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Infantile colic: Is there a role for dietary interventions?

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Infantile colic is a behavioural syndrome of early childhood that is associated with irritability and crying. It self-resolves, but may lead to significant parental strife. The etiology is unknown; however, several investigators have examined the effect of nutrition on infantile colic. For the majority of infants, nutritional interventions appear to have no benefit on infantile colic. However, a minority of infants may display symptoms of infantile colic secondary to a cow's milk protein allergy. In these cases, a maternal hypoallergenic diet for breastfed infants and an extensively hydrolyzed formula for bottle-fed infants may result in resolution of colic. There is no proven role for the use of soy-based formulas or of lactase therapy in the management of infantile colic, and these interventions are not recommended. Currently, there are insufficient data to make a recommendation on the effect of probiotics for infantile colic. In all cases of infantile colic, it is important to ensure that there is sufficient parental support available.

Key Words: *Infantile colic; Nutrition*

The Rome III criteria for functional gastrointestinal disorders defines infantile colic as including all of the following in infants younger than four months of age (1):

- paroxysms of irritability, fussiness or crying that start and stop without obvious cause;
- episodes lasting 3 h or more per day and occurring at least three days per week for at least one week; and
- no failure to thrive.

While the etiologies of infantile colic are unknown, health care professionals often attempt dietary interventions. The present article updates the previous Canadian Paediatric Society practice point concerning the role of dietary modifications for infantile colic.

HYPOALLERGENIC DIETS IN BREASTFEEDING MOTHERS

In a survey, Clifford et al (2) found no association between the prevalence of colic and the source of nutrition (breastmilk or formula). Furthermore, in a crossover trial (3), exclusion of cow's milk by 20 breastfeeding mothers did not reduce colic.

However, in an unblinded study (4), exclusion of cow's milk from the breastfeeding mother's diet resulted in the disappearance of colic in 13 of 18 infants. In a subsequent study (5), 66 breastfeeding mothers of colic infants were given a cow's milk-free diet. Colic disappeared in 35 infants, but reappeared in 23 following the reintroduction of cow's milk into the maternal diet. A randomized,

Les coliques du nourrisson : les interventions alimentaires ont-elles un rôle à jouer?

Les coliques du nourrisson sont un syndrome comportemental de la première enfance qui s'associent à l'irritabilité et aux pleurs. Elles sont spontanément résolutive, mais peuvent entraîner d'importantes dissensions parentales. Même si on n'en connaît pas l'étiologie, plusieurs chercheurs ont examiné l'effet de l'alimentation sur les coliques du nourrisson. Pour la majorité des nourrissons, les interventions alimentaires semblent ne rien changer aux coliques. Cependant, une minorité d'entre eux peuvent présenter des symptômes de coliques secondaires à une allergie aux protéines du lait de vache. Dans de tels cas, un régime hypoallergène pour la mère si le nourrisson est allaité et une préparation fortement hydrolysée si le nourrisson est nourri au biberon peuvent résoudre les coliques. Le rôle des préparations à base de soja ou du traitement par lactase n'est pas démontré pour la prise en charge des coliques du nourrisson, et ces interventions ne sont pas recommandées. Pour l'instant, les données sont insuffisantes pour formuler une recommandation sur l'effet des probiotiques sur les coliques du nourrisson. Dans tous les cas de coliques du nourrisson, il est important de s'assurer d'un soutien parental suffisant.

double-blind crossover trial (5) of cow's milk whey protein was conducted on 16 of these 23 mother-infant pairs. Of the 10 infants analyzed, nine exhibited colic following maternal ingestion of whey. The loss of six infants from the analysis and no report of crying times weakened the study (6).

Hill et al (7) studied the effect of diet change in 38 bottle-fed and 77 breastfed colic infants. Bottle-fed infants were randomly assigned to receive either a casein hydrolysate or standard formula. Breastfeeding mothers were randomly assigned to receive either a low-allergen diet (milk, egg, wheat and nut free) or an unrestricted diet. In a combined analysis, distress was reduced by 39% and 16% in infants receiving the hypoallergenic and control diets, respectively.

Another randomized, controlled trial (8) assessed the effect of maternal dietary elimination (dairy, soy, wheat, eggs, peanuts, tree nuts and fish) in 90 exclusively breastfed infants with colic. After one week, there were significantly more responders (reduction of 25% or greater in crying/fussiness duration) in the low-allergen group (74% versus 37%), for an absolute risk reduction of 37% (95% CI 18% to 56%).

Comment

Some studies have demonstrated a reduction in colic when breastfeeding mothers consumed a hypoallergenic diet, although there is conflicting evidence. Maternal consumption of a hypoallergenic diet may reduce colic in a small number of infants.

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HYPOALLERGENIC FORMULAS (EXTENSIVELY HYDROLYZED CASEIN/WHEY PROTEIN, AND AMINO ACID BASED) IN BOTTLE-FED INFANTS

Twenty-four colic infants who improved on an extensively hydrolyzed casein formula were randomly assigned to a double-blinded, placebo-controlled crossover trial of whey protein (9). Eighteen infants receiving whey protein and two infants receiving placebo reacted with colic. Four did not react to either intervention.

In a randomized, double-blinded multiple-crossover trial (10), colic infants alternately received a casein hydrolysate or a standard formula over four-day periods. With the first formula change, there was significantly less crying and colic associated with the casein hydrolysate formula. With the second change, there was less colic associated with the casein hydrolysate formula but not significantly less crying. By the third change, there were no significant differences between formulas. This study had a dropout rate of 47%, and an intention-to-treat analysis was not performed.

