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The Effect of Fennel on Infantile Colic: A Systematic Review and Meta-Analysis

Hoda Shojaei[1], Seyedeh Mozhgan Heidary[1], Robabeh Moosavi Nezhad[1], Sara Rahafard[2], Azadeh Seydmohammadkhani[1], Mohadeseh Khakpour[1], *Sara Ghahremani[3], Jaleh Salari nasab[4], Hamed Jafarpour[5]

[1]Pediatrician, Department of Pediatrics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. [2]Pediatric specialist, Golestan University of Medical Sciences, Gorgan, Iran. [3]Assistant Professor Of Pediatrics, Department of Pediatrics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. [4]Students Research Committee, Razi School of Nursing and Midwifery, Kerman University of Medical Sciences, Kerman, Iran. [5]Student Research Committee, Mazandaran University of Medical Sciences, Sari, Mazandaran, Iran.

Abstract

Background

The colicky infants generally present around 6–8 weeks postpartum then then is suddenly relieved by 3-4 months. A few studies assessed the effect of fennel on colicky infants. The aim of this systematic review and meta-analysis was to assess whether fennel is effective on infantile colic.

Materials and Methods: Two independent authors separately searched the articles on the national (Irandoc, Magiran, Medlib, SID, and Barakatkns), and the international databases (Medline, EMBASE, Web of Science, Scopus and Cochran Central Register of Controlled Trials) without any time limitation since the inception to August 2019. The keywords of the search were: (Colic) AND (Foeniculum OR Fennel OR Foeniculum vulgare) AND (Infant OR Children OR Baby).

Results: Four studies were conducted to assess the impact of fennel on the infantile colic. A Foeniculum Vulgarein in combination with other herbal medicines was found to be more effective than control group on crying time on infantile colic (SMD= O.708; 95% CI= -0.951 to -0.465; P<0.001). Heterogeneity was 0% and non-significant. According to one study, in the 3rd and 7th days of the treatment in comparison with the previous times, both the fennel group (P=0.004, P=0.05, respectively), and the gripe water group (P=0.037, P=0.002, respectively) indicate the statistically significant difference. Moreover, none of the infants cried for more than 2 hours in the two groups. After treatment, an insignificant difference between the two groups (fennel and gripe water groups) was observed.

Conclusion

Fennel alone or in combination with other herbal medicine is effective on infantile colic. Concerning the high heterogeneity, there is a need of future trials to reach a certain conclusion.

Key Words: Effect, Fennel, Infantile Colic.

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Corresponding Author:

Sara Ghahremani, Department of Pediatrics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

Email: ghahremanis@mums.ac.ir

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1- INTRODUCTION

The colicky infants generally present with the symptoms such as the inordinate flatulence and persistent crying; they are unreasonably and acutely agitated, fussy, and bad-tempered. Suffering from pain, they draw up their knees as well as arch their back, which is another symptom, the peak is around 6–8 weeks postpartum then it is relieved in 3-4 months (1). Given the effect on the approximately 16 to 26% of neonates in the first months of life, the colic remains a challenging issue for both the parents and the caregivers (2).

Infantile colic has been determined as the reason of 10 to 20% of all the pediatrician visits in the initial 4 months of life. Although the infantile colic is prevalent and incites considerable distress in parents and pediatricians, its etiology is still undetermined even after 40 years of research. Numerous aetiopathogenetic hypotheses have been requested to specify the cause of this problem under the title of the organicism and behavioral; it would seem that the infantile colic is the consequence of the synergistic interaction between both factors. The abnormal gastrointestinal function and allergic disorders subtitled in the organicism hypothesis lead to interventions such as substituting cow's milk with soy milk, protein hydrolysate (hypoallergenic), and using herbal tea (3). The infantile colic is a prevailing condition affecting 5 to 28% of the infants in the initial months of life (1).

Furthermore, the infantile colic probably precedes the unnecessary hospitalizations, the problematic parent–infant relationship, marital problems and infant maltreatment (4). The efficient treatment for the infantile colic is still unclear (5). There are various strategies for controlling the disease; these include behavioral, pharmaceutical, and dietary, herbal medicines with less by-products, but few studies have assessed the effect of fennel on colicky infants. The aim of this systematic review and meta-analysis was to assess whether fennel is effective on infantile colic.

