

## The effect of maternal pre-cesarean oral carbohydrate supplementation on neonatal jaundice: A randomized, double-blind clinical trial

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### ABSTRACT

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**Background:** Lack of breastfeeding initiation in the first hours after birth is an influencing factor in the incidence of jaundice. Given the effectiveness of oral carbohydrate before the cesarean section on maternal breastfeeding in the first days of birth, this study was conducted to investigate the effectiveness of oral carbohydrate on the incidence of neonatal jaundice.

**Methods:** In this randomized, double-blind clinical trial study, a total of 91 women scheduled for elective cesarean surgery were randomly divided into intervention (oral carbohydrate before surgery, N=45) and placebo (flavored water before surgery, N=46) groups. The intervention group received 400 + 800 ml of a carbohydrate-rich solution 20 to 24 hours before surgery, while the placebo group received the same amount of flavored water. Until the end of the first week of birth, subjects were followed-up for neonatal jaundice incidence through the information contained in the medical records.

**Results:** In the intervention group, 6 infants developed jaundice. In contrast, in the placebo group, 25 infants developed jaundice. The number of infants with jaundice was significantly lower in the group receiving oral carbohydrate than in the group receiving placebo (n = 25 (54.3%) VS. n = 6 (13.3%), p< 0.001).

**Conclusion:** Carbohydrate could be used as a preventive dietary supplement against neonatal jaundice, which occurs due to the lack of breastfeeding. However, further clinical trials are needed to confirm our results and to investigate the role of other influencing factors on jaundice such as G6PD deficiency status.

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#### Introduction

Neonatal jaundice is one of the prevalent health problems in infancy, which during the first week of the birth is observed in 60% of term infants and 80% of preterm infants [1]. The increased bilirubin levels in these patients could

affect the brain and eventually cause encephalopathy and kernicterus. This disease can be fatal and can cause mental retardation and neurological disorders [2-4]. Due to the dangerous complications of jaundice, early diagnosis and treatment of this disease is crucial. Currently, the most effective and most common treatment for neonatal jaundice is phototherapy, and in refractory cases and those with both kernicterus and high bilirubin level, blood replacement in conjunction with phototherapy is the main therapeutic measure [5]. However, prevention, rather than early detection and treatment, might be the best approach to the management of neonatal jaundice, but no well-known effective measure for the prevention of this disorder is available. Lack of adequate breastfeeding in the first hours and days of birth is one of the risk factors of jaundice in newborns [6]. Inadequate intake of milk in the first few days of birth leads to the exacerbation of enterohepatic cycle, jaundice, and infant weight loss. In these circumstances, the kidneys of infants act as a defense mechanism, resulting in hypernatremia through urinary sodium reabsorption and fluid retention [7]. Moreover, insensible excretion of fluids from the body and lungs due to the lack of sufficient skin maturity could exacerbate dehydration in infants [8, 9]. Reduced breast milk intake and subsequently reduction in calorie intake not only reduces gastrointestinal motility but also leads to intensifying of the enterohepatic cycle [10]. Both of these factors delay the maturity of the bilirubin-conjugating enzyme in the liver and are in association with increased jaundice incidence related to the inadequate breastfeeding of infants in the first two weeks of life [11, 12]. Given the importance and high prevalence of jaundice in newborns, one of the strategies for prevention of this disease is a faster onset of breastfeeding, especially in the first hours of birth.

Breastfeeding in the first hours and days after cesarean section is negatively affected by several factors, including pain, nausea, vomiting, stress, anxiety, hunger, thirst, and insulin resistance (insulin resistance reduces milk production via inhibition of intracellular signaling of lactiferous cells) [8, 13]. It has been shown that oral carbohydrate intake decreases pain, nausea, vomiting, stress, anxiety, hunger, thirst and insulin resistance [14-20]. These findings led us to the hypothesize that oral carbohydrate might improve breastfeeding in women undergoing cesarean surgery through the

reduction of negative influencing factors on breastfeeding, and thus might prevent from neonatal jaundice, which is caused due to the insufficient breastfeeding. Accordingly, this study was conducted to assess the effectiveness of pre-cesarean oral carbohydrate on neonatal jaundice incidence.

### Materials and methods

This randomized clinical trial was conducted in Shabihkhani Hospital, Kashan, Iran. The study protocol was approved by the Ethics Committee of Tehran University of Medical Sciences (IR.TUMS.REC.1395.2636), and registered under the code number of IRCT2016072629082N1 at the Iranian Center of Clinical Trials (<http://www.IRCT.ir>). Informed consent was obtained from all participants. From May 2016 until the end of August 2016, 150 individuals were assessed for eligibility, of whom, 120 individuals agreed to participate in the study. The CONSORT diagram of the study is given in Figure 1.

