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COW'S MILK ALLERGY

Generating new evidence to demonstrate the role of nutrition support in optimising patient and health economic outcomes

Intended for Healthcare Professional use only

SYNBIOTIC CONTAINING EXTENSIVELY HYDROLYZED FORMULA IMPROVES GASTRO-INTESTINAL AND A TOPIC SYMPTOM SEVERITY, GROWTH, CAREGIVER QUALITY OF LIFE, AND HOSPITAL-RELATED HEALTHCARE USE IN INFANTS WITH COW'S MILK ALLERGY

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Background:

Healthy gut microbiota is important for prognosis in cow's milk allergy (CMA). The application of synbiotics (specific pre- and probiotics) in extensively hydrolyzed formulae (eHFs) is a relatively new concept.

Aims:

To evaluate a synbiotic-containing, whey-based eHF (SeHF) with galacto-oligosaccharides, fructo-oligosaccharides, and bifidobacterium breve M-16V in infants with CMA.

Method:

A 31-day one-arm pilot study in 29 infants with CMA (mean age 30.8 weeks [SD 11]) was undertaken, with outcomes including gastrointestinal tolerance, atopic dermatitis symptoms, dietary intake, growth, SeHF acceptability, caregiver quality of life, and hospital-related healthcare use.

Results:

Significant improvements ($p<.05$) in the severity of abdominal pain (in 57%), burping (in 46%), flatulence (in 79%), constipation (in 14%), rhinitis (41%), and itchy eyes (73%), as well as atopic dermatitis in those with severe baseline symptoms (PO-SCORAD© reduction: 34.7–18.2 ($p=.003$), $n=6$) were observed over time. Growth and caregiver quality of life scores significantly increased (+26.7%, $p<.05$) over time. Hospital visits and medications significantly reduced (–1.61 and –2.23, respectively, $p<.005$) in the 6 months after SeHF initiation

Conclusion:

In this small, single-arm, pilot study, the use of SeHF enhanced the management of infants with non-IgE mediated CMA who were already established on eHF. Conclusion: Whilst this study adds to the evidence base for the use of SeHF in CMA, further robust research to explore the longer-term benefits of synbiotics, specifically the blend used in this study, for the clinical management of infants with CMA is warranted.

IMPROVED CLINICAL OUTCOMES WITH AN AMINO ACID FORMULA CONTAINING SYNBIOTICS IN INFANTS WITH COW'S MILK ALLERGY

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Presented at Nutrition and Growth 2022

Introduction:

Cow's milk allergy (CMA) is common and costly. Clinical trials of infants with CMA have shown that use of an amino acid formula containing pre- and probiotics (synbiotics) (AAF-S) may lead to significant reductions in infections, medication prescriptions and hospital admissions, compared to AAF without synbiotics[1]. These effects are yet to be confirmed in real-world settings.

Method:

This retrospective matched cohort study examined clinical and healthcare data from The Health Improvement Network (A Cegedim Proprietary Database) from 148 infants with CMA (54% male, mean age at diagnosis 4.69m) prescribed either AAF-S (probiotic Bifidobacterium breve M16-V; prebiotics including chicory-derived oligo-fructose and long chain inulin) or AAF. Outcomes including symptoms, infections, healthcare usage (medication prescriptions, healthcare contacts) and time to asymptomatic management without hypoallergenic formula (clinical course of symptoms) were measured from diagnosis (mean observation period 1.19 years for both cohorts). Statistical tests included Fisher's exact or chi squared, where appropriate, for proportional data; Poisson for rates; and Cox proportional hazards regression for clinical course of symptoms. A simple cost analysis, based on published UK healthcare unit cost tariffs and accounting for the cost of the AAF powders, compared healthcare costs between groups, using healthcare usage rates extrapolated over the respective median clinical course of symptoms for each group.

Results:

AAF-S was associated with lower rates of symptoms (-37%, p<0.001), infections (-35%, p<0.001), medication prescriptions (-19%, p<0.001) and healthcare contacts (-18%, p¼0.15) vs AAF. Infants prescribed AAF-S had a significantly higher probability of achieving asymptomatic management without hypoallergenic formula (HAF) (adjusted HR 3.70, 95% CI 1.97x-6.95, p<0.001) with a shorter median time to asymptomatic management without HAF (1.35y vs 1.95y). AAF-S was associated with potential cost-savings of £452.18 per infant over the clinical course of symptoms. This may be attributable to the effect of the specific synbiotic on the gut microbiome. Further research is warranted to explore this.

Conclusion:

This real-world study provides evidence consistent with clinical trials that AAF-S may produce clinical and healthcare benefits with potential economic impact.

