventually had a normal delivery of a live male infant.

The patient booked for confinement at 16 weeks. At initial booking her haemoglobin was 9·3 g/100 ml, the reticulocyte count 11%, serum iron 91 μg/100 ml, serum UIBP 340 μg/100 ml, serum folic acid level in excess of 28 pg/100 ml. She was maintained on the standard alkali and folic acid regime, but was admitted to hospital at 26 weeks of pregnancy because of pain in the right elbow and right knee. Her symptoms subsided but recurred 5 weeks later. Itano solubility at this time showed 85% sickle haemoglobin, and in view of her history of recurrent crises in previous pregnancies and during the current pregnancy, she was admitted to the ward at 35 weeks. A small exchange transfusion was carried out in the manner previously outlined, 600 ml of blood being removed and 1000 ml being replaced. A post-transfusion blood sample showed 87% insoluble haemoglobin present.

Despite transfusion the haemoglobin did not rise above 8·0 g/100 ml. The pregnancy remained uneventful and she was induced at 38 weeks in accordance with normal practice, intravenous sodium bicarbonate being given during labour. She had a normal delivery of a live male infant, weight 2·24 kg. Manual removal of the placenta was required due to failure to separate, under intravenous pethidine and promethazine. The puerperium was uneventful, and there was no abnormality at post-natal examination, the haemoglobin at this time being 7·4 g/100 ml.

**Simple transfusion: history of crisis in previous pregnancies**

Case No. D.18709: West Indian, aged 32; gravida 4. The patient had had three previous pregnancies, two elsewhere and one observed in this hospital. In the two elsewhere she had had repeated crises during pregnancy. At the one observed in this hospital she had been maintained on the standard alkali/folic acid regime and remained crisis-free during the whole of the pregnancy and labour. (She was, however, admitted to hospital 6 months after delivery with a pulmonary infarct.) She attended for booking in the present pregnancy when 20 weeks pregnant. There was no obvious abnormality on examination.

**Investigations:** Haemoglobin 7·5 g/100 ml. Stool and urine analysis normal. Itano solubility showed 96·6% sickle haemoglobin. She was maintained on the alkali/folic acid regime, and her haemoglobin remained between 8 and 9 g/100 ml until the 34th week of pregnancy, at which date it fell to 7·8 g/100 ml. She was admitted 10 days later for the transfusion of 1000 ml of fresh blood which was given without untoward reaction. The Itano solubility 48 hr after transfusion showed 61% sickle haemoglobin and the haemoglobin level 9·2 g/100 ml.

The patient went into spontaneous labour at 38 weeks and after a rapid first stage had a spontaneous delivery of a live male infant, weight 3·0 kg. Forty-eight hours after delivery the patient was taken to theatre where Pomeroy sterilization was carried out under general anaesthesia. Subsequent to operation the patient developed a mild temperature and pain in the right chest. She was thought to have had a local sickle infarct in the lung, but no further management was found necessary. She made an uneventful recovery, and was discharged 14 days after delivery.

**Simple transfusion: history of crises before pregnancy**

Case No. D.74492: West Indian, aged 23; primigravida. The patient attended for booking at 16 weeks of pregnancy. There was no history of previous hospital admissions, but the patient stated she had experienced intermittent bone and joint pains for some years. Examination revealed no enlargement of the liver or spleen though there were numerous old scars on the legs.

**Investigations:** Haemoglobin 8·3 g/100 ml. Itano solubility showed 89% sickle haemoglobin. Haemoglobin genotype SS: stool analysis negative: urine culture negative: serum iron 127 μg/100 ml: serum UIBP 190 μg/100 ml: serum folic acid 2·8 pg/ml.

She was commenced on the standard routine and seen frequently. The haemoglobin level remained between 8 and 9 g/100 ml, and she was admitted for blood transfusion at 32 weeks gestation, being given 1000 ml of fresh heparinized blood, without reaction.
Subsequently, the haemoglobin level rose to 10 g/100 ml and the Itano solubility showed 80% sickle haemoglobin present.

Further transfusion was carried out at 37 weeks' pregnancy, 1000 ml of fresh heparinized blood being given. The patient experienced generalized aching and pyrexia towards the end of transfusion, the symptoms subsiding on intravenous chlorpromazine, 10 mg. The post-transfusion level was 8-3 g/100 ml, compared with a pre-transfusion level of 7-6 g/100 ml.

The patient experienced further joint pains 1 week later and was admitted to hospital. Symptoms were mild and subsided with analgesics and, as the patient had reached the 38th week of pregnancy, labour was induced in accordance with standard practice in the unit. Spontaneous delivery of a live female infant, weight 2-68 kg, occurred 7½ hr after induction, the patient being maintained on intravenous sodium bicarbonate during and for a period of 48 hr after delivery. She was thereafter maintained on oral alkali until discharge from hospital on the 10th post-partum day. The puerperium was uneventful.

Discussion

Management of patients with sickle-cell disease during pregnancy has included supplementary dietary folic acid, administration of alkali to reduce the risk of acidosis, and the administration of intravenous bicarbonate and magnesium sulphate during crises (Anstall et al., 1959; Apthorp, Meadday & Lehmann, 1963; Buckle 1968). Treatment of bone-pain crises with low molecular weight Dextran has been reported by Barnes, Hendrickse & Watson-Williams (1965). More recently the use of 'Arvin' has been used to produce therapeutic defibrination in Nigerian children suffering from sickle-cell crises (Gilles et al., 1968) with encouraging results.

An alternative method of management of crises in pregnancy is by exchange transfusion, a large percentage of abnormal cells being removed and replaced by normal cells. Ricks (1965, 1968) has reported on this procedure, and has also utilized exchange transfusion in the last 8 weeks of pregnancy to avoid crises in patients with sickle-cell anaemia or SC disease. In his series, blood less than 48 hr old was employed and an average of 2700 ml was replaced. A total of seven patients (four SC and three SS) were so managed, two (one SC and one SS) being carried out for the management of crises. There were no untoward reactions, and the remainder of pregnancy, labour and puerperium were uneventful. There are obvious dangers, however, from transfusions and Henderson (1950) reported seventeen reactions and three deaths in forty-four transfusions in sickle-cell anaemia. Apart from the hazards always associated with blood transfusions, additional dangers in massive exchange transfusion include possible incompatibilities between donors, haemorrhagic complications with thrombocytopenia and blood coagulation disorders, biochemical disturbances and, in sickle-cell anaemia and SC disease, the induction of crises. The latter are related to increased blood viscosity and perhaps the use of blood taken into acid–citrate–dextrose; heparinized fresh blood minimizes many of these hazards. The artery–vein method of exchange transfusion has been used to a limited extent (though not yet in pregnancy) and appears to be the most efficient method.

The dramatic response to exchange transfusion in sickle-cell crisis is well illustrated by the first case in this paper. By exchange transfusion, the danger of circulatory overloading is avoided and adult haemoglobin substituted for a limited period of time, lessening the risks of crises.

Whether the management of cases, judged by previous history to be at particular risk, by partial exchange transfusion or simple transfusion is justified, is less easy to determine. Certainly our experience to date suggests that it is of value but we feel that final assessment must await a larger series analysis.

References


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