

Formula Change for Difficult Infant Behavior - Why Are We Still Discussing This?

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Source: Sherman AL, Anderson JA, Rudolf CD, et al. Lactose-free milk or soy-based formulas do not improve caregivers' distress or perceptions of difficult infant behavior. [J Pediatr Gastroenterol Nutr. 2015;61\(1\):119-129](#); doi:10.197/0000000000000743. See [AAP Grand Rounds commentary by Dr. Ronald Holmes](#) (subscription required).

PICO Question: Among infants with feeding problems, do caregivers' distress or perceptions of infant behaviors improve by feeding lactose-free milk-based or soy-based formula compared to milk-based, lactose-containing formula?

Question type: Treatment

Study design: Double-blind randomized controlled

This study, which was funded by an infant formula company (and 1 of the 4 study authors is an employee of the company), did not support switching to lactose-free milk or soy-based formulas to alleviate perceived feeding problems (fussiness, crying, cramping, gas, or diarrhea) in formula-fed infants 2 - 12 weeks of age. My bias on the subject tells me this is probably true, but I think this study has serious flaws that prevent any conclusions from being drawn.



Depiction of colic in a 1910 textbook by Henry Koplik (yes, the one who described Koplik spots in measles). He recommended increasing sugar to fat ratio in formula fed infants or attending to hygiene of the wet nurse for breast fed infants. There was no mention of sherry. By SteinsplitterBot via Wikimedia. First, the study appears to be underpowered. The authors calculated they would need 100 infants in each of the 3 formula groups (milk-based lactose-containing formula, lactose-free milk formula, or lactose-free soy formula) in order to detect a statistically significant difference among the groups. (Estimates for their power analysis included an assumption of 30% of infants in the control group A resolution of symptoms, plus considering a 20% difference between control and lactose-free groups as being important. They didn't allow for any infants withdrawing or being lost to follow-up. Although they did enroll and randomize around 100 infants in each group, many fewer completed the study: 85 in the control group, 80 in the lactose-free milk group, and 69 in the lactose-free soy group. Since the purpose of performing a power analysis is to make sure the study has enough patients to exclude the possibility that a finding of no difference wasn't just the result of having insufficient numbers of patients, this is a problem.

Second, investigators would ordinarily perform an intention-to-treat analysis, where all study subjects

actually randomized are included in a final analysis, usually counting the subjects not completing the study as treatment failures. An ITT analysis can minimize problems with crossover (e.g. if a mother didn't stick with the assigned formula) and early dropout, problems that can occur even in a blinded study. These investigators performed a different ITT analysis called last value carried forward, which might be a little kinder to the study results (i.e. less likely to show treatment failures). I have emailed the study's senior author to ask her about the low study power and choice of ITT analysis. If she answers me, I'll post it.

Getting back to my son, he wouldn't have qualified for this study since he was breast fed. His pediatrician's intervention was followed by an astounding resolution of his colicky symptoms. I wonder if, in retrospect, this was the start of my interest in evidence-based medicine - well-designed randomized controlled trials always should trump anecdotal experience. I suspect my son's "cure" was coincidental, or perhaps more likely related to his new parents finally being able to relax for a night.

Further Reading

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