



Interview with Dr. Chow Chung Mo

The management of infant feeding intolerance in clinical practice

This article incorporates expert opinion by Dr. Chow Chung Mo and findings from a recently published double-blind randomized controlled trial by Vivatvakin *et al.* (2020), exploring how different nutritional components may help to alleviate infant feeding intolerance.



Dr. Chow Chung Mo

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CCM: Dr. Chow Chung Mo **R:** Reporter

R: Is infant feeding intolerance a common problem in Hong Kong and what are the common reasons for causing it?

CCM: There is no data in Hong Kong, but this is a common phenomenon globally where nearly half of the infants would occasionally have symptoms of feeding intolerance¹. When parents first observe these symptoms, they often reach out to family members, friends, babysitters and online social media to seek advice instead of going to a healthcare professional directly.

The underlying etiology of feeding intolerance is often multifactorial and elusive, with possible reasons including biological disturbances due to an immature gastrointestinal (GI) tract, neurodevelopmental changes, psychosocial and environmental factors²⁻⁶. Alterations in the infant gut microbiome may also contribute to the symptoms of feeding intolerance^{2,7,8}.

R: According to a newly published paper by Vivatvakin *et al.* (2020), infants may go through formula change due to parent-perceived feeding intolerance², when do you think a change is properly indicated?

CCM: The decision is not always straight forward and the key is to first determine whether the intolerance is a normal phenomenon or rather, caused by an underlying medical condition with similar symptoms. Common manifestations of feeding intolerance include infrequent stooling and hard stools, spitting-up, gassiness and behaviours of discomfort such as fussiness, crying and dysregulated sleep^{2,3,9,10}. Taking a good history and conducting a physical examination are important to check on the general condition and nutritional status of the child, which can help to identify warning signs

pointing to other diseases. For example, symptoms like vomiting with coffee ground vomitus, suboptimal weight gain and back arching during feeding may indicate gastroesophageal reflux disease (GERD). Food allergies such as cow's milk protein allergy (CMPA) can also be presented with constipation or vomiting. If the child has a family history of allergy or atopy, and a physical examination shows features of atopic dermatitis, it is more suggestive of CMPA than feeding intolerances.

To note, feeding intolerance is not limited to formula-fed infants. In my experiences, I have seen breastfed infants with infrequent bowel opening, with the most extreme case being on a biweekly basis. The parents are understandably stressed but if the child is clinically fine nor showing any abdominal distention, there is no indication to recommend a change from breastfeeding to other formulas.



R: How do you think specific nutrients contribute to feeding intolerance?

CCM: Breast milk is the best food for babies. However, some nutritional components with potential to improve symptoms include whey and partially hydrolysed protein, *sn-2* palmitate fatty acids and lowered lactose content. There is some scientific base to these nutritional changes, both in animal studies and in human studies^{2,10-18}, such as with the improved sleep, reduced crying and vomiting observed in the study by Vivatvakin *et al.* (2020)². However, further high-quality studies are warranted to confirm efficacy.

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Another consideration regarding the digestibility of protein includes A2 β -casein protein, which has been shown in some studies to have faster GI transit time than the A1 variant, reducing the likelihood of constipation and feeding intolerance^{9,20}.

R: Any tips you wish to share with healthcare professionals regarding the management of these pediatric cases?

CCM: Reassurance to parents is essential. If no underlying medical disease is identified and it is a confirmed case of feeding intolerance, reassure parents that the infant will recover with natural course. This will help to ease the anxiety and stress of the parents, which often arises from symptoms such as infantile colic with prolonged crying periods. Breastfed infants should continue with their feeding. On the other hand with some scientific base and clinical data, formulas with adjusted nutritional components may be provided to infants who are formula-fed.

