

Why we are still doing so many exchange blood transfusion for neonatal jaundice in Nigeria

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Background: Since exchange blood transfusion (EBT) is associated with serious complications, phototherapy has been made more powerful to reduce the need for EBT in the developed world. This study was undertaken to determine the indications for EBT in neonatal jaundice (NNJ) at our unit and what proportion of EBTs was possibly avoidable.

Methods: All the babies who had EBT for hyperbilirubinemia over a three-year period were included. Age, sex, weight, place of delivery, blood group of baby and mother, other investigations, management, and the outcome of the babies were recorded.

Results: Of the 1686 babies admitted to the neonatal unit, 90 (5.3%) had EBT. Fourteen (15.6%) were inborn while 76 (84.4%) were out-born babies. Fifty-six (62.2%) babies were admitted primarily for NNJ while 34 (37.8%) developed NNJ during admission. Thirty-six (40.0%) of the babies had phototherapy for more than 24 hours prior to EBT either because they were of very low birthweight or NNJ was detected very early and therapy was so commenced. Sixty-eight (75.6%) babies had single EBT while the remaining 22 (24.4%) had two sessions of EBT. Factors associated with severe NNJ in babies requiring EBT included low birthweight (<2500 g, 44.4%), ABO incompatibility (30.0%), glucose-6-phosphate dehydrogenase deficiency (34.4%) and septicemia (26.1%). Twenty-seven (30.0%) of the neonates developed features of kernicterus: 26 before admission while 1 during admission; all except one were delivered outside the hospital.

Conclusions: The EBT rate in our center was high.

With more effective phototherapy, EBT could be avoided in most of the babies who initially had phototherapy for more than 24 hours before EBT and repeated EBT sessions. Health education of the population at risk, especially pregnant women, and early referral at the primary health care level will reduce the burden of severe NNJ.

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Key words: exchange blood transfusion; hyperbilirubinemia; neonatal jaundice; phototherapy

Introduction

Neonatal jaundice (NNJ) is a common cause of neonatal morbidity and mortality.^[1-5] A previous report showed that NNJ was the commonest cause of neonatal morbidity in our newborn unit.^[4] Severe neonatal jaundice is a pediatric emergency because it may cause kernicterus which can result in death or irreversible brain damage in those who survive,^[1,6,7] resulting in chronic handicapping conditions like cerebral palsy or sensorineural deafness.^[1,8]

The goal of the management of severe NNJ is therefore to rapidly reduce the serum bilirubin level to prevent death or handicaps. Phototherapy and exchange blood transfusion (EBT) are the two common treatment modalities that are routinely used all over the world.^[1] The fact that EBT is now rarely used in the developed countries confirms the efficacy of phototherapy for regulating plasma bilirubin concentrations.^[9] EBT is the most rapid method for reducing serum bilirubin (SBR) and the risk of kernicterus in severe NNJ. Indications for EBT in NNJ are described in standard texts.^[1]

However, EBT is associated with complications arising from umbilical catheterization like air embolism, lower limb gangrene, necrotizing enterocolitis and cardiac arrhythmias. Other complications of EBT include metabolic disorders like hypoglycemia, acidosis, hypocalcemia and hyperkalemia and transmission of

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infectious diseases like viral hepatitis, HIV/AIDS, malaria, and syphilis and blood transfusion reactions.^[1]

In the developed countries of North America and Europe, EBT is now rarely done because of the availability of powerful and efficient phototherapy units.^[10-12] In addition, recently introduced interventions like the use of supplementary fibreoptic phototherapy blankets,^[13] prophylaxis with metalloporphyrins^[14] and casein-containing infant formulae are also being used.^[15,16] For various reasons, including shortage of facilities and late presentation in the hospital, it is almost impossible to rely mainly on phototherapy in treating severe NNJ in the developing countries. Unfortunately, the other new methods of treating NNJ are often not available in the developing countries.

The aim of the present study was therefore to determine the frequency of EBT in our unit, the reasons for EBT, the morbidity and mortality among babies who had EBT, and to determine what proportion of EBTs was possibly avoidable.

