IMPACTING HEALTH IN THE NEW NORM WITH SPECIALISED NUTRITION

COWS' MILK PROTEIN ALLERGY SUMMARY

Nutricia Global Virtual Conference, 22 May 2021

For Healthcare Professionals only

The Nutricia Global Virtual Conference was a one-day CPD-accredited event with over 60 international speakers discussing current trends and understanding in specialised nutrition. Here we provide key findings from presentations relating to the management of cows' milk protein allergy (CMPA).

For access to the full recordings, please visit www.DanoneNutriciaCampus.org

Practical view on the diagnosis and management of CMPA
Chair: Dr Mário Vieira (Hospital Pequeno Príncipe, Brazil)

'Hints and tips on the diagnosis of CMPA' was delivered by Dr Carina Venter (University of Colorado, USA). Focusing on IgE-mediated (immediate reaction) and mild-to-moderate non-IgE-mediated (delayed reaction) CMPA, a key emphasis of her talk was that successful diagnosis depends on taking both a detailed clinical and dietary-focused allergy history.

For IgE-mediated CMPA, Dr Venter warned that specific IgE and skin prick tests should only be performed if results can be interpreted correctly and in context of the patient's history, noting that sensitisation does not necessarily mean allergy. Food challenges remain the gold standard for diagnosis and updated publication from the American Academy of Allergy, Asthma & Immunology provides practical guidance on milk oral food challenges.

Diagnosis of non-IgE-mediated CMPA remains an issue in clinical practice. Dr Venter advised that these infants will generally present with 2 or more symptoms (gastrointestinal, dermatological, respiratory) and highlighted that international guidelines now state that where troublesome reflux is present, first line of treatment should be a cows' milk protein elimination diet. For non-IgE-mediated CMPA, an elimination diet followed by home reintroduction after 2–4 weeks should be performed.

Concluding her talk, Dr Venter last tip to attendees was provide families of infants with CMPA with a lot of support outside of managing the symptoms.

Tasked with the job to decipher the numerous guidelines that exist on the management of CMPA, Dr Rosan Meyer (Imperial College, London) took attendees through a case study of a 12-week old girl to provide a *'Practical approach to choosing the right hypoallergenic formula for an infant with CMPA'*.

Presenting with symptoms of non-IgE mediated CMPA, the infant's mother was first provided with support to Continue breastfeeding but also wanted a formula suggestion for when she returned to work.

Initially treated with an extensively hydrolysed formula (eHF) (noting that soy is contraindicated in infants <6months), the infant demonstrated an overall improvement of symptoms but was now demonstrating faltering growth. Dr Meyer provided further insight into the clinical indications of faltering growth, explaining that despite symptom improvement, faltering growth can be an indicator of ongoing inflammation, which may contribute to the development of atopic comorbidities later in life.

In this case and in-line with guideline recommendations, the infant was subsequently switched to an amino acid-based formula (AAF). Dr Meyer, further highlighted that where more severe cases of CMPA occur, including failure to respond to eHF and faltering growth, use of amino acid-based formula should be considered.

Providing practical advice on pre- and probiotics in hypoallergenic formulas, Dr Meyer's take home message was that not all strains are the same and that only formulas containing strains that have been researched and demonstrated to provide benefit should be considered.

Key take-home messages

- Successful diagnosis of CMPA depends on a detailed history
- Specific testing should be used with caution in the diagnosis of IgE-mediated CMPA
- Non-IgE mediated CMPA will generally present with 2 or more symptoms
- eHF is suitable first line treatment for most infants with CMPA who are unable to be breastfed
- AAF should be considered for more severe cases of CMPA, including failure to thrive eHF and faltering growth

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Synbiotics in allergy management: Gut microbiota and immune defence in CMPA
Chair: Dr Mário Vieira (Hospital Pequeno Príncipe, Brazil)

Gut microbiota dysbiosis has now been shown to precede many chronic inflammatory diseases, such as asthma, atopic eczema and food allergy. Speaking on the *'Cause and effect of an imbalanced GI microbiota in early life,'* Prof Harald Renz of Philipps-University Marburg, Germany, provided his insights into the fascinating new research on mechanisms of host–microbe interactions.

