

Comparison of the Effect of Cotoneaster Manna Drop (Bilineaster) and Massage on Bilirubin in Neonates under Phototherapy

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J Babol Univ Med Sci; 19(11); Nov 2017; PP: 21-7

Received: Mar 11th 2017, Revised: May 29th 2017, Accepted: Sep 21st 2017.

ABSTRACT

BACKGROUND AND OBJECTIVE: Neonatal jaundice is one of the most common problems in neonatal period. Considering that the most effective and most commonly used neonatal jaundice treatment is phototherapy, the use of complementary therapies such as massage and herbal medicines is common in our society to reduce jaundice. Therefore, the present study was conducted to compare the effect of cotoneaster manna drop (bilineaster) and massage on bilirubin in neonates under phototherapy.

METHODS: This clinical trial was conducted on 68 neonates admitted to the pediatric ward of Vali-Asr Hospital in Birjand in 2015. The neonates were randomly divided into three groups. The control group (n=21) received the routine care. The massage group (n=23) received massage by field technique, three times a day for 15 minutes in addition to phototherapy. The cotoneaster manna drop (bilineaster) group (n=24) received three oral drops of bilineaster for every eight kilograms of body weight in addition to phototherapy. Then, the rate of reduction in neonatal bilirubin was compared in the three groups (IRCT: 2016101830370N1).

FINDINGS: The mean reduction rate of bilirubin per hour in the first 24 hours was 0.27 ± 0.19 in the control group, 0.23 ± 0.17 in the massage group and 0.25 ± 0.18 in the bilineaster drop group. In addition, the mean reduction rate in the second 24 hours was 0.4 ± 0.26 in the control group, 0.22 ± 0.18 in the massage group and 0.26 ± 0.22 in the bilineaster drop group. In the third 24 hours, the mean reduction rate was 0.19 ± 0.17 in the control group, 0.9 ± 0.13 in the massage group and 0.7 ± 0.1 in the bilineaster drop group, which had no significant difference ($p > 0.05$).

CONCLUSION: The results of this study showed that field massage and administration of cotoneaster manna drop (bilineaster) during neonates' hospitalization had no effect on the reduction of bilirubin in neonates under phototherapy and these interventions cannot be effective.

KEY WORDS: Neonatal Jaundice, Cotoneaster manna drop (bilineaster), Field Massage.

Please cite this article as follows:

Rahani T, Boskabadi H, Sadeghi T, Boskabadi MH, Gharaei R, Pasban F. Comparison of the Effect of Cotoneaster Manna Drop (Bilineaster) and Massage on Bilirubin in Neonates under Phototherapy. J Babol Univ Med Sci. 2017;19(11):21-7.

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Introduction

Neonatal jaundice is one of the most common problems in neonatal period, and nearly 60% of term neonates and 80% of premature neonates suffer from this issue. Various factors such as the blood group and Rh⁺ mother play a role (1, 2). This high prevalence imposes huge costs on society (3).

The importance of neonatal jaundice is not due to its prevalence, but because of the dangerous side effects of bilirubin deposition in the brain (4), which, if left untreated, can lead to serious complications such as kernicterus, that is often followed by life-long disability (1, 4, 5). Nowadays, the most effective and most common method for treating jaundice is phototherapy. In cases of lack of response or if the level of bilirubin exceeds the risk level, exchange transfusion is used as the last way to reduce bilirubin. Phototherapy, however, has many side effects, including skin complications, eye injury, subtle excretion of liquids, fractures in the DNA chain, loose stool, damage to the reproductive system, bronze baby syndrome, thrombocytopenia and patent ductus arteriosus (6).

In addition, phototherapy is costly and, since the neonate is hospitalized and his eyes are covered, the relationship between the mother and the neonate is disturbed. Factors that can speed up the response to phototherapy can greatly help the neonate and his parents and reduce the cost of treatment (7, 8). Therefore, neonatal practitioners have always been looking for new and less costly treatments that would reduce phototherapy period or replace it (4, 9). During 1970 – 1980, new methods were introduced as a substitute for common and traditional healthcare, which they called alternative medicine or complementary medicine (9).