Methods

Materials

This was a retrospective analysis of data of babies admitted to the Newborn Unit of Wesley Guild Hospital (WGH), Ilesa. The hospital is an arm of Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Osun State, South Western Nigeria. The topography and the range of services provided by this unit are as previously described.^[4] Data of all babies who had EBT for severe NNJ between January 2001 and December 2003 were obtained from admission records of the individual case files.

The following data were obtained from the records: age on admission and at the time of EBT, birthweight and weight on admission, sex, place of delivery, time of onset of jaundice, duration of phototherapy prior to EBT and the presence or absence of features suggestive of kernicterus on admission. The total and direct SBR levels on admission, and immediate pre-EBT SBR levels,

blood group of baby and mother, glucose-6-phosphate dehydrogenase (G-6-PD) status of baby and blood culture reports if available were recorded. The duration and outcome of hospitalization were also recorded.

Management

Phototherapy and EBT were the treatment modalities employed in our center. Very low birthweight (VLBW) infants with birthweights less than 1500 g were routinely commenced on prophylactic phototherapy. In other babies, the SBR levels at which phototherapy was commenced was variable depending on postnatal age, weight and associated clinical problems. In otherwise healthy normal weight (≥ 2500 g) babies, phototherapy was commenced at SBR greater than 204 $\mu\text{mol/L}$. Unconjugated SBR levels of ≥ 20 mg/dL were taken as absolute indications for EBT in apparently healthy term infants. In preterm VLBW infants, a much lower SBR value was used as an indication for EBT (10-12 mg/dL for a 1000 g preterm infant in the first week of life). In a very ill term infant or an infant with features of kernicterus, a SBR level lower than 20 mg/dL was sometimes used as an indication for EBT.

Statistical analysis

The data were analyzed by simple descriptive statistics like Chi-square, Student's *t* test using SPSS software. A *P* value < 0.05 in two-tailed test was taken as statistically significant.

Results

Overall clinical features of the babies

Of the 1686 babies admitted over the period, 90 (5.3%) had EBT for severe NNJ. The 90 babies consisted of 48 males and 42 females, giving a male-to-female ratio of 1.1:1. The weight (kg) on admission ranged from 0.85 to 3.80 with mean and standard deviation (SD) of 2.30 and 0.79, respectively (Table 1). The ages in hours at admission ranged between 0.42 and 168 (mean and SD

Table 1. Clinical features of the 90 babies

Parameters	Range	Mean	SD	Remarks
Weight (kg)	0.85–3.80	2.299	0.791	LBW 40/90 (44.4%)
Age on admission (h)	0.42–168	68.27	50.20	Admission for other reasons
Age when NNJ was noticed (h)	12–168	82.51	36.99	Depends on caregiver
Duration of NNJ before admission (h)	0–120	17.96	25.30	34/90 (37.8%) developed NNJ after admission
Interval between admission and EBT (h)	3–120	22.34	28.78	Not necessarily due to delay in EBT
First SBR ($\mu\text{mol/L}$)	78–629	365	146	-
Pre-EBT SBR ($\mu\text{mol/L}$)	184–629	400	121	First and pre-EBT same for some babies
Number of EBT sessions	1–2	1.24	0.43	22/90 (24.4%) had 2 EBT sessions

SD: standard deviation; NNJ: neonatal jaundice; EBT: exchange blood transfusion; SBR: serum bilirubin; LBW: low birthweight.

Table 2. Morbidity and mortality in relation to places of delivery

Places of delivery	<i>n</i>	Mean birthweight (SD)	Kernicterus (SD)	Mortality (percentage)	Low birthweight (SD)
WGH	14	2.225 (0.964)	1 (7.1)	0 (0.0)	8 (57)
Church	11	2.558 (0.600)	2 (18)	1 (9.1)	2 (18)
Home	18	2.339 (0.724)	6 (33)	3 (16.7)	8 (44)
PRIV	32	2.289 (0.753)	12 (38)	3 (9.4)	14 (44)
GH	4	2.400 (1.211)	1 (25)	0 (0.0)	2 (50)
PHC	11	1.965 (0.820)	5 (45)	2 (18.2)	6 (55)

WGH: Wesley Guild Hospital; GH: general hospital; PRIV: private clinic; PHC: primary health care center.

