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EAACI PAAM Paediatric Allergy and Asthma Meeting

Symposium **Speaker**

Prof.
Hania Szajewska
(Poland)

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The Value of Gut Modulating Ingredients in Cow's Milk Allergy (CMA) Treatment

Professor and Chair of the Department of Paediatrics at the Medical University of Warsaw. Editor in Chief of the Journal of Paediatric Gastroenterology and Nutrition. General Secretary of the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN). Board of Directors of the International Scientific Association for Probiotics and Prebiotics (ISAPP)

Introduction

The European Academy of Allergy and Clinical Immunology (EAACI) Paediatric Allergy and Asthma Meeting brings together leading experts and emerging professionals in paediatric allergy and asthma. In November 2023, important topics including research on environment and immunomodulation, food allergy, and the epigenetics of allergy in children were discussed. In this summary booklet, we provide you with a summary of the scientific discussion presented by Professor Hania Szajewska.

The Value of **Gut Modulating Ingredients** in **CMA Treatment**

In her presentation, Professor Szajewska explained that there is a growing interest in ingredients that can modulate the gut microbiota due to the importance of gut microbiota in general. She addressed the most common question of the features of gut microbiota dysbiosis in food allergies, noting that there is no consensus on how to define dysbiosis, but it can be referred to as altered gut microbiota. She explained that one common feature of dysbiosis is reduced diversity in the gut microbiota, emphasising the importance of a diverse microbiota. Professor Szajewska explained how the reduction of short-chain fatty acid producing bacteria is significant because short-chain fatty acids contribute to the production of regulatory T cells, which help suppress excessive immune responses. This aligned with the findings mentioned in Professor Knol's presentation.

Professor Szajewska addressed the practical concerns of patients and clinicians. She explained that patients are primarily concerned with whether diseases can be prevented, treated, or cured, rather than the science and microbiology behind it. This led to Professor Szajewska discussing strategies for modulating the gut microbiota, of which, diet is a strong modulator. However, other strategies exist including biotics (probiotics, prebiotics, synbiotics, postbiotics) and faecal or vaginal microbiota transfer. She provided the definitions of probiotics, prebiotics, synbiotics and postbiotics (table one, below).

Term	Definition
Probiotic[1]	Live microorganisms that, when administered in adequate amount, confer a health benefit on the host.
Prebiotic[2]	A substrate that is selectively utilised by host microorganisms conferring a health benefit.
Synbiotics[3]	A mixture comprising live microorganisms and substrate(s) selectively utilised by host microorganisms that confers a health benefit on the host.
Postbiotics[4]	A preparation of inanimate microorganisms and/or their components that confers a health benefit on the host.

Guidelines, Randomised Trials, and Real-World Evidence

Professor Szajewska summarised guidelines from different organisations regarding the benefit of microbiota-modulating ingredients in non-breastfed infants, highlighting some differences in the recommendations in relation to cow's milk allergy (table two, below). She noted that these recommendations were based on a detailed review of the same evidence.

"What does no recommendation for or against mean in practice? Different choices will be appropriate for different people and clinicians should help individuals make decisions that suit their needs."

Table Two: Comparison between GA2LEN and ESPGHAN recommendations

Recommendation	GA²LEN, 2022	ESPGHAN, 2023
First choice in CMA	Extensively hydrolysed cow's milk formula (EHF) or amino-acid formula (AAF), if better tolerated or more appropriate	EHF is the first choice for a therapeutic elimination diet, while AAF should be reserved for severe cases or in infants with an absent or partial response to EHF.
For or against biotics use	No recommendation for or against any prebiotics, probiotics or synbiotics that have been evaluated so far for managing food allergy, whether used as a supplement or added to infant formula.	There is insufficient evidence demonstrating that the addition of pro-, pre-, or synbiotics studied so far to EHF and AAF improves their therapeutic efficacy (in infants with CMA).

GA2LEN, Global Allergy and Asthma European Network; ESPGHAN, European Society for Paediatric Gastroenterology Hepatology and Nutrition

Guidelines, Randomised Trials, and Real-World Evidence continued

Professor Szajewska emphasised that each formula and each biotics needs to be evaluated separately. She described the potential mechanisms of action for probiotics, prebiotics and synbiotics, emphasising their impact on the immune system and the gut microbiome.

The findings of several studies, including randomised controlled trials and systematic reviews related to different interventions such as extensively hydrolysed formula and amino acid formula supplemented with specific prebiotics, probiotics or synbiotics were discussed. The potential benefits of these interventions, including a reduction in infection risk and medication use are presented in table three, below.

Table Three: Overview of research evidence to support hypoallergenic formula supplemented with specific prebiotics, probiotics or synbiotics

EHcF + LGG	EHwF + HMO-analogues	AAF + prebiotics#/B. breve M-16V
Three RCTs showed improvement in symptoms and tolerance.	A single study supported normal growth and suggested protection against respiratory and ear infections.	A review of seven studies showed lower rates of infection, higher rates of bifidobacteria and a reduction in use of antibiotics.

AAF, amino-acid formula; B. breve M-16V, probiotic strain bifidobacterium M-16V; EHcF, extensively hydrolysed casein formula; EHwF, extensively hydrolysed wheat formula; HMO, human milk oligosaccharides; LGG, Lactobacillus rhamnosus GG; RCTs, randomised controlled trials.

"It's important to differentiate between HMOs naturally occurring in human breast milk, and those that are synthetically produced."

Professor Szajewska highlighted the evolving landscape of evidence-based medicine, emphasising the growing importance of real-world data in addition to traditional randomised controlled trials. She presented results from three studies using real-world data to (1) evaluate the impact of amino-acid formula with synbiotics, (2) extensively hydrolysed formula with synbiotics, and (3) infants with cow's milk allergy versus healthy infants.

Although each study had inherent limitations, collectively, the results showed reductions in symptoms, infections, and medication use, as well as improvements in quality of life.

Professor Szajewska concluded her presentation by acknowledging that the audience needed to make their own predictions on the benefits of real-world data and on the use of gut microbiota modulators.

References

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