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Exchange Transfusion with Fresh Heparinized Blood is a Safe Procedure

Experiences from 1 069 Newborns

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ABSTRACT. Hovi, L. and Siimes MA. (Children's Hospital, University of Helsinki, Helsinki, Finland). Exchange transfusion with fresh heparinized blood is a safe procedure. Experiences from 1 069 newborns. Acta Paediatr Scand 74: 360, 1985.

1 069 newborns were subjected to exchange transfusion with fresh heparinized blood in the years 1968, 1971, 1974, 1977 and 1981. There were 258 infants with Rh disease, 328 with hyperbilirubinemia with ABO incompatibility, 436 with hyperbilirubinemia without ABO incompatibility and 47 infants without hyperbilirubinemia or evidence of hemolytic disease. The total annual number of infants decreased gradually from 279 in 1968 to 130 in 1981. A total of 48 infants of the 1 069 newborns died during neonatal period but the death was possibly related to exchange transfusion in four of them. There were serious complications in 14 infants during and in only five infants after the procedure. Morbidity related to exchange transfusion was the highest among newborns with serious basic disease. Using the presented bilirubin nomograms and fresh heparinized blood we have not found that the hazards of exchange transfusion would have overgone the risks of hyperbilirubinemia. *Key words: Newborn, hyperbilirubinemia, exchange transfusion, heparinized blood.*

In the early 1950s exchange transfusion had established its role in the treatment of erythroblastosis fetalis. In those cases it was an effective way both in treating anemia and hypoproteinemia, and in preventing kernicterus. Subsequently, exchange transfusion was found to be useful also in hyperbilirubinemias of other origin.

The need of exchange transfusions clearly decreased since the late 1960s due to the invention of Rh prophylaxis with anti-D-globulin and phototherapy, the reduction in family size being another though less important reason. On the other hand, there have emerged factors which have increased the use of exchange transfusions. Prematures and asphyctic infants of any gestational age have been observed to develop kernicterus even on relatively low bilirubin levels (1, 2). In addition, after early 1970s exchange transfusions have been used increasingly also in the treatment of other neonatal diseases including IRDS and septicemia (3, 4, 5).

Complications are connected with exchange transfusion (6). Most of the published series are, however, from the 1960s and may not be relevant to the present situation. At the Helsinki Children's Hospital fresh heparinized blood has been used for exchange transfusions since 1948. We wanted to analyze this large, homogenously treated and thoroughly recorded material in order to get more information of the current situation. In this paper we report about the changes which have taken place during the last decade and about the complications and mortality in this material.

SUBJECTS AND METHODS

The newborns. This study is based on the medical records of all newborn infants who were subjected to one or more blood exchange transfusions in the Children's Hospital, University of Helsinki, during the selected years: 1968, 1971, 1974, 1977 and 1981. The Children's Hospital is connected with the Departments of Obstetrics and Gynecology, University of Helsinki, which is a referral center for risk pregnancy groups, including Rh immunized and diabetic mothers. In addition, some newborns are also referred directly from other maternity hospitals.

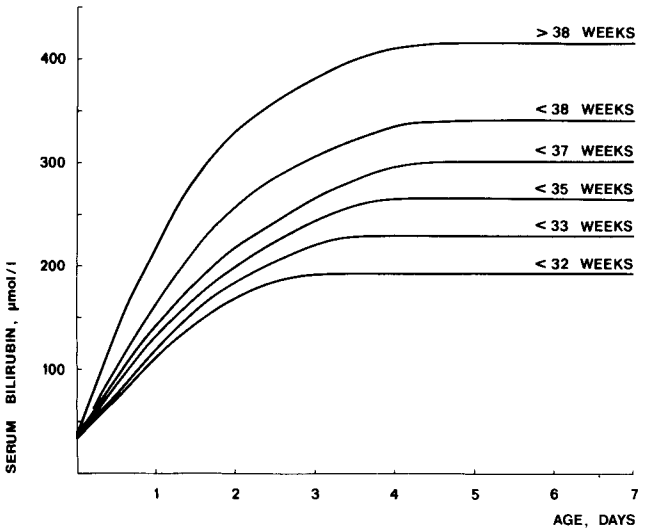

Fig. 1. Serum bilirubin levels indicative for exchange transfusion. The infants were treated according to gestational age but when additional risk factors such as asphyxia, hypoglycemia and neurological symptoms occurred, they were treated as if belonging to the next lower curve.

Thus the Children's Hospital has served a general population of about 3.5 millions. Exchange transfusion was performed on a total of 1 069 infants during the five years. There were 258 infants with Rh disease, 328 with hyperbilirubinemia with fetomaternal ABO incompatibility (all mothers blood group O), and 436 with hyperbilirubinemia without ABO incompatibility. 201 of the 436 had some evidence of co-occurring hemolysis. Lastly, there were 47 infants who did not have hyperbilirubinemia or evidence of hemolytic disease but were exchange transfused for suspected or documented septicemia (n=43), bleeding tendency (n=3) and severe anemia and hypoproteinemia due to feto-fetal transfusion (n=1).

