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Original Article

Effect of Topical Chamomile Oil (*Matricaria chamomile* L.) as a Supplementary Method on Colic Symptoms in Infants: A Randomized Placebo-controlled Clinical Trial

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ABSTRACT

Background: The aim of this study was to evaluate the efficacy of the topical use of chamomile oil as a complementary method in the improvement of infantile colic symptoms.

Methods: This randomized controlled trial was carried out on 74 infants with colic at Sabzevar University of Medical Sciences in Sabzevar, Iran. The infants were randomly allocated into two groups. In the intervention group, chamomile oil was applied topically on the abdominal region three times a day for 14 days. The placebo group received paraffin oil in a similar manner. A data collection form was daily filled out for all infants by their parents. Number and duration of crying episodes and duration of sleep were assessed at the baseline and on the 7th and 14th days of the intervention.

***Results*:** Results showed that there was a significant difference in the crying time of the two groups on days 7 and 14 as compared to that at the baseline (P=0.03 and P=0.002, respectively). There was a significant increase in sleep duration only on the 14th day of treatment as compared with that at the baseline (P=0.01). Although the number of crying episodes in both groups decreased, there was no significant difference between the two groups (P=0.08). Based on the regression test, although the values obtained on days 1 and 7 were not statistically significant, compared to those at the baseline, the number of crying episodes decreased on the 14th day (95% CI: -115.39 to -15.04; P=0.012).

Conclusion: Topical consumption of chamomile oil may be used as a complementary, safe, and cost-effective way to improve and reduce the symptoms of infantile colic.

Keywords: Infant, Chamomile, Colic, Complementary medicine

Introduction

Infantile colic is one of the most common abdominal disorders based on the Wessel criteria. This condition is defined by the crying and belching of healthy eaters for 3 h a day, three days a week for at least three continuous weeks with an unknown cause (1). According to previous studies, this disorder affects approximately 10-40% of infants (2). Moreover, the prevalence of this disorder in Iranian neonates is 20% (3,4). When a baby cries as a result of colic, it can cause anxiety in relationships, lack of lactation, postpartum depression, unexpected visits to the doctor, and child abuse (5).

The etiology of neonatal colic is not well known yet. The proposed psychological theory, infant's inability to modulate internal and external stimuli, disturbs proper parent communication with one another or with the infant, as well as maternal anxiety in creating infant colic (6). The physiological theory is based on digestive factors, which include increased intestinal movements, increased gas in the stomach and intestine, and visceral pains (7). However, no study has the ability to conclusively prove these factors as the

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causes of colic, and there is no effective and standard treatment for this common disorder (2).

Several complementary and alternative treatments are applied for the management of infantile colic, such as herbal medicine and massage (8-14). Many studies suggest that aromatherapy massage is a treatment for some disorders, including digestive problems (15-17). Chamomile is among the most important herbal medicines that has a significant effect on the digestive system when used orally, and its antispasmodic property is recommended to relieve colic pains in infants (18-20). These properties are the results of the high absorption rate of apigenin and flavonoids in chamomile oil. Chamomile oil is one of the most important oils used in aromatherapy massage (21,22).

Based on several studies, infantile colic is an irritating problem for both the parent and infant, and its treatment should be among the healthcare objectives. Therefore, we conducted a randomized controlled trial to assess the efficiency of the topical application of chamomile oil in the management of infantile colic.

Methods

The present study was an experimental double-blind randomized clinical trial that was conducted to determine the effect of topical chamomile oil on the improvement and reduction of colic symptoms in infants.

Participants

The study population included infants with colic admitted to the Pediatric Clinic of Sabzevar University of Medical Sciences, Sabzevar, Iran, from February 2016 to April 2017. The inclusion criteria for participation in the study were infantile colic (based on Wessel criteria []) and pediatrician diagnosis), age of 2 weeks to 4 months, gestational age of more than 37 weeks at birth, birth weight of > 2,500 gr, and lack of underlying diseases or congenital anomalies. The exclusion criteria were impaired growth, major medical illnesses (e.g., immunodeficiency, growth and developmental disorders, and genetic disorders), skin lesions in the topical drug use site, parents' unwillingness to continue the study, change of infant milk, and use of other drugs for colic during the study.

For all participants, oral and practical explanations were given to their mothers about the method of research. The selected samples were entered into the study after completing the written consent form by parents. This study was approved by the Ethics Committee of Sabzevar University of Medical Sciences (code: IR.MEDSAB.REC.1395.130) and registered in the Iranian Registry of Clinical Trials (IRCT2017032818951N2).

