

Two-hourly Feeding versus Three-hourly Feeding for Attaining Early Enteral Feed in Low-birth-weight Preterm Babies: A Randomised Controlled Trial

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ABSTRACT

Introduction: There has been no consensus on whether a two-hour or three-hour feeding interval is safe and economical for preterm neonates. The parameters like feeding tolerance, the occurrence of infection and time required to attain full enteral feed and other outcome need to be clinically proven.

Aim: To investigate whether two-hourly or three-hourly feeding interval is better in preterm neonates to ensure full enteral feeding in lesser time.

Materials and Methods: The present randomised controlled trial was conducted in the Department of Paediatrics, Kempegowda Institute of Medical Sciences, Bangalore, Karnataka, India, from January 2021 to June 2021. Hundred preterm neonates, less than 36 weeks of gestation with birth weights between 1 kg and 1.8 kg, were included in the study. Group 1 was subjected to three-hourly feedings and group 2 were subjected to two-hourly feedings. An

independent t-test or Mann-Whitney U test was used to analyse GA, birth weight and time of achievement of full feeds. In addition, Chi-square test was used to analyse categorical data.

Results: Total 100 neonates were included, in which the age ranged from 5-13 days. There were 50 male and 50 female babies in the present study. Mean time of attainment of full feeds in group 2 was significantly higher (13.72 ± 3.54 days) than group 1 (11.94 ± 3 days). The mean time of achievement of full feeds birth weight 1-1.5 kg was 12.86 days in 3-hourly schedules, and 14.67 days in 2-hourly schedules. When the gestational age increased, the time of achievement of full feeds decreased.

Conclusion: The time to achieve full feeds was better in 3-hourly feeding schedules compared to 2-hourly schedules. The feed tolerance was also better in 3-hourly feeding schedules. The incidence of complications was lesser in 3-hourly compared to 2-hourly feeding schedules.

Keywords: Infant feeding, Intolerance, Neonates, Oral gastric tube

INTRODUCTION

Preterm newborns have a greater risk of neonatal death and stunting, postneonatal death, and long-term neurodevelopmental damage during childhood [1]. Most deaths in this category may be avoided by paying particular attention to warmth, infection control, and, most importantly, appropriate intervals of enteral feeding. Feeding very low birth weight preterm infants is relatively difficult because of their poorly developed feeding skills and feeding intolerance [2,3]. The introduction of enteral feeding of mother's milk is preferred for preterm newborns that not only helps in preventing gastrosatrophrophy but also improves motility [4-6].

There have been research regarding different feed intervals, favouring three-hourly feed over two-hourly feed as it reduces the frequency of physical contact with newborns hence reducing the chance of acquiring infection and also reducing the workload of medical assistants [7]. On the contrary, a three-hourly feed interval leads to a higher volume per feed that can compromise the feed tolerance [8]. Two-hourly feeds are reported to be better tolerated by the preterm babies causing less gastric distension and gastroesophageal reflux as it delivers a lesser volume of feed [8]. Morgan J et al., discovered that three-hourly feeding in low birth weight neonates was associated with rapid progression to full enteral feeding (median 26 days vs 20 days). Also, observed that two-hourly feedings were linked with decreased stomach distension leading to enhanced respiratory tolerance and higher intestine motility with higher faecal bilirubin excretion [8]. In another retrospective study, DeMauro SB et al., found that babies given two-hourly feed attained full enteral feeding 3.7 days sooner, and were less likely to have full parenteral nutrition over >28 days [9]. Other authors found no

variation in the number of days to acquire full enteral feeding when comparing two-hourly vs three-hourly feeding intervals in neonates with a relatively higher mean birth weight of 1,300 gms [10,11]. This could be due to the higher average birth weight of neonates involved. Similarly, there has been a report of the increased risk of invasive infection with delayed full enteral nutrition [3].

It is still unknown what feeding schedule achieves full enteral feeding the fastest and what frequency of feeding intervals is the most appropriate. Hence, this randomised clinical trial was conducted to compare the 2-hourly and 3-hourly feeding intervals to ensure full and quicker enteral feeding time in preterm neonates. Outcome of the study were time to achieve the full feed and complications related to feeding.

