

pain within 24 hours could have been switched over to oral drugs therapy and the same was also done by us. However, as our study end point was achieved, we have not mentioned these in our manuscript.

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Feeding Schedule in Preterm Infants: Two hourly versus Three Hourly

We read with interest the recently published randomized controlled trial by Yadav, et al. [1] comparing two-hourly and three-hourly feeding schedule in very-low-birth-weight neonates. We seek the following clarifications:

- i) It is not clear whether the neonates were randomized at birth, at the time of introduction of feeds or at a specific time point within the first 96 hours. This is important, the time of randomization has a direct bearing on the primary outcome.
- ii) The authors mention that the subgroup analysis was as per birthweight (1000-1250 grams vs >1250 grams), however, the same is not reported here. This subgroup analysis is vital and will help in increasing the generalizability in babies <1250 grams.
- iii) In this trial, 40% of the enrolled neonates were small for gestational age (SGA) who are at higher risk for feed intolerance, hypoglycemia, and necrotizing enterocolitis (NEC) [2]. Therefore, it is desirable to have a subgroup analysis for SGA neonates for the above-said outcomes.
- iv) What was the rationale for excluding infants with the absent or reversed end-diastolic flow? A recent large body of evidence did not show any interaction between antenatal absent or reversed end-diastolic umbilical flow and feeding advancement [3].
- v) One of the major rationales of doing this trial was that three hourly feeding intervals might reduce nursing time in a resource-constrained setting. The previous study has shown that three hourly feedings are associated with shorter nursing time per infant [4]. It is desirable to have this data.
- vi) Probiotic use can have a direct impact on mortality and NEC rates and may act as a confounder. Therefore, it is desirable to compare the probiotic use among two groups.
- vii) Though the authors have presented time to full enteral feeds, many preterm neonates (<1250 grams) must be on tube feeds at the time of enrolment. It will be interesting to know whether there was any difference among the two groups in the time to reach full oral feeds (spoon/paladi/cup) and the duration of the transition in neonates who were on tube feeds at enrolment.

Recently a group of researchers advocated that the clinical trials should choose uniform outcome measures and report all clinically relevant outcomes for uniformity [5]. For trials related to feeding a set of important clinical outcomes shall also include weight gain (g/kg/d), time to regain birth weight, length of hospital stays, duration of parenteral nutrition, sepsis rates, along with other vital outcomes like retinopathy of prematurity and bronchopulmonary dysplasia. The authors should report this data to improve the generalizability of the study.

We sincerely believe that the clarification of the above points shall be immensely helpful for the clinicians and researchers.

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REFERENCES

1. Yadav A, Siddiqui N, Debata PK. Two-hourly versus three-hourly feeding in very low birthweight neonates: A randomized controlled trial. *Indian Pediatr.* 2021;58:320-4.
2. Ree IMC, Smits-Wintjens VEJ, Rijnjtes-Jacobs EGJ, et al. Necrotizing enterocolitis in small-for-gestational-age neonates: A matched case-control study. *Neonatology.* 2014;105:74-8.
3. Dorling J, Abbott J, Berrington J, et al. Controlled trial of two incremental milk-feeding rates in preterm infants. *N Engl J Med.* 2019;381:1434-43.
4. Dhingra A, Agrawal SK, Kumar P, et al. A randomised controlled trial of two feeding schedules in neonates weighing d"1750 g. *J Matern-Fetal Neonatal Med.* 2009;22:198-203.
5. Webbe JWH, Duffy JMN, Afonso E, et al. Core outcomes in neonatology: Development of a core outcome set for neonatal research. *Arch Dis Child Fetal Neonatal Ed.* 2020;105:425-31.

AUTHORS' REPLY

We appreciate the readers' interest in our study [1], and provide the clarifications:

- i) The neonates were approached for randomization within first 96 hours and were enrolled as soon as the participants were deemed fit for inclusion. However, we did not record exact time of randomization or initiation of feeding.
- ii) We agree with the point about subgroup analysis based upon weight and small for gestational age status. Detailed analysis shall be published later. There was no difference in time to reach full enteral feed, hypoglycemia, feed intolerance or necrotizing enterocolitis (NEC) among small for gestational age (SGA) neonates too (**Table I**). This finding is reassuring and indicates the applicability of