The total annual number of infants exchange transfused decreased gradually from 279 in 1968 to 130 in 1981. The number of exchange transfusions decreased from 405 to 218, respectively. The decrease was a constant finding in all groups except in infants without hyperbilirubinemia or hemolytic disease which increased from 4 in 1968 to 27 in 1981.

About half of the infants were prematures (<38 weeks of gestation) as shown in Table 1.

Our indications for exchange transfusions followed standard criteria (7). However, after 1976 the co-existing risk factors including prematurity, asphyxia, hypoglycemia, neurological symptoms etc. had an increased influence on the indications (Fig. 1).

During the exchange transfusion each infant was kept warm with preheated restraints and radiant heat from above. Fresh heparinized blood, mostly within two hours and always within six hours after donation, was used in 1 524 exchanges. On two occasions citrate blood was used. Protamine sulphate was given to neutralize the effect of heparin at the end of the transfusion. During the procedure the clinical condition of the infant was carefully followed and recorded by a nurse. The heart rate was counted at least once in every five minutes. Venous pressure was measured at the beginning and during the procedure by holding the umbilical catheter vertically and measuring the column of blood. No routine electronic monitors were used but during the last year of the study monitoring of ECG, continuous electronic blood pressure measurement and transcutaneous oxygen measurement were used in some cases.

RESULTS

Mortality. A total of 48 of the 1 069 newborns exchange transfused died during neonatal period (Table 1). Most of these newborns were small and sick prematures. After going over the charts of the newborns we came to the conclusion that in 4 of the 48 cases death was possibly related or due to the exchange transfusion (Table 1). The first patient was severely affected after Rh immunization, exchange transfused six times and died of necrotizing enterocolitis at five days. The second patient was also severely affected after Rh immunization and died of Pseudomonas septicemia after five exchange transfusions at

the age of five days. The third patient had hyperbilirubinemia and signs of septic infection already prior to the exchange transfusion. He died of necrotizing enterocolitis at three weeks. The fourth patient was a term baby with clinical signs of 21 trisomy and bacterial septicemia prior to the exchange transfusion. He died of necrotizing enterocolitis at the age of two days. In the other 44 cases death could not be attributed to exchange transfusion but to severe underlying disease such as septicemia, respiratory distress syndrome, or Rh disease.

Complications during exchange transfusions. There were 14 infants whom we classified with a major complication during the exchange transfusion (Table 2). Seven of the infants were in good or relatively good condition prior to exchange transfusion and the other half was in poor general condition already before the procedure. Among this latter group there were five severely affected Rh infants with cord hemoglobin concentration from 24 to 90 g/l, one infant with a hemoglobin of 36 g/l and hypoproteinemia due to feto-fetal transfusion and one with hypoplastic left ventricle and aorta. In these seven infants the complications could be considered to have resulted at least in part from their disease. For the infants who were in good condition prior to the exchange transfusion explaining factors for the complications could be found in three cases: accidental dilution of hemoglobin from 113 to 77 g/l in one case, administration of excess protamine sulphate in one case, and use of six days old citrated blood by mistake in one case. In the remaining four cases no explaining factors—apart from the procedure itself—could be found. In addition to the complications already mentioned some infants had milder symptoms which might be attributed to the exchange transfusion. Such symptoms are for instance mild bradycardia, restlessness and vomiting during the procedure. These are probably not so carefully

Table 1. *Mortality and gestational age*

Gestational age (weeks)	No. of infants	No. of deaths	No. of deaths possibly related to exchange transfusion
<30	33	10	–
>30–32	46	9	–
>32–34	67	6	2
>34–36	114	9	1
>36–38	247	6	–
>38–42	538	7	–
>42	24	1	1
Total	1 069	48	4

Table 2. *Complications during exchange transfusion*

IHB = idiopathic hyperbilirubinemia

	Rh	ABO	IHB	Others	Total
Respiratory arrest	3				3
Pulmonary oedema and cardiac insufficiency	3	1			4
Cardiac arrest	1		1		2
Bradycardia					
<60/min	5		1	1	7
60–100/min	41	30	37	4	112

recorded—except bradycardia—that any further conclusions could be made about their frequency. These noted milder symptoms seem to be scattered in all etiological groups (Table 2).

Complications after exchange transfusion. Some problems which may appear only a few days after the exchange transfusion, as for instance infections, are known to be possible sequalae of this procedure. Five infants had a major complication of this kind. Three of them had necrotizing enterocolitis and two had bacterial septicemia. All three with necrotizing enterocolitis died later. One of them was a severely affected Rh infant, one had 21- trisomy and one had signs of bacterial infection already before the exchange transfusion. The bacterial septicemias were due to St. Aureus and Peudomonas. The latter developed in a severely affected Rh infant after five exchage transfusions and he died later. The other infant with septicemia after exchange transfusion made full recovery. He was a premature baby with symptomatic hypoglycemia. Thus not one of these five infants with serious late reactions after exchange transfusion was in good condition or without major clinical problems before the exchange transfusion.

