Management of Cow's Milk Protein Allergy in Infants

Dr Liew Woei Kang
Consultant Paediatrician
Paediatric Allergy & Immunology
SBCC Baby & Child Clinic, Gleneagles Medical Centre

President, College of Paediatrics and Child Health,
Academy of Medicine Singapore
Immediate Past President, Asthma and Allergy Association, Singapore

Understanding cow's milk protein allergy

Estimated to affect 2-4 percent of children worldwide[1], cow's milk protein allergy (CMPA) is an immunologically-mediated reaction to cow's milk proteins that may involve the gastrointestinal tract, skin, respiratory tract, or multiple organs, causing systemic anaphylaxis.[2] CMPA can be either immunoglobulin E (IgE) or non-IgE mediated; IgE-mediated reactions typically occur immediately after ingestion whereas non-IgE mediated reactions may take up to two days to develop, but still involve the immune system.[3] The symptoms of non-IgE mediated disease, such as erythema, atopic eczema, abdominal pain or constipation, are commonly mistaken as symptoms of lactose intolerance.[3]

It is important to differentiate CMPA from lactose intolerance as confusion may result in unnecessary dietary restriction or avoidable reactions.[3] Moreover, the management of CMPA is distinctly different from that of lactose intolerance. Lactose intolerance results from a reduced capacity to digest lactose, the primary sugar present in breast milk. Lactose intolerance exclusively causes symptoms in the bowel, but does not cause rectal bleeding.[3] It is managed by reducing lactose in the diet, though breast feeding should continue despite high lactose content present in breast milk. Primary lactose intolerance happens when lactase naturally declines, usually after the age of 3 years, but symptoms usually manifest in adults.[3]

Secondary lactose intolerance, which occurs due to mucosal damage, such as in severe gastroenteritis, is usually reversible once the epithelial lining has recovered, and lactose can be tolerated again by 6 weeks.[3]

CMPA is managed by removing the allergenic protein from the diet.[3] If CMPA is suspected in an infant, lactating mothers should not consume cow's milk and its derivatives.[3] In formula-fed infants, the type of formula is determined by the severity of symptoms.[3] As the degree of allergenicity decreases as cow's milk protein gets increasingly broken down, infants with milder symptoms may try an extensively hydrolysed formula (eHF). Amino acid formulas are reserved for infants with severe symptoms or those not responding to eHF.

Lactose-containing eHFs are safe and effective for infants with CMPA

There is no need to restrict lactose in infants with CMPA, unless there is an enteropathy, with small bowel damage causing secondary lactose intolerance.[3] The ESPGHAN guidelines state that adverse reactions to lactose in CMPA are not supported in the literature, and complete avoidance of lactose is not warranted.[4] eHFs containing purified lactose have been found safe and effective in the treatment of CMPA.[4]

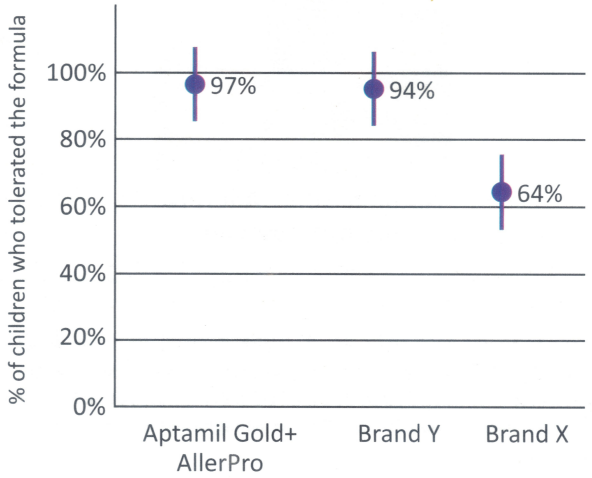
Aptamil Gold+ AllerPro has proven efficacy in CMPA management

