

## Original Article

# A Comparison of the Effect of Probiotic *Lactobacillus Reuteri* and Syrup-Caraway Mixture in the Treatment of Infantile Colic: A Randomized Clinical Trial Study

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## Abstract

**Background and Aim:** Infantile colic is a relatively common behavioral syndrome in infancy. The main mechanism of colic is still unknown and no effective treatment is indicated for it. Recently, a relation between colic-infected children and the microbial balance changes in their intestines has been reported. Accordingly, we decided to compare the effect of probiotics with the syrup-caraway mixture on colic.

**Materials and Methods:** In this clinical trial study, 86 infants with colic were included. Data were collected by a checklist including the duration of crying, severity of crying, crying frequency and complications of treatment which were completed during the course of the treatment through the follow-up of the infants. Infants were randomly divided into two equal-size groups based on random block design. The first group received probiotic *Lactobacillus reuteri* (17938 DSM), and the second group received syrup-caraway mixture. The collected data were analyzed by statistical methods in SPSS version 24.

**Results:** The mean age of the patients was 30.58±14.18 days. Two groups were similar according to age, sex, birth weight, parental education level, history of atopy in the family, history of colic in previous children and crying at presentation. There was no difference between the groups based on the crying frequency, severity of crying and duration of crying on the 7<sup>th</sup> and 15<sup>th</sup> days. Moreover, there was no difference in terms of drug side effects between two groups in the seventh and fifteenth days of treatment.

**Conclusion:** Both probiotics and syrup-caraway mixture are effective in the treatment of colic in infancy.

**Keywords:** Colic, Probiotic, Caraway Mixture, Crying

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## Introduction

Infantile colic is a fairly common behavioral syndrome in infancy whose prevalence ranges from 10% -40% in different communities (1). Its prevalence was estimated in a study by Talachian *et*

*al.* to be about 20% in Iran in 2008 (2). Colic usually begins around the second to the third weeks of birth, reaches its peak amount during the first two months, subsides at three months, and disappears in three to four months (3). Infantile colic syndrome was firstly defined by Wessel in 1954 as continuous

crying and restlessness with facial flare for at least three hours a day and repeated at least 3 days per week which usually starts at three weeks and continues up to three months (4). Infants suffering from colic cry and whine at certain times during the day, mostly in the afternoon, in the evening and at night (5).

Infantile colic usually occurs in the first months of birth and leads to unsuccessful lactation. Due to the mother's dietary pattern (allergens consumption) and inappropriate breastfeeding pattern (over-lactation and lactose intolerance), the infant has insufficient lactase to digest milk and develops heartburn (6). However, the underlying mechanism of colic is still unknown and no effective treatment has been identified for it, though there are different hypotheses, including the behavioral hypothesis and the organic hypothesis for the cause of colic in infants whose microbial balance changes in their intestines (7). The behavioral hypothesis involves inadequate interaction between mother and infant, and maternal anxiety and stress, whereas the organic hypothesis involves improper digestive function and allergic reactions (8).

Although many investigations have been carried out on infantile colic, no definitive cure has been found for it to date. Nevertheless, various treatments for colic have been suggested. Determining the appropriate and effective strategy for infantile colic improves the quality of life of families. The most commonly used drug treatment today is the consumption of dicyclomine, but it has side effects such as respiratory problems, muscle hypotension, apnea, seizures, asphyxia and death (9). Research has also indicated that treatments such as hypoallergenic or hydrolyzed formulas and drugs such as antirefluxes, dimethicones, anticholinergics, as well as baby hugs, play insignificant roles in controlling infantile colic (10). Lack of safe and efficient pharmacological interventions has highlighted alternative and complementary therapies in the management of infantile colic among which probiotics and herbal supplements are pivotal in the treatment of infantile colic (11-12). Hence, this study aimed to compare the effect of probiotic *Lactobacilli reuteri* and syrup-caraway mixture in the treatment of infantile colic.

## Materials and Methods

### Ethical approve and IRCT registration

This study was approved by Ardabil University of Medical Sciences Ethics Committee, and was registered with the code IR.ARUMS.REC.1397.214. Following informing the parents of the infants thoroughly of the details, the informed consent form was signed by the parents and then the infants entered the study. Moreover, this study was registered at the Iran Clinical Trial Center with the code IRCT20190530043761N1.

As a single blind randomized clinical trial study, the present research was carried out on 86 infants with colic. All infants were randomly divided into two groups, and the first group received probiotic *Lactobacilli reuteri* (13) daily, five drops in dose ( $1 \times 10^8$  per drop), for 7 days. The second group received syrup-caraway mixture, 10 ml daily for 7 days. The researcher was not blind to the grouping of the patients.

