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Original Article

Efficiency of Dimethicone and Symbiotic Approaches in Infantile Colic Management

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ABSTRACT

Background: Infantile colic (IC) (a frequent reason for infantile referral to pediatricians) is a common indiscoverable problem posing concerns for parents. Varieties of theories for the etiology of IC have been raised, and different therapeutic approaches have been recommended in this regard. This study aimed to assess and compare the efficiency of dimethicone versus symbiotic in the treatment of IC.

Methods: This randomized clinical trial was conducted on 149 infants with the diagnosis of IC based on the Wessel criteria from 2017 to 2018. The study population was randomly divided into two groups of Dimethicone (n=73) (five drops of dimethicone, three times a day for three weeks) and Symbiotic (n=76) (five daily drops of symbiotic for three weeks). Utilized symbiotic contained fructooligosacharide periodic and probiotic of 10^9CFU of Bifidobacterium lactis. Duration of an infant crying per day, numbers of crying per day, sleep duration per day, and number of defecation per day were obtained prior to the study and at the end of each week.

Results: There was no statistically significant difference between the groups regarding age, gender, and values of breastfeeding (P>0.05). Crying duration, numbers of crying, and sleep duration per day improved significantly in the dimethicone group (P<0.05) within the time as the symbiotic-treated group (P<0.05); however, the comparison of the two groups for IC treatment revealed no statistical differences (P>0.05).

Conclusion: The findings of the current study presented that dimethicone and symbiotic could successfully improve IC symptoms regarding crying times, as well as the duration and sleeping time per day. Comparison of these two remedies for IC treatment revealed no significant differences.

Keywords: Dimethicone, Infantile colic, Symbiotic

Introduction

Infantile colic (IC) as a frequent underlying reason for infantile referral to the healthcare systems occurs in 10%-30% of the infants. Furthermore, it is a common disturbing indiscoverable problem posing significant concerns for parents (1). Researchers have raised various theories for the etiology of IC in order to provide an appropriate approach for the treatment of this complication. Painful contraction due to the presence of excessive gas in the gastrointestinal tract following excessive aerophobia is a common hypothesis about the etiology of IC. This idea has been supported by the studies comparing expiratory H_2 excretion of infants with the diagnosis of IC and normal ones (2).

Another theory is in favor of the type and amount of colonized microbiota in the infants' gastrointestinal tract (3). Gastrointestinal immaturity leading to inflammation and also motility dysfunctions is the other aspect that has been raised by the authors about the etiology of IC (4, 5). Based on the mentioned theories about the etiology of IC, numerous treatments with controversial outcomes have been experimented previously. Dimethicone/ simethicone (methylpolysiloxane) is an old agent that has been used for this aim to reduce gas

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production (6); however, studies in this regard presented controversial outcomes as some were in favor of this agent (7). On the other hand, others presented no superiority of dimethicone, compared to placebo (8).

Probiotics have been abundantly used for infants resenting from IC. Although the use of these compounds has been accompanied by acceptable crying control, inadequate studies support the general use of probiotics for this target group (9). On the other hand, the prebiotic plus probiotic synergistic combination is known as symbiotic. Symbiotics are considered superior to either mere prebiotics or probiotics for numerous aspects while limited studies have been conducted to assess the efficiency of symbiotics in IC management; moreover, among the assessed ones, the ultimate outcomes and the best components are still of great question (10). Based on the review of the literature, there was no comparative study assessing the outcomes of dimethicone versus symbiotic in the treatment of IC; therefore, the current study aimed to compare the efficiency and outcomes of dimethicone and symbiotic in the management of IC.

Methods

Study population

This randomized clinical trial was conducted on infants referred with the chief complaint of IC to the Pediatric Clinic of Alzahra Hospital affiliated to Isfahan University of Medical Sciences, Isfahan, Iran, from 2017 to 2018 (IRCT2015042 3021910N5). This study was extracted from a research project conducted at Isfahan University of Medical Sciences, Isfahan, Iran (IR.MUI.REC. 1396.3.482)

Inclusion and exclusion criteria

The inclusion criteria were: 1) term birth infants with two-week to two-month age under exclusive breastfeeding, 2) no congenital abnormalities, and 3) no medical diseases (e.g., renal, hepatic, gastrointestinal diseases) and/or gastroenteritis. In addition, the included cases were supposed not to have the previous history of antibiotic, prebiotic, and/or probiotic use.