References:

1. Sorensen, K et al. Nutrients 2021, 13 (3), 935.

THE CLINICAL BURDEN OF COW'S MILK ALLERGY IN EARLY CHILDHOOD: A RETROSPECTIVE COHORT STUDY

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Introduction:

Cow's milk allergy (CMA) is common in infants and children. Clinical presentations may vary, with a range of symptoms affecting the gastrointestinal (GI), skin and respiratory systems. Whilst the primary focus of research to date has been on the management of these symptoms, studies investigating the broader clinical burden of CMA are limited.

Method:

We performed a retrospective matched cohort study examining clinical data, including allergic symptoms and infections, extracted from case records within The Health Improvement Network database. A total of 6998 children (54% male) were included in the study, including 3499 with CMA (mean age at diagnosis 4.04 months) and 3499 matched controls without CMA, observed for a mean period of 4.2 years.

Results:

GI, skin and respiratory symptoms affected significantly more children with CMA ($p<.001$), which recurred more often ($p<.001$), compared with children without CMA. More children with CMA had symptoms affecting multiple systems ($p<.001$). CMA was associated with a greater probability of these symptoms requiring hypoallergenic formula (HAF) prescription persisting over time (log-rank test $p<.0001$, unadjusted hazard ratio [HR]: 0.81, 95% confidence interval [CI]: 0.76–0.85, $p<.001$), with a longer median duration of symptoms and HAF prescription compared with the duration of symptoms in those without CMA (3.48 vs. 2.96 years). GI, skin, respiratory and ear infections affected significantly more children with CMA than those without, increasing by 74% ($p<.001$), 20% ($p<.001$), 9% ($p<.001$), and 30% ($p<.001$) respectively. These infections also recurred more often among children with CMA, increasing by 62% for GI infections, 37% for skin and respiratory infections, and 44% for ear infections ($p<.001$).

Conclusion:

This real-world study provides evidence to suggest that CMA presents a significant clinical burden to children, which has implications for the healthcare system. Further research is warranted to understand the health economic impact of this, and the phenotypes, factors and management approaches which may affect clinical outcomes.

AMINO ACID FORMULA CONTAINING SYNBIOTICS IN INFANTS WITH COW'S MILK ALLERGY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction:

Cow's milk protein allergy (CMPA) is associated with dysbiosis of the infant gut microbiome, with allergic and immune development implications. Studies show benefits of combining synbiotics with hypoallergenic formulae, although evidence has never been systematically examined.

Method:

This review identified seven publications of four randomised controlled trials comparing an amino acid formula (AAF) with an AAF containing synbiotics (AAF-Syn) in infants with CMPA (mean age 8.6 months; 68% male, mean intervention 27.3 weeks, n = 410).

Results:

AAF and AAF-Syn were equally effective in managing allergic symptoms and promoting normal growth. Compared to AAF, significantly fewer infants fed AAF-Syn had infections (OR 0.35 (95% CI 0.19–0.67), p = 0.001). Overall medication use, including antibacterials and antifectives, was lower among infants fed AAF-Syn. Significantly fewer infants had hospital admissions with AAF-Syn compared to AAF (8.8% vs. 20.2%, p = 0.036; 56% reduction), leading to potential cost savings per infant of £164.05–£338.77. AAF-Syn was associated with increased bifidobacteria (difference in means 31.75, 95% CI 26.04–37.45, p < 0.0001); reduced Eubacterium rectale and Clostridium coccoides (difference in means –19.06, 95% CI –23.15 to –14.97, p < 0.0001); and reduced microbial diversity (p < 0.05), similar to that described in healthy breastfed infants, and may be associated with the improved clinical outcomes described.

Conclusion:

This review provides evidence that suggests combining synbiotics with AAF produces clinical benefits with potential economic implications.

THE USE OF AN AMINO ACID FORMULA CONTAINING SYNBIOTICS IN INFANTS WITH COW'S MILK PROTEIN ALLERGY—EFFECT ON CLINICAL OUTCOMES

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Introduction:

Cow's milk protein allergy (CMPA) is common and costly. Clinical trials of infants with CMPA have shown that the use of an amino acid formula containing pre- and probiotics (synbiotics) (AAF-Syn) may lead to significant reductions in infections, medication prescriptions and hospital admissions, compared to AAF without synbiotics. These effects have not yet been confirmed in real-world practice.

Method:

This retrospective matched cohort study examined clinical and healthcare data from The Health Improvement Network database, from 148 infants with CMPA (54% male, mean age at diagnosis 4.69 months), prescribed either AAF-Syn (probiotic Bifidobacterium breve M16-V and prebiotics, including chicory-derived oligo-fructose and long-chain inulin) or AAF.

