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Infants With NAS - Is One Formula Better Than Another?

by Lydia Furman MD, Associate Editor, Pediatrics

Blog author note: Three of the study authors are from my home institution.

In a recently released issue of *Pediatrics*, Dr. Heather Kaplan and colleagues (10.1542/peds.2019-0914) from the Ohio Perinatal Quality Collaborative (OPQC) used a technique called "Orchestrated Testing" to reduce length of stay and improve non-pharmacologic care of infants with Neonatal Abstinence Syndrome (NAS) who were receiving formula for feedings. Orchestrated Testing "…is an application of planned experimentation that allows simultaneous examination of multiple practices (bundle elements) to determine which intervention or combination of interventions affects the outcome…"[1] This type of quality improvement is well suited to multi-center collaborative work, and in fact the participating OPQC centers represented all level-3 and 89% of the level-2 neonatal intensive care units (NICUs) in the state of Ohio at the time of the project. Interestingly, the OPQC had previously recommended use of low lactose, high calorie formula based on expert consensus and preliminary data, but adherence across centers was suboptimal, with <60% of infants receiving low lactose formula and <20% receiving high calorie formula. Rather than doubling down on implementation strategies, the study team made this a unique opportunity to study whether standardizing formula type could actually improve care by reducing length of hospital stay for infants with NAS.

Thus each participating center across Ohio self-selected into one of 4 groups: low lactose formula, standard lactose formula, high calorie formula (22 calories per ounce term formula) and standard calorie formula, based on the formula type each NICU staff and faculty felt most confident they could adhere to throughout the study period. Ultimately 47 sites caring for 546 infants with NAS born at ≥37 weeks of gestation were included, while 2985 infants not receiving pharmacologic treatment for NAS and 65 exclusively breastfed infants were excluded from the trial. (A word about breastfeeding shortly!) Each center was responsible for its own quality and reliability processes, attended monthly webinars and reported data on which formula was used (>90% of the time during pharmacologic treatment), and on primary outcomes (length of stay) and secondary outcomes (such as failed opioid wean or >10% drop below birthweight in the first 7 days) during the Orchestrated Testing (OT) phase. During the 12 months-long implementation phase that followed the sharing of OT phase results, reporting of formula type use was simplified to use ">50% of the time during pharmacologic treatment". Viewing Figure 1-3, and toggling up to the Analysis section which explains clearly what is displayed, is a helpful way to understand the analysis of the OT phase results.

The OT phase demonstrated that the use of high calorie formula, regardless of lactose content, was optimal, and the collaborative was able to decrease length of stay over the period of the study. As the authors note, skin-to-skin care, rooming in and breastfeeding whenever possible, are all interventions that significantly improve outcomes among infants with NAS undergoing treatment.[2-4] However, not all mothers of infants with NAS are

able to be supported to exclusively breastfeed. The very specific focus of this study by Kaplan and colleagues on the precise type of formula that is best for those infants is exemplar in several ways. The study design and methods are accessible and well explained. The study also sets a beautiful example of how thoughtful, collaborative, and yet rigorous studies can deliver key information, and demonstrates how a large group of centers can work together in a mutually respectful way to improve care. Kudos to the OPQC and the authors for this work and for sharing it in this important article

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- Diagnosis Codes and Case Definitions for Neonatal Abstinence Syndrome
- Introduction of a Neonatal Abstinence Syndrome Non-Pharmacologic Interventions Bundle to Improve Care of At-Risk Newborns
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