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Continuous versus bolus nasogastric tube feeding in premature neonates: Randomized controlled trial*

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ABSTRACT

Background: Whether premature infants should be fed by bolus or continuous gavage feeding, is still a matter of debate. A recent Cochrane analysis revealed no difference. Study design and methods: We carried out a randomized controlled trial in premature infants on continuous versus bolus nasogastric tube feeding, to search for differences with respect to number of incidents, growth, and time to reach full oral feeding. In total, 110 premature neonates (gestational age 27 - 34 weeks) were randomly assigned to receive either continuous or bolus nasogastric tube feeding. Basic characteristics were comparable in both groups. Results: No significant difference in weight gain could be detected between the two groups, mean weight gain amounting 151.6 (108.9 - 194.3) and 152.4 (102.2 - 202.6) grams per week in the continuous and bolus group, respectively. No significant differences were found between both groups in the time needed to achieve full oral feeding (8 oral feedings per day), full oral feeding being achieved at day 31 (range 19 - 43) and day 29 (range 18 - 40) of life in the continuous and bolus group, respectively. We also found no significant differences in the number of "incident-days" (three or more incidents a day): 3.5 (0 - 9) versus 2.7 (0 - 6.5) days in the continuous and bolus group, respectively. Conclusion: No significant differences were found in weight gain, time to achieve full oral feeding and number of incident-days between preterm infants enterally fed by nasogastric tube, according to either the bolus or continuous method.

Keywords: Premature; Infant; Tube Feeding; Bolus Feeding; Continuous Feeding

1. INTRODUCTION

Most premature infants must initially be fed by gastric tube because of their inability to either suck effectively or coordinate sucking, swallowing and breathing.

Several approaches exist as to tube feeding of preterm infants. An important difference in approach is whether to feed them continuously or by intermittent bolus.

Advantages of bolus feeding mentioned in the literature are the natural character of this type of feeding. Cyclical surges of various gastrointestinal tract hormones occur after feeding preterm infants by bolus [1-3].

On the other hand, continuous feeding would be less exhausting and lead to less incidents than intermittent feeding [4,5]. Also, functional limitations of the premature infant's gastrointestinal system such as delayed gastric emptying or intestinal transit could hinder its ability to handle bolus milk feeds, resulting in feeding intolerance [6-11].

Studies investigating the superiority of either type of feeding (bolus or continuous) are characterized by small numbers, poor definitions of patient groups and poor definitions of parameters to evaluate the differences, such as time to full oral feeds and number of incidents.

While we were writing this manuscript, a Cochrane analysis of studies investigating bolus versus continuous feeding occurred, revealing that time to achieve full oral feeds did not differ between the two methods used in infants of less than 1500 grams [12]. No significant differences in somatic growth and incidence of necrotizing enterocolitis (NEC) occurred between feeding methods irrespective of gastric tube placement. However, small sample sizes, methodologic limitations, inconsistencies in controlling variables and conflicting results make it difficult to make universal recommendations regarding the best tube feeding method for premature infants.

We present a large randomized study with sufficient power on bolus versus continuous enteral feeding in premature infants with a nasogastric tube in order to detect any difference in clinical effects between the two

*In patients that could not be fed human milk, premature formula was kindly provided by FrieslandCampina. Authors MvdS, BS and ES have no financial relationships with FrieslandCampina.
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types of feeding.

2. METHODS

2.1. Study Design

This non-blinded randomized study was performed at the neonatal unit of the Canisius-Wilhelmina Hospital, a level 2 hospital, in Nijmegen, the Netherlands. Infants were enrolled within the first days of life, directly after birth or after discharge from the neonatal intensive care unit of the adjacent level 3 university hospital. They were assigned randomly to continuous nasogastric feeding (CNF) or intermittent bolus nasogastric feeding (IBNF). The randomization assignment was performed using sealed envelopes.