Inclusion criteria were pregnant women scheduled for elective cesarean section with regional anesthesia (spinal), age 20-35 years, gestational age  $\geq 38$  weeks, and body mass index 25-37 kg/m<sup>2</sup>. Exclusion criteria were those with a history of gastrointestinal disorders; diabetes mellitus; gastrointestinal surgery (stomach and intestine); liver, kidney and cardiovascular disorders; complications related to the current pregnancy (preeclampsia, high-risk pregnancy, gestational diabetes mellitus); use of general anesthesia; intraoperative blood loss more than 1000 ml; bowel and bladder injury during surgery; use of dextrose during surgery; failure to follow the instructions for the use of oral carbohydrate or placebo; any problem in the baby keeping the mother from breastfeeding; surgery longer than 45 minutes; RH incompatibility and subject's unwillingness to continue participation in the study.

The subjects were randomized into two study groups: oral carbohydrate (OCH) and flavored water. Randomization of the subjects was done by applying a table of random numbers. The patients, investigator, nurses, surgeon, and anesthesiologist were all blinded to the OCH and placebo. Weight, height, and BMI of the subjects were measured at the time of admission. Also, daily intake of energy, carbohydrate, protein, and fat was assessed using a 24-hour recall questionnaire at the time of admission. OCH and placebo had the same taste and were provided in

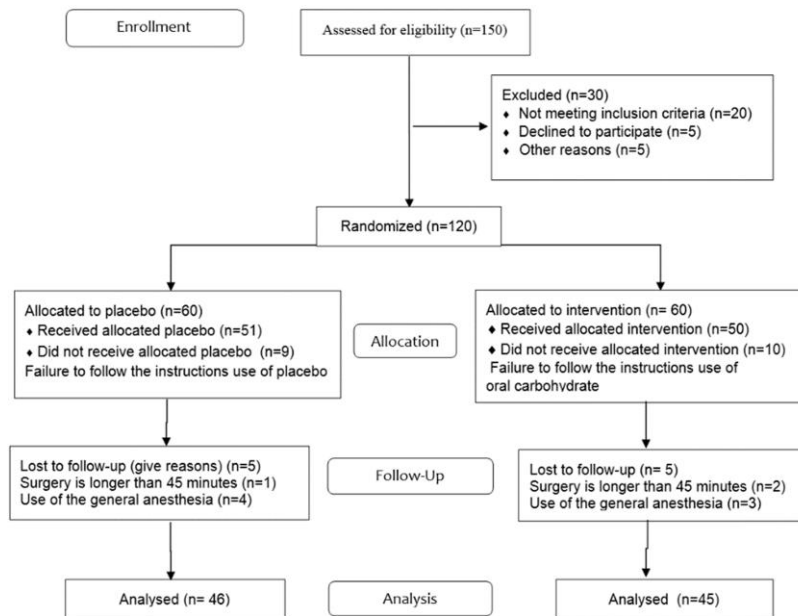


Fig. 1. CONSORT diagram for the trial

identical packaging. OCH group ingested 800 ml of a carbohydrate-rich drink (12.5% carbohydrates, 50 kcal/100 ml, 290 mOsm/kg, pH 5.0, Nutricia Preop; Numico, Zoetermeer, the Netherlands) 20 to 24 hours before surgery. The control group consumed the same amount of flavored water (0 kcal/100 ml, pH 5.0). There was no food or drink restriction before midnight. After midnight, the subjects were allowed no oral intake except another 400 ml of the same drink 2 hours before the initiation of anesthesia in OCH and control groups. The subjects were similar in terms of the method of anesthesia, drugs used for anesthesia, surgical procedure, and surgeon. The blood group of mother and

neonate and bilirubin of neonate were evaluated. Until the end of the first week of birth, subjects were followed-up for neonatal jaundice incidence through the information contained in the medical records.