Chamomile preparation method

Chamomile oil was prepared in the Traditional Pharmacy Laboratory of the Faculty of Traditional Medicine. The dried flowers of *Matricaria chamomile* var. were used after confirmation by the botanist, and then recorded in each herbarium and assigned the herbarium number (PMP-336). The flowers were soaked five times in water for a night, and then cooked on a gentle heat until a quarter of the content was left. Afterward, the water is smooth and add sesame oil to its weight and put it on a gentle heat until the water was completely evaporated and the oil remained. The standardization of the product was based on the identification and determination of the amount of chemical compounds present in the preparation by a gas chromatography mass spectrometry device.

Intervention

On the first visit, the diagnosis of the pediatrician was based on the Wessel criteria, and the subjects were checked in terms of the inclusion and exclusion criteria. The infants were randomly divided into the intervention and placebo groups. The infants were subjected to a thorough examination by the physician, and the initial questionnaire was completed after the explanation of the study procedure. After checking the skin sensitivity in the infants' arms, they were randomly divided into two groups of intervention and placebo respectively administered chamomile oil and paraffin oil for 14 days.

Both parents received verbal explanations on topical application and massaging of chamomile oil on the abdomen of children in case of colic. One day before the treatment, the parents were asked to record the duration of crying, number of crying episode, and duration of sleep in minutes in a special form. During the study, a whole day (i.e., 24 h) was considered from 6 a.m. to 6 a.m. the following day. Both parents were trained to begin treatment on the first day. The chamomile oil or placebo was applied topically on the infant's abdomen.

To prevent skin sensation and redness at the massage site, the mothers were advised to apply five drops of oil on the abdomen of the infants.

This intervention was repeated three times a day (i.e., morning, evening, and night) for 14 days. On the 1st, 7th, and 14th days, the researcher reminded parents to register the infant's symptoms in the registration form through a telephone call and asked to refer to the pediatric clinic for an appointment, child's examination, and collect and check the registration forms on the last day of the intervention.

Also, on the first day, all parents were given the researcher's contact number for asking probable questions, reporting the status of the child, or declaring unwillingness to continue participating in the study. A physician conducted all the pediatric visits and therapies for all infants in both groups. Furthermore, the use of medicine and placebo and also education for parents were the same for all infants.

Assessments and outcome

In this study, the primary outcome was the duration of infant's crying in 24 h. The secondary outcomes included the frequency of infant crying and the duration of sleep in 24 h. The data were recorded before the treatment and on days 1, 7, and 14 of the treatment in a specific form by the parents. The participants' data were compared with the baseline data and those of the placebo group.

Sample size

The sample size was determined so that the study was able to detect the difference of at least 30 with averages of 150 and 120 in the intervention and placebo groups, respectively. With the type I error of 5%, type II error of 10%, and standard deviation of 25 for the control and intervention groups, the maximum sample size was calculated as 34 for each group. Considering 10% attrition, it was considered 37 cases for each group, and the calculations were performed by G* Power software.

Randomization and blinding

A block randomization list was generated for 74 infants based on a computer-generated random allocation sequence with four sequences in each block without stratification. Randomization to two groups, namely intervention (chamomile oil) and placebo (paraffin oil), occurred at the pretreatment stage. Allocation was carried out by the research assistant one day before treatment after obtaining informed consent. Group assignment was performed using sealed, numbered, and opaque envelopes. The parents and the investigator were blind to treatment assignment in the intervention and placebo groups.

Statistical analysis

The continuous variables were described as mean and standard deviation, and the categorical variables were presented as number and percentages. To compare the mean of the quantitative outcomes between the two groups, t-test or its nonparametric equivalent (i.e. Mann-Whitney U test) were employed. Furthermore, in terms of the qualitative variables, Chi-square test or Fisher's exact test was used. In order to determine the intra-group differences (before and after the treatment), the paired-sample t-test or its nonparametric equivalent (i.e., Wilcoxon Signed Rank test) was run.

To compare the variables at different times, repeated measures ANOVA was used for the two groups. If there was a needed to control the basic variables, appropriate regression models were applied. Data analysis was performed using Stata software (version 12). P-value less than 0.05 was considered statistically significant.

Results

Totally, 81 infants were assessed in this study. Out of all enrolled samples, 74 participants were eligible based on the inclusion and exclusion criteria. The participants were randomly allocated into the intervention (chamomile oil, n=37) and placebo (paraffin oil, n=37) groups. During the study, six infants were excluded from the study; in this regard, two parents terminated the study on the first week of treatment due to missing recording the data, and four others left the study during the second week because of the nonrecovery of colic symptoms in their child. Finally, 68 infants (i.e., 34 infants in the intervention group and 34 infants in the placebo group) completed the study and were analyzed statistically. The details of research data through the trial are summarized in Figure 1.

