

Nutritional intervention in infantile colic: mini review

Abstract

Background: Infantile colic is a severe irritable or crying which bothers babies and parents. The etiology of infantile colic is not known until now and nutritional intervention is often used as a treatment for colic symptom.

Objective: To determine the role of nutrition in the management of infantile colics.

Method: This review article on infantile colic used several electronic databases such as Google, Pubmed, Ebscohost, American Academy of Pediatrics Publications and Cochrane databases

Results: Three studies of infantile colic on breast-fed infants and six studies of infantile colic on infants who consumed formula milk were found.

Conclusion: Low-allergen diet consumption in mothers who breast-fed infants or infants who consumed extensive hydrolyzed casein-based formula can improve symptom of infantile colic. There is no strong evidence for now to recommend the use of soy protein-based formulas and low-lactose formula as the management of infantile colic in infants.

Keywords: infantile colic, nutritional intervention.

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Introduction

Infantile colic is a symptomatic disorder characterized by paroxysms of fussing, agitation or crying, lasting more than three hours a day and occurring more than three days a week for at least three weeks.¹ In addition to this definition, diagnostic criteria of Rome III for functional gastrointestinal disorder defines infantile colic as a condition that includes all of the following symptoms in infants aged less than 4months, such as (1) paroxysms of irritability, fussing or crying that start and stop without obvious cause, (2) episodes lasting for three or more hours per day and occurring at least three days per week for at least one week, and (3) there is no failure to thrive.² The main symptoms are excessive and persistent crying which tend to occur at night. During each episodes, the child appears distress, irritable, fussy, becomes red faces, contracted legs, and frequent borborygmi.³ This condition occurs in 10-40% of infants worldwide and peaks at around 6weeks, then disappears by 3-6months. The incidence of infantile colic is similar in both male and female infants. There are also no relationships between infantile colic and feeding types (breast-fed or formula), gestational age, or socioeconomic status. The definite cause of infantile colic is unknown. Several causes of infantile colic have been proposed such as microfloral changes in faecal content, cow's milk or lactose intolerance, gastrointestinal immaturity or inflammation, increased serotonin secretion, inappropriate breast-feeding techniques, and maternal smoking or nicotine replacement therapy.⁴

Infantile colic is a diagnosis of exclusion; established only after careful history and physical examination have excluded some dangerous causes including morbus hirschprung, incarcerated hernia, testicular torsion, child abuse, gastroesophageal reflux disease, pyloric stenosis, anal fissures, etc. Parental support and reassurance are key components of colic management.⁴ Various studies have

analyzed the management of infantile colic with mixed results. These include: (1) probiotic *Lactobacillus reuteri* (strain DSM 17938), drugs such as simethicone, dicyclomine, and proton pump inhibitors, (3) dietary modification, (4) physical therapy including chiropractic and osteopathic manipulation, massage, and acupuncture, (5) herbal therapy including *Mentha piperita* (peppermint) and various other herbal teas such as fennel, chamomile, vervain, lemon balm, and licorice, and (6) other modalities including 12% sucrose solution, "Gripe water" which consists of dill seed oil, bicarbonate, and hydrogenated glucose, the use of a vented bottle or swaddling.⁴ This review only discusses the role of nutrition in the management of infantile colic.

Methods

This review used Google, Pubmed, Ebscohost, American Academy of Pediatrics Publications and Cochrane databases with infant and colic as the keywords. The inclusion criteria in this review were studies which involved infant as the subject's research and had been published during 1980 - 2016. The studies included in this review were studies that met the inclusion criteria and focuses only on infants who were breast-fed and infants receiving hydrolyzed protein-based formula, soy protein-based formula, and low-lactose formula.

Results

There were 3 studies on infants with infantile colic who were breast-fed and 6 studies on infants with infantile colic who received formula milk (Table 1) (Table 2). Studies on nutritional intervention as the management of infantile colic in breast-fed infants showed various results (Table 1). Jakobsson et al.⁵ Hill et al.⁶ and Hill et al.⁷ showed that there were improvements of colic symptoms in breast-fed infants if mother avoided cow's milk, eggs, peanuts, wheat,

soy, and fish in their diet (low-allergen diet). Several studies which used infant formula as nutritional intervention in infants suffering from infantile colic also gave varying results (Table 2). Studies by Lothe et al.⁸ Lothe et al.⁹ Lucassen et al.¹⁰ and Savino et al.¹¹ that used hydrolyzed casein-based formula (Nutramigen) or hydrolyzed whey-based formula showed improvements of colic symptoms and crying duration. However, the administration of capsules containing whey powder extracted from cow's milk caused colic symptoms

to reappear in 75% of infants who showed improvement of colic symptoms after consumption of hydrolyzed casein-based formula (Nutramigen).⁹ Consumption of soy protein-based formula either resulted in improvement of colic symptoms in 18% of infants with colics⁸ or reduced duration of colic symptoms,¹² whereas Infante et al.¹³ showed in their study improvement in excessive gas production, abnormal feeding pattern, and crying duration in infants with colics who received low lactose-based formula for 15 days.

