Neonatal Jaundice in Full-term Infants

Role of Breast-feeding and Other Causes

M. Jeffrey Maisels, MB, BCh, Kathleen Gifford, RNC

- Serum bilirubin determinations were performed on 264 term infants who were consecutively delivered via the vaginal route. Forty-one infants (15.5%) had serum bilirubin concentrations greater than 12 mg/dL. No cause for this was found, initially, in 23 (56%) of these infants. On the third hospital day, the mean (± SD) serum bilirubin level was 6.5±3.6 mg/dL in breast-fed infants and 6.5±3.2 mg/dL in bottle-fed infants. Of the 23 infants without obvious cause for hyperbilirubinemia, eight (four bottle-fed and four breast-fed infants) had serum bilirubin concentrations greater than 12 mg/dL on the third hospital day, whereas in 15 (14 breast-fed infants and one bottle-fed infant), the elevated serum bilirubin level occurred on day 4 or 5. Breast-feeding does not seem to affect the total serum bilirubin level in the first three days of life but may be associated with an increased incidence of hyperbilirubinemia subsequently. In a normal full-term population, routine investigations do not disclose a cause for hyperbilirubinemia in about half of the patients.

(Am J Dis Child 1983;137:561-562)

An association between breast-feeding and increased levels of serum bilirubin has been reported by some investigators but not by others. Nevertheless, many pediatricians believe that breast-fed infants have higher serum bilirubin levels during the first week of life than bottle-fed infants. We, therefore, conducted a prospective study of the relationship between neonatal jaundice and breast-feeding. In addition, we examined the causes of hyperbilirubinemia in a group of full-term infants.

PATIENTS AND METHODS

Serum bilirubin determinations were performed on 264 Caucasian term infants who were consecutively delivered via the vaginal route. The total serum bilirubin level was determined in every case on the third hospital day and was repeated if clinically indicated. Measurements were performed by a modified chloroform method using an automatic clinical analyzer (ACA III Instrument Manual, DuPont Co, Clinical Systems Division, Wilmington, Del). At serum bilirubin levels of 2.5, 4.2, and 19.4 mg/dL (Omega chemistry control sera, Hyland Diagnostics Corp, Bannockburn, Ill), 30 repeated determinations showed SDs of 0.1, 0.18, and 0.3 mg/dL with coefficients of variation of 4.6, 4.2%, and 1.5%, respectively. If clinical jaundice was noted in the first 24 hours, the serum bilirubin concentration increased by more than 5 mg/dL/day, or if it exceeded 12 mg/dL, the following additional investigations were carried out: ABO and Rh blood typing, direct Coomb's test, reticulocyte count, hematinocrit reading, WBC and differential cell counts, smear for RBC morphology, total and direct serum bilirubin concentrations, and a total serum protein level. With the exception of two infants (excluded from analysis), breast-fed infants were not supplemented with formula or water. The data were analyzed using the nonpaired, two-tailed t test and Fisher's exact test.

RESULTS

Forty-one infants (15.5%) had serum bilirubin concentrations greater than 12 mg/dL. A cause for this was found in 18 infants as follows: ABO incompatibility (n = 6), peripheral hematomas (n = 2), bruising (n = 2), and asphyxia (n = 2). Initially, no cause for the hyperbilirubinemia was found in 23 infants, although in three infants, the subsequent course suggested the diagnosis of "true" breast milk jaundice. (In those three otherwise normal infants, indirect hyperbilirubinemia (serum bilirubin level, >6 mg/dL), associated with breast-feeding, persisted for four to seven weeks and then spontaneously resolved. There was no evidence of hemolysis, and thyroid function was normal.) Two hundred twenty-three infants had a serum bilirubin level of 12 mg/dL or less. The 18 infants with a documented case for jaundice were excluded from the original cohort of 264, leaving 246 study infants (Table). In this group, the serum bilirubin concentration at a mean age (± SD) of 67.6±8 hours was 6.7±3.4 mg/dL, with a range of 0.5 to 14 mg/dL. Two breast-fed infants were supplemented, and, therefore, excluded from further analysis, leaving a final group of 115 who were totally breast-fed and 129 who were bottle-fed.

