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Efficacy of Maternal Chicory Aroma Water Consumption for Neonatal Jaundice: A Randomized Single-Blind Clinical Trial

Mohsen Manouchehrian¹, Mehrdad Shakiba², Mamak Shariat³, Mohammad Kamalinejad⁴, Mehdi Pasalar⁵, Ali Akbar Jafarian⁶, Mohammad Hassan Lotfi⁷, Naeimeh Keighobady⁸

¹Department of Traditional Medicine, Faculty of Persian medicine, Shahid Sadoughi University of Medical Sciences, Ardakan, Yazd, Iran

²Pediatric Department, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

³Maternal, Fetal & Neonatal Research Center, Tehran University of Medical Sciences, Tehran, Iran

⁴School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

⁵Research Center for Traditional Medicine and History of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

⁶Department of Anesthesiology, Iran University of Medical Sciences, Tehran, Iran

⁷Department of Biostatistics & Epidemiology, Health Faculty, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

⁸Department of Biostatistics and Epidemiology, Faculty of Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Abstract

Background: Although neonatal jaundice occurs in 60% of term infants, very little evidence is available on how to prevent it. Given the ethno-medical use of chicory aroma water (CAW) for the management of jaundice by Iranian pregnant women, the aim of this study was to evaluate whether the frequent CAW consumption was associated with fewer jaundice symptoms after 40 days. **Materials and Methods:** A single blind randomized controlled trial was designed to enroll participants from Lolagar Hospital, Tehran, Iran. Pregnant women (n=80) were randomly divided into two groups. The trial group was provided with common diet and an instruction to consume CAW. The control group was maintained on common diet. The proportion of phototherapy and mean value of bilirubin were measured and compared between the two groups. (IRCT registry number: IRCT2017041633475N1) **Results:** There was no statistically significant difference in the mean value of bilirubin between the women with frequent CAW consumption compared with the control. Also, the intake of CAW was not associated with a marked improvement in the need for phototherapy ($P > 0.05$). **Conclusion:** The findings of this study highlighted that the intake of CAW by pregnant women failed to ameliorate neonatal jaundice. [GMJ.2017;6(4):312-8] DOI: 10.22086/gmj.v6i4.973

Keywords: Chicory; Phototherapy; Neonatal Jaundice; Pregnancy; Persian Medicine

Introduction

Jaundice is one of the most common medical complications among infants. It has been reported that jaundice affects approxi-

mately 60% of term infants as well as 80% of immature and preterm neonates [1, 2]. The incidence of severe hyperbilirubinemia was reported ranging from 12 to 15% in various geographical parts of Iran. Since the neona-

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Tel/Fax: +98 71 36474503
PO Box 7193616563
Email: info@gmj.ir



✉ **Correspondence to:**

Mehdi Pasalar, Research Center for Traditional Medicine and History of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
Telephone Number: +987132338476
Email Address : pasalar@sums.ac.ir

tal liver might not be well-developed to clear bilirubin from the blood quickly enough, the excessive formation of bilirubin would occur; this, in turn, leads to hyperbilirubinemia [3]. In some cases, this might be associated with serious health issues. For instance, an elevated level of unconjugated bilirubin in the blood causes irreversible impairments to the brain cells (kernicterus). It can inflict various permanent adverse effects on the central nervous system and on hearing ability, particularly in pre-mature neonates [4]. The proportion of the hospitalization and readmissions caused by jaundice is considerable, reaching to 75% of all infants [3, 5]. The newborns should be monitored continuously to detect those who are at risk of developing serious elevated unconjugated bilirubinemia [6]. Consequently, medical scholars have called for new preventive measures capable of normalizing the bilirubin level [7]. There are different methods to treat hyperbilirubinemia, including transfusion, phototherapy and pharmacological agents. Each of these may bring about some adverse consequences. Despite promising outcomes of phototherapy and blood exchange for hyperbilirubinemia, there have been some reports concerning corona infliction, impaired reproductive organs, dehydration, diarrhea, bronze baby syndrome and risky adverse effects like thrombocytopenia or apnea [8-10]. Finding new modalities—to decrease the duration of treatment—is of major concern. In this regard, herbal medicine has recently emerged as a new management strategy to decrease the level of bilirubin [11]. Various traditional branches of Complementary and Alternative Medicine (CAM) have recently focused on herbal remedies alongside their preventive principals, despite the fact that some topics such as women's life style, nutrition and using some special medicines during pregnancy have been discussed for purposes of demonstrating them as effective factors on infants' health [8, 12-14]. Chicory (*Chicorium intybus*), a fairly woody permanent herbaceous plant of the family Asteraceae, is one of the most widespread plants in Iranian diet in the form of decoction, aroma water and so on. It is a rich source of inulin, fructan family, a good water soluble agent which is rarely hy-

