

News from congresses, symposia, workshops, medical-scientific meetings and conferences

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7th European Pediatric GI Motility Meeting

Hilton Sorrento Palace Hotel, Sorrento, Italy

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At the beginning of October, the seventh European Gastrointestinal Pediatric Motility Meeting was held, to discuss relevant topics in paediatric gastroenterology. Overall, functional gastrointestinal disorders (F GI D) represent one of the most common and stressful conditions for babies and their parents: the most recent evidence on incidence, aetiology, impact and management of the various types of F GI D was thus reviewed in depth during the congress and new evidence on the possible therapeutic approaches was presented.

In particular, on the morning of Friday, 2nd October, a session of three lectures on F GI D received great attention from the audience. The speakers at these lessons were Prof. De Vos from the Netherlands, Prof. Vandenplas, from Belgium, and Prof. Miele from the nearby Naples University.

The microbiome/microbiota represents a "hot topic", since its implications for both the body and the brain are generating a lot of interest, posing a number of challenges and generating new concepts. In particular, since factors altering intestinal microbiota can start a vicious circle leading to chronic diseases such as I BS and even I BD, there could be a window of opportunity to impact later life health with a proper selection of the right intestinal microbial species in early life. An interesting observation is that children with colics show a delayed development of intestinal bacterial flora diversification, further supporting the concept of a targeted intervention on the intestinal microbiome (1). A further interesting concept is that maternal stress, through increased cortisol levels, can negatively impact intestinal flora. In particular, high levels of cortisol in mothers have proven to be associated with an unfavourable intestinal microbiota profile, while lower levels of cortisol are associated with a more favourable one, characterized by an increase in *Bifidus spp.* and a reduced proliferation of *E. coli* strains. As a consequence, this aberrant colonization pattern was related to more maternally reported infant gastrointestinal symptoms and allergic reactions (2).

Considering the importance of the microbiota diversity, a proper and limited use of antibiotics in children is strongly advised, to avoid an imbalance and negative selection of intestinal bacterial species.

This session also dealt with the issue of F GI D in the first year of life, a condition affecting about one child in two. In the setting of F GI D, colics have a highly prominent role, since colicky children show an incidence of other F GI D (i.e.: nausea, reflux diarrhoea...) nearly twice as high as non-colicky ones (F I P S study, in preparation). The results of an international consensus on F GI D confirmed an approach based on reassurance and the use of the safest type of intervention, such as herbal remedies, probiotics or a combination of the two, and was the base for the development of a smartphone app to help GPs deal with the issue of F GI D.

One of the remarks of this lecture was that in F GI D there are more reviews than original studies: this could

be partly changed from the preliminary data of a study presented in this congress, regarding the treatment of colics with a standardized, composite herbal remedy. Infant colic is a complex theme, already from its definition: currently, there are more than ten definitions available of this disorder that are mainly based on the duration of infant crying and its impact on the parent. In spite of relatively small differences between them, this variety of definitions can produce a great difference in the estimated rate of colics.

Today, the accepted incidence of colics is 10-30% of children aged between two weeks and four months, with no differences linked to sex, type of feeding or type of delivery (3). This high prevalence is supported by the evidence that colics are responsible for nearly one pediatric consultation in four in the first four months of life, with a huge impact for the healthcare system.

Overall, colics tend to arise in the first three weeks of life and disappear within the fourth month, and have a complex and multifactorial aetiology (Fig. 1).



Colics represent a benign and usually self-limiting condition and – clinically – the only caution is represented by a proper differential diagnosis to exclude other conditions (such as infections) according to the "IT- CRI ES" criteria and other alerting signals such as the Sandifer position (4,5).

Even if benign, self-limiting and transient in nature, colics must not be underestimated, due to their impact not only on babies but also on their parents, who can suffer a huge amount of stress. Their inability to cope with this stress can have serious consequences, the most dramatic of which is the so-called "shaken baby syndrome," currently the most frequent non-natural cause of death in infants (6). Moreover, excessive infant crying is usually addressed as one of the main causes of maternal postnatal depression (7). Once the need for intervention in colics has been addressed, an analysis of the available treatment approaches underlines the substantial lack of a standard of care. Beyond reassurance, that remains the cornerstone of colics management, the evidence available for drugs is either weak (cimetropium bromide) or absent (symethicone) or there is evidence of efficacy but coupled with severe side effects (dicyclomine).

A more robust evidence seems to be available for probiotics, and in particular for *Lactobacillus reuteri*, through two meta-analyses dating from 2013: at any rate, as stressed by the speaker himself, the three studies included in these publications have relevant methodological limitations, such as the lack of objective measures of crying. More recently, another trial provided substantially positive results for this approach but, overall, the evidence on probiotics is controversial, with a mix of positive and negative results not clarified even by metanalysis that does not allow a clear recommendation on this topic.

Regarding treatment for infant colics, an analysis of the available herbal treatment shows that this approach has already demonstrated some encouraging results and reassuring safety profile in small or non-controlled trials, that have yet to be confirmed in larger randomized studies.

To overcome this limitation, Prof. Miele and his group performed a well-designed, multicentre prospective, randomized comparative study on 133 infants with colic according to Rome III criteria, who were assigned at random to receive a preparation with *Chamomilla L.*, *Melissa officinalis L.* and tyndallized *Lactobacillus acidophilus* (HA122) (Group A; n = 45), *Lactobacillus reuteri* DSM 17938 (Group B; n = 45) or symethicone (Group C; n = 43) for 21 days, with an overall four-week follow-up. Treatment success was assessed at the end of study period through daily crying and fussing times, recorded in a structured diary, and maternal questionnaires that assessed changes in infant colic symptoms and adverse events. Overall, groups A and B had a superior results when compared with group C. A similar pattern was observed for the percentage of responder patients, i.e. those with a mean reduction in crying time greater than 50% from baseline, that proved to be highest with the combined approach with *Chamomilla L., Melissa officinalis L.* and tyndallized *Lactobacillus acidophilus* (HA122), followed by probiotic alone and with symethicone being the least effective intervention.

A positive impact of *Chamomilla L., Melissa officinalis* L. and tyndallized *Lactobacillus acidophilus* (HA122) was also observed in terms of reduced mean daily fuss time and increased sleep duration, with a significant improvement in both parameters *versus* symethicone. None of the three treatment approaches produced any relevant side effect.

Thus, this study suggests that administration of *Cha*momilla L., *Melissa officinalis L.* and tyndallized *Lacto*bacillus acidophilus (HA122) – commercially available



Mean daily crying of the three different groups' treatment at enrolment, T14 and T28: Chamomile L., Melissa officinalis L. and tyndallized Lactobacillus acidophilus (HA122) (n=45), Lactobacillus reuteri DSM 17938 (108 CFU) (n=45), Symethicone (n=43). Follow-up: four weeks

as *Colimil Plus* - and *Lactobacillus reuteri* DSM 17938 are significantly more effective than symethicone in improving colic symptoms and indicates the use of a combined approach with herbal extracts and tyndalized probiotics as a new and valuable therapeutic strategy in the management of colicky infants. This result is in line with the available evidence that says that, considering the multifactorial nature of colics, the most effective approach should be a well-tolerated, multifactorial and personalized strategy.

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