"There is a clear small window of opportunity in early life where we set the stage for the rest of life."

While the detailed cellular cause and effect relationship may not yet be fully understood, Prof Renz stated that "there is a clear small window of opportunity in early life where we set the stage for the rest of life." Factors impacting early colonisation include prenatal (e.g., obesity, smoking, air pollution and antibiotics use) and perinatal (e.g., c-section) risk factors. In the postnatal space, Prof Renz focused on the importance of breastfeeding to establish a healthy microbiome characterised by Bifidobacterium and Lactobacillus. However, he noted that any changes in diet and health can dramatically shift the composition, and that these changes that can either help prevent or promote inflammation. This point was demonstrated with a discussion on the latest findings establishing short-chain fatty acids as a driver of tolerogenic T-cells.

Prof Renz finished his talk with a proposal of an individualised risk score to identify children at risk of chronic inflammation and who might benefit from the use of pre- and probiotics.

The presentation on *'Biotics from science to clinical application – where are we*?' took the form of an interactive discussion, between Prof Udo Herz (Global Industry, Medical and Science Director, Danone Nutricia) and Prof Seppo Salminen (University of Turku, Finland). After providing clear definitions on the biotic family, Prof Herz challenged Prof Salminen to provide clarity on a few key puzzle pieces.

- Why is early colonisation of the infant gut so important?

"The gut microbiota in a healthy state protects us from exposures later on" was Prof Salminen concluding remark. He reemphasised that the development of the microbiome begins before birth and that natural pre-, pro- and synbiotics already play an essential role to promote a beneficial environment in these early stages, with the predominance of Bifidobacterium and Lactobacillus considered integral to a healthy developing newborn gut microbiome.

- How does the biotic concept support infants with CMPA?

Prof Salminen explained that the biotic concept is based on the components of human milk. Through breastfeeding, infants are supplied with key probiotics and prebiotics in the form of human milk oligosaccharides (GOS/FOS), which contribute to a synbiotic environment. Similarly, the biotic concept is designed to try to mimic these effects in infants with CMPA and to help rebalance the gut microbiota.

- Why are the use of biotics not included in management guidelines?

Prof Salminen believes that this is a case of science being a forerunner and regulations playing catch-up. Studies for the use of biotics has mainly been performed in adults, leading to confusion around efficacy; however, evidence is now growing for the use of pre- and probiotics in infants, and they are increasingly being recommended by medical and nutritional societies, including the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPHGAN), World Allergy Organization (WAO) and most recently, the American Gastroenterological Association (AGA).

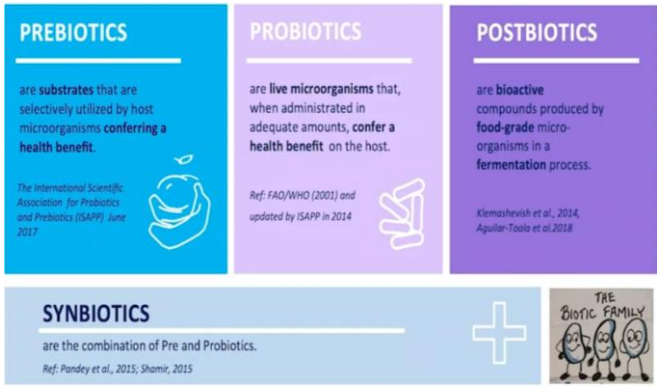

Image presented by Prof Seppo Salminen.

- What does the future look like for the composition of hypoallergenic formula?

With more than 200 human milk oligosaccharides, more research is needed to understand the role each of these plays. Prof Salminen also acknowledged that more research is needed into the gut microbiota composition, but concluded that our current knowledge, in combination with the availability of biotics, puts us in a good standing for the management of CMPA.

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Prof Anna Nowak--Węgrzyn from NYU Langone Hospital, USA, concluded the session by specifically focusing on the '*Clinical benefits of synbiotics beyond the dietary management of infants with cows' milk allergy*'.