MATERIALS AND METHODS

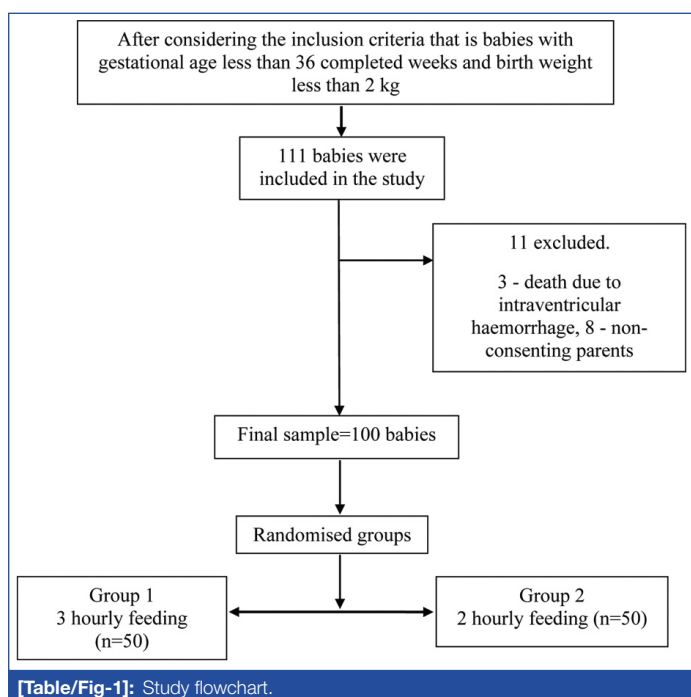
The present randomised controlled trial was conducted in the Department of Paediatrics, Kempegowda Institute of Medical Sciences, Bangalore, Karnataka, India, from January 2020 to June 2021. The study was approved by the Institutional Ethical Committee (KIMS/IEC/DOS4/2019), and informed written consent was taken by the parents of each participant neonatal.

Inclusion criteria: Preterm neonates of less than 36 weeks of gestation admitted to the Neonatal Intensive Care Unit (NICU) (weight range-1.0 kg to 1.8 kg) were included in the study. The enteral feeding was started within 96 hours after birth.

Exclusion criteria: Neonates with major congenital malformations, (chromosomal malformations, oesophageal atresia, tracheoesophageal fistula) and perinatal asphyxia were excluded from the study.

Study Procedure

Early full enteral feeding was defined as newborn infants receiving all of their prescribed nutrition as milk feeds (either human milk or formula) and no supplemental parenteral fluids or nutrition. Newborns fulfilling the inclusion criteria were randomised using the block randomisation technique with varying block sizes. The allocation of neonates was kept confidential. As soon as the neonates were stable, feeding was started as expressed breast milk or preterm formula at 10-20 mL/kg via oral gastric tube by gravity technique. Group 1 was provided with enteral feed every three hours and group 2 every two hours. All the feeding protocols were followed uniformly for both groups. The patients were assessed before the next meal. Parameters like abdominal girth were assessed every 12 hours, gastric residual was checked incase there was an incidence of vomiting. In case of feed intolerance or the presence of bile or blood stain in the stomach residual, feeds were withheld for atleast 24 hours and resumed once the issue was resolved [Table/Fig-1].



STATISTICAL ANALYSIS

Data were presented as mean, standard deviation, frequency and percentage. Continuable variables were compared using Independent samples t-test. Categorical variables were compared using Pearson's Chi-square test. Significance was defined by p-values less than 0.05 using a two-tailed test. Data analysis was performed using IBM Statistical Package for the Social Science (SPSS) software version 21.0 (IBM-SPSS Science Inc., Chicago, IL).

RESULTS

All the baseline demographic and clinical parameters were statistically comparable between the two subject groups. The age range was from 5-13 days and 50 males and 50 females babies were included. At baseline, the birth weight, gestational age were similar between the groups [Table/Fig-2]. Various complications arising during the study were monitored and have been represented in [Table/Fig-3].

Neonates with Gestational Age (GA) between 28-32 weeks showed a delayed time of achievement of full feeds than other GA. Neonates with BW between 1-1.5 kg attained full feeds significantly later than others. Also, the neonates with 3-hourly feeding schedule reached full feeding earlier than the 2-hourly group [Table/Fig-4].

[Table/Fig-3] shows the model with the predictors that explain 54.89% variability of time of achievement of full feeds. As the gestational age increased, the time of achievement of full feeds

Variables	Feeding schedule		Total n (%)	Fisher's exact p-value	
	2-hourly n (%)	3-hourly n (%)			
Gestational age	<28 weeks	3 (100)	0	3 (100)	0.096
	28-32 weeks	22 (48.88)	23 (51.11)	45 (100)	
	33-36 weeks	25 (48.07)	27 (51.92)	52 (100)	
Mean gestational age (weeks)	31.98±1.96	32.51±2.28			0.215
Birth weight	<1 kg	4 (57.14)	3 (42.85)	7 (100)	0.104
	1-1.5 kg	24 (52.17)	22 (47.82)	46 (100)	
	1.5-2 kg	22 (46.8)	25 (53.19)	47 (100)	
Mean birth weight (kg)	1.39±0.22	1.47±0.29			0.123
Tolerance of feeding	Not tolerated	18 (36)	18 (36)	36 (36)	1.000
	Tolerated	32 (64)	32 (64)	64 (64)	

[Table/Fig-2]: Gestational age, birth weight and tolerance of feeding in the study population.