Proposed therapies along with phototherapy include complementary therapies such as use of clofibrate, herbal medicine, enema and massage (10–15). In Iran, plants such as *Fumaria officinalis*, *Jujube*, *Chicory*, *Alhagi camelorum* and *Cotoneaster* are used in the treatment of hyperbilirubinemia (16 and 18). *Cotoneaster* is a white, slightly yellowish, and sweet substance known as purgative manna. This substance is in the *Cotoneaster* SPP species and is a member of the *Rosaceae* family, and its most important compositions are carbohydrates, including mannitol, fructose, glucose and sucrose, which causes osmotic diarrhea, and may reduce the level of bilirubin (17). *Bilineaster* Oral Drop is one of the industrial products

made from *Cotoneaster* that is available at pharmacies. According to the studies of Azadbakht and Khoshdel, the effect of *Cotoneaster* on jaundice has been evaluated (17,18). Studies by Mansoori et al. and Shahfarahat et al. did not evaluate the effect of *Cotoneaster* to be positive (19,20).

Due to the fact that this medicinal plant is traditionally used in the treatment of neonatal jaundice in Iran, there is a need for more scientific studies in this field. Another supplement therapy is to reduce the jaundice in the neonatal massage. Today, in India, Pakistan and some African countries, as well as in the American Indians, massage for neonates and children is part of their everyday life, and neonates are given massage at birth (25).

Many studies have been conducted on the effects of massage, including the study of Field et al. about the effect of massage on reducing the pain of teething, constipation and colic (21). Several studies have evaluated the effect of massage on neonatal jaundice (22–25). Chen et al. and Lin'an et al. showed that jaundice index was lower in the neonates of the massage group (11, 23). However, there was no difference in the two groups, according to the study of Seyyedresouli et al. (24).

Since the reduction of neonatal jaundice complications by improving the quality and quantity of neonates' healthcare is necessary, this study was conducted to compare the effect of *cotoneaster* manna drop (*bilineaster*) and massage on bilirubin in neonates under phototherapy.

Methods

This clinical trial study was approved by the Ethics Committee of the Mashhad University of Medical Sciences (code of ethics: IR.MUMS.REC.1394.510; clinical trial entry number: 2016101830370N1), and was conducted among 'term' and 'near – term' neonates (35 – 42 weeks of gestation) and above 2 kg who were admitted in the pediatric ward of Vali-e-Asr Hospital in Birjand in 2015 due to hyperbilirubinemia. In order to increase the age range of neonates under study, near – term infants also entered this study. To determine the sample size based on preliminary studies (17, 25), the common variance rate was calculated to be 2.31. Considering the type I error of 0.05, and the test power of 0.87 at the significance level of 0.95, the sample size was estimated to be 20 neonates in each group. To predict the drop in the research units, the

sample size increased to 25 neonates per group. Of total 75 studied neonates (50 infants in intervention groups and 25 neonates in the control group), five neonates were excluded from the study due to fast discharge with their parent's consent, one was excluded due to prolonged treatment-resistant jaundice, and one neonate was excluded because the parents were not willing to cooperate.

Finally, 68 neonates were studied; 21 neonates in the control group, 23 neonates in the massage group and 24 neonates in the cotoneaster manna drop (bilineaster) group. Neonates with gestational age of 35 – 42 weeks, birth weight over 2000 gr, high total serum bilirubin (12 – 24 mg/dl) (17, 25), absence of apparent anomalies in physical examination, hematocrit less than 65%, or hemoglobin less than 20, no abnormalities of ABO or RH, no disruption of the G6PD enzyme and no positive coombs test result, were included in the study. In case of need for ventilation or exchange transfusion, infections, asphyxia and parents' unwillingness to cooperate, neonates were excluded from the study. Data were collected by a personal information questionnaire (including neonate, mother and father's information), a daily information checklist (including information such as birth weight (gr), body temperature (°C), frequency of defecation, and total serum bilirubin level (mg/dl) that was completed daily for neonates of all three groups), and a checklist for recording the interventions (specially for the massage group and the bilineaster group, specifying the type of intervention and hours of intervention).

After obtaining permission from the Ethics Committee of the Mashhad University of Medical Sciences for mothers who were willing to participate in the project, it was necessary to make a face-to-face description of the purpose of the study, how to use the bilineaster drop and how to massage the neonates. In addition, mothers were convinced of the complication-free nature of these methods. The Demographic Information Questionnaires and Written Consent were completed at the same time. Neonates entered the study by a convenient sampling method and were randomly assigned to one of the three groups.