Table 1 Studies on the effect of diet in breast-fed infants

Researchers	Sample	Study Design	Interventions	Results	NNT
Jakobsson et al. ⁵	66 breast-fed infants with infantile colic	Randomized, double-blind, crossover trial	<p>I. Step I: mothers eliminated cow's milk for 1 week. Then, cow's milk were reintroduced in their diet twice.</p> <p>II. Step II: subjects whose colic symptoms disappeared on elimination of cow's milk and reappeared on mother's milk challenges, the mothers were asked to participate in a randomized double-blind crossover trial using gelatinous capsules filled with either cow's milk whey protein or potato starch powder. Twelve capsules were taken by the mothers per day based on a scheme: three capsules four times a day. The amount of whey protein in those capsules corresponded to the amount of whey in about 320 mL of cow's milk. The capsules were taken on day 1 and day 3. After the additional two days, the mothers were asked to drink one half to one glass of milk three times daily</p>	<p>I. The elimination of cow's milk from the mother's diet resulted in the colic disappearance in 35 infants (53%).</p> <p>II. Colic symptoms reappeared after reintroduction of cow's milk into the mother's diet in 23 out of 35 infants (35%).</p> <p>III. A randomized double-blind crossover trial was done in 10 infants. Colic symptoms reappeared in 9 out of 10 infants after their mothers ingested the capsules containing cow's milk whey protein and also when the mothers were drinking milk directly afterwards.</p>	2.9
Hill et al. ⁶	38 bottle-fed and 77 breast-fed colicky infants	Randomized, double-blind, placebo-controlled trial	<p>I. All mothers of breast-fed infants were started on an artificial color-free, preservative-free, additive-free diet and also randomized to an active low allergen diet (milk-, egg-, wheat-, nut-free) or a control diet.</p> <p>II. Bottle-fed infants were randomized into either hydrolyzed casein-based formula group or cow's milk formula group.</p>		5.4

Table Continued...

Researchers	Sample	Study Design	Interventions	Results	NNT
Hill et al. ⁷	90 exclusively breast-fed infants presenting with colic	Randomized, controlled trial	<p>I. Mothers in the intervention group (low-allergen diet) excluded cow's milk, eggs, peanuts, tree nuts, wheat, soy, and fish from their diet.</p> <p>II. Mothers in the control group continued to consume these foods.</p>	<p>I. After interventions were done for one week, there were significantly more responders in the low-allergen group compared to control group (74% vs 37%), and absolute risk reduction of 37% (95 confidence interval: 18-56%).</p> <p>II. Cry/fuss duration per 48 hours was reduced by a substantially greater amount in the low-allergen diet group with an average reduction of 21% (95% confidence interval: 3-37%).</p>	2.7

Note NNT, Number Needed to Treat

Table 2 Studies on the effect of diet in infants who received formula milk

Researchers	Sample	Study design	Interventions	Results	NNT
Hypoallergenic formula					
Lothe et al. ⁸	60 colicky infants	Double-blind study	<p>I. 60 colicky infants were given a cow's milk- and soy-based formula</p> <p>II. Hydrolyzed casein-based formula were given to infants whose symptoms were unchanged or worse when they were fed cow's milk- and soy-based formula.</p> <p>III. Challenges with cow's milk-based formula were at approximately 3, 6 and 12 months of age.</p>	<p>I. Eleven infants (18%) were free of symptoms while receiving soy-based formula</p> <p>II. Symptoms of 32 (53%) infants were unchanged or worse when they were fed cow's milk- and soy-based formula, but symptoms disappeared when they were fed hydrolyzed casein-based formula (Nutramigen).</p> <p>III. Symptoms of 17 (29%) infants were not related to the diet, so these infants continued to consume cow's milk-based formula.</p> <p>IV. Challenges with cow's milk-based formula at 3, 6, and 12 months of age caused infantile colic symptoms in 22 (36%), 11 (18%), and 8 (13%).</p>	3.5

Table Continued...