Parameters	Feeding schedule, n (%)		p-value
	2-hourly (n=17)	3-hourly (n=15)	
Abdominal distension	7 (14)	7 (14)	1.00
Apnoea	14 (28)	2 (4)	0.001
Feeding intolerance/RT aspirate	9 (18)	5 (10)	0.249
GERD	1 (2)	1 (2)	1.00
New	3 (6)	2 (4)	0.318
Sepsis	4 (8)	1 (2)	0.152
Vomiting	12 (24)	10 (20)	0.629

[Table/Fig-3]: Complications with feeding schedule distribution.

Parameters	Feeding schedule		p-value	
	2-hourly (Mean±SD)	3-hourly (Mean±SD)		
Gestational age	<28 weeks	16±1	-	-
	28-32 weeks	15.45±3.25	12.87±3.11	0.009
	>32-36 weeks	11.92±3.08	11.15±2.71	0.344
Birth weight	<1 kg	18±1.83	16.67±1.53	0.341
	1-1.5 kg	14.67±3.41	12.86±3.01	0.063
	>1.5-2.0 kg	11.91±2.84	10.56±2.16	0.076
Time of achievement of full feeds (days)	13.72±3.54	11.94±3		0.008

[Table/Fig-4]: Time of achievement of full feeds with feeding schedule in days stratified with birth weight and gestational age. p-value in bold font represents statistically significant values

decreased. As the birth weight increased, the time of achievement of full feeds decreased [Table/Fig-5].

Predictors for time of achievement of full feeds	Adjusted B (95% CI)	p-value	Adjusted R ²
Gestational age	-0.285 (-0.52-0.05)	0.018	0.549
Birth weight	-6.018 (-7.88-4.16)	<0.0001	
Feeding schedule	-1.686 (-2.62-0.75)	0.001	

[Table/Fig-5]: Linear Regression for predicting the time of achievement of full feeds.

DISCUSSION

The study was conducted as a randomised controlled trial with 100 subjects to determine a better feeding schedule, either 2-hourly or 3-hourly enteral feeding in preterm infants with low birth weight. The mean gestational age (weeks) was 32.51±2.28 weeks ranging from 26-36 weeks. Forty seven (47%) had 1.5-2 kg birth weight followed by 46 (46%) had 1-1.5 kg birth weight and least 7 (7%) with <1 kg birth weight. The mean birth weight among the subjects was 1.47 (±0.29) kg ranging from 0.84-1.88 kg.

Rüdiger M et al., did a retrospective study to define which among the two 2-hourly or 3-hourly feeding intervals was better for extremely low body weight neonates. Charts were analysed for all Extremely

Low Birth Weight (ELBW) infants during a period of two years. They found that the weight gain and time required to accomplish complete enteral nutrition were similar in 2-hourly and 3-hourly feeding regimes. Infact, their findings suggest an advantage of 2-hourly feedings which contradicts the present study observation. This could be due to special physiological conditions of infants of body weight less than 1.2 kg suffering from apnoea and infants under phototherapy [7].

Similar findings were demonstrated by DeMauro SB *et al.*, where the neonates showed improved feeding tolerance when fed more frequently. They observed that infants fed at a 2-hourly interval reached full feedings 2.7 days earlier than the infants fed at a 3-hourly interval. After adjustment for confounders, 2-hourly fed infants reached full feedings 3.7 days earlier. Infants fed 3-hourly were more likely to receive >28 days of parenteral nutrition, and were more likely to have feeds held for ≥ 7 days [9]. Furthermore, it was shown that 3-hourly feeding was comparable with 2-hourly feeding to achieve full enteral feeding without any evidence of increased adverse effects. Dsilna A *et al.*, found that the mean time for full enteral feeding was 11.3 days in the 3-hourly group and 10.2 days in the 2-hourly group (mean difference 1.1 days; 95% CI-0.4 to 2.5; p-value=0.14). The mean time to regain birth weight was shorter in the 3-hourly group (12.9 vs 14.8 days, p-value=0.04) [5].

A similar observation has been reported by Yadav A *et al.*, to prove that a 3-hourly feeding schedule is feasible to reach full enteral feeds without increasing harm to the neonate, so that the nursing time consumed in the feeding of Very Low Birth Weight (VLBW) babies could be reduced. The time to achieve full enteral feed was comparable in the two feeding schedule groups (median 5 days). Moreover, there were no significant differences in incidence of hypoglycaemia, feed intolerance, and necrotising enterocolitis in either of the groups. Thus, a 3-hourly feeding regime could be adopted safely to reduce the nursing time without any adverse effects [12].