On the other hand, the exclusion criteria included: 1) lack of adherence to the study protocol considering the regular use of remedies, 2) concurrent maternal therapeutic drug use, 3) incidence of any harmful complication during the study attributed to the remedies, 4) presence of other medical conditions justifying colic symptoms (e.g., allergy to cow's milk protein), 5) use of any antibiotic during the study period, and 6) over 20% of deficiencies in the obtained data.

The study protocol was approved by the Ethics Committee of Isfahan University of Medical Sciences, Isfahan, Iran. Subsequently, the legal guardians of the infants were provided with all required information about the study by the author (resident of pediatrics responsible for conducting the study). Following that, written informed consent was obtained from them regarding their child's participation in the study.

Considering a 10% attrition rate, one would need to complete at least 50 patients per arm to be able to notice any degree of confidence whether a difference exists between the two groups (19). Accordingly, for more accuracy, 149 infants were selected through convenience sampling with an absolute diagnosis of IC by a target neonatologist considering the Wessel criteria (11).

Afterward, the study population was randomly divided into two groups. Randomization was performed using Random Allocation software in a way that each infant was provided with a specific number. The even and odd numbers were attributed to groups A (Dimethicone treatment) and B (Symbiotic treatment), respectively. It should be mentioned that the neonatologist and parents were blinded to the treatment approach used for each infant as the agents were blindly provided to parents (in sachets similar in shape, size, and color); moreover, the assessments were obtained from the blinded parents and presented to the neonatologist that was blinded to the type of the agents prescribed for each of the groups.

Study procedure

Prior to the treatment initiation, duration of crying per day, numbers of crying per day, sleep duration per day, and number of defecation per day were obtained from mothers. Subsequently, group A was treated with five drops of dimethicone (Razi Company; Iran) three times a day for four weeks. On the other hand, group B received five drops of symbiotic daily for a similar duration. The utilized symbiotic was BBC (Zist-takhmir Company; Iran) containing fructooligo-sacharide periodic and probiotic of 10^9 CFU of Bifidobacterium lactis. Thereafter, the mentioned variables above were recorded within a week, two weeks, and three weeks following the interventions in the study checklist.

Furthermore, other variables including infant's weight gain, numbers of physician visit requirements, and intervention associated complications were evaluated and recorded in this

study. Parents' adherence to interventions and checklist completion were also checked by the pediatric resident responsible for the study through a twice-a-week telephoning schedule, and the required information about the study was provided to the parents if needed. In addition, the parents were asked about the probable complications associated with the use of dimethicone/symbiotic to be recorded in threatening conditions to cease the intervention and be eliminated from the study.

Statistical analysis

The ordinal proportional odds model was used to investigate the effect of the intervention on the interest outcomes using the generalized estimating equation method. The model included the intervention effect (dimethicone as the reference group), time effect (in a week), baseline value, and interaction effect of time, as well as intervention (week×group). When the interaction effect of week×group was not significant, the results were reported according to the model without it. The obtained data were analyzed in SPSS software (version 20). Furthermore, the independent t-test was employed to compare the means, and McNemar's chi-squared test was utilized to compare the abundance between the two groups. A two-tailed statistical significance probability was considered less than 0.05, and a p-value less than 0.05 was considered statistically significant.

Results

The current study was conducted on 149 infants, who were divided into two similar groups regarding gender distribution (P=0.949) and type of feeding (P=0.912) (Table 1). All individuals had more than three hours of crying per day. According to the results, there was no significant difference between the two groups regarding the distribution of sleep duration (P=0.556) and number of defecation per day (P=0.250) at the baseline. However, a significant difference was observed between the two groups in terms of the number of crying at the baseline (P=0.005). Figures 1 a-d visualize the number of individuals at different levels of outcomes (crying duration, numbers of crying, sleep duration, and numbers of defecation per day) at baseline and the weeks after the intervention. Table 2 represents the effect of symbiotic, compared to dimethicone, on each outcome during follow-up using separate ordinal logistic models.

