

Bilinorm administration combined with Phototherapy in the management of neonatal jaundice: a hospital based clinical trial

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Summary:

Background: Neonatal jaundice (NJ) is a common problem worldwide and frequent in Iraq . Several reports were published on prevalence, distribution, causes and treatment of NJ. This clinical trial was carried out to demonstrate the effect of combinations of Castrol oil, riboflavin and magnesium in mechanical elimination of bilirubin after enhancing hepatic excretion by phototherapy.

Patients & methods: This clinical trial included a total of 61 significantly jaundiced neonates who were admitted to the special care baby unit of Children Welfare Teaching Hospital, medical city complex, Baghdad, Iraq, during the period June 1st to Dec.31st 2007. Phototherapy was applied alone in 30 neonates (group 1) and phototherapy with Bilinorm in 31 neonates (group 2), (Bilinorm oral gel constituted of riboflavin sodium phosphate, magnesium oxide and castor oil). Student's t test was used to examine the differences in variables between the two groups.

Results: There were no significant differences between the two groups in body weight, age of onset of jaundice, age on admission, and TSB on admission ($p = 0.9, 0.4, 0.4, 0.4$, respectively). A significant difference in total decrease in TSB was noticed between group II (7.2 ± 2.4) and group I (5.9 ± 1.8) ($p = 0.02$). Days of hospitalization were significantly lower in group II (2.4 ± 0.8 days) than in group I (3.3 ± 1.5 days) ($p = 0.009$), and hours of phototherapy were significantly lower in group II (47.4 ± 19.7 hours) than in group I (66.8 ± 27.4 hours) ($p = 0.002$).

Conclusions: There was a statistically significant difference regarding total decrease in TSB, days of hospitalization and hours of phototherapy when both Bilinorm and phototherapy were used than when phototherapy was used alone. So mechanical elimination of bilirubin from intestinal lumen may enhance the effect of phototherapy.

Keywords: Bilinorm, Phototherapy, neonatal, jaundice.

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Introduction:

Neonatal jaundice (NJ) is a common problem worldwide 1 and frequent in Iraq 2. Several reports were published on prevalence, distribution, causes and treatment of NJ 3-5. The principle effect of the phototherapy treatment is not photodegradation of bilirubin, but conversion of the pigment to structural isomers that are more polar and more readily excreted than the normal, more toxic "dark" form of the pigment. This, coupled with some photooxidation of bilirubin, diminishes the overall pool of bilirubin in the body and lowers plasma levels. In the future, phototherapy may be supplanted by pharmacologic treatment. 6 It appears that during phototherapy in the newborn infant there is a decrease of the blood level of riboflavin reaching up to hypovitaminotic values and a transient biliverdin level elevation. Oral riboflavin administration may maintain this level within physiological range and at the same time shorten the necessary duration of phototherapy. The short-term phototherapy not only results in decreased Glutathione reductase activity in red blood cell, but also results in hemolysis of the newborn. This side-effect can be prevented by oral administration of Vitamin B2. 7, 8

There is possible neuroprotective role or compensatory mechanism in ionized magnesium increase against emerging toxicity risk of increasing serum bilirubin level. 9 Castor oil is well known to enhance elimination of intestinal contents including bilirubin. This work was carried out to demonstrate the effect of combinations of Castrol oil, riboflavin and magnesium in mechanical elimination of bilirubin after enhancing hepatic excretion by phototherapy.

Patients and methods:

A total of 61 significantly jaundiced neonates admitted to the neonatal care unit (NCU) of Children Welfare Teaching Hospital, medical city complex, Baghdad, Iraq, were included in the study. This clinical trial was conducted for the period June 1st to Dec.31st 2007. The Children Welfare Teaching Hospital is tertiary referral hospital with 250 beds including 25 incubators in NCU and 50 beds for pediatric surgical ward. The NCU receiving out born neonates from different hospitals in Baghdad & other governorates plus private clinics & hospitals, including neonates with significant neonatal jaundice that requiring phototherapy and exchange transfusion. The inclusion criteria included neonates with significant jaundice, with good general health, term or preterm of > 32 weeks gestation, and of < 10 days old. The exclusion criteria included preterm neonates of < 32 weeks, significant direct bilirubin