Researchers	Sample	Study design	Interventions	Results	NNT
Hypoallergenic formula					
Lothe et al. ⁹	27 infants with severe colic	Double-blind crossover study	<p>I. All infants were given hydrolyzed casein-based formula (Nutramigen).</p> <p>II. Infants whose colic symptoms disappeared after receiving hydrolyzed casein-based formula (Nutramigen) were given one identical capsule and mixed it into the bottle of Nutramigen (capsule A) at each meal five times a day on the sixth day. For the second challenge, the same procedure was performed with capsule B on the tenth day</p> <p>III. Capsule A contained 135 mg of bovine whey protein powder containing 90 mg of whey protein, 26 mg of carbohydrates, 2 mg of fat, electrolytes, and minerals. Capsule B contained 135 mg of human albumin powder used as placebo. Nutramigen was added to a weight of 200 mg to each capsule.</p> <p>IV. The amount of whey protein in five capsules corresponded to the amount in about 70 mL of whole cow's milk</p>	<p>I. 24 out of 27 infants who received hydrolyzed casein-based formula had the reduced symptoms of crying, gas-formation, hiccup, and disturbed sleep compared to cow's milk-based formula ($p < 0.001$).</p> <p>II. 18 infants receiving the whey protein-containing capsules reacted with colic, 2 infants receiving placebo reacted with colic ($p < 0.001$), and 4 infants did not react at all</p> <p>III. Crying hours per day for the 24 infants receiving cow's milk-based protein and hydrolyzed casein-based formula were 5.6 hours and 0.7 hours ($p < 0.001$).</p> <p>IV. Crying hours per day for the infants receiving whey protein capsules and placebo were 3.2 hours and 1.0 hour ($p < 0.001$)</p> <p>II. Around 5 out of 43 infants were withdrawn during the intervention week because of less data.</p>	1.8
Lucassen et al. ¹⁰	43 healthy, formula-fed infants aged <6 months old with infantile colic	Randomized, double-blind, parallel trial	<p>I. 20 infants were fed hydrolyzed whey-based formula and 18 infants were fed cow's milk-based formula.</p>	<p>III. After adjusted for the confounders in 38 infants, such as infant's gender and the duration of crying during the qualification period, the difference of the decrease in crying time between hydrolyzed whey-based protein and cow's milk-based protein was 47 minutes/day ($p = 0.04$)</p>	8.2*

Table Continued..

Researchers	Sample	Study design	Interventions	Results	NNT
Hypoallergenic formula					
Savino et al. ¹¹	267 formula-fed infants, aged <4 months old with infantile colic	Prospective randomized controlled trial	<p>I. Intervention group received new formula containing partially hydrolyzed formula supplemented with fructo- and galacto-oligosaccharides and high palmitic acid for 14 days.</p> <p>II. Control group received standar formula and 6 mg/kg of simethicone twice daily.</p>	<p>I. Out of the 199 infants who completed the study, 96 infants were treated with the new formula and 103 infants were not treated.</p> <p>II. On day 7, infants receiving the new formula had a significant decrease in colic episodes (2.47 ± 1.94 at day 7 vs 5.99 ± 1.84 at the study entry) compared to infants receiving the standard formula (3.72 ± 1.98 at day 7 vs 5.41 ± 1.88 at the study entry) ($p < 0.0001$).</p> <p>III. On day 14, the crying episodes were clinically different between the two groups of infants (1.76 ± 1.60 in intervention group vs 3.32 ± 2.06 in control group) ($p < 0.0001$).</p>	CC
Soy protein-based formula					
Campbell ¹²	19 infants with infantile colic	Randomized, double-blind, crossover trial	10 infants were given soya milk for one week followed by standard modified cow's milk formula in the following week, and 9 infants had standard milk followed by soya milk	<p>I. The duration of colic symptoms was significantly reduced during the week on soya milk ($p < 0.01$).</p> <p>II. Out of 19 infants with colic symptoms who received intervention; 11 (58%) infants had intolerance of cow's milk, 2 (11%) infants had intolerance of cow's milk and soya milk, 5 (26%) infants had spontaneous resolved symptoms, and 1 (5%) infants had failure of dietary treatment</p>	CC

Table Continued..

Researchers	Sample	Study design	Interventions	Results	NNT
Low-lactose formula					
Infante et al. ¹³	20 colicky infants	Non-randomized, non-placebo-controlled study	All infants received an adapted low-lactose formula (Novalac AC) for 15 days	<p>I. Symptoms of excessive gas, abnormal feeding, duration of crying for 1-3 hours/day and >3 hours/day at inclusion were found in 17 (85%), 15 (75%), 13 (65%), and 7 (35%) infants.</p> <p>II. Intervention significantly reduced each of the symptoms ($p < 0.01$). Symptoms of excessive gas, abnormal feeding, duration of crying for 1-3 hours/day and >3 hours/day after intervention were found in 5 (25%), 6 (30%), 3 (15%), and 0 (0%) infants.</p> <p>III. Approximately 4 out of 5 patients who still had symptoms of excessive gas were crying for < 1 hour/day.</p> <p>IV. The level of hydrogen expired in hydrogen breath test decreased from 35 ± 3.1 ppm at inclusion to 10 ± 2.5 ppm ($p < 0.01$)</p>	CC