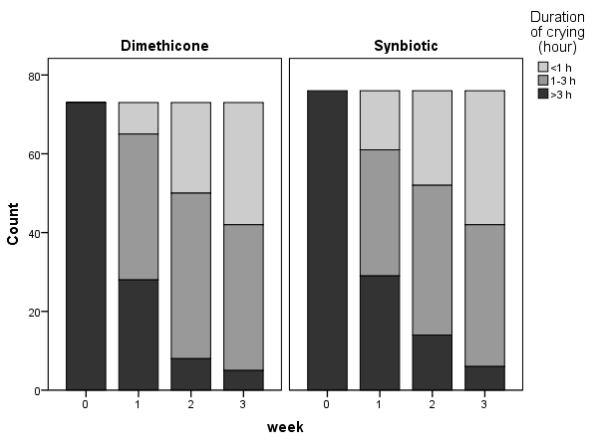
Regarding the non-significant interaction effect of trial groups and time of follow-up, there was no significant difference between the two groups regarding the pattern of decreasing in crying duration (Model 1). Therefore, according to the results of Model 2, crying duration decreased significantly within three weeks following the intervention in both groups (β=-0.84, 95% CI:-1.02, -0.67); however, the effect of symbiotic was not significantly superior to dimethicone (β=-0.03, 95% CI: -0.53, 0.48).

The number of crying also decreased significantly within three weeks following the intervention in both groups (β=-0.74, 95% CI: -1.02, -0.47) (Model 2). In addition, the

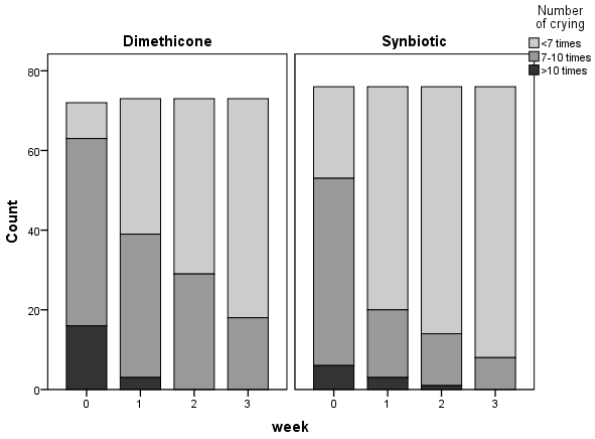
Table 1. Baseline characteristics

		Dimethicone (n=73)	Symbiotic (n=76)	Total	P-value¶
Gender	Female	34 (46.6)	35 (46.1)	69 (46.3)	0.949
	Male	39 (53.4)	41 (53.9)	80 (53.7)	
Feeding type	Exclusive breastfeeding	59 (80.8)	62 (81.6)	120 (81.1)	0.912
	Almost exclusive breastfeeding	8 (11)	9 (11.8)	17 (11.5)	
	High mixed	6 (8.2)	5 (6.6)	11 (7.4)	
Duration of crying (hour)	< 1 h	-	-	-	-
	1-3 h	-	-	-	
	>3 h	73 (100.0)	76 (100.0)	149 (100.0)	
Number of crying	<7 times	9 (12.3)	23 (30.3)	32 (21.5)	0.005
	7-10 times	48 (65.7)	47 (61.8)	95 (63.7)	
	>10 times	16 (22)	6 (7.9)	22 (14.8)	
Sleep duration (hour)	<10 h	12 (16.4)	15 (19.7)	27 (18.1)	0.556
	10-16 h	57 (78.1)	54 (71.1)	111 (74.5)	
	>16 h	4 (5.5)	7 (9.2)	11 (7.4)	
Numbers of defecation per day	<3 times	5 (6.8)	9 (11.8)	14 (9.4)	0.250
	3-5 times	28 (38.4)	42 (55.3)	70 (47.0)	
	>5 times	40 (54.8)	25 (32.9)	65 (43.6)	

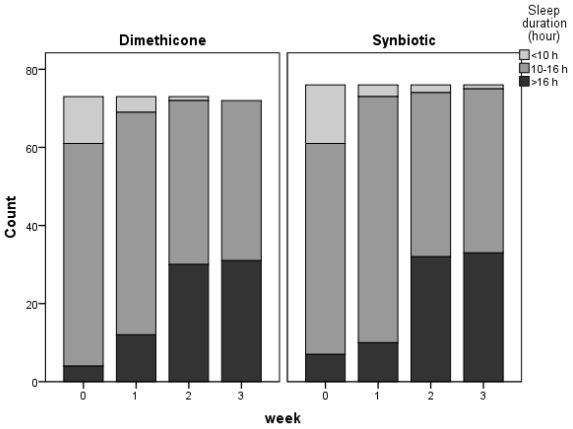
Entries are number (%). ¶ Pearson's chi-square test



