MULTIPLE REPLACEMENT TRANSFUSIONS IN TWO INFANTS
WITH RH ERYTHROBLASTOSIS
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In the management of hyperbilirubinemia during the newborn period, it occasionally becomes necessary to do many replacement transfusions for the same infant. Regardless of the etiology of hyperbilirubinemia, it has been our policy during the first few days of life to keep the free bilirubin in the serum down to reasonable levels. The first few days of life may be defined as the first 5 days in the full-term infant and the first week in the premature infant. Reasonable levels may be defined as approaching 20 mg/100 ml in the first 48 to 72 hours and approaching 25 mg/100 ml for the remainder of the period stated.

The two cases presented here have been selected to demonstrate the feasibility of multiple exchange transfusions.

REPORT OF CASES

Case 1
This 950-gm female infant was transferred from another hospital at 14 hours of age for jaundice and respiratory distress. The mother was gravida III, para III and was Rh-negative. The hemoglobin concentration in cord blood was 9.0 gm/100 ml, and the bilirubin value was 4.75 mg/100 ml. The result of a Coomb's test was positive; the infant's blood was Rh-positive. Physical examination revealed a markedly jaundiced premature infant with moderate respiratory distress. The liver and spleen were not palpable.

The free bilirubin in serum was 24.5 mg/100 ml at 16 hours of age, and the first exchange transfusion was performed; the values for the hospital course are illustrated in Figure 1. Five replacement transfusions were required to control the level of bilirubin. At 78 hours of age the free bilirubin in serum was 14 mg/100 ml. Conjugated bilirubin was measured four times and never exceeded 1.25 mg/100 ml. The jaundice gradually disappeared. When the infant was 52 days of age the hemoglobin concentration was 6.8 gm/100 ml, and 25 cc of whole blood was given. Two days later the value was 11.7 gm/100 ml.

The infant was discharged at 102 days of age, weighing 2,460 gm. Physical examination, including neurologic evaluation, at the time of discharge revealed a normal premature infant.

Case 2
This 2-hour-old full-term female was transferred from another hospital for anemia and edema. The mother was gravida II, para II, Rh-negative, with high titers (1:5000). The hemoglobin concentration in cord blood was 3.8 gm/100 ml. More than 1,000,000 leukocytes were reported at the other hospital.

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ADDRESS: 29th Street and Ellis Avenue, Chicago 16, Illinois.
Physical examination revealed generalized edema and pallor. The central nervous system appeared intact. The heart and lungs were clear. The heart rate was 140 per minute, with a systolic murmur at the apex. The liver was palpated 6 cm below the costal margin, and the spleen was also enlarged. There were no petechiae or any signs of respiratory distress.

Laboratory data on admission were as follows: hemoglobin, 6.3 gm/100 ml; normoblasts, 270 per 100 leukocytes; corrected leukocyte count, 31,000/mm³, with 25% polymorphonuclear cells, 38% band cells, 1% eosinophils, 8% basophils, 12% lymphocytes and 16% monocytes. There was 3 + macrocytosis, 2 + target cell count and 4 + polychromatophilia. The bilirubin in serum was 2.6 mg/100 ml; the result of a direct Coomb's test was positive.

The first exchange transfusion was performed shortly after admission, and the values for bilirubin in serum during the hospital course is illustrated in Figure 2. Eight replacement transfusions were required to control the level of bilirubin in serum. At 96 hours the free bilirubin was 16 mg/100 ml. Conjugated bilirubin never exceeded 2.5 mg/100 ml on five occasions. The jaundice gradually disappeared, but marked pallor was noted. On the sixth day the hemoglobin was 8 gm/100 ml, and the infant was discharged in apparently good condition.

At the age of 2 years the child appeared to be perfectly normal.

Fig. 2. Case 2. Values for bilirubin in serum during the hospital course.