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Latest findings by Vivatvakin *et al.* on infant feeding composition and feeding intolerance (2020)²

Study methods:

- A double-blind randomized 14-day feeding study in six Asian centers (Taiwan, Hong Kong, Thailand and the Philippines)
- Key recruitment criteria for subjects:
 - Exclusively formula-fed infants (**standard, full-lactose, intact cow’s milk protein formula**) aged 30 to 90 days, and;
 - Reported frequent “fussiness and crying” (often, 2-3 hours/day, or very often > 3 hours/day), and;
 - Gassy (moderate or extreme) and/or experiencing stooling difficulties
- Randomly assigned to different feeding for 14 days:
 - Study formula A (FA) ($n = 130$), **100% partially hydrolysed whey protein, reduced lactose (54% of total carbohydrates) and with a fat blend enriched in *sn-2* palmitate**, or;

- Study formula B (FB) ($n = 129$), **α -lactalbumin-enriched formula with 65% intact whey protein, 35% casein, full lactose (100%) and a non *sn-2* palmitate enriched fat blend**

- Measured endpoints include daily duration of fussiness-crying, gassiness, spitting-up, vomiting, sleep pattern, Infant Gastrointestinal Symptom Questionnaire (IGSQ) Index, infant temperament and maternal anxiety

Key findings:

- **Mean duration of fussiness-crying** in the 256 analyzed infants (FA, $n = 127$ and FB, $n = 129$) **significantly decreased from baseline to study end**, with no difference between groups
 - FA: 291 to 140 min/day, -52% ($p < 0.001$)
 - FB: 313 to 153 min/day, -51% ($p < 0.001$)
- Similarly, **gassiness, spitting-up, vomiting, sleep pattern, infant temperament, maternal anxiety significantly improved by study end for both formulas**
- There was a **significant increase in sleep duration (minutes/day) throughout the whole study** ($p < 0.001$), with 10 to 15% more minutes per day compared with baseline in both formula groups
- **Mean IGSQ index scores significantly decreased** from baseline to study end by approximately 35%, **indicating a lower GI burden**, with no difference between groups
 - FA: 44.5 to 28.6 ($p < 0.001$)
 - FB: 44.5 to 29.0 ($p < 0.001$)
- Stool consistency and frequency did not change significantly from baseline in both formula groups

Conclusion:

- **Compositional adjustments in tested infant formulas are favourable for ameliorating GI symptoms and associated behaviours in infants with signs of feeding intolerance**

References: 1. Vandenplas Y *et al.* *Pediatr Gastroenterol Hepatol Nutr.* 2019;22(3):297-216. 2. Vivatvakin B *et al.* *Global Pediatr Health.* 2020;7:1-14. 3. Alarcon PA *et al.* *Nutrition.* 2002;18:484-489. 4. Douglas PS *et al.* *Med J Aust.* 2010;193:533-536. 5. Sherman PM *et al.* *Am J Gastroenterol.* 2009;104:1278-1295. 6. Vandenplas Y *et al.* *Nestle Nutr Inst Workshop ser.* 2016;86:29-37. 7. Partty A *et al.* *PLoS One.* 2012;7:e32495. 8. De Weerth C *et al.* *Pediatrics.* 2013;131:e550-e558. 9. Iacono G *et al.* *Dig Liver Dis.* 2005;37:432-438. 10. Infante Pina D *et al.* *World J Gastroenterol.* 2008;14:248-254. 11. Berseeth CL *et al.* *Clin Pediatr (Phila).* 2009;48:58-65. 12. Indrio F *et al.* *Nutrients.* 2017;9:1181. 13. Mihatsch WA *et al.* *Pediatrics.* 2002;110:1199-1203. 14. Nowacki J *et al.* *Nutrition J.* 2014;13:105. 15. Yao MJ *et al.* *J Pediatr Gastroenterol Nutr.* 2014;59:440-448. 16. Bar-Yoseph F *et al.* *Clinics Mother Child Health.* 2017;14:2. 17. Barr RG. *J Dev Behav Pediatr.* 1991;12:248-253. 18. Kanabar D *et al.* *J Hum Nutr Diet.* 2001;14:359-363. 19. Sheng X *et al.* *J Pediatr Gastroenterol Nutr.* 2019;69:375-382. 20. Sadler MJ and Smith M. *Infant.* 2013;9(5):173-176.

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