Consistent with the present study results, Ehrenkranz RA *et al.*, has shown feed intolerance of 7.4% in 2-hourly and 6.9% in 3-hourly feeding schedules with no significant difference [1]. The proportion of feed intolerance was low in that study since it included babies of more than 1 kg who would have better tolerance compared to the subjects with birth weight less than 1 kg in the present study. The study done by Dsilna A *et al.*, has shown an incidence of 20% of feed intolerance in 3-hourly and 28% in 2-hourly feeding schedules [5]. Shaw S *et al.*, showed 30% of feed intolerance in 2-hourly and 23.3% in 3-hourly feeding schedules [13].

The mean time of achievement of fullfeeds among 2-hourly feeding schedules was more than that among 3-hourly feeding schedules. Dhingra A *et al.*, showed the time to fullfeeds in 3-hourly feeding schedules as 11.3 ± 4.93 days compared to 10.2 ± 3.7 days in 2-hourly feeding schedules. Even though there was a mean difference of 1.07 days between the two feeding schedules, the difference was insignificant [10]. According to Rüdiger M *et al.*, it takes 20 days and 26 days, for the 2-hourly and 3-hourly, respectively, and a longer time to attain complete feeds [7]. Shaw S *et al.*, showed 10 days to fullfeeds in the 2-hourly and 3-hourly feeding schedules [13].

The mean time of achievement of full feeds among subjects with gestational age 28-32 weeks was 12.87 days in 3-hourly schedules, which is earlier by 2.58 days compared to 15.45 days in 2-hourly schedules. Though the achievement of full feeds in other gestational ages was earlier in 3-hourly schedules compared to 2-hourly schedules, they were not statistically significant. Ibrahim NR *et al.*, showed a slightly earlier achievement of full feeds in 2-hourly feeding schedules in less than 32 weeks of gestation and 3-hourly feeding schedules in more than 32 weeks [11].

Among the participants, 39 (78%) of the subjects in 3-hourly feeding schedules had no complications compared to 29 (58%) in 2-hourly feeding schedules. Apnoea was higher in 2-hourly feeding schedule

than 3-hourly feeding schedule. Vomiting and feeding intolerance/ Ryle's Tube (RT) aspirate were higher in both 2-hourly feeding schedule than 3-hourly feeding schedule group.

Yadav A *et al.*, showed Necrotising Enterocolitis (NEC) 2.3% incidence in 2-hourly and 2.9% in 3-hourly feeding schedules [12]. Dhingra A *et al.*, showed no difference in apnoea between the two feeding schedules, with 25% in 3-hourly and 28% in 2-hourly feeding schedules [10]. Ibrahim NR *et al.*, showed 6.7% of NEC in 3-hourly and 12% in 2-hourly feeding schedules [11]. Shaw S *et al.*, reported a similar result of 6.7% incidence of NEC in 2-hourly and 3-hourly feeding schedules. Apnoea was seen in 23.3% of 2-hourly and 16.7% of 3-hourly feeding schedules [13]. Apnoea was the most common complications seen.

The present study showed that as the gestational age increased, the time of achievement of fullfeeds decreased, and it was the same with birth weight too. The time of achievement of fullfeeds decreased 3.38 times for 2-hourly and 5.07 times for 3-hourly feeding schedules.

Other similar studies that show better outcomes in 2-hourly feeding schedules than 3-hourly fail to prove the statistical significance of the difference. However, certain studies [10] significantly favor 3-hourly feeding schedules for better outcomes. Thus, the present study shows a better hand in improving the 3-hourly feeding schedules compared to the 2-hourly feeding schedules in many results.

Limitation(s)

Smaller sample size was also a limitation since, within the study duration, many subjects could not be recruited.

CONCLUSION(S)

The time to achieve fullfeeds was better in 3-hourly feeding schedules compared to 2-hourly schedules, which were also reflected in all gestational age groups. The feed tolerance was also better in 3-hourly feeding schedules. The incidence of complications was lesser in 3-hourly compared to 2-hourly feeding schedules. On the other hand, difficulties like apnoea, NEC and sepsis were more significant among the 2-hourly feeding schedules. Time of achievement of fullfeeds decreases 3.38 times for 2-hourly and 5.07 times for 3-hourly feeding schedules, 0.29 times for each week increase in gestational age and 6.02 times for each kg increase in birth weight. Hence this study implies that 3-hourly feeding schedules are better compared to 2-hourly feeding schedules in preterm low birth weight neonates and also help reduce the incidence of complications and help in the earlier achievement of fullfeeds.

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