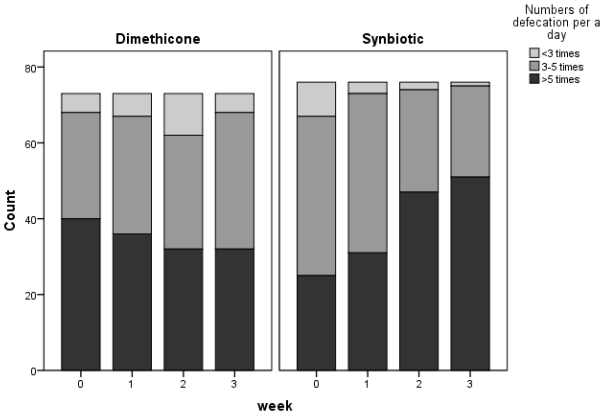
a. Duration of crying (hour)



b. Number of crying (hour)



c. Sleep duration (hour)



d. Numbers of defecation per day

Figure 1. Frequency of different levels of crying duration (a), number of crying (b), sleep duration (c), and number of defecation per day (d) at baseline and each week after the intervention in symbiotic and dimethicone groups.

Table 2. Effect of symbiotic, compared to dimethicone, on crying duration, number of crying, sleep duration, and number of defecation per day

	Model 1				Model 2			
	β	SE	95% CI	P-value	β	SE	95% CI	P-value
Crying duration								
Group (Ref: Dimethicone)	-0.19	0.43	(-1.03 , 0.65)	0.655	-0.03	0.26	(-0.53 , 0.48)	0.919
Week	-0.89	0.13	(-1.14 , -0.63)	<0.001	-0.84	0.09	(-1.02 , -0.67)	<0.001
Group*Week	0.08	0.17	(-0.24 , 0.41)	0.619				
Number of crying								
Group (Ref: Dimethicone)	-0.81	0.56	(-1.91 , 0.28)	0.145	-0.64	0.33	(-1.28 , 0.01)	0.052
Week	-0.78	0.18	(-1.14 , -0.43)	<0.001	-0.74	0.14	(-1.02 , -0.47)	0.00
Group*Week	0.10	0.28	(-0.45 , 0.65)	0.729				
Sleep duration								
Group (Ref: Dimethicone)	-0.20	0.48	(-1.15 , 0.74)	0.675	-0.05	0.27	(-0.57 , 0.47)	0.849
Week	0.73	0.15	(0.44 , 1.02)	<0.001	0.77	0.11	(0.55 , 0.98)	<0.001
Group*Week	0.07	0.21	(-0.34 , 0.49)	0.731				
Number of defecation								
Group (Ref: Dimethicone)	-0.43	0.45	(-1.32 , 0.46)	0.343	0.83	0.25	(0.33 , 1.33)	0.001
Week	-0.09	0.15	(-0.39 , 0.21)	0.568	0.23	0.10	(0.02 , 0.43)	0.029
Group*Week	0.64	0.20	(0.24 , 1.04)	0.002				

Ref: reference category. Model 1: ordinal logistic regression adjusted for baseline value and interaction effect of trial group and follow-up week, Model 2: ordinal logistic regression only adjusted for baseline values.

symbiotic treatment led to a more reduction in the number of crying, compared to dimethicone (β=-0.64, 95% CI: -1.28, 0.01; P=0.052) (marginally significant).

Regarding the non-significant interaction effect of follow-up weeks and intervention groups, variations of sleep duration were not significantly different between the two groups (model 1). According to the results of Model 2, sleep duration increased significantly within three weeks following the intervention in both groups (β=0.77, 95% CI: 0.55-0.98), and the effects of dimethicone and symbiotic were not significantly different (β=-0.05, 95% CI: -0.57, 0.47). Furthermore, the number of defecation per day varied differently in the dimethicone and symbiotic groups (interaction of week and group: P<0.05, Model 1). Although the number of defecation was stable during the study period in the dimethicone group (β=-0.09, 95% CI: -0.39, 0.21), it was increased significantly in the symbiotic group within the second (β=0.86, 95% CI: 0.35, 1.37) and third weeks (β=1.50, 95% CI: 0.81, 2.19) after the intervention (Model 1).

