

Milk Protein Allergy in Breastfeeding Infants

Kimberly Cranford, BS¹

¹Currently studying medicine at the University of Washington School of Medicine (MD candidate May 2015); student member of the American Psychiatric Association, the American College of Physicians, and the American Academy of Family Physicians; Bachelor of Science in Molecular Biology earned from the University of Wyoming; Email: kimboc@u.washington.edu

Abstract *Milk protein allergy (MPA) is a term used to describe various symptoms and clinical presentations thought to be associated with an allergy to cow's milk protein, such as casein. The association between dairy milk consumption and certain symptoms is well known and documented. Controversy exists over whether breastfeeding infants can also have an allergic reaction to cow's milk protein consumed from the breast milk of nursing mothers. The results of several studies show an association between allergic symptomatology in breastfeeding infants and dairy milk consumption in the mothers of those infants. The methodology for diagnosis of MPA is outlined along with treatment options. Studies have found two treatment regimens to be effective for infants with MPA. The best option is for the mother to continue breastfeeding while also doing a trial of dietary restriction of cow's milk protein, then all bovine protein, and possibly other cross-reactive proteins like soy. The second option is for the mother to feed her infant exclusively with formula using extensively hydrolyzed or amino acid-based formulas.*

Introduction

Milk protein allergy (MPA) presents with a multiplicity and a specificity of symptoms ranging from gastrointestinal, colicky, or allergic presentations. The association between these symptoms and the consumption of cow's milk proteins has been widely documented, but the theory that infants can present with a reaction to cow's milk protein consumed from their mothers' breast milk remains controversial. Studies have documented an association between cow's milk proteins in the mother's diet and allergic symptoms in the infant.¹⁻⁴ Reviewed here are studies looking at the association between milk protein allergy in breastfeeding infants and the mother's intake of dairy in her diet. The recommended approach to treatment is also discussed.

Milk protein allergy, a rather elusive

term, will be used in this paper to describe any clinical presentation that is thought to be caused by a reaction to cow's milk proteins in the diet. The various presentations of MPA that have been studied in the literature include colic (also a poorly understood and ill-defined condition in itself), atopic disease (usually IgE-mediated), and gastrointestinal (GI) presentations of allergy. GI presentations can overlap with atopic disease but are often non-IgE-mediated (except in eosinophilic enterocolitis) and therefore more difficult to diagnose. These include enterocolitis, proctocolitis, and esophagitis.²

Literature Review

Two treatment regimens have been found to be effective in the breastfeeding infant presenting with MPA:^{5,6} avoidance

of all dairy products in the maternal diet or switching to feeding the infant with a hypoallergenic formula if maternal dietary restrictions are too difficult or not possible. Methodologically sound randomized control trials (RCT) demonstrating the efficacy of dietary avoidance of dairy are lacking in the literature. Though dietary avoidance cannot be suggested based on studies included in systematic reviews, many studies have demonstrated efficacy.^{3,4,7} Given the large body of evidence outside of RCTs (prospective studies) and the RCTs not included in reviews, the Committee on Nutrition from the American Academy of Pediatrics⁸ does recommend dietary restriction in the mother if MPA in the infant is suspected or diagnosed. This recommendation came from a clinical review in 2008, and recommendations like this one, dealing specifically with the cessation of symptoms in infants with MPA, have yet to be replaced. More recent reviews of the literature make conclusions based only on RCTs and address only the development of atopic disease later in life rather than a decrease in unfavorable symptoms during infancy while still breastfeeding. Studies on this issue have been done but have not yet been systematically reviewed. Therefore, until evidence suggests maternal dietary restriction is inefficacious, mothers should be offered the option of treating MPA in their infants with a hypoallergenic diet.²