NNT, Number Needed to Treat; *, Calculation Used Secondary Outcomes; CC, Can't be Calculated because Data were in Numerical Form

Discussion

Dietary modification is one of the most frequently used management strategies of infantile colic. Infants should be exclusively breast-fed for the first six months of life to achieve optimal growth, development, and health. In situations where infants can't suckle, expressed breast milk (mother own milk) or donor milk that meet safety requirement can be considered.^{14,15} If breast milk is not available, infants may be given formula milk which fulfills the Codex Alimentarius regulation with proper preparation of formula milk.¹⁴

The pathogenesis of infantile colic remains partly unknown. Several main factors are considered to cause colic symptoms, such as immaturity of nervous/digestive system, cow's milk proteins allergy and atopy, altered gut microflora such low Lactobacilli or increased *E. Coli*, and gut hormones such as increased ghrelin and motilin.¹⁶ From (Table 1) (Table 2), the colic symptoms improved in breast-fed infants whose mothers consumed low-allergen diet (free of cow's milk, eggs, wheat, and nuts), and infants who received hydrolyzed casein/whey-based formula. This suggests that infantile colic can be triggered by food allergies, such as cow's milk allergy. The possible relationship between food allergy and infantile colic is based on two evidences, (1) the presence of dysmotility with visceral neuronal hypersensitivity and dysbiosis, and (2) the clinical response to dietary intervention. Although the etiology of infantile colic remains controversial, dysmotility and gut neuronal hyperexcitability have been advocated as pivotal pathogenetic factors. Food allergy induces gut neuronal hyperexcitability which lead to altered perception of physiological stimuli, such as intestinal distention and peristalsis, being perceived as painful events.¹⁷

Hypoallergenic maternal diet may be suggested in breast-fed

infants. Meanwhile, partially hydrolyzed whey protein is the first line-approach and extensive hydrolyzed formula based on casein or whey could be useful in children with severe infantile colic or additional atopic symptoms.^{16,18,19} The use of hydrolyzed casein or whey-based formula led to the improvement of colic symptoms in infants, but Lothe et al.⁹ found that colic symptoms recurred in 75% of infants who received capsules containing whey protein powders extracted from cow's milk. This may be due to β -lactoglobulin which is the largest cow's milk allergen. In fact, β -lactoglobulin is the major component of whey protein in cow's milk, but it is not found in breast milk.²⁰ In the confusion of using partially or extensive hydrolyzed formula, American Academy of Pediatrics (AAP) stated that partially hydrolyzed formulas are not hypoallergenic and should not be used for the dietary management of colic due to cow's milk protein allergy.²¹ Therefore, we suggest that low allergen maternal diet is effective in breast-fed colicky infants and extensive hydrolyzed formula based on casein or whey are effective in formula-fed infants due to the possibility of cow's milk allergy as the cause of infantile colic. Because some infants may still have colic symptoms after the consumption of whey protein, extensive hydrolyzed casein-based formula is preferably to manage infantile colic in formula-fed infants.

Campbell¹² found that colic symptoms were significantly reduced during the consumption of soy protein-based formula, but only 5(17%) out of 19 subjects experienced spontaneous improvement. Cow's milk protein-based formula is the first choice for healthy and term infant who are not exclusively breast-fed,²² whereas soy protein-based formula is indicated for infants with galactosemia, congenital lactase deficiency, or conditions in which parents prefer the vegetarian diet.²³ European Society for Paediatric Gastroenterology Hepatology and Nutrition (EPSGHAN)²² and AAP²³ suggest that the use of soy

protein-based formula is not proven to prevent or manage infantile colic or fussiness in infants. Moreover, soy is an important allergen in infants because approximately 10–14% infants with cow's milk allergy will also have soy protein allergy.²³ In 2009, the Canadian Paediatric Society also stated that “physician should consider limiting the use of soy-based formulas to those infants with galactosemia or those who cannot consume dairy-based products for cultural or religious reasons.²⁴ The use of low-lactose formula in the study by Infante et al.¹³ caused a significant reduction in the number of infants with excessive gas production, abnormal feeding pattern, and duration of crying, due to the inadequate study design. In contrary, there was no evidence of but those results should be considered carefully effect on excessive crying of lowering the lactose content of the formula milk.^{25–27}

Conclusion

Various studies have shown that nutritional intervention is one of the managements which can reduce the symptoms of colics in infants. Breast-fed mothers are advised to consume low-allergen diet, such as free of cow's milk, eggs, wheat and nuts to reduce the symptoms of infantile colic. In the other hand, infants who consume formula milk should be best given extensive hydrolyzed casein-based formula because colic symptoms may still persist after the consumption of whey protein. The use of soy protein-based formula and low-lactose formula does not have a strong evidence to reduce infantile colic symptoms in infants.

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Conflict of interest

Author declares that there is no conflict of interest.

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