Jakobsson et al (11) randomly assigned 22 colic infants to one of two extensively hydrolyzed casein-based formulas. Fifteen infants completed the trial; all experienced a significant decrease in crying duration and intensity. Furthermore, 11 reacted with increased crying time when challenged with bovine milk and whey protein.

Lucassen et al (12) randomly assigned 43 colic infants to either an extensively hydrolyzed whey or standard formula. The hydrolysate formula was associated with a 63 min/day decrease in crying time.

In an uncontrolled study, Estep and Kulczycki (13) fed six colic infants an amino acid formula. All infants improved, with total crying and fussing time being reduced by 45%. Furthermore, all infants displayed increased colic behaviour when challenged with bovine immunoglobulin G.

Comment

Extensively hydrolyzed protein formulas may reduce colic in a small number of bottle-fed infants. Of note, partially hydrolyzed formulas are not hypoallergenic (14) and should not be used for the dietary management of colic due to cow's milk protein allergy.

SOY-BASED FORMULAS IN BOTTLE-FED INFANTS

Remission of symptoms was achieved in 50 of 70 (71%) cow's milk formula-fed colic infants who were fed a soy milk formula (15). All 50 infants redeveloped symptoms on two successive unblinded challenges.

Eleven of 60 hospitalized colic infants receiving cow's milk improved when fed a soy formula (16). Symptoms did not improve in 32 infants when fed a soy formula, but did disappear when infants were fed a casein hydrolysate formula. Of the 43 infants who responded to the exclusion of cow's milk, 11 showed other features of cow's milk allergy by six months of age and five remained cow's milk intolerant at 16 months.

In a randomized crossover trial (17) involving 19 colic infants, the mean weekly duration of symptoms was 8.5 h compared with 18.7 h when fed soy versus cow's milk formula, respectively.

Comment

Soy formulas may reduce the symptoms of colic in some bottle-fed infants. However, the therapeutic use of soy formulas in colic is not recommended because soy protein is a frequent allergen in infancy (9,18-23). In 2008, the American Academy of Pediatrics (21) stated that "the routine use of isolated soy protein-based formula has no proven value in the prevention or management of

infantile colic or fussiness". In 2009, the Canadian Paediatric Society (24) stated that "physicians 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".

EFFECT OF LACTASE TREATMENT

In a crossover study (25), no differences in duration and severity of colic symptoms were observed among 10 infants whose feedings (breastmilk or cow's milk formula) were untreated or treated with lactase. A placebo-controlled crossover trial (26) involving 12 infants showed that taking lactase before breastfeeding had no effect on colic. In a double-blinded crossover trial, 13 infants were randomly assigned to have lactase or placebo added to their formula for one week (27). Lactase treatment reduced crying time by 1.14 h/day compared with placebo. In another double-blinded crossover trial, Kanabar et al (28) randomly assigned 53 infants to 10 days of lactase-treated breastmilk (or formula) or placebo. In 26% (95% CI 12.9% to 44.4%) of the lactase-treated group, breath hydrogen levels and total crying time were reduced by at least 45%. The remainder did not respond to lactase.

Comment

The evidence does not support the use of lactase in the treatment of colic. It is important to emphasize that congenital lactase deficiency is rare (29).

PROBIOTICS AND PREBIOTICS IN INFANTS

Savino et al (30) randomly assigned 199 formula-fed colic infants to either a new formula containing partially hydrolyzed whey proteins, low lactose levels and prebiotic oligosaccharides (96 infants), or a standard formula and simethicone (103 infants). At day 14, the mean (\pm SD) number of crying episodes was significantly lower in the infants receiving the new formula versus the standard formula (1.76 ± 1.60 versus 3.32 ± 2.06 , $P < 0.0001$). Unfortunately, one cannot conclude which component(s) of the new formula may have resulted in the decreased crying.

Subsequently, Savino et al (31) randomly assigned 83 breast-fed colic infants to receive either *Lactobacillus reuteri* (41 infants) or simethicone (42 infants). On day 28, 39 patients (95%) in the probiotic group had a decrease in daily average crying time of at least 50% compared with three patients (7%) in the simethicone group.

Comment

There is insufficient evidence to recommend for or against the use of probiotics or prebiotics in the management of colic.

CONCLUSIONS

Current evidence suggests that dietary modifications may reduce colic in only a very small minority of infants (32). Unfortunately, the evidence is often conflicting and many of the studies were unblinded, suffered from small sample sizes and had inadequate outcome measures. As such, it is very important to avoid making nutritional interventions in the vast majority of infants with colic.

- For infants with severe colic, if there is a concern of cow's milk protein allergy, an empiric time-limited (two weeks) therapeutic trial of a hypoallergenic diet could be considered (1,14,33).
- For the breastfed infant with colic where there is the relatively rare concern of a cow's milk protein allergy, one can consider eliminating cow's milk from the maternal diet (5,7,20). If this

is done, one must ensure that breastfeeding is not prematurely discontinued, and that the mother and infant receive the appropriate nutritional support (ensuring sufficient caloric, calcium and vitamin D intake). If there is no definite benefit after two weeks, the dietary restrictions should be lifted.

- For the bottle-fed infant with colic where there is the relatively rare concern of a cow's milk protein allergy, the use of a time-limited (two weeks) empiric trial of an extensively hydrolyzed formula may be considered (6,11-13,19,20,32).
- The use of soy formulas in the treatment of infantile colic should be avoided (9,18-22).
- Currently, evidence does not support the use of lactase in the management of infantile colic.
- There is insufficient evidence to make recommendations on the use of probiotics or prebiotics.

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