2- MATERIALS AND METHODS

2-1. The Data Sources

The articles published in the national and international databases were enrolled in this systematic review and meta-analysis study. Two independent authors separately searched the articles on the national (Irandoc, Magiran, Medlib, SID, and Barakatkns), and the international databases (Medline [via PubMed], EMBASE, Web of Science, Scopus and Cochran Central Register of Controlled Trials) without any time limitation since the inception to August 1, 2019. Moreover, a manual search was launched in Google motor engine, Google Scholar, and the bibliography of related articles and reviews. The keywords of the search were: (Colic) AND (Foeniculum OR Fennel OR Foeniculum vulgare) AND (Infant OR Children OR Baby). The search query in Medline (via PubMed) is shown in **Table.1**. For the further research, our preference was a hand search on the references' list of the selected articles, previous systematic review and meta-analysis. Additionally, we have called some of the editorial boards of the national journals seeking for the gray literature.

Table-1: Search strategy for Medline (via PubMed).

("colic"[MeSH Terms] OR "colic"[All Fields]) AND (("foeniculum"[MeSH Terms] OR "foeniculum"[All Fields]) OR ("foeniculum"[MeSH Terms] OR "foeniculum"[All Fields] OR "fennel"[All Fields]) OR ("foeniculum"[MeSH Terms] OR "foeniculum"[All Fields] OR ("foeniculum"[All Fields] AND "vulgare"[All Fields]) OR "foeniculum vulgare"[All Fields])) AND (("infant"[MeSH Terms] OR "infant"[All Fields]) OR ("child"[MeSH Terms] OR "child"[All Fields] OR "children"[All Fields]) OR ("infant, newborn"[MeSH Terms] OR ("infant"[All Fields] AND "newborn"[All Fields]) OR "newborn infant"[All Fields] OR "baby"[All Fields] OR "infant"[MeSH Terms] OR "infant"[All Fields])).

2-2. The Inclusion and Exclusion Criteria

We included all clinical trials studies that evaluated the effectiveness of the fennel therapy on the crying time on infantile colic. No time and language limitations were applied. Only the English and Persian articles were included in the study.

2-3. The Data Extraction

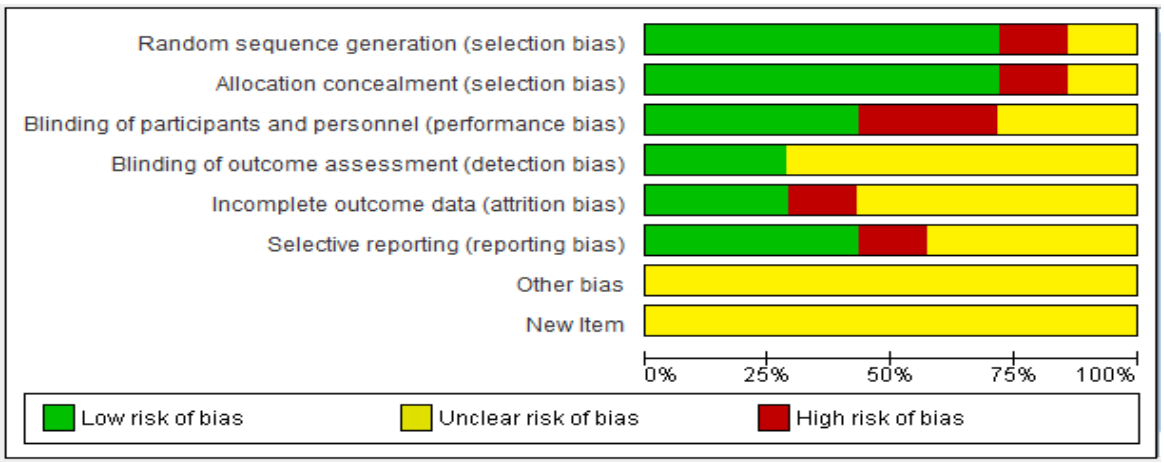
The data extraction and quality assessment of the trials were undertaken by two independent individuals based on the authors, year, region, study design, treatment duration, type and number of treatment and main findings. If there was disagreement, it was resolved by the 3rd reviewer.

2-3. Quality Assessment and Data Extraction

After searching and eliminating some reports and duplicates, two independent authors read the titles and abstracts, and then relevant studies were selected. Any disagreement was solved by discussion among the research team. Data related to the first author of article, years, region, study design, treatment duration, type and number of treatment and main findings were recorded. The quality of the Clinical trial studies was assessed using Cochrane's proposed guidelines (6). Two authors assessed the risk of bias of the included studies independently, using the criteria of the Cochrane Handbook for Systematic Reviews of Interventions (Tarsilla, 2008) that evaluated: (a) random sequence generation; (b) allocation concealment; (c) blinding of participants and personnel; (d) blinding of outcome assessment; (e) incomplete outcome data; (f) selective reporting; and (g) other bias. In this assessment, each item was graded as 'low', 'high' or 'unclear' risk of bias (**Figure.1**).

