COMPARATIVE ANALYSIS OF INTERMITTENT BOLUS VERSUS CONTINUOUS NASOGASTRIC FEEDING IN PRETERM INFANTS

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ABSTRACT

Objective: To compare the effectiveness and complications of bolus versus continuous tube feeding in pre-term newborns <1500 grams.

Study Design: Quasi-experimental study

Place and Duration of Study: Neonatology Department of Pakistan Institute of Medical Sciences Islamabad, from Nov 2014 to Mar 2016.

Methodology: A total of 60 pre-terms; <34 weeks meeting the inclusion criteria, were included in the study and grouped according to birth weight; group A between 1000 to 1250 grams, and group B between 1250 to 1500 grams. Newborns from each group were randomly selected for bolus feeds given intermittently after every 2 hours, and continuous feed given with infusion pump. All infants were maintained in closed incubators until they weighed approximately 1800 g and the neonatal staff followed standard nursery protocols other than for feeding.

Results: There were 10 patients (9 in the bolus group and 1 in the continuous group) who did not reach the end point of 150 mL/Kg/day. One was transferred to another hospital before completing the protocol; 2 were diagnosed with congenital syphilis and Rubella syndrome; 1 switched to breast feeding due to parental concerns; 1 required the surgery for intestinal malrotation, and 5 died. The number of days to achieve full feeding calculated from the initiation of feeding was not significantly different between the groups. The main daily gastric residual volumes were significantly lower in the continuous group than in the bolus group, as was the total number of patients with feeding interruptions.

Conclusion: Birth weight was inversely related to days to achieve full enteral feeding. The method of feeding was not associated with differences in outcome when similar energy intakes were provided and when guidelines for discontinuation of feedings are followed.

Keywords: Bolus, Continuous, Enteral feeding, Necrotizing enterocolitis, Premature infants.

INTRODUCTION

Prematurity is third leading cause of neonatal mortality in Pakistan. In preterm infants, nutritional practices have strong impacts on outcomes[1]. Many studies have explored their complete feeding needs. Studies have shown that early commencement of enteral nutrition aids in rapid weight gain and reduces the time to attain full enteral feedings without increasing the incidence of necrotizing enterocolitis[2,3]. It has direct impact on the duration of hospital stay for preterm babies which reduce the risks of developing infections[4]. Moreover, during this sensitive period of development, insufficient nutrient supply endangers body and organ growth, especially neurodevelopment[5]. There-fore, major goal for all neonates after birth is to achieve adequate nutrition as soon as possible.

For low birth weight infants, it is often difficult to achieve early enteral nutrition because of their medical complications and immaturity of gastrointestinal tract. Even when started early, temporary feeding cessation due to any complication often causes delays in achieving full feeds. This elevates the risk of relative complications e.g. cholestasis, infections and also requires prolonged parenteral nutrition. Early achievement of full enteral feeding reduces these

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risks and promotes the functional development of the gut and the mucosal immune system[6]. Consequently, in many hospitals around the world minimal enteral feeding is started as soon as possible after birth and the amount of enteral feeding is increased daily through tube feeding. Tube feeding can either be bolus every 2 to 3 hours or continuous with an infusion pump. It is still a matter of dispute among neonatologists which mode is effective[7].

Continuous nasogastric feeding improves growth and favors feeding tolerance by improving energy balance through increased energy absorption and decrease energy expenditure. It also improves duodenal motor function and splanchnic oxygenation but there is also a possibility of losing significant number of nutrients to the delivery system. Moreover, there is a possibility that continuous feeding affects the cyclical release pattern of hormones in gastrointestinal tract (gastric inhibitory peptide, gastrin and enteroglucagon) which disturbs lower esophageal sphincter functions supporting the development of gastro-esophageal reflux and affects the metabolic homeostasis[8].

Whereas intermittent feeding could be very significant for the development of gastrointestinal tract as it promotes the normal cyclical release of gastrointestinal tract hormones, feeding tolerance and growth of preterm infants can be negatively affected by significant gastrointestinal limitations like intestinal transit or delayed gastric emptying. Furthermore, ability of premature infant to maintain metabolic homeostasis can be challenged by bolus feeding because of its alternating feeding and fasting cycle. It also aids in the development of gastrointestinal tract and improves protein accretion. However, it may have adverse effects on pulmonary function and premature gastrointestinal tract resulting in feeding related apneas and increased feeding intolerance[9].

The objective of this study was to compare the effects of continuous and intermittent bolus nasogastric milk feeding in premature infants weighing less than 1500 grams.