Mothers who cannot comply with dietary restrictions can feed their infants with a hypoallergenic infant formula. Evidence demonstrates that the use of hydrolyzed infant formulas for infants with MPA reduces the risk of developing atopic disease in the first year of life in those infants that are deemed at high risk of atopic disease—those that have at least one first degree relative with atopy.^{4,8,9,10} Again, it is important to note that these studies and reviews looked at development of atopy after infancy, rather than the immediate effect of hydrolyzed formula feeding on all forms of MPA (not just atopic disease). Systematic reviews of immediate symptomatic relief are warranted. A systematic review of soy milk formulas concludes

that there is insufficient evidence to suggest that soy milk formulas are more efficacious than milk protein formulas in infants diagnosed with MPA.¹¹ Outside of this review's conclusion, a well-designed study¹ does show a significant improvement in colic symptoms in those infants fed a soy milk formula versus the control infants who were fed a cow's milk formula. Other studies also demonstrate that soy milk is a better choice than cow's milk in decreasing symptoms of MPA.¹²⁻¹⁴

Implications for Clinical Practice

In order to apply this inconclusive evidence to clinical practice when MPA is suspected, the first step is to attempt to make a diagnosis using these tests: food challenge tests, skin prick testing, serum IgE testing, and patch testing.² Diagnosis before treatment is important, as there is often a wide discrepancy between parental reporting of symptoms and an actual MPA. MPA has a very low incidence (0.5%). This incidence was discovered in one study⁷ of Scandinavian women and their infants and is cited by most other studies as the true incidence of MPA in all populations. More studies need to be done in various populations to confirm that this is true. If the MPA is IgE-mediated, skin prick testing combined with a serum IgE measurement has a positive predictive value of 95% in diagnosing the MPA. For diagnosis of non-IgE-mediated disease, patch testing shows promise, but diagnosis is more difficult. Recommendations are to combine patch testing with a food challenge test.²

Once diagnosis is made or if a strong clinical suspicion for MPA exists, the breastfeeding mother should eliminate certain foods, beginning with cow's milk protein, then all bovine protein, and possibly other cross-reactive proteins like soy.⁵ If the mother wants to formula feed, either extensively hydrolyzed or amino acid-based formulas should be fed to the infant exclusively.⁶ One should refer to specialists for dietary counseling, suspected anaphylactic allergy, suspected multiple food allergies, significant weight loss, failure to thrive refractory to treatment, or feeding aversion.²

Conclusions

Having reviewed the systematic reviews and literature on MPA in breastfeeding infants, certain conclusions can be made. Many studies previously discussed demonstrate either complete cessation or lessening in severity of MPA-associated symptoms when dairy is avoided in the maternal diet. If the goal is to increase comfort in the infant and prevent illness in the short-term, evidence does demonstrate efficacy.¹⁻⁴ Current systematic reviews focus on whether dietary restriction prevents atopic disease in the future and only considers RCTs that meet certain methodological requirements. The reviews demonstrate that if decreasing the likelihood of developing atopic disease after infancy is the goal, dietary restriction has not been found to be effective.^{15,16} More methodologically sound RCTs specifically studying immediate improvement of symptoms in breastfeeding infants when the mother removes allergens from her diet are warranted. All studies strongly suggest that breastfeeding, regardless of the mother's diet, should be the exclusive method of feeding in high risk infants if possible due to the role breastfeeding plays in producing a healthy immune system in the infant.

One may be led to wonder why so much conflicting evidence surrounding MPA and treatment exists. Some answers lie in the literature, specifically studies performed by immunologists. The immune system is very complicated and still relatively poorly understood. Studies have demonstrated the following immunological defects in children with MPA: defects in regulation of B cells, lower IFN-gamma production, and defective T-cell mediated suppression of the immune system.¹⁷ MPA infants also received less IgA antibodies from mother's milk than asymptomatic infants.¹⁷ Development of a food allergy requires both genetic predisposition and exposure to environmental antigens;^{17,18} therefore, immunologists are not yet sure if the immunological dysfunction found in MPA infants is determined entirely by genetics, regardless of the breast milk composition, or if an infant's first ex-

posure to cow's milk proteins in breast milk triggers a response to create the aforementioned disadvantageous immune system.¹⁷ The development of MPA may be somewhat unpredictable.^{17,19,20} It may, therefore, be wise for mothers of infants with diagnosed MPA to err on the side of caution and avoid dairy products in their diet until the child is ready for solid food.

Competing Interests

The author declares that she has no competing interests.