At the time of admission to hospital, necessary and routine tests including total bilirubin, direct bilirubin, total blood count, G6PD and coombs test were measured. In the bilineaster drop group, the neonates received three drops of bilineaster every 8 hours for each kilogram of body weight by the researcher, in addition to phototherapy. In the massage group, in

addition to phototherapy, the neonates received massage based on Field method (11), three times daily (morning, noon and evening) after breastfeeding and each time for 15 minutes on the neonate's bed, using sunflower oil and gentle mild fingernail after washing and warming the hands. This technique was performed in 3 phases of 5 minutes and a total of 15 minutes. In phases 1 and 3, the neonate was placed on the abdomen and the massage is from the top of the head to the neck and vice versa, from the neck to the shoulders and vice versa, from the back to the waist and vice versa, from shoulder to shoulder and vice versa in both hand, from hip to ankle and vice versa in both feet. In each of the above areas, 12 5 – second moves were performed.

In phase 2, the neonate was placed in a supine position, and the flexion and extension movements were done in 5 1 – minute stages, including the right arm, left arm, right foot, left foot and both feet together. Each stage included 6 10 – second moves. In control group, neonates only received phototherapy and routine measures.

Then, based on neonatal jaundice severity and physician's opinion, total bilirubin and direct bilirubin were measured during the admission period. Phototherapy and routine care measures were performed under the same conditions for all neonates in each of the three groups. The phototherapy equipment in the section was used for neonates in the intervention and control group.

Considering that the bilirubin measurements were different in the neonates in the three groups (depending on the severity of jaundice, the age of the neonate and the level of bilirubin at the time of admission), therefore, to determine the bilirubin drop rate, the level of bilirubin measured at each turn was subtracted from the previous bilirubin and the result was divided by the interval between them, thus serum bilirubin drop rate was calculated for each group.

Variables such as maternal age, type of delivery and neonatal characteristics such as sex, birth rank, fetal age, calendar age, birth weight and bilirubin level at admission were homogenized by random sampling of the research units using statistical tests. To analyze the data, the data were normalized using Kolmogorov-Smirnov test in the three groups. Finally, the data were analyzed by SPSS software Ver. 16 using chi-square, ANOVA, Mann Whitney, Independent t-test and Kruskal-Wallis H test, while $p < 0.05$ was considered significant.

Results

The results showed that the calendar age, sex, birth rank, birth weight, weight at admission and gestational age of neonates were not significantly different in the three groups. The mean neonatal bilirubin at admission was 18.87 ± 2.78 mg/dl in the control group, 16.99 ± 2.91 mg/dl in the massage group and 17.95 ± 2.38 mg/dl in the cotoneaster manna drop (bilineaster) group, which showed no statistically significant difference between the three groups. The mean rate of bilirubin reduction per hour was not significantly different between the

three groups, in the first, second and third 24 hours, and the groups were homogeneous in this regard (table 1). The mean frequency of defecation in the first, second and third 24 hours was not statistically significant (table 2). There was no significant difference in the mean number of days at the hospital in the three groups ($p=0.656$). This mean was 2.14 ± 0.65 days in the control group and 2.09 ± 0.66 days in the massage group and 1.96 ± 0.75 days in the bilirubin drop group.

Table 1. Comparison of the mean reduction rate of total serum bilirubin per hour (mg/dl/hr) in the three groups

Variable	Group	Bilineaster drop Mean±SD	Massage Mean±SD	Control Mean±SD	P-value
First 24 hours		0.18 ± 0.25 (n=24)	0.17 ± 0.23 (n=23)	0.19 ± 0.27 (n=21)	0.97
Second 24 hours		0.22 ± 0.26 (n=19)	0.18 ± 0.22 (n=19)	0.26 ± 0.40 (n=18)	0.74
Third 24 hours		0.7 ± 0.10 (n=8)	0.13 ± 0.9 (n=9)	0.17 ± 0.19 (n=8)	0.41

Table 2. Comparison of the mean frequency of defecation in infants in the three groups

Frequency of defecation	Bilineaster drop Mean±SD	Massage Mean±SD	Control Mean±SD	P-value
First 24 hours	4.1 ± 2.1 (N=24)	4.7 ± 2.4 (N=23)	3.3 ± 1.7 (N=21)	0.115
Second 24 hours	3.8 ± 2 (N=21)	3.7 ± 2.8 (N=19)	2.8 ± 1.7 (N=21)	0.260
Third 24 hours	3.5 ± 0.5 (N=6)	2.6 ± 0.8 (N=6)	2.8 ± 1.5 (N=7)	0.412