COMMENT

We would like to emphasize that we do not take the exchange transfusion procedure lightly. The more experience one has with this procedure, the more respect there is for the potential hazards. Attention to detail is essential to avoid tragedy. It is especially important to be certain that 1) the blood has been adequately cross-matched (Coomb's test); 2) the blood is less than 48 hours old; 3) the infant is warm and the blood is not frigid; 4) a competent observer is assigned to watch the baby, to listen to the heart, to use a pacifier to prevent screaming (especially when venous pressure readings are taken) and to be ready to use oxygen, suction and a laryngoscope as needed; 5) calcium is given slowly; and 6) if necessary the procedure is stopped to allow the baby to rest for a few hours, especially if a large deficit (over 40 cc) is required to reduce venous pressure readings to normal. These are some of the more important details. There are many others.

CONCLUSION

Replacement transfusions via the umbilical vein may be carried out successfully in small premature as well as full-term infants. Many repeat procedures may be necessary to keep down the levels of free bilirubin. With great care, this can be done safely.

REFERENCES


DISCUSSION

VISITING PHYSICIAN: These were very interesting cases. I have a few questions. First, we have been very impressed with the importance of the early treatment of these patients. The first infant
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was not given an exchange transfusion until 15 hours of age, and the second, at 2 hours. We have found that there is a high correlation between the interval of time from birth to the first transfusion and the number of replacements necessary. Second, I wonder about the slope of the increase of bilirubin. What slope do you use before you do your next replacement? Third, I wonder about the indication for packed erythrocytes versus whole blood when the venous pressure is high. Fourth, we have trouble deciding on a small transfusion. How low do you permit the hemoglobin values to go?

Dr. Wishingrad: First, concerning early replacement transfusion, I do not think there is any question, especially in Rh incompatibility, that we want to do the procedure earlier than we did in both of these patients. However, both infants were transferred from other hospitals, and we gave them transfusions as soon as possible. I agree that it is easier to prevent the bilirubin concentration from increasing to high values than it is to bring it down. Concerning the question of slopes, we too are interested in the increment of increase bilirubin. However, for these patients the slope is as it is because there are only two points between exchanges, at the end of the replacement transfusion and 8 to 12 hours later. To do bilirubin determinations more often than every 6 to 8 hours is not very rewarding, except during the first 12 to 24 hours of life. Once the replacement has been done, it takes time for the tissue and extravascular bilirubin to be redistributed and equilibrium re-established. I agree, in the presence of an elevated venous pressure, that the use of packed erythrocytes is a good idea. Regarding small blood transfusions, we use them if the hemoglobin concentration is less than 7 gm/100 cc the first week of life. If the hemoglobin concentration is less than 7 gm/100 cc, the chances are the baby will become severely anemic, because it will be 5 to 6 weeks before the value will start to increase.

Dr. Elegent: Regarding the slope of the bilirubin curve, we figure approximately an increase of 0.75 to 1 mg/100 ml/hour as an indication for the first replacement transfusion.

Visiting Physician (Fargo, North Dakota): I would like to know what the management of these babies is between exchanges. I would think that by the time you get to the eighth exchange you would likely have difficulty. What do you do to prevent infection?

Dr. Wishingrad: We almost always use the umbilical vein, even in premature infants at 4 to 6 days of age, but we never leave the catheter in place. At the end of the procedure we put one suture through the vein; at the time of the next procedure we can find the vein very easily, pick up the suture and remove it; and we are able to cannulate it again. We usually give no feedings orally for 6 hours and administer penicillin and streptomycin until the blood culture is reported sterile.

Visiting Physician (Glencoe, Illinois): I question the value of early transfusion from my experience. As far as the slope of bilirubin, I would like to know how often, for example, the bilirubin is 22 mg/100 ml, and by the time the operator begins to work, it is 18 mg/100 ml. However, they do the exchange transfusion, and the next day the bilirubin concentration is up to 24 mg/100 ml. I wonder how important it really is to measure venous pressure. After you have done a number of exchanges, I think you develop a feeling about these things. You know that you keep a deficit, and rarely get into trouble if you go slowly.

The last point concerns iron. We send a number of children home with a hemoglobin value of 9 or 10 gm/100 ml, and in a week the value begins to decrease. We do not want to give blood, so we give iron, even though the anemia is normocytic normochromic. In a month the hemoglobin value will be back to 10 or 11 gm/100 ml with no blood transfusions. A number of physicians do this.