Human breast milk is the gold standard in infant nutrition but is also the ultimate synbiotic – containing live bacteria, prebiotic oligosaccharides and lactose to stimulate gut microbiota and the immune system.

Traditional hypoallergenic formulas, while mitigating CMPA symptoms, lacked these key microbiota-stimulating factors, potentially further compounding the underlying issue.

New-generation hypoallergenic formulas now contain a synbiotic blend of pre- and probiotics that mimic the components of human milk. A prebiotic mix of scGOS/lcFOS (9:1) or scFOS/lcFOS (9:1) mimics the levels and functionality of human milk oligosaccharides, while inclusion of *Bifidobacterium breve* M16 – predominant in healthy breastfed infant gut – has been shown to reduce allergic response.

Key take-home messages

- Early life is a critical time for the development of the gut microbiota and maturation of the immune system.
- Infants with CMPA often have gut dysbiosis, which can lead to an increased risk of developing chronic inflammatory disease later on in life.
- New-generation hypoallergenic infant formulas (eHF and AAF) with synbiotics have been shown to help rebalance the gut microbiota and replicate the immunomodulatory effects of human milk.
- Pre- and probiotics are being increasingly recommended by international medical and nutritional societies, including ESPGHAN, WAO and AGA.

The biotics family in early life and their role on immunity

Chair: Prof Seppo Salminen (University of Turku, Finland)

If you feed an infant the right prebiotic composition, you can support a healthy gut microbiome in early life – this was one of Prof Mohamad Miqdady (Sheikh Khalifa Medical City, UAE) opening statements in his presentation on '*Feeding the microbiome – prebiotics and human milk oligosaccharides*'.

First providing a breakdown of the composition of human milk, Prof Miqdady highlighted the significance of the prebiotic oligosaccharides, both in their complexity of over 200 structures (of which, only 162 have been identified to date), and in their amount, representing between 12-15g/L – a level higher than the protein content.

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Prof Miqdady concluded his talk by discussing updates to the international recommendations (WAO and ESPGHAN) and added that the role of paediatricians is to not only focus on physical growth and development but to also look further by reducing incidence of GI, respiratory and allergic disease that will impact health in later childhood and adulthood.

Taking attendees through the complex world of synbiotics was Prof Niko Papadopoulos (University of Manchester, UK; OPRI, Singapore) who endeavoured to answer the question '*How can synbiotics modulate the microbiota and shape of the immune system?*'

Prof Papadopoulos began his talk with an overview of the development of the immune system, highlighting that the microbiome reaches a state of maturation relatively early – around the age of 2-3 years – during which, the microbiome plays a key role to aid the immune system in distinguishing self from non-self, and in developing antigen-specific tolerance.

After introducing the synbiotic concept (previously described in this report), Prof Papadopoulos further added to the definition, that two types of synbiotics existed: ones that are complementary and ones that work together to produce a synergistic effect.

To date, not many synbiotics have been evaluated but clinical data so far have supported the use of synbiotics in quickly rebalancing the gut microbiome following c-section to levels similar to an infant delivered via a vaginal birth.

Prof Papadopoulos finished his presentation by looking at the specific combination of scGOS/lcFOS + *Bifidobacterium breve* M16. In a clinical study of 290 infants 6-9 weeks old, those who were supplemented with the scGOS/lcFOS + *Bifidobacterium breve* M16 synbiotic, developed a gut flora microbiome (bacterial type and faecal pH) similar to that of breastfed infants.

Key take-home messages

- Immunity is shaped to a considerable extent through the microbiome.
- Prebiotic mix of scGOS/lcFOS (9:1) has been proven to stimulate growth of bifidobacteria and provide long-term immunomodulatory effects.
- Use of a synbiotic supplementation that works synergistically can provide additional beneficial effects on the gut microbiome.
- The synbiotic scGOS/lcFOS (9:1) + *Bifidobacterium breve* M16 has been shown to quickly promote a gut microbiome similar to that of a breastfed infant.