

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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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

Table I Comparison of Primary and Secondary Outcomes as per Appropriateness for Gestational Age

Outcomes	Two-hourly group (n=110)	Three-hourly group (n=99)
<i>Appropriate for gestational age</i>		
Time to reach full enteral feeds (n=100) ^a	5.27 (1.73)	4.90 (1.17)
Hypoglycemia	4 (3.64)	3 (2.97)
Episodes of feed intolerance	8 (7.27)	5 (5.1)
Necrotising enterocolitis	0	2 (1.98)
<i>Small for gestational age</i>		
Time to reach full enteral feeds (d) ^a	5 (1.49)	5.36 (2.09)
Hypoglycemia	2 (3.08)	4 (5.41)
Episodes of feed intolerance	5 (7.69)	7 (9.46)
Necrotising enterocolitis	4 (6.15)	3 (4.05)

Values in no. (%) except ^amean (SD). All *P* values >0.05.

trial to growth restricted neonates which are considered at higher risk for adverse outcomes. The SGA neonates were overall at significantly higher risk for NEC (7 vs 2; *P*-0.016) as compared to appropriate for gestational age, irrespective of feeding schedule.

iii) We agree with the point raised over excluding neonates with absent or reversed end diastolic flow (A/REDF). However, at the time of commencement of the study (2017) our unit policy was withholding feeds for first 24 hours and thereafter slow advancement of feeds (10-20 mL/kg/day) in neonates with A/REDF [2]. For the index study we planned rapid advancement of feeds (30 mL/kg/day) for all enrolled infants and the team was worried over the rapid advancement of feeds in A/REDF population.

Therefore, inclusion of neonates with A/REDF would have either led to deviation from the protocol. Also, as of now, three-hourly feeding is not a standard of care. Therefore, to ensure uniformity in study protocol and to ensure safety we excluded neonates with A/REDF. We are also aware of the Cochrane review published in 2017 (after commencement of our study) showing no evidence of increase in NEC with rapid advancement of feed in these neonates [3].

iv) We agree that it is an important outcome. However, we did not objectively record this data.

v) None of the neonates in the study received probiotics.

vi) Due to high volume of admissions and rapid turnover we did not record time to reach full oral feeds and the duration of the transition in neonates who were on tube feeds at enrolment. However, as per our policy the spoon feeds are started at 31 weeks of postmenstrual age.

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Artificial Intelligence in Medical Education

Artificial Intelligence (AI) is bringing a great transformation in all spheres of life including healthcare sector. Recent work has proved that AI techniques have a great potential in making healthcare facilities affordable and easily accessible [1]. AI promises early diagnosis of diseases, improved patient care and facilitating continuous monitoring of patients. However, for an optimized use of AI for healthcare, doctors and AI experts need to collaborate. Thus, it is desirable that medical graduates have a good understanding of data science and AI techniques, they are going to need to handle it in the near future.

Researchers have developed powerful high-performance AI tools in healthcare to predict the occurrence of many chronic diseases like cancers, diabetes, etc. [2]. Many AI tools have already been approved by regulatory authorities to diagnose

diseases, and are being used in primary healthcare centres of rural areas in developed countries like USA [3]. As the healthcare policy-makers are looking forward to amalgamating AI in healthcare sector, it is high time that medical education curriculum be updated to include formal education of emerging medical professionals in this technology. Introduction of AI in medical education curriculum has previously also been suggested [4]. Curriculum should be focussed on AI literacy rather than expertise. AI researchers/data scientists may act as resource persons to conduct faculty development programs in AI for medical faculty. The subject must be taught making sure that complex mathematics is avoided, and the concepts are explained in an easy way. For the medical students, emphasis should be laid on population health and evidence-based medicine. Clinicians should have a formal training of using AI tools to spot anomalies, forecast patterns from medical data and make decisions. Medical students may be provided with an opportunity to see and observe simple concepts of data mining working with small data science projects to enable them to use AI techniques to get meaningful information from data.