For protein hydrolysate formulas to support a therapeutic hypoallergenic claim, several authoritative bodies including the American Academy of Pediatrics (AAP), the European Society of Paediatric Gastroenterology and Nutrition (ESPGAN) and the European Society of Paediatric Allergy and Clinical Immunology (ESPACI) recommend that protein hydrolysate formulas should be tolerated by at least 90

percent of children with CMPA.[6] Aptamil Gold+ AllerPro is an extensively hydrolysed whey protein formula, which has been proven by studies to be well tolerated by infants with CMPA and results in an adequate nutritional status.[6] Notably, clinical trial data is the most important measure of efficacy for eHFs, not peptide size.[1,4,5]

In a two-centre study, 32 children with proven CMPA received duplicate skin prick tests (SPT) and took part in a double-blind placebo-controlled food challenge with Aptamil Gold+ AllerPro (extensively hydrolysed), Brand Y (extensively hydrolysed) and Brand X (partially hydrolysed).[6] Skin-prick tests (SPTs) were positive in 19 percent, 15 percent, and 32 percent of children to the three hydrolysate formulas, respectively.[6] The double-blind placebo-controlled oral challenge showed that 97 percent (95 percent CI, 85–100 percent) of the children tolerated Aptamil Gold+ AllerPro, 94 percent (95 percent CI, 75–100 percent) tolerated Brand Y, while 64 percent (95 percent CI, 37–81 percent) tolerated Brand X **(Figure 1)**.[6] This study demonstrates that Aptamil Gold+ AllerPro is well tolerated in a population of children with proven CMPA and is considered safe for its intended use.[6]

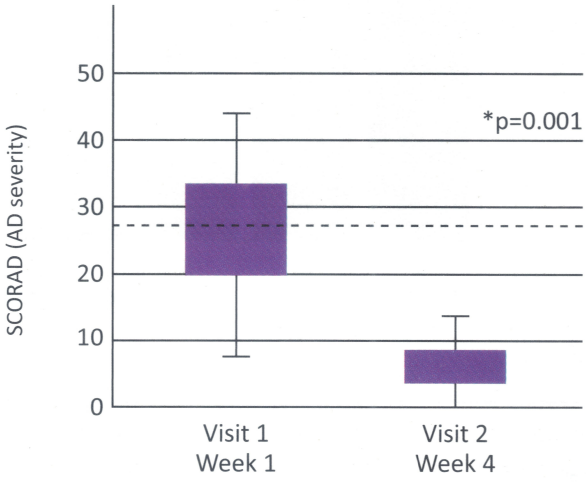
Figure 1. Oral tolerability of three hydrolysate formulas in young children with proven CMPA



Based on data from Giampietro PG, et al. *Pediatr Allergy Immunol* 2001;12(2):83-86.

A multicentre open-label clinical trial in Russia evaluated the efficacy of a whey-based eHF (Aptamil Gold+ AllerPro) in formula-fed infants with atopic dermatitis associated with CMPA.[7] A total of 51 infants with mild-to-moderate atopic dermatitis (SCORAD <40) received the eHF for 4 weeks. Results showed that early use of Aptamil Gold+ AllerPro significantly reduced skin symptoms (p=0.001) **(Figure 2)**. At the end of 4 weeks, the use of glucocorticosteroids, zinc-containing agents, and antihistamines was also significantly reduced (p<0.01).

Figure 2. Resolution of skin symptoms in infants receiving Aptamil Gold+ AllerPro for 4 weeks



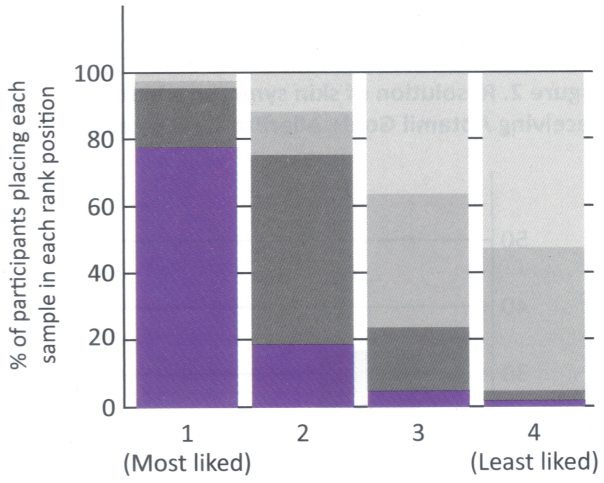
Aptamil Gold+ AllerPro encourages compliance with superior palatability