Results:

AAF-Syn was associated with fewer symptoms (–37%, $p < 0.001$), infections (–35%, $p < 0.001$), medication prescriptions (–19%, $p < 0.001$) and healthcare contacts (–18%, $p = 0.15$) vs. AAF. Infants prescribed AAF-Syn had a significantly higher probability of achieving asymptomatic management without hypoallergenic formula (HAF) (adjusted HR 3.70, 95% CI 1.97–6.95, $p < 0.001$), with a shorter clinical course of symptoms (median time to asymptomatic management without HAF 1.35 years vs. 1.95 years). AAF-Syn was associated with potential cost-savings of £452.18 per infant over the clinical course of symptoms.

Conclusion:

These findings may be attributable to the effect of the specific synbiotic on the gut microbiome. Further research is warranted to explore this. This real-world study provides evidence consistent with clinical trials that AAF-Syn may produce clinical and healthcare benefits with potential economic impact.

THE USE OF AMINO ACID-BASED NUTRITIONAL FEEDS IS EFFECTIVE IN THE DIETARY MANAGEMENT OF PEDIATRIC EOSINOPHILIC OESOPHAGITIS

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Introduction:

Eosinophilic oesophagitis (EoE) is an immune-mediated, chronic disease characterized by eosinophilic inflammation and esophageal dysfunction. Specific food allergens including cow's milk protein, are partially causative to disease progression, and dietary management forms three main options; the elemental diet (ED), the empirical elimination diet (EED), and the targeted elimination diet (TED). The dietary choice should be individualized, however, the European Society for Pediatric Gastroenterology, Hepatology and Nutrition guidelines recommend an ED for pediatric EoE with multiple food allergies, failure to thrive, unresponsive disease or unable to follow a highly restricted diet. The aim of this narrative review was to explore the effectiveness of the ED (using amino acid formula [AAF]), in the management of pediatric EoE.

Method:

Literature searches were performed to identify eligible studies that described outcomes including eosinophil count, clinical symptoms, growth, and medications.

Results:

Overall, 10 eligible studies were found, with n = 462 patients assigned to receive AAF from a total of n = 748 (average age 6.7 years), for a duration of 4 to 8 weeks. The use of AAF reduced eosinophil levels and demonstrated remission (defined as ≤10 eosinophils per high power field) in 75%-100% of children with improvements, if not resolution, in clinical symptoms. AAF was more clinically effective than the use of the EED or TED, where remission rates were 75%-81% and 40%-69%, respectively. Few studies collected growth outcomes, however where documented these were positive for those on AAF. The long-term impacts of each diet were not thoroughly explored.

Conclusion:

The use of AAF is a clinically effective management option for pediatric EoE, and further research is required to guide long-term management.

THE USE OF AMINO-ACID FORMULAS IN THE DIETARY MANAGEMENT OF INFANTS WITH FOOD PROTEIN ENTEROCOLITIS SYNDROME: A LITERATURE REVIEW

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Presented at BSACI 2018. Published in Clinical and Experimental Allergy (2018), Vol. 48 (11): p1550

Introduction:

Recommendations in formula choice for the dietary management of food protein enterocolitis syndrome (FPIES) are not synonymous, although international FPIES guidelines recommend use of amino-acid formula (AAF) in those not responding to extensively hydrolysed formula (EHF) and faltering growth. This literature review was undertaken to summarise existing evidence for use of AAF in the dietary management of infants with FPIES.

Method:

Literature searches were performed (up to Mar 2018) on electronic databases (e.g. PubMed) to identify articles using relevant search terms including: 'elemental', 'amino-acid', all brand names of AAF. Studies describing outcomes (e.g. symptom resolution, growth) with AAF in infants with confirmed FPIES were included.

Results:

Whilst a number of studies described use of AAF in FPIES, no suitable trials with relevant outcomes were found. Five case studies were identified (mean age 42 days; all had poor weight gain at presentation) by four authors (Kelso et al 1993, Anand et al 2006, Mane et al. 2014, Joshi et al. 2018). Intervention with AAF led to symptom resolution (including vomiting, methemoglobinemia and bloody diarrhoea) in all cases, after failure with other formulas (including soya and EHF). Symptom resolution with AAF was reported rapidly (48-72 hours) by Kelso et al 1993 and Anand et al 2006. Improvements in mean weight gain by 51-97g/day were observed in two infants over 6-9 days (Anand et al. 2006) and after 5 months continuation with AAF, growth increased in one infant by 2 centiles (who had initially declined 4 centiles at presentation) (Joshi et al 2018).

Conclusion:

This limited number of case studies show symptom resolution and growth in infants with FPIES on AAF who failed to respond to other formulas. However, stronger research is required to assess the role of AAF in aiding symptom management, nutrient provision and growth in FPIES so clearer evidence-based guidelines can be developed.