2-5. The Statistical Analysis

The Comprehensive Meta-Analysis software was used to analyze the data. Finally, the heterogeneity index was determined between the studies using I^2 and Cochran's Q test. Based on the results suggested by Higgins et al., a value less than 25% was considered as low heterogeneity, a 25-75% value as moderate heterogeneity, and a value over 75% as high heterogeneity (7). Based on the results of heterogeneity, a random or fixed effect model was used to estimate the effect size of the fennel on infantile colic with a 95% confidence interval in forest plot. In this diagram, since the number of articles is less than 10 articles, there is no need for calculation or to draw publication bias plot. The forest plot was used to show the meta-analysis results in which the square size indicates the number of samples in each study. The drawn lines on both sides of the 95% confidence interval (CI) show the effect size of each study.



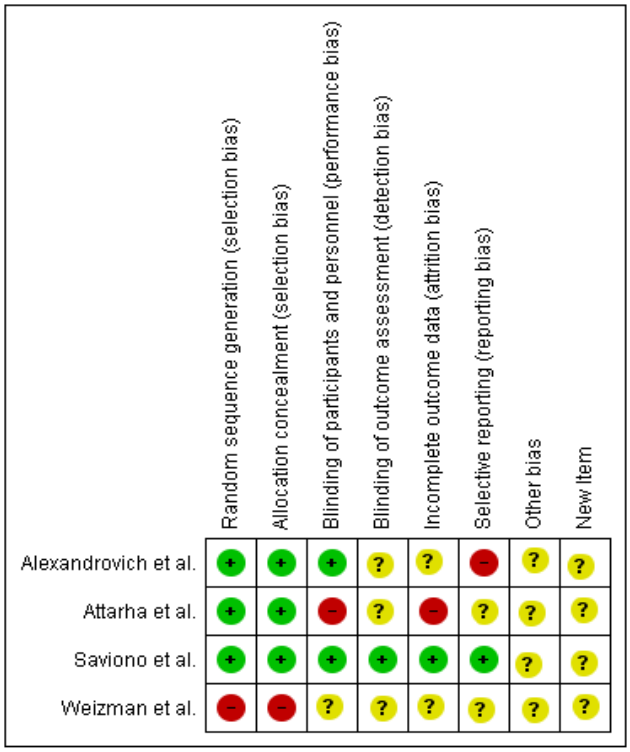


Fig1: Risk of Bias summary.

3- RESULTS

Four studies were conducted to assess the impact of the fennel on the infantile colic (**Table.2**). **Figure.2** displays the process of the articles selection for this systematic review. Three studies had sufficient data to include in meta-analysis (3, 8, 9). A Foeniculum Vulgarein in combination with other herbal medicines was found to be more effective than control group on crying time on infantile colic (Standardized Mean Difference [SMD]=O.708; 95% CI=-0.951 to -0.465; P<0.001, **Figure.3**). Heterogeneity was 0% and non-significant according to studies (10) on the 3rd and 7th days of the treatment in comparison with the previous times, both the fennel group (P=0.004, P=0.05, respectively), and the gripe water group (P=0.037, P=0.002, respectively) indicate statistically significant difference. Moreover, none of the infants cried for more than 2h in the two groups. After treatment, an insignificant difference was observed between the two groups.

Table-2: General characteristics of included studies in systematic review-meta-analysis.

Authors, Years, Region, (Reference)	Study design	Treatment duration	Type and number of treatment	Main findings
Savino et al., 2005, Italy, (3)	Clinical trial	One week	Matricariae recutita, Foeniculum vulgare and Melissa officinalis	Significant difference between two groups.
Alexandrovich et al., 2003, Russia, (8)	Clinical trial	One week	Water emulsion of 0.1% fennel seed oil/ placebo n= 60	Significant difference between two groups.
Weizman et al., 1993, Israel, (9)	Clinical trial	One week	Officinalis fennel licorice(Glycyrrhiza glabra, chamomile (Matricaria chamomilla balm-mint (Melissa officinalis n=36/36	Colic, significant difference between two groups.
Attarha et al., 2008, Iran, (10)	Clinical trial	One week	Fennel n=40, Gripe water syrup n=40	Significant difference between two groups.