METHODOLOGY

It was a Quasi-eperimental study conducted at Department of Neonatology, Children Hospital, PIMS from November 2014 to March 2016. All preterm babies admitted to the neonatal intensive care unit (NICU) were screened for enrolment. Those who fulfilled the inclusion criteria were enrolled in this study. They were recruited into the study if they satisfied all the following criteria: new born with birth weight less than 1500 grams, gestational age ≤34 weeks, need of nasogastric tube feeding and clinically stable condition to start feeding soon after birth (until the third day). Exclusion criteria included all the preterm neonates who had significant asphyxia or resuscitation at birth, maternal history of infections or any congenital malformation. A total of 135 preterm neonates were admitted to NICU during the period of study and 60 of them fulfilled the inclusion criteria and were enrolled in this study. Consecutive sampling technique was used for sampling. We calculated sample size by using WHO sample size calculator. Informed consent was obtained from the parents when the infant was considered eligible for the study. The study design was approved by the institutional review board of the Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad. Since there was no new intervention and feeding was givenper already established protocols therefore, there was no risk of unethical practice during the study.

Intervention: The infants were stratified per birth weight into two groups (group-A weighed between 1000 and 1250 g and group-B weighed between more than 1250 and 1500 g). Infants within each group were randomly assigned to either continuous nasogastric feeding or intermittent bolus feeding by using sequentially numbered opaque sealed envelopes using a table of random numbers. Continuous feedings were delivered via an indwelling 6 Fr nasogastric tube with a continuous infusion pump. Intermittent

bolus feedings were given by gravity every 2 hours for 15 to 30 minutes via an in-dwelling 6 Fr nasogastric tubelike that used for continuous nasogastric feeding. Gastric residuals were measured with the same catheter every 2 hours in the continuous nasogastric feeding group and every 2 hours (pre-feed) in the intermittent bolus feeding group as routinely practiced in our nursery. All infants were nursed per pre-set neonatology protocols other than feeds and were kept until the weight gain of 1800g and attainment of full enteral feeds.

Feeds were discontinued for 3 hours if residuals were excessive and there were no other clinical findings. Guidelines for withholding feeding for longer periods included two or more of the following: excessive gastric residual, increase in abdominal girthby 2 cm or more in 6 hours measured at the umbilicus, occult blood positive in stool, visibly dilated bowel loops and/or abnormal abdominal roentgenograms, possible sepsis, apnea and/or bradycardia* occurring more than 3 times in 8 hour shift (*cessation of breathing for more than 20 seconds and heart rate, 100 beats/min). Any infant whose feeding was withheld for more than 12 hours was considered to have an episode of feeding intolerance (FI). NEC was defined by modified Bell's criteria.

Feeding Protocol: All infants were fed undiluted 24 calories/oz. preterm formula milk or expressed breast milk. Feeding protocols were designed for each 50 to 100 g weight category. Patients were started on 10ml/kg/day feed daily. Feeds were advanced by increment of 10ml/kg/day and it was same in both groups. The caloric and protein intake was identical in the two groups. Successful achievement of enteral feedings was defined as the ability to tolerate enteral feedings of 150 mL/kg/d for at least 72 hours.

Arbitrary guidelines for excessive residual were developed based on consensus among the study staff and the attending neonatologists. Thus, excessive residual was defined in the continuous nasogastric feeding group as residual volume 2.5 times the hourly volume of formula when the rate of infusion was 2 ml/h; 1.5 times when the rate was 2 to 3 ml/h; more than half when the rate was 5ml/h. In the intermittent bolus feeding group, the residual was defined as excessive when the amount was more than half of the preceding feed. Except in rare instances, gastric residual was refed in each group.

After being included inthe study, all patients were inserted with a nasogastric tube. Continuous feeds were delivered by an infusion pump continuously with infusion rate calculated per hour. Bolus feedings were given over 10-20 minutes by gravity drainage every two hours.

Expressed human milk, when available, was the nutrition of choice. When human milk was not available, commercially available preterm formula was used (24kcal/30ml).

A "trial-list" was developed for each infant to be kept on the bedside, on which the nurses noted any incident occurring. The following incidents were recorded: frequency of vomiting, nasogastric aspirates, abdominal distension, signs of necrotizing enterocolitis, breathing difficulty, apnea and cyanosis.

To simplify scoring, three or more incidents a day was scored as one "incident-day".

