Evaluation of an Amino Acid–Based Formula in Infants Not Responding to Extensively Hydrolyzed Protein Formula

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ABSTRACT

Nearly 2% to 3% of infants and children younger than 3 years have confirmed cow’s milk protein allergy with multiple clinical presentations including atopic dermatitis (AD), diarrhea, and vomiting/spitting up. Although most infants with cow’s milk protein allergy experience clinical improvement with the use of an extensively hydrolyzed (EHP) formula, highly sensitive infants may require an amino acid–based formula. In this observational, prospective study, 30 infants (1–12 months of age) with a history of weight loss and persistent allergic manifestations while on an EHP formula were provided an amino acid–based formula for 12 weeks. Mean weight gain (z score change) improved \(+0.43 \pm 0.28\) (mean \(\pm\) standard deviation) after the 12-week feeding period. Improvement was observed for many allergic symptoms including significant decreases in AD severity (\(P = 0.02\)). These results indicate the new amino acid–based infant formula supported healthy weight gain and improvement in allergic manifestations in infants not responding to EHP formulas.

Key Words: allergy, amino acid formula, hydrolyzed formula, infant

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ow’s milk protein allergy (CMPA), the most common food allergy, affects at least 2% to 3% of infants (1,2). CMPA can provoke both IgE-mediated (immediate onset) and non–IgE-mediated (delayed onset) reactions, and result in several clinical symptoms including atopic dermatitis (AD), diarrhea, and vomiting (3–5). Although 80% of children develop a tolerance to cow’s milk protein by 3 years of age, CMPA can significantly reduce infant quality of life and result in poor growth (2,6). Current recommendations for CMPA management include complete avoidance of cow’s milk protein and the initiation of an extensively hydrolyzed protein (EHP) formula (7–9).

Although most of infants with CMPA respond well to EHP formulas and experience adequate growth and reduced allergy symptoms, the formulas may still contain small peptide fragments that can exacerbate allergic reactions in highly sensitive infants (6,10,11). Failure to respond to an EHP formula can result in impaired growth and persistence of symptoms. Therefore, amino acid–based formulas (AAFs) are often recommended for infants with CMPA not responding to EHP formulas (12). AAFs have demonstrated reduced allergy symptoms and improved growth in infants with CMPA (2,6,13). Furthermore, similar growth, tolerance, and safety outcomes were demonstrated in healthy term infants fed AAF compared to infants receiving a control (EHP) formula (6). In recent studies, AAFs were well tolerated and supported growth in otherwise healthy infants without CMPA (6), and in those with CMPA (2). Furthermore, EHP and AAFs have been shown to improve the gut barrier function (14).

Although many studies have demonstrated the safety and efficacy of AAFs in healthy infants, few have examined the role of AAFs in CMPA infants not responding to EHP formulas. Therefore, the objective of the present study was to evaluate the efficacy of an AAF in infants between the ages of 1 and 12 months with a history of weight loss and persistent allergic symptoms while on an EHP formula.
Methods

Methods are available online as Supplemental Digital Content (http://links.lww.com/MPG/A759).

Results

Participant Characteristics

Of the 32 infants consented and enrolled in the study, 2 were discontinued, 30 infants completed the 12-week feeding period. Participants who were enrolled but consumed no study formula (n = 1) were not included in subsequent analyses. Of the participants enrolled, 38.7% (12) were boys and 61.3% (15) were girls. The mean age of participants was 6.6 (standard deviation [SD] = 3.2) months. IgE testing indicated that 76.7% (23) of infants were IgE-negative, whereas 23.3% (7) were IgE-positive. AD was present for 41.9% (13) participants, with a mean scoring atopic dermatitis value of 24.64 (SD = 13.25). At Study Visit 1, 8 infants presented with watery stools. Vomiting/spitting up was reported in 61.3% (15) participants, with 17 infants presenting with a gastrointestinal (GI) symptom score >16.

