ADVANCING THE MANAGEMENT OF COW'S MILK PROTEIN ALLERGY:
Setting the standard for extensively hydrolysed formulas

Breastfeeding is the gold standard for infant nutrition, including infants with CMPA. For the majority of non-breastfed infants with CMPA, an extensively hydrolysed formula (eHF) is recommended first-line. Although the ultimate goals of eHF are the same, which is to ensure normal growth and symptom relief, composition heterogeneity among them leads to variability in clinical efficacy. This may reduce quality of life for infants with CMPA and their caregivers, whilst increasing healthcare costs.

Choosing the most appropriate formula

When exclusive breastfeeding is not possible, extensively hydrolysed formulas (eHF) are recommended first-line formula for the majority of infants with CMPA, while amino-acid based formulas (AAF) are recommended for those with severe symptoms, or those who do not tolerate eHF.[1,2] In order to be confirmed as safe and effective, guidelines recommend that both eHF and AAF should be tolerated by at least 90% of infants and young children with CMPA, with 95% confidence in a randomised, double blind, placebo-controlled trial.[1-4] Excessive usage of AAF in some countries suggests that eHF are not routinely prescribed first-line, or that eHF are not being tolerated by at least 90% of infants,[5,6] potentially reducing quality of life and increasing the cost burden.[7,8] AAF in general have significantly worse palatability than whey-based eHF[8,9] and may be 3x more costly[10], whilst eHF failure will increase the time to symptom resolution and will result in further physician appointments.

The design of an eHF can affect its efficacy

eHF are made by hydrolysing whey or casein protein, cleaving them into peptides, to reduce their allergenicity.[3] A well-designed hydrolysis should markedly decrease, and ideally abolish, the allergenicity of the resulting peptides.[3,11] An additional ultrafiltration step can ensure the removal of residual larger peptides and proteins.[3,11] However, it is worth noting there is no clear definition of an eHF.[2,3] There is no consensus on the degree of hydrolysis and assessment of residual allergenicity.[2,11-13] Fig 1 illustrates the high variability in the level of hydrolysis between commercially available eHF, raising the important question - "are all eHF sufficiently hydrolysed?"[2,11] Several studies have reported allergic reactions to eHF and variability in clinical efficacy.[2,12,14,15] This includes the Dutch cohort of the EuroPrevall study, where an eHF with 5-15% peptides above 1200 Da (Fig 1. orange) did not achieve adequate symptom control in 51% of infants with CMPA, resulting in the reintroduction of an AAF.[14] Differences in the safety and clinical efficacy of eHF may be attributed to residual proteins or larger peptides.[11] It has been suggested that the smaller the peptides, the lower the risk of allergic reaction.[16]

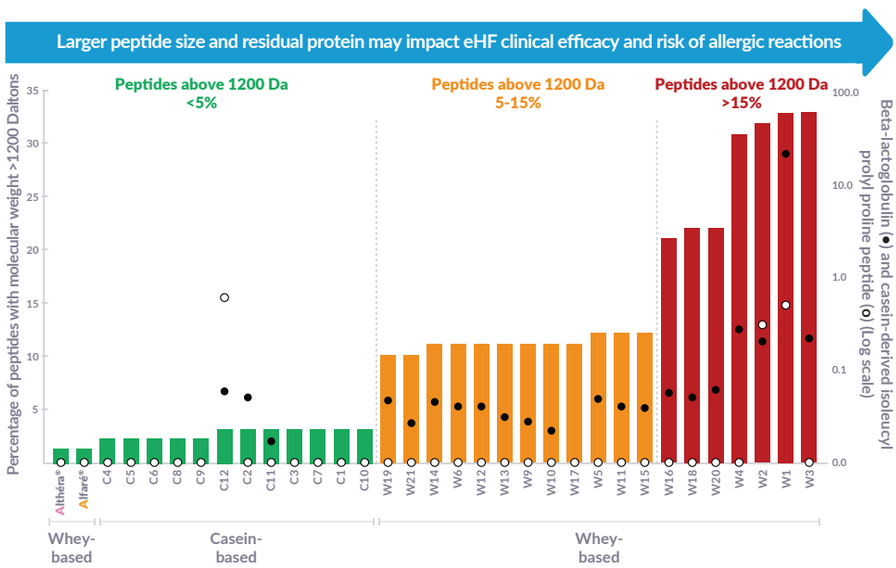

Fig. 1. Level of hydrolysis and residual protein for different eHF. Each bar represents the analytical results of a different eHF brand from around the world and shows the percentage of peptides with molecular weight (MW) >1200 Da and residual protein (e.g. ß-lactoglobulin- or casein) in each formula. Adapted from Nutten et al 2019.[11]

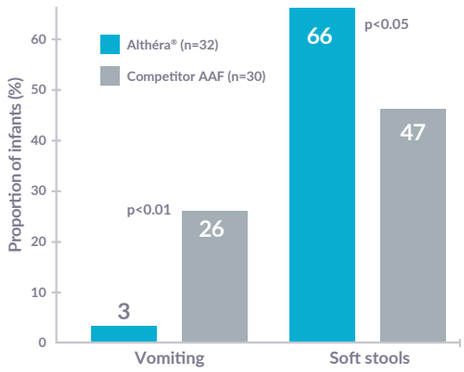

Fig.2. Proportion of infants with CMPA consuming Althéra® and an AAF over 180 days. Adapted from Niggeman 2008.[7]

Guidelines recommend eHF with clinically proven efficacy

Clinical evidence is paramount to prove the safety and efficacy of an eHF.[3] However, many eHF have not been subjected to rigorous clinical testing.[2] Batch-to-batch inconsistencies shown in some eHF also raise doubts on the continued validity of earlier clinical trials.[3,11]

Our clinically proven eHF for CMPA

Decades of research have led to >12 publications* which support Althéra® HMO and Alfaré® HMO for the first-line management of CMPA and/or CMPA with severe GI impairment, respectively.[7,11,17-28] Both are manufactured to the highest standards, including a patented ultra-filtration process, and strict release criteria which includes testing for residual allergenicity in every batch.[3]

Improving first-line outcomes

Althéra® HMO is the most extensively hydrolysed whey-based eHF for the first-line management of CMPA.[11] This is thought to explain why it is the only eHF to show similar efficacy and safety as an AAF in a randomised controlled trial.[7] It was also significantly better tolerated than the AAF (Fig 2).[7]

Althéra® HMO and Alfaré® HMO have proven to be hypoallergenic, provide effective symptom relief and support normal growth and development in infants with CMPA. Their design sets a higher quality and safety standard among an ill-defined category of products. Clinical evidence suggests first-line usage of Althéra® HMO could improve quality of life while reducing the cost burden of CMPA.

IMPORTANT NOTICE: Mothers should be encouraged to continue breastfeeding even when their infants have cow's milk protein allergy. This usually requires qualified dietary counseling to completely exclude all sources of cow's milk protein from the mothers' diet. If a decision to use a special formula intended for infants is taken, it is important to give instructions on correct preparation methods, emphasizing that unboiled water, unsterilized bottles or incorrect dilution can all lead to illness. Formula for special medical purposes intended for infants must be used under medical supervision.

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*Althéra® HMO and Alfaré® HMO share the same protein hydrolysate and production facility. The same strict quality control controls are applied to both. Studies that confirm the efficacy of Althéra® HMO therefore also apply to Alfaré® HMO. As part of our on-going commitment to discovering and following the latest scientific breakthroughs and regulations, product compositions may differ between clinical trials and between countries.

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