Table 3. Possible etiological factors for neonatal jaundice

Low birthweight (40/90, 44.4%)
Very low birthweight (10/90, 11.1%)
Glucose-6-phosphate dehydrogenase deficiency (11/32, 34.4%)
Blood culture positive (6/23, 26.1%)
Direct Coomb's test positive (1/32, 3.1%): baby (A+) and mother (A-)
ABO incompatibility (27/90, 30%): AO (8), BO (19)

of 68.27 and 50.20, respectively).

The distribution of the patients in relation to places of delivery is shown in Table 2. Fourteen (15.5%) of the 90 babies were delivered in Wesley Guild Hospital (WGH) while the remaining 76 (84.5%) at private clinics (PRIV), home, churches, primary health care (PHC) centers and general hospitals (GH), constituting 42.1%, 23.7%, 14.5%, 14.5% and 5.2% of the out-born babies respectively.

Fifty-six (62.2%) babies were admitted primarily for NNJ while 34 (37.8%) developed NNJ during admission. Forty (44.4%) of the patients were of low birth weight (LBW) (<2.5 kg). The LBW babies were admitted primarily because they were LBW but jaundice was subsequently observed in them.

Management in relation to SBR levels

Thirty-six (40%) of the babies had phototherapy for more than 24 hours prior to EBT either because they were of VLBW or jaundice was detected very early and therapy was so commenced. The mean age at which jaundice was noticed was 82.51 hours, which depended largely on the level of awareness of the caregiver. For most babies, especially those who had EBT within three hours of admission, the admission SBR was also the same as the pre-EBT SBR. The mean pre-EBT SBR value was 400 $\mu\text{mol/L}$. Sixty-eight (75.6%) babies had single EBT while the remaining 22 (24.4%) had two sessions of EBT, a total of 112 EBT sessions.

Possible etiological factors

Possible etiological factors for NNJ are shown in Table 3. Forty (44.4%) of the babies studied were of LBW while 10 (11.1%) were VLBW. ABO blood group

incompatibility was suspected in 27 (30%) babies: 19 (70.4%) had BO incompatibility (mother blood group O and baby of blood group B) while 8 (29.6%) had AO incompatibility (baby of blood group A). Direct Coomb's test was positive in only 1 baby (1.1%) who was of blood group A Rh positive while the mother was blood group A Rh negative. G-6-PD status was known in 32 babies and 11 (34.4%) of them were G-6-PD deficient while 21 (65.6%) were G-6-PD normal. Blood culture reports were available in only 23 babies and positive results in 6 (26.1%) of the 23 babies.

Morbidity and mortality (Table 2)

Twenty-seven (30%) of the patients had features of kernicterus: 26 of them were admitted with features of kernicterus while 1 developed kernicterus during admission because the parents refused to give consent for EBT. Features of kernicterus commonly encountered in these neonates included poor feeding, severe hypotonia or hypertonia, depressed neonatal reflexes, very weak cry or gasping or irregular respiration, abnormal movement of the limbs and opisthotonus. All these babies were delivered outside the hospital with the exception of the baby whose parents refused to give consent for EBT. Twenty-one (42%) of the 50 normal weight babies had features of kernicterus compared with 6 (15%) of the 40 LBW babies. The difference was statistically significant ($\chi^2=7.7$, $P<0.01$).

Nine of the 90 babies died, giving an overall mortality rate of 10%. All the deaths were among the 76 babies admitted from outside. The mortality rate among the LBW babies was 12.5% (5 out of 40), which was higher than that of 8.0% (4 out of 50) among the normal weight babies, although the difference was not statistically significant ($\chi^2=0.5$, $P>0.5$).

Discussion

This study showed that about 1 in 20 babies admitted into our newborn unit had EBT and the frequency of EBT was about thirty per year or about one every other week. Such a high rate of EBT has been previously reported from the same center.^[3]

There are two major reasons for so many EBTs in our center: very late presentation of the outborn babies and the inability to carry out intensive phototherapy. For example, 26 of the babies had features of kernicterus on admission. Such babies and others with high SBR on admission required urgent EBT.^[17,18] Early discharge of babies from nurseries is now a major reason for the re-emergence of kernicterus in the developed world.^[14] For this reason efforts are being made to predict the risk of severe jaundice and to identify babies who are likely to be re-admitted because of severe hyperbilirubinemia. This is done by screening with SBR within the first 24 hours of life and risk factors for severe hyperbilirubinemia before discharge from the hospital.^[14,15,17] On the other hand, most of the babies with severe NNJ in the present study were delivered in places where adequate medical and nursing supervision is not available. Jaundice in many of the babies was diagnosed only when they were no longer able to suck.^[3] EBT was therefore indicated in at least 26 (28.9%) of the babies on admission.