In the intervention group, 52.94% (n=18) of the infants were male, and also 91.18% (n=31) of them were from the urban area. The mean age of the infants was 51.02±26.2 days. The details of the demographic data are summarized in tables 1 and 2. Table 3 shows that one day before the treatment, the mean crying durations of the infants in the chamomile and placebo groups were 262.66 and 261.66 min in a 24-h period. Independent t-test showed that the mean crying duration of the participants in both groups was not significantly different (P=0.90), and both

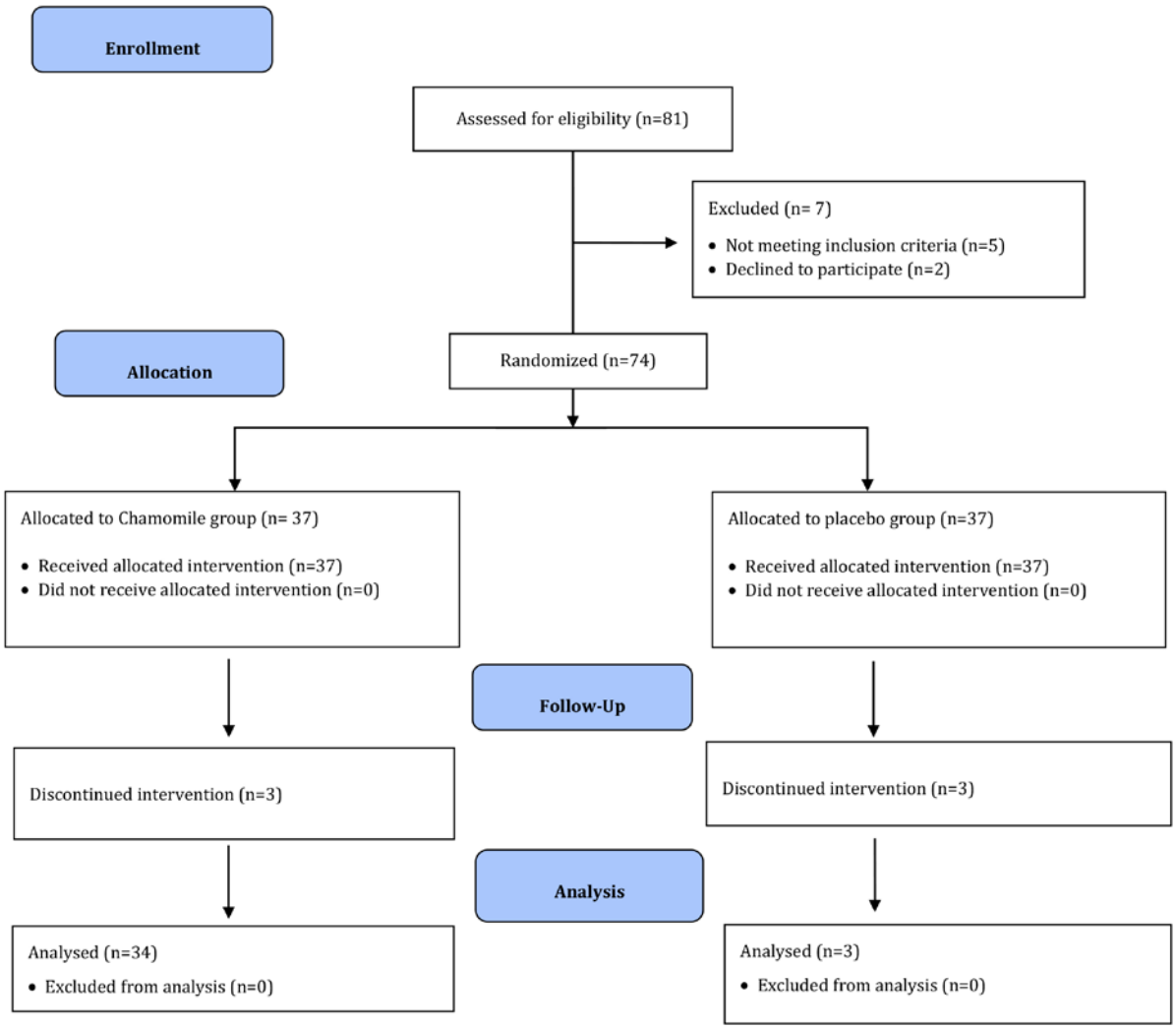

Figure 1. CONSORT diagram of the research process

Table 1. Baseline data for infants in the intervention and placebo groups

Parameter	Treatment group Mean (SD)	Placebo group Mean (SD)	Statistical test (P-value)
Age (day)	51.02 (26.25)	60.02 (21.47)	0.051
Birth weight (g)	3071.17 (430.46)	3203.52 (473.78)	0.212
Current weight (g)	4816.17 (778.37)	4794.11 (907.10)	0.914
Age of the onset of colic symptoms (day)	25.5 (11.76)	22.41 (11.17)	0.154
Gestational age (week)	38.73 (1.16)	38.85 (1.10)	0.670
Mother's age (year)	28.55 (5.63)	29.76 (6.52)	0.417

groups were homogeneous in this regard before the commencement of the treatment.

The results of the ANCOVA test showed that there was no significant difference in the mean crying duration of infants in both groups at the end of the first day of treatment, compared to that recorded one day before the treatment (P=0.63). There was a significant difference in the mean crying duration of the infants in both groups at the end of the 7^{th} and 14^{th} days of the treatment, compared to that obtained the day before the treatment (P=0.032 and P=0.002, respectively).

In terms of sleep duration one day before the intervention, the mean sleep durations of the infants in the chamomile and placebo groups were 748.23 and 646 (min/24 hours), respectively. Independent t-test showed that there was no significant difference in the mean sleep duration of the research samples in both groups (P=0.90). The results of ANCOVA showed that there was no

