

## Dietary manipulations for infantile colic



Infantile colic is characterized by paroxysms of uncontrollable crying or fussing in an otherwise healthy and well-fed infant younger than three months of age with crying that lasts for more than 3 h per day and more than three days per week for at least three weeks (1). The condition can be profoundly disturbing to both the infant and the family (1). There is increasing evidence that bovine milk proteins may play a role in the pathogenesis of infantile colic and that removal of cow's milk from the infant's diet may reduce the symptoms of colic in a small percentage of infants (2-9). We reviewed the literature and want to share with our readers' the current information on the dietary management of infantile colic.

### HYPOALLERGENIC DIETS OF BREASTFEEDING MOTHERS

#### Literature review

Evans et al (10) found that avoidance of cow's milk by 20 mothers who were breastfeeding their infants did not reduce the rate of infantile colic in a double-blind, placebo-controlled crossover trial. However, the rates of colic were significantly higher on days on which mothers consumed chocolate or fruit, regardless of the groups to which they were randomly assigned. Because of the small sample size, this study was not sufficiently powered.

Jakobsson and Lindberg (11) reported that the removal of cow's milk from the breastfeeding mother's diet resulted in the disappearance of colic in 13 of 18 infants. However, this was not a double-blind study and involved a small sample size. In a subsequent study, the same authors put 66 mothers of 66 breastfed infants with infantile colic on a diet free of cow's milk (6). The colic disappeared in 35 infants, but it reappeared on at least two challenges after reintroduction of cow's milk into the maternal diet in 23 of the 35 infants. There was a family history of allergy in 12 of the infants. A randomized, double-blind crossover trial with cow's milk whey protein was performed in 16 of these 23 mothers and infants. Six infants had to be taken out of the study for various reasons. Of the remaining 10 infants, nine displayed signs of colic after their mothers had taken the whey-filled capsules. The lack of information regarding

crying times and the suggestion that colic 'completely' resolved when the mother was on a milk-free diet raise questions about the validity of the conclusions drawn from this study (12).

Hill et al (4) studied the effect of diet change in 38 bottle-fed and 77 breastfed colicky infants in a randomized, double-blind, placebo-controlled trial. Bottle-fed infants were assigned to either casein hydrolysate or cow's milk formula. All mothers of breastfed infants were started on an artificial colour-free, preservative-free and additive-free diet, and were randomly assigned to receive either an active low-allergen diet (milk-, egg-, wheat- and nut-free) or a control diet. In a combined analysis, the authors showed that infants on the active diet had distress reduced by 39% compared with 16% for those on the control diet. Although the authors claimed that their study was double-blind, the formulas had different tastes and the maternal diets had different levels of restriction.

#### Comment

The preliminary data suggest a correlation between infantile colic in breastfed infants and their mother's consumption of cow's milk and allergenic products (evidence level A). Use of hypoallergenic diets by breastfeeding mothers may help to reduce colicky symptoms in some infants.

### USE OF HYPOALLERGENIC FORMULAS IN BOTTLE-FED INFANTS

#### Literature review

In Hill et al's study (4), 38 infants were bottle-fed, but the authors did not specify how many of these infants were on the restricted diet. A stratified analysis of the data showed that children randomly assigned to receive the hypoallergenic formula had significantly greater improvements in clinical scores than did infants on the control diet (13).

One unblinded study showed that colic disappeared in 24 of 27 infants when they were given a hydrolysed casein formula (8). These 24 infants were entered into a randomized, double-blind, placebo-controlled crossover trial of whey protein. Eighteen infants receiving the whey protein

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capsules and two infants receiving placebo reacted with colic while four infants did not react at all.

In a randomized, double-blind, multiple-crossover trial (3), three changes of formulas were made. For each of the four-day periods, colicky infants alternately received a casein hydrolysate formula and a formula containing cow's milk. To introduce the effect of a washout period, only data from the last two days of each period were included in the analysis. With the first formula change, there was significantly less crying and colic in infants when they were fed the casein hydrolysate formula; with the second change, there was less colic when infants were fed the casein hydrolysate formula but not significantly less crying. By the third change, there were no significant differences between formulas. This study had a high dropout rate of 47%.