With intensive phototherapy it was possible to avoid 58 (51.8%) of the 112 EBT sessions. These included the 36 EBTs in babies who had phototherapy for more than 24 hours before EBT and the repeated EBT in the 22 babies.

In the developed countries, a baby may be exposed to two or more powerful and efficient phototherapy units.^[1,9] Such practice has considerably reduced the need for EBT to the extent that a resident doctor may not have the opportunity of doing an EBT.^[1] In Nigeria, on the other hand, two or three may have to share a phototherapy unit of doubtful efficacy.

Although the number of babies who had all the necessary investigations was small, it was remarkable that only one of these babies had confirmed Rhesus incompatibility as a cause of the jaundice. This attests to earlier reports that Rhesus isoimmunization was not a common cause of NNJ in this part of the world.^[3,5] The baby with positive direct Coomb's test in the present study was admitted at the age of about 0.42 hours as a LBW infant of a Rhesus negative mother. He was noticed to be jaundiced at the age of about 12 hours. This emphasizes the need to closely monitor newborn babies, especially LBW, for NNJ. That baby received prompt attention because he was delivered in our hospital. It also calls for a renewal of a sound referral system between the various tiers of health care delivery for outborn babies with risk factors. For example, an 850 g baby who was delivered in a primary health center outside Ilesa was presented very late and had features of kernicterus on admission.

The only baby among those delivered in WGH who had kernicterus was a victim of parental refusal

to receive blood, as dictated by their religion. The parents were of the Jehovah Witnesses and they refused consent for EBT on religious grounds, which resulted in development of overt signs of neurologic damage in the baby. That was indeed a case which should provoke a strong advocacy on the need for the state to protect children by appropriating the right of parenthood in such circumstances.

The levels of bilirubin at which treatment with phototherapy was commenced in our babies were relatively low judging from recent recommendations from developed countries.^[11] Most of these babies could be regarded as having prophylactic phototherapy.^[12] Our practice, as in most other centers in Nigeria, may be due to many local peculiarities including the shortage of modern phototherapy units which can be used to administer intensive phototherapy and the frequent cuts in electric power. Frequent power outages and lack of fuel to run electricity generating plants often marred adequate usage of the available conventional phototherapy.

Early discharge from our hospital was not a major factor in the present series. EBT was avoided in most normal weight babies delivered in our hospital. Most of the babies who had EBT in this group were LBW infants and none of them had kernicterus except the one whose parents refused EBT. Jaundice among inborn babies was detected early and parents were sensitized to risk of jaundice before discharge. Secondly, VLBW infants who were admitted before the appearance of NNJ were usually commenced on prophylactic phototherapy to prevent SBR rising to dangerously high SBR level that would warrant EBT as it is done in many parts of the world.^[1,12]

The trend in which all babies admitted into the newborn units with features of kernicterus were outborn had been previously reported^[4,19,20] and was attributed to the preference of expectant mothers to use un-orthodox delivery services for economic and religious reasons.^[21] This might be a major reason for clinicians practicing in such an area being rather "vigintiphobic".^[22] Even the recommendations by the American Academy of Pediatrics recognized local variations and therefore added a footnote that "The recommendations in this guideline do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate."^[23]

In conclusion, two major factors were responsible for the high EBT rate in the present series: late presentation and lack of facilities to deliver intensive phototherapy. Overhauling the existing health facilities such that with provision of intensive phototherapy in adequate quality and quantity will reduce avoidable risks associated with

EBT among the LBW infants. This form of therapy has been known to reduce the requirement for EBT.^[12] There is also the need to intensify health education of generality of the population on the risk of NNJ and especially pregnant women at the primary health care level and the need for early referral.

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