All infants were weighed each morning, naked, before feeding, on one same electronic weighing scale with one-gram accuracy. Growth

Table-I: Demographic and clinical features of both groups.

Features/Groups	Continuous (n=30)	Bolus (n=30)
Birth weight (grams)	1005 ± 168	995 ± 142
Gestation week (weeks)	28.8 ± 1.9	28.99 ± 2.1
Apgar (1 min)	5.6 ± 2.0	4.9 ± 1.8
Apgar (5 min)	7.6 ± 1.1	7.0 ± 1.9

Table-II: Gender distribution among bolus and continuous feeding groups.

Number (n)/ gender	Males n(%)	Females n(%)
Continuous (n=30)	23 (76.67%)	7 (23.33%)
Bolus (n=30)	17 (56.67%)	13 (43.33%)

was assessed from birth to the day of tolerating full feeds. Weekly weight increments were noted.

All the study data and procedures were performed by the researcher to decrease the chance of bias. Statistical analysis was done using SPSS version 19.0. Two sample t-test was used to on continuous data. Statistical significance was checked at $p \leq 0.05$ value.

RESULTS

A total of 135 preterm neonates underwent randomization and 60 were included in the analysis; 85 didn't fulfill the inclusion criteria. Demographic and clinical characteristics of the 60 preterm neonates at the onset of the study were given in table-I. The male babies were 40 (66.67%) and females were 20 (33.33%) (table-II). The number of infants in each birthweight category was 1000-1250g (n=30) and 1251-1500g (n=30). No significant differences were found between both groups. There were 30 patients in each bolus and continuous group.

Table-II & IV showed the **primary and secondary outcomes**. There were 10 patients (9 i.e. 30% in the bolus group and 1 i.e. 3.33% in the continuous group) who did not reach the end of 150 mL/kg/day. One was transferred to another hospital before completing the protocol; 2 were diagnosed with congenital syphilis and Rubella syndrome; 1 switched to breast feeding due to parental concerns; 1 required the surgery for intestinal malrotation and 5 died.

The number of days to achieve full feeding calculated from the initiation of feeding was not significantly different between the groups. The daily gastric residual volumes were significantly lower in the continuous group than in the bolus group, as was the total number of patients with feeding interruptions. Stratification for birth-

Table-III: Analysis of outcome based on weight groups.

Days of Feeding (Number of days)	Weight (1000-1250g)		*p*-value	Weight (1251-1500g)		*p*-value
	Continuous feed (n=15)	Bolus Feed (n=15)		Continuous Feed (n=15)	Bolus Feed (n=15)	
Regain Birth Weight	12.8 ± 6.3	12.9 ± 3.9	0.9	12.5 ± 4.0	12.0 ± 3.4	0.6
Full Enteral Feeds	19.7 ± 6.7	18 ± 5.4	0.2	13 ± 5.2	12.4 ± 3.9	0.6
Reach Discharge weight	68 ± 7.2	68 ± 11.6	1.0	49 ± 9.0	48 ± 3.0	1.0

Table-IV: Comparison of infants with and without feeding intolerance.

	Feeding Intolerance	No Feeding Intolerance	*p*-value
Birth Weight (g)	1150 ± 124	1326 ± 164	0.03
Reach Full Feeds (days)	23.1 ± 8.8	13.1 ± 3.4	<0.001
Regain Discharge Weight (days)	69.3 ± 13.6	57.1 ± 11.0	<0.001
Intermittent Mandatory Ventilation	13.7 ± 11.2	7.1 ± 9.2	0.02
Gestation (week)	28.4 ± 2.0	29.2 ± 2.1	0.13
Initial Feeds (days)	6.3 ± 1.9	5.3 ± 2.2	0.06
Regain Birth Weight (days)	13.0 ± 5.3	12.4 ± 3.9	0.6

Table-V: Outcomes of the study.

Outcome (n=number)	Continuous Feed n (%)	Bolus Feed n(%)	*p*-value	Odds Ratio
Death (n=5)	1(3.3%)	4 (13.3%)	0.07	14.53
Apnea (n=3)	1 (3.3%)	2(2.6%)	0.4	2.85
Abdominal Distension (n=7)	3(10%)	4(13.3%)	0.4	1.96
Vomiting (n=3)	1(3.3%)	2(6.6%)	0.4	2.85
Tachypnea (n=0)	-	-	-	1.34
Nasogastric aspirates (n=3)	-	3(10%)	0.12	10.75

weight revealed that birthweight was inversely related to days to achieve full enteral feeding.

