

# Rebound hyperbilirubinaemia in neonates admitted to Mofid Children's Hospital, Tehran, Iran

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**Introduction and aim.** Approximately 60% of term neonates and 80% of preterm neonates develop hyperbilirubinaemia in the first week of life. Rebound hyperbilirubinaemia may occur after cessation of phototherapy, especially when the Coombs test is positive, in premature infants, and in those treated with phototherapy for less than 72 hours. The main aim of this study was to evaluate the bilirubin level 24 and 48 hours after cessation of phototherapy in neonates admitted to our hospital with jaundice. We also evaluated haemoglobin (Hb) levels and duration of phototherapy for a possible association with rebound hyperbilirubinaemia.

**Patients and methods.** The study was a clinical trial in term neonates (gestational age  $\geq 37$  weeks) with hyperbilirubinaemia who were admitted to the Department of Neonatology at Mofid Children's Hospital, Tehran, Iran. Exclusion criteria were neonatal infection, glucose-6-phosphate dehydrogenase deficiency, a history of neonatal exchange transfusion, and parental refusal. Phototherapy was delivered via a Philips TL 45/20W at 15 - 20 cm distance from the skin. We discharged patients after cessation of phototherapy. Total serum bilirubin (TSB) was checked in the neonates 24 and 48 hours after cessation of phototherapy. We included patients in whom follow-up tests were completed at 24 and 48 hours after discharge. Chi-square and Student's *t*-tests were used for data analysis using SPSS version 13.0 (SPSS Inc., Chicago, IL, USA).

**Results.** Twenty-five girls and 37 boys were included in the study. The mean admission age was 5.4 (standard deviation (SD)  $\pm 0.5$ ) days for girls and 8.0 (SD  $\pm 0.6$ ) days for boys ( $p=0.041$ ). The mean Hb values for the girls and the boys were 15.0 (SD  $\pm 0.39$ ) g/dl and 15.9 (SD  $\pm 0.36$ ) g/dl, respectively ( $p=0.108$ ). The mean TSB levels for the girls and the boys were 322.6 (SD  $\pm 9.4$ )  $\mu\text{mol/l}$  and 322.3 (SD  $\pm 7.3$ )  $\mu\text{mol/l}$ , respectively ( $p>0.05$ ). The mean admission and pre-discharge TSB levels of 322.3 (SD  $\pm 5.6$ )  $\mu\text{mol/l}$  and 187.9 (SD  $\pm 3.2$ )  $\mu\text{mol/l}$  were significantly different ( $p=0.0$ ). The mean TSB levels 24 and 48 hours later were 197.8 (SD  $\pm 4.6$ ) and 195.1 (SD  $\pm 5.3$ )  $\mu\text{mol/l}$ , respectively, with no significant difference between them ( $p>0.05$ ).

**Conclusion.** We found no significant differences between mean TSB levels at the time of termination of phototherapy and 24 and 48 hours later. We therefore do not recommend checking for rebound bilirubinaemia after phototherapy.

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Hyperbilirubinaemia is a common problem in daily practice for paediatricians and neonatologists. It affects about 60% of all newborns.<sup>[1]</sup> Rebound hyperbilirubinaemia may occur after cessation of phototherapy, especially if the Coombs test is positive, if the infant was born prematurely, and if the duration of phototherapy was less than 72 hours.<sup>[2]</sup> Although the American Academy of Pediatrics has recommended that infants need not be kept in hospital for measurement of bilirubin levels in case of rebound after discontinuation of phototherapy,<sup>[1]</sup> we decided to perform a study to evaluate the optimal timing of measurement of bilirubin to assess potential rebound. We also evaluated haemoglobin (Hb) levels and duration of phototherapy for possible associations with a rebound in the bilirubin level.

## Patients and methods

This prospective study was conducted at Mofid Children's Hospital, a tertiary paediatric referral hospital in Tehran, Iran. The hospital does not have an obstetric or postpartum ward, so all jaundiced newborns were referred from outside. All healthy term neonates (gestational age  $\geq 37$  weeks and birth weight  $> 2500$  g) with indirect hyperbilirubinaemia ( $\geq 256.5 - 290.7$   $\mu\text{mol/l}$ ) who were admitted to the neonatology department during the 6 months October 2007 - March 2008 were included in the study. Exclusion criteria were neonatal infection, haemolysis, direct hyperbilirubinaemia (serum conjugated bilirubin  $> 17.1$   $\mu\text{mol/l}$  if the total serum bilirubin (TSB) was  $< 85.5$   $\mu\text{mol/l}$ , or  $> 20\%$  of TSB if the TSB was  $> 85.5$   $\mu\text{mol/l}$ ), glucose-6-phosphate dehydrogenase

**Table 1. Comparison between patients with a duration of phototherapy of <48 hours and those with a duration of ≥48 hours**