### Inclusion and exclusion criteria

Based on Wessel criteria, infants with colic (crying more than 3 hours per day for more than 3 days per week over 3 weeks), with birth weight between 2500 and 4000 gr, breast fed, between the ages of 15 to 60 days, without known underlying and gastrointestinal diseases were included into the study. Illness (infants suffering from pneumonia and gastroenteritis) a history of hospitalization, the use of other medications during the study, being withheld from prescribed medications were the criteria that excluded certain infants from the study.

### Measurement Outcomes

During the treatment, the frequency, duration, severity of infant crying and treatment related complications were recorded on the 15th day after the treatment by telephone contact with parents. All information were recorded in the checklist.

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**Statistical Analysis**

Data analysis was carried out using SPSS version 24 via descriptive statistical methods such as Mean±SD. Moreover, frequency, percentage and analytical statistical methods such as T-test were used to compare the quantitative data between the two groups. Finally, the chi-square test was used to compare two qualitative data. The significance level was considered less than 0.05 in all statistical tests.

**Results and Discussion**

In this research, 86 out of 100 infants completed the study and 14 infants were excluded. The average age of all the infants was 30.3±14.4 days. Of all the

infants, 51 (59.3%) were male and 35 (40.7%) female. No significant distinction was observed between the two groups in terms of gender, age, birth weight and weight in the referral time (Table 1). The average gestational age of the infants was 38.34 ± 1.08 weeks. 64 (74.4%) of all deliveries were cesarean section and the rest were normal. Nineteen (22.1%) mothers had illnesses during pregnancy. The majority of them (15) suffered from hypothyroidism (78.9%) (Table 2). There was no significant difference between the two groups regarding mothers' education. With regard to the history of colic in previous children, infants who were the first child of the family were excluded from the study. Twenty-five infants from the probiotic group and 24 infants from the syrup-

**Table 1:** Demographic data of infants in two groups.

Variables	Probiotic group (n=44)	mixing cavari syrup (n=42)	p-value
Age (days)	32±14.3	28.54±14.4	0.83
Weight in birth time (gr)	3233.5±461.1	3226.8±525.8	0.7
Weight in admission time (gr)	4096.6±879.8	4126.8±886.6	0.74
Sex (n,%)	Boys	27(61.4)	0.8
	Girls	17(37.6)	

**Table 2:** Demographic data of infant’s mothers in two groups.

Variables	Probiotic group (n=44)	mixing cavari syrup (n=42)	p-value	
Gestational age (weeks)	41±1.3	40.5±1.4	0.83	
Delivery type	CS	33 (75)	0.87	
	Normal	11 (25)		11 (26.2)
Underlying diseases	HTN	1(2.3)	3(7.1)	0.26
	Hypothyroidism	10(22.7)	5(11.9)	
	none	33(75)	34(81)	

caraway mixture group were excluded. Of the remaining 37 infants, 18 families (48.6%) had a history of colic in their previous infants but there was no significant difference between the two groups. At baseline, the two groups had no remarkable distinction in the frequency, severity and duration of crying (Table 3).

It was found on the 7th day follow-up that no significant difference could be observed between the

two groups in terms of infant crying variables such as the frequency, severity and duration of crying (Table 4).

On the 15th day of the treatment, the two groups did not differ significantly in the duration, intensity and frequency of crying per day (Table 5).

On the 7th day of the treatment, 7 cases (15.9%) of the probiotic group compared to 12 cases (28.6%) in the syrup-caraway mixture group confronted drug side

**Table 3:** Compare two groups in terms of crying variables.

Variables	Probiotic group (n=44)	mixing cavari syrup (n=42)	p-value
Number of crying (Mean±SD)	6.54±2.91	5.9±2.8	0.3
Severity of crying (Mean±SD)	6±2.02	5.61±1.82	0.36
Duration of crying (Mean±SD)	123.3±69.03	130.6±56.9	0.59

**Table 4:** Compare two groups in terms of crying variables in 7 th day.

Variables		Probiotic group (n=44)		mixing cavari syrup (n=42)		p-value
		n	%	n	%	
Number of crying	Decreased	30	68.2	24	57.1	0.54
	Increased	7	15.9	8	19	
	Without change	7	15.9	10	23.8	
Severity of crying	Decreased	31	70.5	25	59.5	0.55
	Increased	6	13.6	7	16.6	
	Without change	7	15.9	10	23.8	
Duration of crying	Decreased	31	70.5	25	59.5	0.44
	Increased	7	15.9	7	16.6	
	Without change	6	13.6	10	23.8	

**Table 5:** Compare two groups in terms of crying variables in 15 th day.

Variables		Probiotic group (n=44)		mixing cavari syrup (n=42)		p-value
		n	%	n	%	
Number of crying	Decreased	34	77.3	31	73.8	0.92
	Increased	2	4.5	2	4.8	
	Without change	8	18.2	9	21.4	
Severity of crying	Decreased	35	79.5	31	73.8	0.8
	Increased	2	4.5	2	4.8	
	Without change	7	15.9	9	21.4	
Duration of crying	Decreased	34	77.3	32	76.2	0.9
	Increased	2	4.5	2	4.8	
	Without change	8	18.2	8	19	

effects but there was no significant difference between them. Furthermore, there was no significant difference between the two groups in terms of drug side effects on the 15<sup>th</sup> day.