drolyzed by gastrointestinal human enzymes resulting in different health benefits including digestive and cardiovascular problems [15-17]. Persian medicine (PM) sages believe that chicory is cold and dry in temperament with its diuretic, appetizer and cholagogue features. They note that extra warmness of the liver causes its dysfunction leading to weakened activities [14, 18]. Considering the cold temperament of chicory, some selected folk medicinal benefits are reported including decrease in bile concentration, protective action against jaundice, and amelioration of liver activity [19, 20]. There exists a number of anecdotal evidence in support of chicory aroma water (CAW) supplementation during pregnancy, specifically in the course of the last trimester of pregnancy when the warmness of the pregnant woman's body temperament increases to the highest point [14, 18, 19]. Nevertheless, it needs to be approved through comprehensive clinical trials. Accordingly, this study was intended to examine the effects of frequent consumption of CAW in pregnant women on the course of neonatal jaundice.

Materials and Methods

This single blind, randomized controlled trial was performed in Lolagar Hospital, Tehran, Iran from April to June 2015. The protocol of the present study was approved by the Ethics Committee on Human Research affiliated to Shahid Sadoughi University of Medical Sciences, Yazd, Iran. Furthermore, all the participants filled out informed consent forms. The clinical trial was registered in the Iranian Registry of Clinical Trials (IRCT) database (IRCT2017041633475N1). As this was a pilot study, a number of 40 people for each group were assigned by a statistician. Consequently, a total of 80 healthy nulipar pregnant women whose ages were between 18 and 35 years were recruited. The following factors were considered to exclude participants: diseases such as diabetes, hypertension or hypothyroidism; having neonatal birth-weight less than 2.5 kg and more than 4 kg; a neonate with Apgar score of less than 8; neonatal congenital disorders (including hypothyroidism, glucose-6-phosphate-dehydrogenase deficiency,

phenylketonuria); infants with jaundice within the first day of birth; and neonatal infections within the first week of birth. Thereafter, the eligible participants were randomly assigned to two groups based on routine random number tables regarding their clinic chart numbers by a research assistant; the control group received a common diet and the trial group was provided with common diet and an instruction to consume CAW (200 mL twice a day; morning and evening) for 40 days prior to delivery. Both groups were in the last trimester of pregnancy. The study started at the 34th week of pregnancy and continued until delivery. The CAW with a density of 25 kg aerial parts/100 L water was provided by the Zahra Company (Kerman, Iran). The CAW was packed in 2 liters dark plastic jar with a label showing the university logo, manufacturer's company name and expiration date. All quality control tests were performed before the trial onset by the company. Since there was no evidence regarding the side effects of chicory use on maternal or fetal participants, Shahid Sadoughi University of medical sciences ethics committee issued necessary legal health permissions. CAW packages were distributed to the pregnant women weekly by a research assistant who was available in the clinic every working day. A diary was handed over to the pregnant mothers to register any probable daily side effects related to CAW consumption and also a phone number of a physician for emergen-

cy situations. Following delivery, they were asked to bring their neonates to the hospital for the measurement of bilirubin, using bilitest within the first day of life; in case of visible icterus, the mothers were advised to bring babies immediately during the first week after birth. Throughout each visit, the study nurses, who were independent of the nurse staff, collected the pertained data concerning parturition, the health of the neonate, and the serum bilirubin concentrations. As for data analysis, SPSS 18 was used to perform paired comparisons; the difference between the bilirubin Mean of two groups was evaluated by t-test and the chi-square test used for independence to conclude whether there is a significant relationship between hyperbilirubinemia and demographic variables. The power of study was set at 80% and P values less than 0.05 were considered as significant.

Results

A flow chart for the study is shown in Figure-1. Upon recruitment, 80 pregnant women (in their third trimester) out of 97 were substantiated to be between 18 and 35 years. Of all participants, half served as the control group while the other half comprised the study group. Four subjects failed to complete the study, due to their child's sickness. From those in the trial group, six cases were further dropped out since they could not stick to the

Table 1: Variables of the Participating Mothers and Their Children at Recruitment

	Control group N=36	Trial group N=34	P-value
Mean mother's age, year (SD)	23.3 (3.6)	24.9 (4.0)	0.09
Mean mother's BMI, kg/m² (SD)	22.2 (3.9)	23.85 (3.0)	0.054
Mean mother's weight gain, kg (SD)	16.9 (6.6)	14.8 (7.3)	0.22
Type of delivery (%)			
Vaginal			0.12
Caesarian section	17(47.2)	10(29.4)	
	19(52)	24(70.6)	
Mean neonate's birth weight, kg (SD)	3334.7(348.0)	3397.0(390.4)	0.48
Neonates' gender (%)			
Female			0.62
	18(50)	15(44.1)	
Male	18(50)	19(55.9)	