Growth and Allergy Symptoms

A mean weight z score change of +0.433 (SD = 0.281) was observed after the 12-week feeding period, and was not significantly different from the inclusion criteria z-score change of 0.5 (P = 0.1938). Improvement was observed for all allergic manifestations, both in terms of the number of infants presenting symptoms and symptom intensity. The incidence of AD significantly decreased from 13 participants at visit 1 to 7 participants at visit 3 (Table 1). The mean scoring atopic dermatitis score of the 7 patients still experiencing AD significantly decreased from 32.73 (SD = 10.30) at visit 1 to 9.04 (SD = 5.94) at visit 3 (P = 0.0156). The number of infants experiencing vomiting/spitting up (as defined by a GI symptom score >16) decreased from 17 at visit 1 to 4 at visit 3 (Table 1). A statistically significant decrease was observed in the GI symptom score (P < 0.0001), with a mean change of −10.5 (SD = 1.8) (Table 2).

Discussion

The present study demonstrated improved weight gain and decreased allergic manifestations in suspected CMPA infants.
receiving an amino acid–based infant formula. Before the initiation of an AAF all study participants were below the 50th percentile of the WHO reference population for weight and were experiencing allergic symptoms while on an EHP formula. Following the 12-week feeding period, there was an increase in weight (+0.433 z score change), relative to the WHO reference population. Although not statistically significant, participant length was increased during the 12-week feeding period. These results indicate that the AAF provided adequate nutrition while managing CMPA symptoms. These findings are in agreement with previous studies, which demonstrate that AAFs provide healthy growth when provided to CMPA infants (6,11). In healthy infants, AAFs provided similar weight and growth compared to infants given EHP formula (6). A similar study demonstrated weight and length gains in infants with CMPA not responding to EHP formulas when fed AAF for 11.4 months (16).

Recommended management of CMPA includes complete elimination of cow’s milk protein and the initiation of a hydrolyzed protein formula (7). Although 90% of infants exhibit healthy growth and reduced allergic symptoms on an EH formula, highly sensitive infants may require an AAF. Before initiation of an AAF, infants in the present study had not responded to various EHP formulas, including cow’s milk based EHP formulas and hydrolyzed rice protein formulas. Although previous studies have demonstrated that hydrolyzed rice protein formulas are well tolerated in CMPA infants unable to tolerate other cow’s milk–based EHP formulas, the findings from the present study suggest that infants with severe CMPA may require an AAF (17–19). Furthermore, it is possible that infants with non–IgE-mediated allergies, a group highly represented in the study, may be more susceptible to persistent allergic manifestations and unable to tolerate traditional EHP and hydrolyzed rice protein formulas.

Significant improvement was demonstrated in all allergic manifestations in the present study indicating that the AAF properly managed CMPA symptoms. Incidence and severity of AD and vomiting/spitting up were significantly reduced during the 12-week study period. Furthermore, all 8 infants experiencing watery stools at visit 1 had recovered after 12 weeks of receiving study formula. These results are in agreement with the demonstration that short-term feeding of AAF in infants with CMPA reduces the presence and severity of allergic manifestations (2,6,15). In a prospective, controlled study, atopic infants with CMPA receiving an AAF for 6 months demonstrated clinical improvement and growth compared with infants fed an EHP formula (20). In another study, data suggested that hypoallergenic (AAF) formulas improved the gut barrier function and minimized gastrointestinal complications in atopic infants (14). Similarly, when fed an AAF, infants with CMPA with multiple food allergies demonstrated reduced allergic symptoms and normal growth (15,21,22). The results in the present study indicated that longer-term feeding of an AAF in infants with poorly managed CMPA, improved long-term allergy management.

There were some limitations of the present study, with 1 being the observational, nonrandomized nature of the study design. Another limitation was the relatively small sample size of study participants. Despite these limitations, the present study, however, provided support for the use of this new amino acid–based infant formula in infants with suspected CMPA not responding to EH formulas. The results of the present study build on the past literature supporting the efficacy and safety of AAFs for CMPA management. The new amino acid formula in the present study supported healthy weight gain and improvement in allergic symptoms in CMPA infants not responding to EHP formulas.