DISCUSSION

The decrease in the number of exchange transfusions between 1974 and 1977 is very striking. There were no changes in the number of referral hospitals of newborns during these years. Thus the decrease indicates a decline in the frequency of exchange transfusions. The decrease was anticipated in the infants with Rh disease due to the Rh prevention program in effect in Finland since 1969. The increased use of phototherapy might be the main reason for the decrease of exchange transfusions in the hyperbilirubinemic groups.

The role of exchange transfusion and the indications of exchange transfusion in the treatment of septicemia of newborns remain to be determined. As a whole, the question about who and when should be treated with exchange transfusion has not become any easier to answer during the last decade, vice versa. In the hyperbilirubinemic groups the role of prematurity continues to be unclear and the safe top value of serum bilirubin concentration in fullterm healthy infants is also without a definite answer. Nevertheless, in the near future the serum concentration of bilirubin continues to form a basis for indications of exchange transfusion in newborns and we would like to emphasize that the gestational age and the general condition of the newborn should be taken into account when considering an exchange transfusion (Fig. 1).

Table 3. *Reported mortality of exchange transfusions (ET)*

IHB = idiopathic hyper-bilirubinemia

					Total mortality	
Source of data	Diagnosis	No. of infants	No. of ETs	Total deaths	Per infants	Per ETs
Boggs & Westphal, USA (8) 1960	Rh ABO, IHB	519	875	38	7.3	4.3
Taylor, Edmonton, Alta (9) 1962	Rh ABO, IHB	104	150	8	7.7	5.3
Panagopoulos et al., Athens, Greece (10) 1969	Rh ABO	502	606	18	3.6	3.0
Tan et al., Singapore (11) 1976	ABO IHB	122	140	2	1.6	1.4
Present study	Rh ABO, IHB	1022	1472	26	2.5	1.8

Our data suggest that exchange transfusion when performed with fresh heparinized blood is a safe procedure resulting only rarely in serious complications. The mortality rate in this series was lower than previously reported by many other investigators (Table 3). However, it is difficult to compare the different studies because the characteristics of the patient material and the mode of tretment—other than exchange transfusion—of the newborns may vary considerably from one study to the other. In order to reduce this variation the infants of this study who were exchange transfused for other reasons than hyperbilirubinemia or Rh disease have been excluded in the comparison in Table 3. The incidence of sudden cardiac arrest during exchange transfusion was lower in this series than that reported in most previous studies (12). An explanation might be that the risk of hyperkalemia, acid base disturbances and citrate toxicity are mostly avoided by the use of fresh heparinized blood and associated with use of citrated blood especially after its storage. According to Ellis et al. (12) the appearance of sudden circulatory arrest during exchange transfusion was about 1.5 per 100 transfusions. In our series two infants had cardiac arrest, subsequently successfully resuscitated. One of the two occurred immediately after the administration of protamine sulphate and the other at the end of the exchange transfusion which was erroneously performed with six days old citrated blood. We were not surprised to learn that morbidity related to exchange transfusion was concentrated in newborns with other, often multiple, serious problems. In fact, only 7 out of 19 infants with major complications connected with exchange transfusion were in good or relatively good condition prior to the exchange transfusion.

Certain side effects, especially hypoglycemia and rise in nonesterified fatty acids during exchange transfusion have been attributed to heparinized blood. According to Schiff et al. (13) hypoglycemia was mild and concentration of fatty acids was back to normal in three hours. In this study these parameters were not regularly measured.

Exchange transfusion at too fast a rate has been claimed to cause unfavourable symptoms and signs in the infant (14, 15). The actual momental speed of blood flow, in or out, is probably a more important factor than the total time spent on the procedure. This speed was not measured in this study and thus a causal relationship to complications of exhange transfusion could not be ascertained. However, in this series there were four infants who had severe bradycardia of unknown reason during exchange transfusion. It could be envisaged that too fast a speed may have been one etiological factor in these cases.

The procedure of exchange transfusion contains many possibilities of human errors which may uncommonly end up in complications. In this work such mistakes as selection of wrong blood and dilution of hemoglobin concentration of the infant during the exchange transfusion were found to be associated with subsequent cardiorespiratory problems. The increasing experience of the personnel should minimize the risks of complications due to human errors but in addition to that, many technical devices have shown to be useful in following the condition of the sick infants during the procedure. Such devices include those which monitor continuously body temperature, blood pressure, ECG and transcutaneous oxygen pressure. However, the experience and skill of the personnel cannot be replaced by any technical devices and thus these properties should be maintained by performing enough exchange transfusions in any particular pediatric unit.

We conclude that the general condition of the infant prior to the exchange transfusion, the rate of exchange transfusion, the quality of blood and human errors are important factors in determining the risks for complications during the exchange transfusion.

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