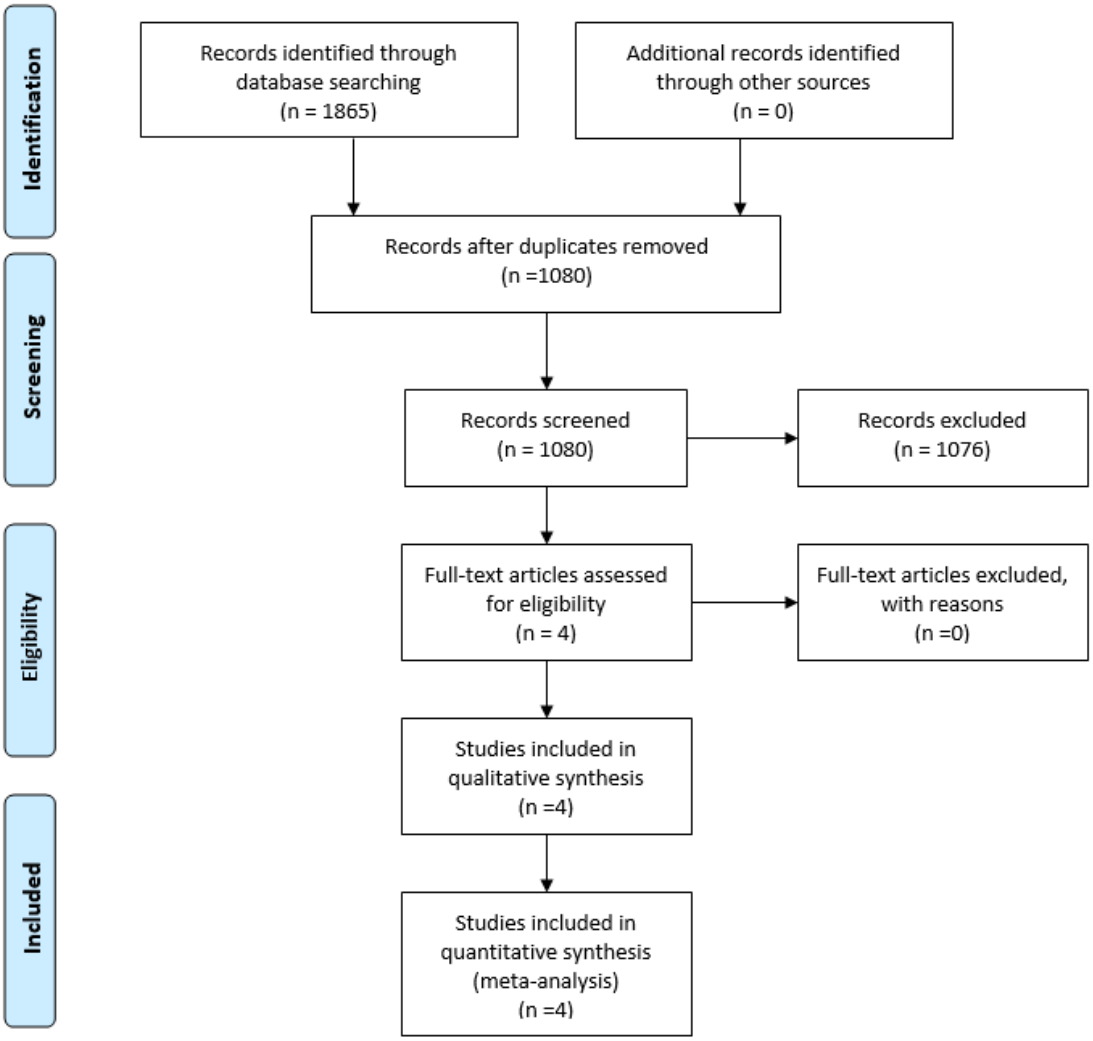


Fig.2: PRISMA flowchart.