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level, current neonatal sepsis, dehydration, tracheoesophageal fistula, intestinal obstruction, and congenital biliary atresia. Neonates who had serum bilirubin levels close to exchange transfusion were also excluded from the study. The need for phototherapy was determined using the American Academy of Pediatrics Clinical Practice guidelines for management of hyperbilirubinaemia in newborn 5. Phototherapy was applied alone in 30 neonates (group 1) and phototherapy with Bilinorm in 31 neonates (group 2). Badeli HR et al 10 method of application of phototherapy was used. Bilinorm oral gel constituted of riboflavin sodium phosphate 13.7 micrograms BP, magnesium oxide 274 micrograms USP and castor oil 2 grams BP. Each 5 mls of Bilinorm gel contained 5 grams of the combinations. It was given in a dose of 5 mls /kg/day in 3 divided doses for 3-5 days. The parents` consent, the agreements of manager and ethical committee of the hospital were taken to use the gel. The requested data were age on admission, total serum bilirubin (TSB), type of feeding, direct bilirubin, reticulocyte count, G₆PD deficiency, coomb`s test and blood glucose, hospitalization days, decrease in TSB, TSB on admission and on discharge, body weight and age of onset of jaundice. Student`s t test was used to examine the differences in variables (TSB on admission and at end of treatment, total decrease in TSB, days of hospitalization, hours of phototherapy, age of onset, body weight and age on admission) between the two groups (neonates treated with phototherapy alone and those treated with phototherapy and Bilinorm). P value less than 0.05 was considered as significant.

Results:

There were no significant differences between the groups 1 and 2 in body weight, age of onset of jaundice, age on admission, and TSB on admission (p =0.9,0.4, 0.4, 0.4, respectively). There were no statistical significant variation in TSB at the end of treatment between groups I (10.7 ± 1.5) and group II (9.9 ± 1.6) (p = 0.05).Table 1 A significant total decrease in TSB was noticed between group II (7.2 ± 2.4) than group I (5.9 ± 1.8)(p = 0.02). Days of hospitalization were significantly lower in group II (2.4 ± 0.8 days) than that in group I (3.3 ± 1.5 days) (p = 0.009), and hours of phototherapy were significantly lower in group II (47.4 ± 19.7 hours) than that in group I (66.8 ± 27.4 hours) (p = 0.002). Table1

Table 1: Distribution of studied variables in group 1 and 2

Characteristics	Phototherapy alone 1	Phototherapy with Bilinorm 2	P value
Body weight	2.9 ± 0.6	2.9 ± 0.6	0.9
Age of onset of NJ	2.6 ± 1.3	2.8 ± 0.9	0.4
Age on admission	5.6 ± 2.1	5.2 ± 1.4	0.4
TSB on admission	16.8 ± 2.1	17.1 ± 1.5	0.4
TSB on end of treatment	10.7 ± 1.5	9.9 ± 1.6	0.05
Total decrease in TSB	5.9 ± 1.8	7.2 ± 2.4	0.02
Days of hospitalization	3.3 ± 1.5	2.4 ± 0.8	0.009
Hours of phototherapy	66.8 ± 27.4	47.4 ± 19.7	0.002

*P < 0.05 was considered significant

Discussion:

Neonatal hyperbilirubinaemia is usually due to combination of increased bilirubin load and decreased bilirubin excretion of unconjugated bilirubin. In this form, bilirubin subjected to enterohepatic circulation, and the true efficacy of phototherapy will be blunted. 5 The finding of significant decrease in TSB in group II (treated with phototherapy and bilinorm) than the decrease in group I (treated with phototherapy alone) support the hypothesis that sequestration of luminal unconjugated bilirubin would enhance the efficacy of phototherapy in jaundiced infant. Bilinorm constitutes of magnesium oxide and Castrol oil in addition to vitamin B2, and hence, it enhances the mechanical elimination of bilirubin. This finding is consistent with that of other workers 4. They used agar ingestion to enhance luminal elimination of bilirubin. Other workers 5 reported that ingestion of agar does not supplement the effect of phototherapy. Severe unconjugated hyperbilirubinaemia, seen mainly in neonates, may cause kernicterus and death. Conventional treatment for severe unconjugated hyperbilirubinaemia consists of phototherapy and exchange transfusion. The later is associated with significant morbidity and mortality 2, so there is a need to develop alternative pharmacological treatment strategies for unconjugated hyperbilirubinaemia 11. Generally these strategies aim to decrease the plasma concentration of unconjugated bilirubin by inhibiting production, stimulating hepatic clearance or interrupting the entrohepatic circulation of pigment. Several pharmacological therapies such as metalloporphyrins 12, 13, clofibrate 10, bile salts, laxatives and bilirubin oxidase may meet the criteria in future. There was a statistically significant difference regarding total decrease in TSB, days of hospitalization and hours of phototherapy when both Bilinorm and phototherapy were used than when phototherapy was used alone. So mechanical elimination of bilirubin from intestinal lumen may enhance the effect of phototherapy.

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