Time of obtaining sample	Duration of phototherapy (hours)	N	TSB (µmol/l), mean (±SD)	p-value
Admission	<48	29	319.4 (±8.3)	0.628
	≥48	33	325.6 (±8.0)	
On discontinuation of therapy	<48	29	190.1 (±4.7)	0.427
	≥48	33	184.4 (±4.8)	
24 hours after discontinuation of therapy	<48	29	193.8 (±8.2)	0.570
	≥48	33	201.4 (±5.2)	
48 hours after discontinuation of therapy	<48	29	191.9 (±8.6)	0.258
	≥48	33	198.0 (±6.7)	

deficiency, a history of neonatal exchange transfusion, and parental refusal. Parents had to give signed consent before enrolment in the study. Phototherapy was delivered via a Philips TL 45/20W at a 15 - 20 cm distance from the skin. A TSB level of ≥205.2 - 222.3 µmol/l was considered the threshold for cessation of phototherapy, and all the infants were examined by a neonatologist. TSB was measured for each neonate at admission, on discontinuation of phototherapy, and 24 hours and 48 hours later. Student's *t*-test was used to compare the means, and the chi-square test was used to compare qualitative variables. SPSS version 13.0 (SPSS Inc., Chicago, IL, USA) was used for analysis.

## Results

Twenty-five female and 37 male term neonates with indirect hyperbilirubinaemia were included. The mean admission age was 5.44 (standard deviation (SD)) 0.52 days for the girls and 7.19 (SD ±0.59) days for the boys ( $p=0.041$ ). In 29 of the 62 cases (46.8%) the duration of phototherapy was less than 48 hours. There were no significant differences between girls and boys with regard to admission TSB (322.6 (SD ±9.4) µmol/l and 322.3 (SD ±7.3) µmol/l, respectively), Hb concentrations (15.0 (SD ±0.39) g/dl and 15.9 (SD ±0.36) g/dl, respectively), duration of phototherapy (46.7 (SD ±2.7) hours and 43.9 (SD ±2.4) hours, respectively), or TSB level before discontinuation of therapy (198.0 (SD ±4.6) µmol/l and 186.9 (SD ±4.6) µmol/l, respectively). TSB levels 24 hours after discontinuation of therapy were 186.0 (SD ±7.1) µmol/l and 205.7 (SD ±5.8) µmol/l in girls and boys, respectively ( $p=0.04$ ). There were no significant differences between patients with a duration of phototherapy <48 hours and ≥48 hours with regard to bilirubin level at admission, before discharge, and 24 hours and 48 hours after discharge ( $p>0.05$ ) (Table 1). The mean TSB levels 24 and 48 hours later were 197.8 (SD ±4.6) and 195.1 (SD ±5.3) µmol/l, respectively, with no significant difference between them ( $p>0.05$ ). Of the patients, 4 had duration of phototherapy of ≥72 hours. These 4 infants had a significantly lower bilirubin level 48 hours after termination of phototherapy ( $p=0.039$ ), but otherwise there were no significant differences between the patients with duration of phototherapy <72 hours and ≥72 hours. Only 1 of our patients was readmitted due to rebound hyperbilirubinaemia.

## Discussion

A review of published studies suggests that significant rebound hyperbilirubinaemia after discontinuation of phototherapy is rare,<sup>[3,4]</sup> although some authors have reported it in 5.1 - 13.2% of cases.<sup>[2,5,6]</sup> The variation in reported proportions of neonates who required further phototherapy may be due to different definitions of rebound bilirubin level. Kaplan *et al.*<sup>[2]</sup> concluded that 'post-phototherapy neonatal bilirubin rebound to clinically significant levels may occur, especially in cases of prematurity, direct Coombs test positivity, and those treated ≥72 hours'.<sup>[2]</sup> Maisels and Kring found that 14 of 303 term and near-term infants who received phototherapy were

readmitted with rebound hyperbilirubinaemia.<sup>[7]</sup> They concluded that it is unnecessary to keep infants in hospital to check rebound, but recommended follow-up measurement of the bilirubin level for infants who required phototherapy during hospitalisation and for those with haemolytic disease.<sup>[7]</sup>

Some of the differences between the studies may also be due to local differences (e.g. hospitals with and without midwifery wards), funding policies of medical insurance organisations, and socio-economic factors – many mothers and their babies are discharged less than 48 hours or even less than 24 hours after birth. In our study, all the neonates with hyperbilirubinaemia had been discharged. Only term neonates without a positive Coombs test were included, and only 1 patient was readmitted with rebound hyperbilirubinaemia (this was thought to be due to breastmilk jaundice). Our findings are therefore similar to those of Del Vecchio *et al.*,<sup>[8]</sup> who reported that 1 in 48 newborns required readmission for phototherapy.

A guideline from India (Symposium on AIIMS Protocols in Neonatology-II) recommends that discharge from hospital need not to be delayed to observe infants for rebounds.<sup>[9]</sup> However, the authors suggest that a repeat TSB measurement or clinical follow-up 24 hours after discharge is a useful option.<sup>[9]</sup>

Our findings concur with the American Academy of Pediatrics guideline, according to which infants without haemolytic disease do not require observation for rebound hyperbilirubinaemia and may be discharged from the hospital after discontinuation of phototherapy.<sup>[11]</sup> Yetman *et al.* also concluded that follow-up of infants discharged after termination of phototherapy solely for rebound hyperbilirubinaemia is unnecessary.<sup>[10]</sup>

## Conclusion

We did not find significant differences between TSB at the time of termination of phototherapy and 24 hours and 48 hours after cessation of phototherapy. We therefore do not recommend checking the TSB level for rebound hyperbilirubinaemia.

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**Conflict of interest.** Nothing to declare.

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