*Statistical analysis*

Statistical analysis was performed with SPSS version 16 software. The normal distribution of the quantitative variables was assessed using Kolmogorov-Smirnov test. Quantitative variables are reported as mean and standard deviation (SD) and were compared between the two groups using independent sample t-test. Qualitative variables are reported as percentage

Table 1. Demographics and basic information

Parameter	OCH (n=45)	Placebo (n=46)	P-value
Age (year)	30.20(3.37)	29.46(3.52)	0.307
Weight (kg)	81.71(8.98)	83.33(8.06)	0.370
Height (cm)	165.04(5.75)	167.46(8.62)	0.120
BMI(kg/m <sup>2</sup> )	30.09(3.20)	29.79(2.45)	0.620
Gestational age (weeks)	38.32(0.42)	38.62(0.71)	0.69
previous cesarean (n)	2.27(0.86)	1.91(0.59)	0.26
Infant weight (g)	3306.67(371.973)	3397.83(333.659)	0.221
Gravidity(n)			
0	9(20%)	10(21.7%)	
1	32(71.1%)	32(69.6%)	0.972
2	4(8.9%)	4(8.7%)	
Baby's gender			
Girl	25(55.6%)	25(54.3%)	
Boy	20(44.4%)	21(45.7%)	0.908

Data are presented as mean±standard deviation or number

**Table 2.** Daily nutrient intakes

Parameter	OCH (n=45)	Placebo (n=46)	P-value
Energy(kcal)	2217.46(463.48)	2120.82(458.00)	0.320
Carbohydrate(g)	347.74(107.58)	416.83(401.51)	0.265
Protein(g)	91.10(25.89)	80.31(23.15)	0.39
Fat(g)	60.77(21.54)	57.33(15.51)	0.386

Data are presented as mean±SD

and were compared between the groups using the chi-square test.

### Results

At the baseline, a total of 120 women participated in this study, of them, 29 subjects were excluded, and 91 women were finally included in the study (Figure 1). Daily intake of energy, carbohydrate, protein, fat, and participants' characteristics including age, height, weight, body mass index, gestational age, gravidity, history of cesarean, and sex and birth weight of infants are summarized in Table 1 and 2. No statistically significant difference was found in these variables between the two groups.

The comparative rates of neonatal jaundice incidence in the intervention and placebo groups are reported in Table 3. In the intervention group, in which mothers received oral carbohydrate before the cesarean section, 6 infants developed jaundice. All these cases were infants with blood group of A or B from mothers with blood group of O. In contrast, in the placebo group, 25 infants developed jaundice, of them, 5 cases were infants with blood group of A or B from mothers with blood group of O (n= 25 (54.3%) vs. n= 6 (13.3%), p< 0.001).

### Discussion

Since breastfeeding in the first hours and days of birth reduces the risk of jaundice, in this study, the effect of oral carbohydrate intake on the breastfeeding of mothers and incidence of neonatal jaundice was examined. To the best of our knowledge, until now, no study has investigated the prevention of neonatal jaundice associated with insufficient breastfeeding worldwide. This study revealed that pre-cesarean oral carbohydrate intake could prevent the development of jaundice, which is caused by insufficient breastfeeding in the first few days of birth. Salas et al. [21] showed that 60% of infants with premature jaundice have an insufficient breastfeeding, and more than 10% weight loss was observed in these infants. In the present study, 54.3% of infants in the control group were affected by jaundice. The study by Salas et al. [21] was a case-control study in

design, while the present study was a clinical trial, containing information that could not be found in other studies. The results of our study showed that in women receiving oral carbohydrate due to better well-being and reduced insulin resistance in the early hours after surgery in the OCH group and enhanced serotonin synthesis, early recovery and reduced nausea, vomiting, and pain, the first time of breastfeeding after cesarean section was initiated earlier than the placebo group. Furthermore, the number of breastfeeding episodes and the duration of breast-feedings in these women were remarkably higher than those in the women receiving placebo. Breastfeeding was assessed by a questionnaire completed by the researcher. It was found that in the group receiving oral carbohydrate, 6 infants were affected by jaundice, and the ABO group incompatibility between mother and fetus was detected in all these patients. Although, it is likely that factors other than ABO group incompatibility such as G-6PD enzyme deficiency might also be involved in this process. But, except for these 6 infants, other newborns in the intervention group did not develop this disorder. On the other hand, 25 infants in the placebo group were affected by jaundice, which the ABO incompatibility was observed in 5 cases. Our assessment showed that the infants in this group had not an adequate breastfeeding. Therefore, it can be suggested that oral carbohydrate intake increases breastfeeding, which subsequently enhances bilirubin excretion in the feces. This indicates that maternal pre-cesarean oral carbohydrate supplementation might have a beneficial impact on neonatal jaundice. Nevertheless, additional clinical trials are needed to confirm our findings and to investigate the role of other influencing factors on jaundice.

In conclusion, this study demonstrated that oral carbohydrate supplementation before the cesarean section is associated with reduction in neonatal jaundice incidence through improvement of breastfeeding and bilirubin clearance.

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### Disclosure Statement

The authors declared no conflicts of interests.

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