

## **RIBOFLAVIN IN THE TREATMENT OF NEONATAL HYPERBILIRUBINEMIA\***

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Riboflavin was found to sensitize bilirubin against the effect of light and therefore phototherapy combined with riboflavin has been suggested in the treatment of hyperbilirubinemia<sup>1-4</sup>. We have attempted to evaluate the value of oral riboflavin in the treatment of neonatal hyperbilirubinemia in our patients.

### **Material and Methods**

This study consisted of 124 consecutive full-term newborns with indirect hyperbilirubinemia who did not present with hemolytic disease nor with other major medical problems but in whom phototherapy was required. Excluded from this study were newborns who required phototherapy for less than eight hours and who were subsequently exchange transfused. During phototherapy, the newborns were undressed and only their eyes were shielded. Except during nursing, there was a continual exposure to light. A bank of six natural white bulbs (Phillips<sup>R</sup>), 20 W each, were kept at a distance of 40 cm above the baby. From birth and extending throughout the study all subjects were on breast milk.

Within half an hour of initiation of phototherapy, riboflavin as a single oral dose of 3 mg/kg body weight in drinking water was administered to 50 of the 124 newborns with indirect hyperbilirubinemia who were chosen at random. The control group consisted of the remaining 74 newborns; they were not given riboflavin.

The serum bilirubin level was determined at the introduction of therapy and this value was deemed to be the 0-hour level. Serial determinations were made at 4-6 hourly intervals until the termination of therapy. At the conclusion of this study, the total duration of phototherapy and the flowing rate of the serum indirect bilirubin levels were calculated. Results were expressed as the mean  $\pm$  standard error of the mean and the Student's *t* test was used to compare the results.

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## Results

Table I summarizes the results of this study. The birth weight of the patients and their postnatal age at admission to phototherapy were similar in both groups ( $p>0.05$ ).

In this study it has been determined that the total duration of phototherapy and serum indirect bilirubin falling-velocity were similar in newborns with hyperbilirubinemia who required phototherapy irrespective of whether they received oral riboflavin ( $p>0.05$ ).

TABLE I: Data Regarding Newborn Infants Treated with Phototherapy Alone or Riboflavin Combined with Phototherapy

|                                                              | Riboflavin plus<br>phototherapy<br>(n: 50) | Phototherapy<br>alone<br>(n: 74) | Statistical<br>significance |
|--------------------------------------------------------------|--------------------------------------------|----------------------------------|-----------------------------|
| Birth weight (gm)                                            | 3201 $\pm$ 80*<br>(488)                    | 3250 $\pm$ 53<br>(457)           | NS**                        |
| Postnatal age at the<br>introduction of<br>therapy (day)     | 2.6 $\pm$ 0.1<br>(0.7)                     | 2.5 $\pm$ 0.1<br>(0.6)           | NS                          |
| Duration of<br>phototherapy (h)                              | 55.0 $\pm$ 4.4<br>(29.7)                   | 45.7 $\pm$ 3.2<br>(27.5)         | NS                          |
| Falling-velocity of<br>serum Indirect<br>bilirubin (mg/dl/h) | 0.09 $\pm$ 0.02<br>(0.11)                  | 0.07 $\pm$ 0.01<br>(0.19)        | NS                          |

\* Mean  $\pm$  standard error of the mean (standard deviation).

\*\* NS: Nonsignificant ( $p>0.05$ ).

## Discussion

Recent observations have shown that during phototherapy<sup>1,2,5</sup> photoisomerization is the basic factor in bilirubin metabolism. Although some authors suggest that riboflavin enhances the effect of phototherapy in babies with hyperbilirubinemia<sup>2-4</sup>, our findings do not support their suggestions. It has also been shown that there is transient riboflavin depletion both in healthy and jaundiced newborns who have been fed breast milk during the first week of life and riboflavin depletion is much more severe in babies with hyperbilirubinemia during phototherapy<sup>6,7</sup>. It has also been suggested that newborns fed human milk may be more sensitive than

formula-fed infants to phototherapy-induced riboflavin depletion, because infant milk formulas contain three times more riboflavin than human milk<sup>4</sup>. In this study all babies received human milk throughout phototherapy, and we therefore can exclude this possibility. We prefer to use a single oral dose of riboflavin because of the potential side effects of light-exposed riboflavin<sup>8</sup>. It is our opinion that further data with regard to the content of riboflavin in the milk of Turkish nursing mothers be obtained so that it may be determined whether or not riboflavin supplementation might be necessary in healthy breast-fed infants and also in those babies receiving phototherapy.

## Summary

This study, regarding the effect of riboflavin in the treatment of neonatal hyperbilirubinemia was carried out on 124 full-term healthy newborns with indirect hyperbilirubinemia who required phototherapy. No evidence of hemolytic disease and/or other associated disease were observed in these babies. Within half an hour of the initiation of phototherapy, 50 neonates received riboflavin in a single oral dose of 3 mg/kg body weight. At the end of the study, it was determined that the total duration of phototherapy and the serum indirect bilirubin falling-velocity were similar in both groups ( $p>0.05$ ).

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