Table 2. Baseline data for infants in the intervention and placebo groups

Parameter		Intervention group N (%)	placebo group N (%)	Statistical test (P-value)
Residential area, Urban		31 (91.18)	29 (85.29)	0.71
Gender, Male		18 (52.94)	16 (47.06)	0.62
Birth order	First	14 (41.18)	17 (50.00)	0.01
	Second	18 (52.94)	9 (26.47)	
	Third or above	2 (5.88)	8 (23.53)	
Nutritional diet	Breastfeeding	25 (75.53)	29 (85.29)	0.21
	Powdered milk	0 (0)	1 (2.94)	
	Complex	9 (26.47)	4 (11.76)	
Mother's education level	Under Diploma	4 (11.76)	4 (11.76)	0.83
	Diploma	9 (26.47)	13 (38.24)	
	Associate diploma	8 (23.53)	5 (14.71)	
	Bachelor	11 (32.35)	10 (29.41)	
	Master	2 (5.88)	2 (5.88)	

Table 3. Mean distribution and standard deviation of the Crying, Sleep, and NumCrying of research samples in study groups

Plan	Before the treatment		First day of treatment		Analysis Test	Seventh day of treatment		Analysis Test	Fourteenth day of treatment		Analysis Test
Parameter	Intervention group Mean (SD)	Placebo group Mean (SD)	Intervention group Mean (SD)	Placebo group Mean (SD)	P-value*	Intervention group Mean (SD)	Placebo group Mean (SD)	P-value *	Intervention group Mean (SD)	Placebo group Mean (SD)	P-value*
Crying duration (Min/Day)	262.6 (140.4)	266.6 (133.4)	222.6 (144.8)	231.1 (130.5)	0.63	150.3 (121.1)	204.5 (123.7)	0.03	113.3 (90.1)	190.7 (133.4)	0.002
Sleep (Min/Day)	748.2 (239.5)	646.1 (250.4)	727.1 (201.4)	767.2 (243.2)	0.55	770.1 (208.8)	781.6 (223.8)	0.24	793.8 (183.4)	767.1 (228.7)	0.01
Number of crying (N/Day)	7.94 (4.3)	7.35 (4.5)	6.1 (3.8)	7.41 (5.7)	0.27	4.35 (4.1)	6.08 (3.6)	0.08	3.76 (4.1)	5.38 (3.3)	0.09

*ANCOVA test
* These measures are adjusted by age group and gender
** ANCOVA test

Table 4. Effect of intervention on the outcomes of the study (linear regression test)*