Discussion

Based on the results of this study, bilineaster drop and massage did not accelerate the rate of bilirubin reduction and shorten the duration of hospitalization, and these interventions did not affect the reduction of neonatal bilirubin levels under phototherapy. The results of this study showed that there was no significant difference between the massage and control groups regarding the rate of serum bilirubin reduction per hour. In a study conducted by Seyyedresouli et al., the findings showed that there was no significant difference in bilirubin levels and the frequency of defecation from the first day to the fourth day in the two groups (24). Moreover, Karbandi et al. showed that performing Field massage for 5 days in premature infants who were admitted to NICU could not significantly decrease the level of bilirubin (26), which

is consistent with the results of the present study. The Field massage technique was also used in these studies. The results of a study by Chen et al. indicated that infant massage with Field technique from day 1 to day 5 could significantly decrease the level of bilirubin (days 2 - 5) and total serum bilirubin on day 4 (11). The results of a study by Lin'an et al. showed that jaundice index was significantly lower in massage group during the second to fifth day of massage, and the hours of light therapy in the neonates of the massage group were less than the control group (23), which is not consistent with the results of the present study. The insignificant decrease in the rate of bilirubin per hour between the two groups in this study can be due to the low duration of massage intervention, because the study of Chen et al., and Lin'an et al.

showed a faster decrease in the bilirubin level in the intervention group compared to the control group after 5 days of massage (11,23). Furthermore, it seems that another reason for the lack of significant correlation between massage and the rate of bilirubin reduction in this study is the lack of massage in the early hours of jaundice or early admission of the infant, because the study of Chen et al. showed that fewer infants in the massage group who were massaged from birth (compared to the control group) needed phototherapy. In this study, the neonates were massaged after becoming yellow and immediately after admission to the hospital; most neonates were hospitalized at the night shift while receiving the first massage a few hours after admission and in the morning. In this study, massage was carried out in three sessions, in the morning, at noon and in the evening (with an interval of about four hours).

There are large amounts of bilirubin in meconium, which increase with gentle massage of skin blood flow and lymphatic drainage (27). Perhaps this increase in the skin blood flow and soft tissue below it may be effective in disposing of various types of bilirubin spatial changes. According to the WHO, 80% of the world's population uses medicinal herbs (28). In Iranian traditional medicine, cotoneaster is used to treat neonatal jaundice. The name of this plant is mentioned in Avicenna's Book of Law, Razi's Al-Hawi, and Aghili Khorasani's Makhzan-al' advieh (18). The results of this study showed that there was no significant difference between the bilineaster drop group and control group in terms of the rate of serum bilirubin reduction, and contrary to the indigenous beliefs, the use of cotoneaster had no effect on the reduction of jaundice in neonates. The result of this study was consistent with studies of Shahfarahat et al.,

which showed that administration of 6 grams of cotoneaster in a single dose had no effect on the reduction of neonatal jaundice (20), and Mansoori et al., who reported that five drops of bilineaster, three times a day for three days had no preventive effect in neonatal jaundice on day 3 to 5 after birth (19). On the other hand, according to the study of Khoshdel et al., the decrease in bilirubin levels in bilineaster drop groups was higher compared to the control group receiving placebo and light therapy (17). The result of this study is not consistent with the present research. Azadbakht et al., demonstrated that decline in bilirubin level due to the use of bilineaster drops in neonates treated with phototherapy was very rapid in the first 3 days compared to the control group, and there was a significant difference between the two groups (18). The result of this study is not consistent with the present study.

The results of this study indicate that the Field massage and administration of cotoneaster manna drop (bilineaster) during neonate's hospitalization have no effect on the reduction of bilirubin levels in neonates under phototherapy. The short duration of intervention due to the early discharge of some infants (before 48 hours) and small sample size of study were among the limitations of this study. However, due to numerous studies in this field and the ineffectiveness of these interventions, further research on this topic in the future is not recommended.

Acknowledgments

Hereby, we express our deepest sense of gratitude and indebtedness to Deputy of Research and Technology of Mashhad University of Medical Sciences for their financial support.

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