For non-breastfed infants with CMPA, selecting a palatable eHF formula is crucial, as flavour affects acceptability and modulates intake. In eHF, proteins are broken down into shorter peptides which reduce the number of conformation and sequential epitopes, hence decreasing allergenicity.[8] However, the shorter peptides are often bitter and sour-tasting with a volatile odour, leading to the perception of poor palatability.[8] Studies have demonstrated that many infants older than 7 months tend to dislike and reject these formulas, but are more likely to accept them if they have been exposed to them at 3.5 months.[8]

In a recent independent taste panel of 100 dietitians and GPs, Aptamil Gold+ AllerPro was ranked the most liked formula on the UK market, with 77 percent of participants choosing it as the most palatable, significantly higher than other eHFs (p<0.0001) **(Figure 3)**.[8] In addition, nearly all participants (96 percent) expected that a better tasting EHF would result in an increased chance of non-rejection, more content families (92 percent), and decreased healthcare costs and waste (90 percent).[8]

The superior palatability of Aptamil Gold+ AllerPro has been attributed to it being a whey-based formula that contains

Figure 3. Palatability ranking of eHF by a blinded taste panel of 100 healthcare professionals



lactose.[8] The results are consistent with other studies that show that whey-based eHFs have superior palatability than casein-based eHFs.[9–11] Studies have also shown that lactose-containing formulas are more palatable than lactose-free formulas.[10,11] Besides enhancing palatability, lactose is also beneficial for infant gut microbiota and calcium absorption.[5]

Conclusions

CMPA is managed by the strict avoidance of cow's milk protein. For breastfed infants, the mother should avoid CMP from her diet. Non-breastfed infants should receive an eHF with proven efficacy and tolerability in clinical trials. Aptamil Gold+ AllerPro is an extensively hydrolysed whey protein-based, lactose-containing formula, which has been proven by studies to be efficacious and safe in the management of infants with CMPA. It has superior palatability which encourages infant acceptance and compliance.

"Aptamil Gold+ AllerPro has a unique formulation of extensively hydrolysed whey formula containing lactose, which enhances its palatability and is shown to be effective in the management of infants with cow's milk protein allergy"

Aptamil Gold+ AllerPro (From birth onwards)

References:

1. Meyer R. *Complet Nutr Focus* 2014;6:50-53. **2.** Bahna S. *Ann Allergy Asthma Immunol* 2002;89:56-60. **3.** Walsh J, et al. *Br J Gen Pract* 2016;66(649):e609-e611. **4.** Koletzko S, et al. *J Pediatr Gastroenterol Nutr* 2012;55(2):221-229. **5.** Host A, et al. *Arch Dis Child* 1999;81:80-84. **6.** Giampietro PG, et al. *Pediatr Allergy Immunol* 2001;12:83-86. **7.** Pampura AN, et al. *Ros Vestn Perinatol Pediat* 2014;4:91-99. **8.** Maslin K, et al. *Pediatr Allergy Immunol* 2018;doi:10.1111/pai.12979. **9.** Pedrosa M, et al. *Investig Allergol Clin Immunol* 2006;16:351-356. **10.** Miraglia Del Giudice M, et al. *Ital J Pediatr* 2015;41:42. **11.** de Jong N, et al. *Ann Allergy Asthma Immunol* 2014;113:235-236.

NUTRICIA
LIFE-TRANSFORMING NUTRITION

Sponsored as a service to the medical profession by Nutricia.
Editorial development by MIMS.

MIMS

MIMS Pte Ltd
438A Alexandra Road
Alexandra Technopark
#04-01/02 Singapore 119967
Tel: +65 6290 7400 | Fax: +65 6290 7401
Email: enquiry.sg@mims.com