In this study, there was no significant difference between the Probiotic Lactobacillus Reuteri and caraway mixture groups in terms of the severity, duration and frequency of crying in infants with infantile colic on the 7<sup>th</sup> and 15<sup>th</sup> days after the treatment. In the probiotic group, the frequency of crying was decreased 68% and the intensity and duration of crying decreased 70% on the 7<sup>th</sup> days after the treatment compared to the baseline for which these values were about 57% with regard to the crying frequency and 59% for the intensity and duration of crying in the caraway-mixture group. Considering the non-significant distinction between the two groups on the 7<sup>th</sup> and 15<sup>th</sup> days, it could be stated that the effect of caraway-mixture syrup was similar to the probiotic. Moreover, in this study the, treatment groups were similar in terms of side effects on the 7<sup>th</sup> and 15<sup>th</sup> day after the treatment. In a study conducted by Attarha *et al.* (14), it has been shown that in the treatment of infantile colic,

the effect of fennel is similar to the effect of grape water syrup (as a conventional treatment) which was in line with the results of our study. Alexandrovich *et al.* (15) also indicated that fennel could significantly reduce and abolished infantile colic symptoms and no specific side effects were reported in their study. The results of this research also confirm our findings because they were the same both in terms of fennel efficacy and side effects. Savino *et al.* (16) showed that the extract of fennel could significantly reduce the average crying rate of infants with colic which is similar to the present study. Furthermore, the fennel extract has no specific side effects.

Alves *et al.* (17) found that peppermint extract was influential in reducing the frequency and duration of crying in infants. This study is in line with the results of our research. Alves *et al.* did not examine the severity of infant crying but the peppermint extract was influenced by two other variables; i.e. the frequency and duration of crying in our study. The results reported by Rafiei *et al.* are similar to our findings (18). In this study, the probiotic group and the treatment group had no significant difference in the number of infant crying. There were no

differences between the two groups in terms of sleep duration, frequency of bowel movement, infant appetite and referral to a pediatrician. These studies have shown that treatment with mint and fennel herbs is effective in the treatment of neonatal colic which are consistent with the findings of our research. The major difference between our research and the studies mentioned above is that these studies used placebo as the control group. We compared the caraway-mixture with probiotics in our research. Moreover, some studies do not consider probiotics to be effective in treating infant with colic. Ben *et al.* investigated the effect of probiotic-containing milk powder on the reduction of colic symptoms. In this study, probiotics were found to improve the frequency of bowel feces and microflora but did not have any impact on the frequency of crying and vomiting in neonates (19). Inefficiency of probiotic effect on infants' crying frequency was inconsistent with the results of our study. Savino *et al.* compared *Lactobacilli reuteri* and the placebo groups for colic variables, and they showed that the severity of crying was remarkably higher in the intervention group than the placebo group (20).

Sung *et al.* investigated the effect of *Lactobacillus reuteri* on infant colic in their research. In this study, 167 infants were divided into probiotic and placebo groups. The results of this study showed that since the frequency of crying was similar between the two groups, this probiotic was not effective in treating infantile colic which was not in line with our study results (21). Roos *et al.* contend that the use of probiotics is effective in children who have been exposed to altered fecal bacteria in the microbiota (22). Differences in the type of probiotics, the dose used, duration of administration and studied population might also be the possible causes of the differences between the results of different studies with our study results.

## Conclusion

The results of the present study indicated that caraway mixture is effective in the treatment of neonatal colic like probiotics. The availability and cheaper price of the syrup-caraway mixture compared to probiotics make this drug a better and

safer choice in the treatment or alleviation of infantile colic symptoms. Improper drug consumption and failure to take it on time by some people as well as the use of traditional medicines during the intervention and subsequent follow up without informing the researcher led to the exclusion of infants from the study. It is suggested that researches comprising larger populations be conducted to investigate the drug side effects in future. In this study, some of the infants were excluded due the failure to take the drug in a timely manner and also because of the use of traditional medicines during the intervention and subsequent follow-up without informing the researchers. These limitations led to the reduction of sample size in the two groups.

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## Conflict of Interest

The authors declare that they have no conflict of interest.

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