References

1. Campbell JP: Dietary treatment of infant colic: a double-blind study. *JR Coll Gen Pract*, 1989; 39(318): 11-14.
2. Brill H: Approach to milk protein allergy in infants. *Can Fam Physician*, 2008; 54: 1258-1264.
3. Hill DJ, Hudson IL, Sheffield LJ, et al: A low allergen diet is a significant intervention in infantile colic: results of a community-based study. *J Allergy Clin Immunol*, 1995; 96(6 Pt 1): 886-892.
4. Ram FS, Ducharme FM, Scarlett J: Cow's milk protein avoidance and development of childhood wheeze in children with a family history of atopy. *Cochrane Database Syst Rev*, 2002; (3): CD003795.
5. Jarvinen KM, Mäkinen-Kiljunen S, Suomalainen H: Cow's milk challenge through human milk evokes immune responses in infants with cow's milk allergy. *J Pediatr*, 1999; 135: 506-512.
6. Terheggen-Lagro SW, Khouw IM, Schaafsma A, et al: Safety of a new extensively hydrolysed formula in children with cow's milk protein allergy: a double blind crossover study. *BMC Pediatr*, 2002; 2: 10.
7. Host A, Husby S, Osterballe O: A prospective study of cow's milk allergy in exclusively breastfed infants. *Acta Paediatr Scand*, 1998; 77: 663-670.
8. [No authors listed]. American Academy of Pediatrics. Committee on Nutrition. Hypoallergenic infant formulas. *Pediatrics*, 2000; 106(2 Pt 1): 346-349.
9. Osborn DA, Sinn J: Formulas containing hydrolysed protein for prevention of allergy and food intolerance in infants. *Cochrane Database Syst Rev*, 18; (4): CD003664.
10. Lucassen PL, Assendelft WJ, Gubbels JW, et al: Infantile colic: crying time reduction with a whey hydrolysate: A double-blind, randomized, placebo-controlled trial. *Pediatrics*, 2000; 106(6): 1349-1354.
11. Osborn DA, Sinn J: Soy formula for prevention of allergy and food intolerance in infants. *Cochrane*

- Database Syst Rev*, 2006; (4): CD003741.
12. American Academy of Pediatrics. Committee on Nutrition. Soy protein-based formulas: recommendations for use in infant feeding. *Pediatrics*, 1998; 101: 148-153
 13. Lothe L, Lindber T, Jakobsson I: Cow's milk formula as a cause of infantile colic: a double-blind study. *Pediatrics*, 1982; 70(1): 7-10.
 14. Forsyth BW: Colic and the effect of changing formulas: a double-blind, multiple-crossover study. *J Pediatr*; 1989; 115(4): 521-526.
 15. Kramer MS, Kakuma R: Maternal dietary antigen avoidance during pregnancy or lactation, or both, for preventing or treating atopic disease in the child. *Cochrane Database Syst Rev*, 2012; 9: CD000133.
 16. Greer FR, Sicherer S, Burks W; American Academy of Pediatrics Committee on Nutrition; American Academy of Pediatrics Section on Allergy and Immunology: Effects of early nutritional interventions on the development of atopic disease in infants and children: the role of maternal dietary restriction, breastfeeding, timing of introduction of complementary foods, and hydrolyzed formulas. *Pediatrics*, 2008; 121: 183-191.
 17. Järvinen KM, Suomalainen H: Development of cow's milk allergy in breast-fed infants. *Clin Exp Allergy*, 2001; 31:978-987.
 18. Jakobsson O, Lindberg T: A prospective study of cow's milk protein intolerance in Swedish infants. *Acta Paediatr Scand*, 1979; 68:853-859.
 19. Fukushima Y, Kawata Y, Onda T, et al: Consumption of cow milk and egg by lactating women and the presence of Beta-lactoglobulin and ovalbumin in breast milk. *Am J Clin Nutr*, 1997; 65: 30-35.
 20. Sorva R, Mäkinen-Kiljunen S, Juntunen-Backman K: Beta-lactoglobulin secretion in human milk varies widely after cow's milk ingestion in mothers of infants with cow's milk allergy. *J Allergy Clin Immunol*, 1994; 93: 787-792.
-