Jakobsson et al (7) studied the effectiveness of two extensively hydrolysed casein-based formulas in 22 infants with severe colic in a randomized, double-blind, placebo-controlled crossover fashion. One infant was considered as a treatment failure and six infants as protocol failures. The remaining 15 infants showed a significant decrease in the lengths of time they cried, as well as a decrease in the intensity of their crying on both formulas. When the infants were challenged in a double-blind design with capsules containing bovine milk powder, bovine whey protein concentrate or placebo, 11 infants reacted with an increase in crying time to bovine milk and bovine whey protein.

Lucassen et al (9) randomly selected 43 healthy infants with colic to receive whey hydrolysate formula or standard cow's milk formula in a double-blind, placebo-controlled trial. Thirty-eight infants completed the trial, of whom 20 were fed whey hydrolysate formula. These investigators found a decrease in the average duration of crying of 63 min per day in those infants fed with whey hydrolysate formula. Concerning the question of blinding, six parents indicated that they were possibly aware of the formula their infant had been fed, but only four parents correctly identified the formula as whey hydrolysate. Sensitivity analysis, removing these four infants from the analysis, revealed an adjusted effect of 58 min per day.

Estep and Kulczycki (2) studied six colicky infants using Barr-type infant behaviour diaries for three to six days on their current formula and then for five to 17 days on an amino acid-based formula (14). All infants tolerated the amino acid-based formula well and all improved, usually within one to two days. The total crying and fussing time was reduced by an average of 45%. After symptoms of colic had improved, these infants were challenged with oral doses of 75 mg of bovine immunoglobulin G, which resulted in increased crying and fussing behaviour. The drawbacks of this study were its small sample size and the lack of a control group or placebo intervention.

#### Comment

For bottle-fed infants, hypoallergenic formulas may have a beneficial effect in the management of some infants with colic (evidence level A).

### USE OF SOY-BASED FORMULAS IN BOTTLE-FED INFANTS

Iacono et al (5) put 70 cow's milk formula-fed infants with severe colic on a soymilk formula. In 50 infants, there was a remission of symptoms when cow's milk protein was eliminated from the diet. Two successive challenges caused the return of symptoms in all 50 infants. Follow-ups were conducted after a period that averaged 18 months. The results showed that 22 of 50 infants (44%) who had cow's milk protein-related colic and one of 20 infants (5%) with non-cow's milk protein-related colic developed an overt form of alimentary intolerance.

Lothe et al (15) reported that 11 of 60 hospitalized colicky infants receiving cow's milk responded to soy formula. The symptoms of 32 infants were unchanged or deteriorated when they were fed cow's milk and soy formula, but the symptoms disappeared when they were fed a casein hydrolysate formula. Of the 43 infants who responded to the exclusion of cow's milk, 11 infants showed other features of cow's milk allergy by the age of six months and five infants were still intolerant to cow's milk at 16 months of age. This study has been criticized because the patients were highly selected; the protocol was not truly double-blind because the two formulas can be distinguished by taste, smell and texture; there was a lack of suitable controls; and objective data of crying or fussing were not obtained (16).

In a randomized, double-blind, placebo-controlled crossover trial involving 19 colicky infants, Campbell (17) found that the mean weekly duration of colicky symptoms during treatment with soy formula was 8.5 h compared with 18.7 h during the control period. Again, this study was not truly double-blind because no attempt was made to render the two formulas indistinguishable from one another.

#### Comment

For bottle-fed infants, soy formulas may be effective in reducing the symptoms of infantile colic (evidence level B). However, the use of soy formulas in the treatment of infants with colic should be avoided because soy protein is an important allergen in infancy (evidence level A) (1,8,13,18-20).