Although the rate of major complications was higher in bolus group as compare to continuous, however no significant association was found between bolus feeding method and death (OR=14.53, *p*=0.07). Total number of patients with feeding interruption was lower in continuous group as compared to bolus group (OR= 12.43, *p*=0.021) (table-IV).

No significant differences were seen between the continuous and bolus groups at the onset of the study. In addition, there were no differences between the groups in the number of days spent on the ventilator (continuous 8.9 ± 10.9 days' vs bolus 9.4 ± 9.8 days). Feeding intolerance was diagnosed in 10 patients, 9 in bolus group and 1 in continuous group.

In general, a larger proportion of infants whose feedings were discontinued because of excessive residual were in the bolus group, the odds ratio for apnea and tachypnea was OR=2.85, (positive effect) *p*=0.4; OR=1.34, (positive effect) *p*=0.88 respectively. While selecting the bolus group as exposed group, the odds ratio for vomit and distension was OR=2.85, (positive effect) *p*=0.4; OR= 1.96, (positive effect) *p*=0.4 respectively. Infants with feeding intolerance were smaller at birth, so they need longer time to reach discharge weight. Feeding intolerance was associated with time to reach full enteral feedings as well as with time to reach discharge weight most likely because 8 of the 10 infants with FI weighed less than 1250 g at birth(table-V).

DISCUSSION

This study exhibited that for preterm low birth-weight infants; there were no differences in days to reach full enteral feeding or weight gain in both feeding groups. There is also no significant difference of safety between continuous or intermittent bolus feeding. Optimizing enteral nutrition is very significant for improving subsequent health 10, but only few studies have compared different feeding methods.

As shown in Cochrane meta-analysis[11], our study also revealed that both feeding methods take same time to reach full enteral feedings. However, there was a significant difference between feeding intolerance of both feeding strategies. The study by Schanler *et al* also supports these findings. Their study showed that percentage gastric residual exceeds by 50% of the 3-hour feeding volume was almost twice higher in the continuous feeding versus the bolus feeding. But they also observe a time difference to reach full enteral feedings in low birthweight infants with a gestation age of 26-27 weeks between both feeding methods[12].

Current study showed a statistical difference between number of patients having feeding interruptions and gastric residual volume in both groups. These both outcomes are strictly linked to each other because feeding interruptions occurs if gastric residual increases 3 times for the volume of preceding bolus in continuous or bolus groups.

Sometimes gastric residual is used as a marker for the evaluation of feeding intolerance; however, it is also used as a warning symptom for the necrotizing enterocolitis[13]. According to recent studies only hemorrhagic residuals elevate the chances of necrotizing enterocolitis. Bertino *et al*[14] has found no consensus in literature about the clinical relevance of gastric residual. Therefore, the use of gastric residual as diagnostic sign is decreasing. The current study also endorses this decline because this doesn't cause any difference for days to achieve full enteral feeding in both groups. From current study, we can conclude that the higher amount of gastric residual in patients of bolus group explains the increased number of patients with feeding interruptions.

In contrast with Corvaglia *et al*[7] our study showed increased number of apneas in bolus group. However, their study was specifically designed to study the cardiorespiratory events with bolus versus continuous enteral feeding. In this study, full enteral feeding was defined as enteral feeding of >72 uninterrupted hours; which is ideal as it shows complete comparisons

between studies. But Berseth *et al*[5], used a full enteral feeding of >140 mL/kg/day. Their study also explains that instead of enforcing that one feeding causes the necrotizing enterocolitis more often, it's possible that the rapidity of feeding advancements may lead to increased occurrences of necrotizing enterocolitis.

Continuous methods have been recommended as a way of increasing energy efficiency because of improved absorptive capacity by the gut as a means of decreasing the amount of time required to reach full feedings and as the best method for infants with intestinal disease[15-18].

In general, the literature suggested that birth weight is usually regained in an inverse relation to birth weight. In our study, birth weight was regained at similar times regardless of method of feeding or birth weight category, this was most likely attributable to the early and liberal use of parenteral nutrition (on day 2 or 3) when the infants were considered metabolically stable. Our study may have set higher arbitrary guidelines for excessive GR than used by others. Had these guidelines been lower, an even greater number of infants would have had feedings discontinued for more than 3 hours.

CONCLUSION

Continuous feeding may be preferable but it allows less parental involvement in feeding. But the final choice of method of feeding remains that of clinical judgment based on the tolerance and the clinical condition of the infant.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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