Plan	First day of treatment		Statistical test	Seventh day of treatment		Statistical test	Fourteenth day of treatment		Analysis Test
Parameter	Coefficient of regression	[95% CI]	P-value**	Coefficient of regression	[95% CI]	P-value**	Coefficient of regression	[95% CI]	P-value**
Crying duration (Min/Day)	- 7.78	[-56.23, 40.49]	0.746	- 46.03	[-96.74, 4.68]	0.074	- 65.21	[-115.39, - 15.04]	0.012
Sleep (Min/Day)	- 14.03	[-111.27, 83.20]	0.774	1.22	[-91.56, 94.10]	0.979	38.63	[-53.05, 130.33]	0.403
Number of crying (N/Day)	- 0.94	[-3.36, 1.47]	0.437	- 1.38	[-3.23, 0.45]	0.136	- 1.36	[-3.16, 0.43]	0.134

significant difference between the mean sleep duration of the infants in both groups at the end of the 1st and 7th days of the treatment, compared to that reported for the day before the treatment (P=0.55 and P=0.09, respectively). There was a significant difference in the mean sleep duration of the infants in both groups at the end of the 14th day of the treatment, compared to that recorded the day before the treatment (P=0.01).

Regarding the number of crying episodes one day before the treatment, the mean numbers of crying episodes were 7.94 and 35.7 during 24 h in the chamomile and placebo groups, respectively. The results of independent t-test showed that the mean number of crying episodes in the two groups did not have a significant difference (P=0.58). Moreover, according to the ANCOVA test, there was no significant difference in the mean number of crying episodes in the infants in both groups at the end of the 1st, 7th, and 14th days of the treatment, as compared to that obtained the day before the treatment (P=0.26, P=0.08, and P=0.09, respectively).

Regarding Table 4, the effect of the intervention (i.e., topical use of chamomile oil) on the primary and secondary outcomes of the study on days 1, 7, and 14 of the treatment was investigated using regression test. Based on this test, although the values obtained for days 1 and 7 were not statistically significant as compared to that recorded the day before the treatment, the number of crying episodes was treated at the end of the 14th day (95% CI: -115.39 to -15.04; P=0.012).

Discussion

This is the first study, which investigates the effect of the topical application of chamomile oil on the management of infantile colic in form of a clinical trial. The Mann-Whitney U test showed a significant difference between the treatment and placebo groups. We also used a crying diary before and during the study in most of the infants. Both groups showed a reduction in hours of crying per day during the study, but there was a significant difference between the intervention and placebo groups.

The efficacy of oral chamomile on infantile colic has been demonstrated in several studies (23-27). The results of this study are in agreement with those obtained by Martinelli et al. demonstrating that an oral herbal formula, containing *Matricaria chamomilla* L., M*. officinalis* L., and *Tyndallized* L., can significantly reduce infant's crying duration in 28 days (18). In addition, Savino et al. examined the efficacy of an oral herbal formula containing *Matricaria recutita* L. on infants with infantile colic (20).

In this study, we demonstrated that the topical form of chamomile oil had similar properties to its oral form. The efficacy of chamomile could be partially explained by the hypothesis that infantile colic is related to gastrointestinal (GI) motor dysfunction due to the dysregulation and immaturity of intestinal motility (28). Many studies have revealed that *Matricaria chamomilla* has antispasmodic and anti-inflammatory properties (29). The antispasmodic activity seems to be mainly effective on the GI smooth muscle due to the essential oil and flavonoid components, particularly apigenin and bisabolol (22).

In a recent study, Arikan et al. examined the effectiveness of massage alone in the treatment of infantile colic (30). In addition, another study demonstrated that massage could be effective in the management of infantile colic (31). In many parts of the world, massage aromatherapy is used as a traditional treatment for relieving the symptoms of colic and other pains (8, 15, 32). However, in this study, we demonstrated that topical chamomile oil was more effective than the topical placebo oil, which was not aromatherapy oil.

Chamomile oil is one of the most common oils used in aromatherapy. Infantile colic is related to the distension of the bowels and activation of the autonomic nervous system. Topical application of chamomile oil can influence both autonomic nervous system and visceral pain. The studies on rats suggested that chamomile may influence the intestinal digestive and absorptive functions (33) that could explain the mechanism of topical chamomile on infantile colic.

One of the limitations of this study is that we utilized no validated diary for the duration of infant crying and used parents' reports on the duration of crying. The mothers filled out the form hourly during the day to minimize recall bias. Furthermore, we did not report some potential confounders, such as maternal diets, maternal lifestyle, and early use of drugs.

Conclusion

This is the first trial that investigates the effect of the topical application of chamomile oil on infantile colic. Results of this trial suggested that the topical application of chamomile oil had potential alleviating effects on reducing infantile colic symptoms. As there is no standard management for infantile colic symptoms, a variety of management modalities have been proposed to decrease the symptoms. However, further studies are needed to confirm the findings of the present study. Future researchers are suggested to use a larger sample size and a longer follow-up period.

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Conflicts of interests

The authors declare that there is no conflict of interest.

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