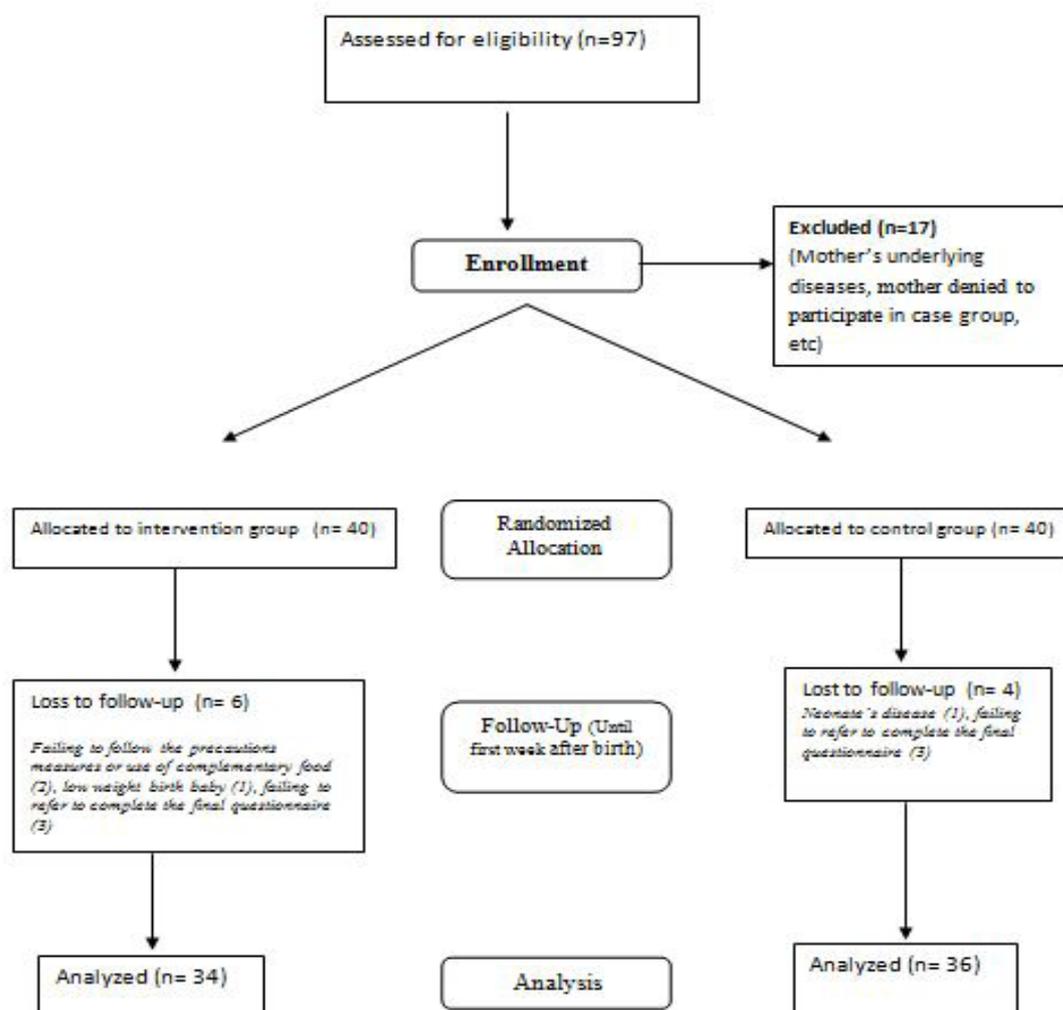


Figure 1: The Consort Flowchart

diet or did not like to follow. As seen in Table 1, the mothers and their neonates were similar in terms of some baseline characteristics. All the babies in the intervention group were breastfed except for five of them who took formula and breast milk simultaneously. The latter figure was 3 babies in the control group (P -value >0.05). The number of babies needed phototherapy in trial and control groups were 11(32.4%) and 11(30.6%), respectively. It was indicated that there was no significant difference between the two groups regarding the need for phototherapy (P -value = 0.87). Likewise, neonates in the control and trial groups showed mean values of 9.81 ± 4.51 and 9.52 ± 4.65 , respectively (P -value = 0.79).