Dr. Wishingrad: The first question concerns the advantages of early exchange transfusion. Our experience is quite different from yours. If a family has a previous history of severe erythroblastosis, the baby is Rh-positive and the result of Coomb's test is positive, we find early replacement transfusion essential. There are other indications for early replacement transfusion as well. If we do not exchange until the bilirubin value is 18 or 20 mg/100 cc, and the tissues are saturated, the management is much more difficult. As for the measurement of venous pressure, I think it is of extreme importance not to depend upon our feelings in this situation. Each baby is different. The infant with hydrops discussed today required very little deficit to control elevated venous pressure. There have been other babies, who did not look nearly as ill, but had very high venous pressures. If we decrease the venous pressure in these patients too rapidly with a great deficit, we may well contribute to mortality. I think the measure of venous pressure is a crucial part of the replacement transfusion. I am certain that iron has absolutely nothing to do with the response of the bone marrow following erythroblastosis. At about 6 weeks of age, a spontaneous regeneration of erythrocytes occurs. The anemia appears to be the result of a physiologic hypoplasia that is more marked in the baby with hemolytic disease of the newborn. I agree that we ought to try to keep small transfusions to a minimum, but I know that iron therapy does not make any difference. Would you mind repeating the second question?

Visiting Physician: Have you had the experience of the bilirubin in serum decreasing sharply between the time you decided to do a replacement and the time the replacement actually begins?
DR. WISHINGRAD: There is a standard error of about 5 to 10% in bilirubin values. I think 18 mg/100 ml is essentially the same as 20. If we decide to go ahead with the procedure for a baby whose bilirubin concentration is 22, and the repeat determination at the time of exchange is 18, we would not be concerned. I do not think the conjugation of bilirubin in the liver starts between one determination and the next. Every newborn baby is conjugating to a certain degree, and as time passes, the conjugating ability increases. If one has a good indication for a replacement at 6:00 P.M., and the procedure is started at 8:00 P.M., the value at 8:00 P.M. should not influence the decision one way or the other.

DR. METCOFF: I think there are two points to be made. First, the usual procedures with exchange transfusions is not to do eight exchange transfusions for an infant. I trust it is not necessary to affirm this to this audience. Dr. Wishingrad and Dr. Elegant chose cases to illustrate one extreme, that it may be essential to be prepared to carry out many repeated procedures. The second point I cannot emphasize strongly enough is that there is an error in any determination that one chooses to make in any laboratory at any time. There is no such thing as an absolute value. All values have a range. The range is dependent upon variations between patients, as well as variations of technicians, reagents, etc. An error of 5% in the determination of bilirubin concentration by an excellent laboratory and excellent technicians is almost a minimum error. All errors are plus and minus errors. If the error is 2 mg/100 ml, that means that there would be a range of 4 mg/100 ml. All values from 16 to 20 mg/100 ml would be exactly the same value.

DR. H. J. COHEN (New York): Have you ever seen phlebitis with eventual abscess formation. We did an exchange, and the child developed a mass. Eventually the mass pointed and had to be incised. The child eventually recovered. I would like to know if you had any similar experiences and whether you use antibiotics?

DR. WISHINGRAD: Up to very recently, the use of antibiotics was an individual decision of the attending physician. Some used it and some did not. We were unable to recognize any difference in the outcome of our patients. However, now we are engaged in a more formal program of recording what is happening to the babies who receive replacement transfusions. Concerning the question of liver abscess, I have experienced just about every complication from this procedure, except that one.

DR. VAN GELDIN (Louisiana): I would like to know if you have encountered any difficulties with calcium.

DR. WISHINGRAD: We have been very unhappy with the administration of calcium. We started giving it rapidly. We soon learned to give it slowly. Now we dilute it with 10 ml of blood and practically drip it in. Our usual dosage is 1 ml of 10% calcium gluconate for every 100 ml of blood transfused. We give about half this amount to the premature infant because of a few experiences with small infants who required resuscitation after calcium administration. I think it would be better to treat tetany than cardiac arrest. Yes, we have had difficulties with calcium.
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