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REFERENCES
1. Sicherer SH, Sampson HA. Food allergy: epidemiology, pathogenesis, diagnosis, and treatment. J Allergy Clin Immunol 2014;133:291–307.
2. Nowak-Wegrzyn A, Czerkies LA, Collins B, et al. Evaluation of hypoallergenicity of a new amino acid-based formula. Clin Pediatr (Phila) 2015;54:264–72.
3. Host A, Hakken S, Cow’s milk allergy: where have we come from and where are we going? Endor Metab Immune Disord Drug Targets 2014;14:2–8.
4. Lifschitz C, Sajewska H. Cow’s milk allergy: evidence-based diagnosis and management for the practitioner. Eur J Pediatr 2015;174:141–50.
5. Dominguez-Ortega G, Borrelli O, Meyer R, et al. Extraintestinal manifestations in children with gastrointestinal food allergy. J Pediatr Gastroenterol Nutr 2014;59:210–4.
6. Burks W, Jones SM, Berseth CL, et al. Hypoallergenicity and effects on growth and tolerance of a new amino acid-based formula with docosahexaenoic acid and arachidonic acid. J Pediatr 2008;153:266–71.
7. AAP American Academy of Pediatrics. Committee on Nutrition. Hypoallergenic infant formulas. Pediatrics 2000;106(2 pt 1):346–9.
8. Koletzko S, Niggemann B, Arato A, et al. Diagnostic approach and management of cow’s milk protein allergy in infants and children: ESPGHAN GI Committee practical guidelines. J Pediatr Gastroenterol Nutr 2012;55:221–9.
9. Dupont C, Chouraqui JP, De Boissieu D, et al. Dietary treatment of cows’ milk protein allergy in childhood: a commentary by the Committee on Nutrition of the French Society of Paediatrics. Br J Nutr 2012;107:325–38.
10. Hoffmann KM, Sampson HA. Serum specific-IgE antibodies to peptides detected in a casein hydrolysate formula. Pediatr Allergy Immunol 1997;8:185–9.
11. De Boissieu D, Dupont C. Allergy to extensively hydrolyzed cow’s milk proteins in infants: safety and duration of amino acid-based formula. J Pediatr 2002;141:271–3.
12. Isolauri E, Sutas Y, Mäkinen-Kiljunen S, et al. Efficacy and safety of hydrolyzed cow milk and amino acid-derived formulas in infants with cow milk allergy. J Pediatr 1995;127:550–7.
13. Hill DJ, Murch SH, Rafferty K, et al. The efficacy of amino acid-based formulas in relieving the symptoms of cow’s milk allergy: a systematic review. Clin Exp Allergy 2007;37:808–22.
14. Arvolta T, Molislan E, Vuento R, et al. Weaning to hypoallergenic formula improves gut barrier function in breast-fed infants with atopic eczema. J Pediatr Gastroenterol Nutr 2004;38:92–6.
15. Dupont C, Kalach N, Soulaines P, et al. Safety of a new amino acid formula in infants allergic to cow’s milk and intolerant to hydrolysates. J Pediatr Gastroenterol Nutr 2015;61:456–63.
16. De Boissieu D, Dupont C. Time course of allergy to extensively hydrolyzed cow’s milk proteins in infants. J Pediatr 2000;136:119–20.
17. Fiocchi A, Restani P, Bernardini R, et al. A hydrolysed rice-based formula is tolerated by children with cow’s milk allergy: a multi-centre study. Clin Exp Allergy 2006;36:311–6.
18. Fiocchi A, Travaini M, D’Auria E, et al. Tolerance to a rice hydrolysate formula in children allergic to cow’s milk and soy. Clin Exp Allergy 2003;33:1576–80.
19. Reche M, Pascual C, Fiandor A, et al. The effect of a partially hydrolysed formula based on rice protein in the treatment of infants with cow’s milk protein allergy. Pediatr Allergy Immunol 2010;21(4 pt 1):577–85.
20. Niggemann B, Binder C, Dupont C, et al. Prospective, controlled, multicenter study on the effect of an amino acid-based formula in infants with cow’s milk allergy/intolerance and atopic dermatitis. Pediatr Allergy Immunol 2001;12:78–82.
21. Sicherer SH, Noone SA, Koerner CB, et al. Hypoallergenicity and efficacy of an amino acid-based formula in children with cow’s milk and multiple food hypersensitivities. J Pediatr 2001;138:688–93.
22. Dupont C, Kalach N, Soulaines P, et al. A thickened amino-acid formula in infants with cow’s milk allergy failing to respond to protein hydrolysate formulas: a randomized double-blind trial. Paediatr Drugs 2014;16:513–22.