Discussion

The study showed that maternal daily consumption of CAW with special diet for 40 days would not affect the bilirubin level of neonates. It did not decrease the need for babies' phototherapy in comparison to the control group who merely followed a particular regimen. Medicinal plants are prevalently used for treatment of neonatal jaundice in PM and other traditional systems. Most of them are applied for neonates. However, according to PM textbooks, the mothers' diet has a key role to prevent upcoming jaundice [12, 18]. Despite many studies on the treatment of jaundice through herbal medicine, to the best of our

knowledge, no effort has been made to investigate the role of a phytochemical entity in prevention of neonatal jaundice [21]. There are a few reports describing the inability of some traditional herbal and/or CAM remedies for improvement of neonatal jaundice. Boskabadi and colleagues—in a descriptive study performed in north-east of Iran—demonstrated that some traditional therapies like flix-weed seeds or camel's thorn during the first week of the birth have no effect on bilirubin reduction in infants [22]. This finding is in accordance with ours, although we should bear in mind that the methodologies are completely different from each other. The differences in methodologies between our study and that of Boskabadi *et al* made the mentioned resemblance undoubtedly unstable. In a randomized controlled trial in southwest Iran, 70 term infants admitted due to hyperbilirubinemia were assessed to investigate the effect of phototherapy plus *Hordeum vulgare L.* seed flour. The results showed that a herbaceous plant could cause decline in indirect bilirubin of hospitalized neonates [23]. The effect of *H. vulgare* is attributed to its antioxidant content while chicory lacks this substance. *Chicorium intybus* (English: Chicory; Persian: *Kāsni*) is a member of the Asteraceae family. Its major constituents are: inulin, fructooligosaccharide, coffee acid derivatives, flavonoids, and polyphenols [24]. This affirmative effect compared to the current study could be allied to the main ingredients, the route of prescription and the target population neonates instead of mothers. Similar findings showed that total serum bilirubin declined and a reduced number of babies' hospitalization was reported by Zahedpasha *et al.* through the application of clofibrate. They showed the safety and efficacy of this drug in a randomized controlled trial in the northern part of Iran [25]. Our findings are in line with this study in terms of safety profile. Of course, this makes the use of such pilot herbal studies more reasonable. The hypolipidemic effect of soluble fibers like inulin has been demonstrated in previous *in vitro*, *in vivo* and human trials. This effect is related to increased fecal lipids, cholesterol and bile acids [15]. The ability of main chicory ingredient; inulin, to improve lipid, cho-

lesterol and bile acid levels in the mothers' liver may play a significant role to prevent neonatal jaundice in their babies. This finding is of more concern when we consider the relationship and material exchange between maternal and fetal blood through intrauterine membranes – the decreasing effect of bilirubin level in babies' blood might be attributable to maternal substance catabolism and excretion of waste materials [26]. In accordance with PM masterpieces, pregnant women are advised to avoid consuming pepper owing to its warm temperament [20] which, in turn, increases the whole body warmth, especially the liver temperament [19]. From this perspective, there is a close connection between the fetus as well as the mother's temperament; intake of food with warm quality by mother makes the uterus' and the resulting blood's temperament warm. Such warming of both the uterus and its throughput blood has adverse effects on the fetus. Therefore, the fetus' liver may be inflicted with the mother's temperament presenting all main signs of liver dysfunction in the first days of birth. The dysfunction of the neonate's liver within these fate-determining days is associated with interference in the process of bilirubin conjugation; this condition is regarded as a significant contributor to jaundice because of lack of bilirubin clearance. The ethno-medical use of herbal preparations such as CAW for the management of jaundice is prevalent among Iranian pregnant women [12]. Moreover, there exists a body of literature in PM texts, indicating that the use of chicory is beneficial for the cure of liver disorders including jaundice, improvement of its function and removal of its weakness (*Za'fe*) [19, 27]. Use of medicinal herbs as preventive or protective agents, is an established issue in current literature originating from traditional systems like PM [28]. One of the limitations of the current study is that the main components of chicory were not analyzed first. Moreover, the mechanism of action for this material was not assessed thoroughly; we reviewed the mechanism based on PM textbooks and suggested a hypothesis supported by current literature. The prescription of PM scholars in suggesting chicory plant is the decoction of aerial parts

and not its aroma water. However, one could guess the component since the taste of the decoction of chicory plant is bitter it is for this reason that pregnant women show very little interest in drinking it. On the other hand, it could act as a preliminary pilot study for future investigations in the field of pediatrics, focusing on maternal diet as a cost-effective way of prevention.

Conclusion

The findings of the present study indicated no considerable differences between the two groups following frequent consumption of CAW. Thus, it was concluded that CAW failed to appear influential on the prevention of

jaundice, implying that aerial parts-extracted CAW is a highly dilute compound with partial therapeutic effects. Therefore, other types of chicory-derived products such as juice as well as decoction might show a marked enhancement for the preventive management of neonatal jaundice. Regarding the decrease of the warmth and the strengthening of the liver function, other options such as oxymel (*Sekán-jebin*) and barley juice (*māo-sháir*) – a kind of non-alcoholic beer with special traditional recipe—have been prescribed in PM masterpieces, which could be studied in the future studies.

Conflict of Interests

Authors have no conflict of interests.

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