### USE OF LOW LACTOSE FORMULAS IN BOTTLE-FED INFANTS

#### Literature review

In a double-blind, placebo-controlled crossover study, 10 infants with infantile colic were fed breast milk and cow's milk formula, untreated and treated with lactase (21). The study found no evidence that low lactose milk reduced the daily duration and severity of colic.

In another double-blind, placebo-controlled crossover trial, 12 infants were given either lactase or placebo within 5 min of breastfeeding (22). In the study, lactase had no significant effect on the duration of crying and fussing.

In a third double-blind, placebo-controlled crossover trial, 13 infants were randomly assigned to have lactase or placebo added to their formula for one week, followed by a

two-day 'washout' (23). The addition to the formula was changed for the second week so that subjects served as their own control. The study found that lactase-treated formula reduced crying time by 1.14 h per day.

#### Comment

Congenital lactase deficiency is exceedingly rare and there is no solid evidence that low lactose formulas are an effective therapy for infantile colic.

### USE OF FIBRE-ENRICHED FORMULAS IN BOTTLE-FED INFANTS

#### Literature review

In one study, 27 colicky infants were randomly assigned in nine-day periods to a sequence of placebo (soy formula) followed by fibre-supplemented formula (soy formula plus soy polysaccharide) or the reverse (24). There was no significant difference in time spent crying or in time spent crying plus fussing among the 27 infants while they were consuming the fibre-supplemented formula compared with placebo.

#### Comment

There is no evidence that fibre-enriched formulas are effective for infantile colic.

### CONCLUDING REMARKS

Dietary modification is a treatment option for the management of some patients with infantile colic (25). Bovine milk proteins can elicit symptoms of infantile colic in certain infants (2-9). Studies have shown that removal of cow's milk from the infant's diet may result in a significant reduction of the symptoms of colic in a certain percentage of infants (evidence level A) (2,5,8,9). It is probable, though not proven, that atopic infants with severe colic would benefit most from the elimination of cow's milk (evidence level C) (5,26). It has been suggested that mothers who breastfeed their infants should, with appropriate nutritional support, consider eliminating cow's milk from the diet and avoid potentially allergenic substances such as caffeine, chocolate, eggs and nuts (4,6,18). If breastfeeding is not possible, the use of a hypoallergenic formula should be considered (2,7,9,12,13,18,25). The use of soy formulas in the treatment of infantile colic should be avoided because soy protein is an important allergen in infancy (1,8,13,18-20). There is no evidence that low lactose milk formulas and fibre-enriched milk formulas are effective cow's milk formula substitutes.

The literature on colic is very susceptible to observer bias. We are dealing with a condition that universally improves over time. There is a huge placebo effect and a 'tincture of time' effect resulting from any intervention. Therefore, it is very risky to draw conclusions unless studies are rigorously controlled and outcomes are determined by blinded observers. There is also a decided 'publication bias' for studies that show an effect of intervention and discount the many studies that show 'no effect'. Studies rarely stratify populations into children prone or not prone to atopy and

often reflect the referral bias of the particular institution or country. Moreover, there can be nutritional, monetary and attitudinal consequences derived from the recommendation of maternal exclusion diets or the use of 'hypoallergenic' formulas in a large percentage of the population.

Most of the studies have, so far, involved a small sample size, and some of the studies have methodological flaws. It is hoped that future well-designed, large-scale, randomized, double-blind, placebo-controlled studies will provide more information in this area. A well-designed study should include the use of a common case definition, objective outcome measures, appropriate washout times in crossover trials, adequate blinding and repeated blind challenges of the proposed intervention to account for spontaneous resolution with increasing age (12,13). Until results from such trials are available, no unequivocal recommendation can be made. In the meantime, temporary dietary modification should be considered for infants with severe colic, especially for those with atopic features or a strong family history of atopy (25). Periodic challenges at monthly intervals are used to ensure that the improvement is related to dietary modification and not a result of natural resolution.

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The recommendations in this statement do not indicate an exclusive course of treatment or procedure to be followed. Variations, taking into account individual circumstances, may be appropriate.