Discussion

The current study was conducted to compare the efficiency of symbiotic (a remedy that has recently gained considerable attention) versus dimethicone (an agent abundantly used for the treatment of IC in the literature) on the IC treatment (12). The study participants were not statistically different regarding gender distribution, breastfeeding status, and duration of daily crying. This similarity showed that probable confounding variables affecting the outcomes of the interventions were eliminated in this study. The evaluation results of the efficiency of symbiotic showed successful outcomes regarding colic symptoms rehabilitation and improved quality of sleep. Mentioned findings were also achieved by dimethicone. Comparison of the interventions showed that symbiotic was neither superior nor inferior to dimethicone in terms of IC symptoms and quality of life but for the numbers of defecation per day that was considerably higher among those under symbiotic treatment.

The use of methylpolysiloxane, dimethicone, and simethicone, has a great history for IC treatment since four decades ago. As mentioned above, one of the theories about the etiology of IC was gastrointestinal wall tension due to excessive gas production. In this term, methylpolysiloxane derivates were considered to reduce produced gas in the gastrointestinal tract leading to fewer IC symptoms (13). Further comparative studies went on to assess the efficiency of dimethicone in IC, and although most of them presented satisfactory effects of dimethicone/simethicone on the IC symptoms control (especially crying), dimethicone comparison with placebo revealed no significant superiority of this agent (8, 14, 15). A study was conducted by Wiberg et al. to assess the efficiency of short-term spinal manipulation in exclusive breastfed infants resenting from IC. They compared their outcomes with dimethicone and found that spinal manipulation was as successful in IC symptoms control as dimethicone; however, their comparison showed the superiority of spinal manipulation on the first days while this superiority diminished by time (16).

Another theory about the etiology of IC has been attributed to the intestinal microflora that posed scientists to perform studies assessing the amount of gut microbiota. These evaluations revealed fewer colony counts of lactobacilli in the intestinal tract of colicky infants, compared to normal ones. Following that, the ideas about the efficacy of probiotics for the treatment of IC were ignited (17, 18). Savino et al. conducted a comparative study assessing the use of probiotics containing Lactobacillus reuteri on the IC improvement and compared their outcomes with simethicone. The probiotics were superior to simethicone regarding earlier colic attack rehabilitation (19). Other studies assessing probiotics containing Lactobacillus reuteri on IC presented well tolerability of this agent by colicky infants. In addition to satisfactory symptoms control, they presented the superiority of probiotics to whether placebo or simethicone (11, 20). Therefore a theory has been raised that intestinal microbiota change following Lactobacillus reuteri use has led to colic attack improvement (11).

Prebiotics have been scarcely considered for the IC treatment with diverse and also controversial outcomes. While no benefit of prebiotic use for the IC treatment was presented by Ben et al.(21), another study revealed well tolerability, reduced crying time, intestinal microbiota improvement, and promoted intestinal immune cell interactions as the advantages of prebiotics for the IC treatment (22). What mentioned above deviated the thoughts toward symbiotic use for the treatment of IC since prebiotics can pose better survival of probiotics bacteria and host endogenous immune cells activation (23). The latter (endogenous immune

response modulation) seems to effectively reduce food hypersensitivity as well (11, 24).

Mugambi et al. performed a study in 2012 to assess the effectiveness of symbiotic on diverse entities, including restlessness, colic frequency, crying duration, and colic incidence. They eventually presented no benefit of this agent on their assessed colicky infants (25). On the other hand, Kianifar et al. compared the symbiotic with placebo and showed significant superiority of symbiotic as they presented even up to 90% of reduction in daily crying time of their study participants (1). The efficiency of symbiotic in the IC treatment was also confirmed by Vandenplas et al. (26). A point about the efficacy of symbiotic, notified by authors, is about the contents of prebiotic and probiotics that may notably affect symbiotic effectiveness in colic. Other factors that should be considered for the study interpretation and also generalization are ethnicity, treatment duration, and dosage of treatments (27, 28). Therefore, further studies in different ethnicities comparing different strains are strongly recommended.

Regarding the strengths of the current study, one can refer to the comparison of symbiotic with dimethicone (an old agent abundantly used for IC) and the assessment of factors, such as sleep duration and defecation that rarely has been evaluated previously among colicky infants.

Conclusion

The findings of the current study presented that dimethicone and symbiotic could successfully improve IC symptoms regarding crying times, as well as the duration and sleeping time per day. However, the comparison of these two remedies for IC treatment revealed no significant differences.

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Conflicts of interest

There are no conflicts of interest.

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