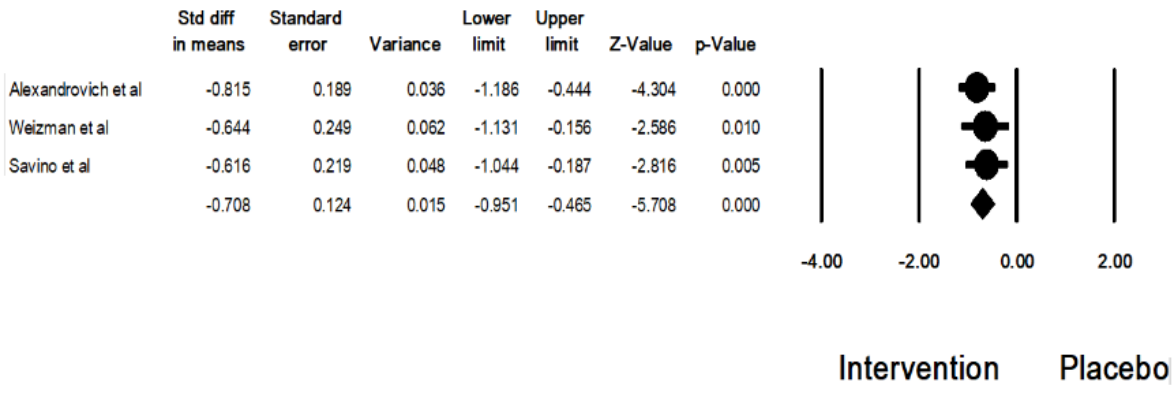


Fig.3: The effect of Foeniculum Vulgarein in combination with other herbal medicines on crying time on infantile colic. The square size indicates the number of samples in each study; the drawn lines on both sides of the 95% confidence interval.

4- DISCUSSION

The aim of this systematic review and meta-analysis study was to assess whether fennel is effective on Infantile Colic. Four studies (3, 8-10) were included into systematic review and meta-analysis. In Savino et al.'s study crying time had been reduced in 85.4 and 48.9% of subjects for the phytotherapeutic agents and the placebo ($P < 0.005$), respectively. There were no reports of reaction. After one week of treatment, the breastfed infants with the colic were treated with the extracts of the Matricariae recutita, the Foeniculum vulgare and the Melissa officinalis (3). In a study by Alexandrovich et al., according to the Wessel criteria (10), the infants in the treatment group in comparison with the infants in the control group had better reaction to the usage of the fennel oil emulsion eradicating the colic, 65% (40/62), and 23.7% (14/59) ($P<0.01$) of each group, respectively. The treatment group compared to the control group indicated a significant improvement in the colic treatment (8). In a study by Weizman et al., the effect of an herbal tea preparation on the infantile colic was examined in the double-blind study. The tea usage eradicated the colic in 33 infants out of 49 (57%).

Nevertheless, the placebo merely effected on 9 infants out of 35 (26%) ($P < 0.04$). The infants who were under the tea treatment, showed a considerably improved mean colic score. Regarding the incidence of the night wake ups, there was no considerable difference between the two groups (9). According to the study by Attarha et al. (10), on the 3rd and 7th days of the treatment in comparison with the previous times, both the fennel group ($P=0.004$, $P= 0.05$, respectively), and the gripe water group ($P=0.037$, $P=0.002$, respectively), indicated the statistically significant difference. Moreover, none of the infants cried for more than 2 hours in the two groups. After receiving treatment, an insignificant difference was observed between the two groups. The fennel (Foeniculum vulgare) as a plant belonging to the Umbelliferae (Apiaceae) family was discovered and has been utilized by the humans since the olden days. Since the fennel has a good flavor, it was cultivated in every country nearby the Mediterranean Sea. The fennel is an edible fragrant plant whose seed are used in the savory formulations, sauces, liqueurs, confectionaries, and so forth (11). It has been reported that the fennel essential oil usage is beneficial in the pediatric colic and some respiratory disorders due to its anti-spasmodic effect (12, 13).

4-1. Study Limitations

Our systematic review was multi-dimensionally limited; despite an exhaustive search, we might have failed to find some published trials. Moreover, we did not form the connection with the regarded experts; it is noteworthy that if we had contacted the experts, we would have found further studies. The small sample size could be recognized as another limitation of the included studies. To confirm this conclusion the requisite factors were the larger RCTs with more reliability and better design. Our analysis was fundamentally limited by taking into consideration the CONSORT checklist to enhance the methodological quality as well as the heterogeneity of the included studies for the supplementary trials. The heterogeneity might be varied by the diversity of the fennel products, the dosage, the therapy duration, and the treatment received by the control group. Another latent limitation of our systematic review was the methodological defects of the numerous included studies, which can affect our findings in terms of the reliability and the validity.

5- CONCLUSION

Fennel alone or in combination with other herbal medicine are effective on infantile colic. With regard to the high heterogeneity, there is a need for future trials to reach a definite conclusion.

6- CONFLICT OF INTEREST: None.

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