In the breast-fed infants, the mean (± SD) serum bilirubin level at 68±7.8 hours was 6.9±3.6 mg/dL. In the bottle-fed infants, the serum bilirubin level at 67±7.8 hours was 6.5±3.2 mg/dL (P > .1). Eight infants (four breast-fed and four bottle-fed infants) had total serum bilirubin concentrations greater than 12 mg/dL on the third hospital day. An additional 15 infants had total serum bilirubin levels greater than 12 mg/dL (range, 12.2 to 15.4 mg/dL; mean, 13.1 mg/dL) on day 4 or 5. Fourteen of these infants were breast-fed, and one was bottle-fed (P = .01, Fisher's exact test). The
Jaundiced breast-fed infants with serum bilirubin concentrations greater than 12 mg/dL had a cumulative weight loss of 6.3% ± 2.9% of their birth weight, while that of the non-jaundiced breast-fed infants was 5.7% ± 3.3% (*P* = .57).

**COMMENT**

Results of our studies confirm observations made by others that the serum bilirubin concentration on the third day of life in breast-fed infants is not significantly different from that of bottle-fed infants.

On the other hand, there were significantly more breast-fed than bottle-fed infants with hyperbilirubinemia on the fourth and fifth days of life. These latter data must be interpreted with caution because the majority of the infants were discharged on day 4 and did not have serum bilirubin determinations on the fourth and fifth days. The infants who remained in the hospital for more than four days did so because they appeared to be jaundiced or because an elevated serum bilirubin level on day 3 had failed to decrease. Nevertheless, a significantly greater proportion (14/15) of these infants was breast-fed. Similar observations have been made by McConnell et al. and by Gould and coworkers who found increased serum bilirubin levels in breast-fed infants on the fifth and sixth days of life when compared with bottle-fed infants.

We have previously reviewed the data from eight prospective studies of breast- and bottle-fed infants. Composite data from 680 infants at 3 to 4 days of age disclosed mean serum bilirubin concentrations of 6.2 ± 0.54 mg/dL in 278 breast-fed infants and 5.4 ± 0.96 mg/dL in 402 bottle-fed infants. On the fifth to sixth day of life, 493 breast-fed infants had mean serum bilirubin concentrations of 6.2 ± 2.3 mg/dL, and 455 bottle-fed infants had values of 5.3 ± 2.6 mg/dL. It is possible that large studies of infants 4 to 6 days old might produce unequivocal data supporting the contention that breast-fed infants of this age have higher mean serum bilirubin levels and/or a greater incidence of hyperbilirubinemia than their formula-fed peers. This remains to be proved, however, and even if it were so, the differences would be small and of questionable clinical significance.

It is not surprising that we could not find an obvious cause for hyperbilirubinemia in 20/41 (49%) of our infants. The plasma bilirubin concentration is a reflection of the cumulative bilirubin load and its clearance. Thus, an increase in load (which may include a significant enterohepatic circulation) or a decrease in clearance, or both, may produce jaundice. On the other hand, a modest increase in load might be accompanied by an increased clearance, leaving the serum bilirubin levels relatively unaffected. In the absence of overt laboratory indications of hemolysis, eg, abnormalities of RBC morphology, reticulocytes, and positive Coombs' test, more subtle increases in RBC turnover are not detectable by the usual laboratory methods. Furthermore, to our knowledge, no clinical method exists for the measurement of enterohepatic circulation of bilirubin. We are, thus, effectively prevented from more clearly defining the cause of hyperbilirubinemia in a significant proportion of infants. Measurements of serum carboxyhemoglobin levels, corrected for the ambient carbon monoxide concentration, may provide information about increased RBC turnover that is not otherwise apparent by the usual laboratory techniques. Our population contained no black infants, and screening for glucose 6-phosphate dehydrogenase deficiency was not carried out routinely. In the 23 infants without obvious cause for hyperbilirubinemia, reticulocyte counts and RBC morphology were normal. In our experience, investigations other than those listed (see “Methods” section) have not been useful in defining the cause of jaundice.

**Addendum**

Since this article was accepted for publication, we have had the opportunity to analyze serum bilirubin measurements on 2,241 consecutive infants admitted to our well-infant nursery. Of the infants with no identifiable cause for hyperbilirubinemia (serum bilirubin level, >12.8 mg/dL), 22.7% were breast-fed (*P* < .0001). Of 57 infants with no apparent cause for their hyperbilirubinemia on the third hospital day, 40 were breast-fed, eight were bottle-fed, and two were breast-and-bottle-fed (*P* < .0001). These data thus confirm that there is a significant association between breast-feeding and the incidence of physiologic jaundice in a normal newborn population as early as the third day of life. This study also confirmed that the routine investigations did not disclose a cause for hyperbilirubinemia in about half of these infants.

**References**

E2 or oxytocin. Lancet 1974; i:1338-1342.