In a preceding pilot study in 19 patients with continuous feeding, we observed a mean number of incidents of 2.1 (SD 1.7). Assuming that the standard deviation in the bolus group would also be 1.7, and based on an unreliability of 5% and a power of 80%, it was calculated that 51 patients would be needed in either group, to show a mean difference of maximal one incident per day. Informed written consent was obtained from both parents and the study protocol was approved by the local research ethics committee. The study was performed according to GCP-guidelines.

2.2. Study Population

A total of 110 premature infants were enrolled between November 2001 and September 2004. They were recruited into the study if they satisfied all the following criteria: gestational age 27 - 34 weeks; need of nasogastric tube feeding; clinically stable condition to start feeding soon after birth (until the third day); informed consent from both parents. Infants were excluded if they had a severe congenital malformation, used prokinetics, or had evidence of infection (clinical signs and symptoms of infection and elevated C-reactive protein).

Infants were followed until they tolerated full oral feeds and had no longer need of their nasogastric tube (which for this reason was removed).

2.3. Feeding Protocol

After entry into the study, all patients received a nasogastric tube. Continuous feeds were delivered by an infusion pump over 1 - 2.5 hours, an infusion time of 1 hour being used only in case of 24 feedings a day. Bolus feedings were given over 10 - 20 minutes by gravity drainage every two or three hours.

On day one, feeds were started at 60 mL/kg/day, with a daily increment of 20 mL/kg. Full fluid and energy requirements were met at 160 - 180 mL/kg/day. This feeding protocol was similarly used in both groups.

Expressed human milk, when available, was the nutrition of choice. When human milk was not available, preterm formula (335 kJ/80 kcal per 100 mL, Frisopré, FrieslandCampina, The Netherlands) was used.

According to the local feeding protocol, breastmilk fortifier (1.75 g (6 kCal) per 50 ml breast milk, Friso BMF, FrieslandCampina) is added in infants of both groups, as soon as fluid intake reaches 50 mL/kg/dag. Non nutritive sucking is introduced as soon as gestational age reaches 32 weeks and/or body weight reaches 1500 g. In infants on bottle feeding, a bottle is presented as soon as gestational age reaches 34 weeks and/or body weight reaches 1500 g.

2.4. Outcome Measures

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 apnea, bradycardia and desaturations.

An apnea was defined as a cessation of inspiratory gas flow for a duration of 20 seconds (on cardiorespiratory monitor). The nurses noted the frequency of apneas during their shift, including the time period during which breathing stopped, until the infant's complete recovery of respiration and oxygen saturation.

Bradycardia was defined as a decline in heart rate at less than 80 beats per minute. The nurses also noted the frequency, the period of time, the lowest heart rate reached and the recovery.

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

All infants were weighed each morning, naked, before feeding and bathing, on one same electronic weighing scale with a one-gram accuracy. Growth was assessed from birth to the day of tolerating full feeds. Weekly weight increments were noted.

Feeding tolerance was assessed by recording the number of days the infant needed to tolerate full milk feeds (8 oral feedings per day) and by the number of "incident-days" (days with more than 3 incidents).

2.5. Data Analyses

Data were analyzed with the SPSS 15.0. An independent T-test and the Mann-Whitney test were used for assessing differences between groups (CNF and IBNF) since the Kolmogorov-Smirnov test assumed parameters to be normally distributed.

3. RESULTS

Of all eligible infants born between November 2001 and September 2004, 110 were randomly assigned to the feeding groups. Seven infants (6.4%) were excluded after randomization because of serious gastro-esophageal reflux

(0.9%), incarcerated hernia (0.9%), suspected necrotizing enterocolitis (1.8%), feeding problems needing tube feeding at home until the age of 2 years (0.9%), and unacceptable growth needing extra supplements (0.9%). One patient was missed (0.9%). The two infants with suspected necrotizing enterocolitis were given bolus feeding; the diagnosis could not be confirmed, infants were treated conservatively and had no further intestinal problems (both Bell's stage 1).

There was only one refusal for the study, This concerned an infant whose parents insisted to have their infant on continuous feeding, since they felt it would be better tolerated.

There were no statistically significant differences between infants in both groups in baseline demographic and clinical characteristics at study entry (**Table 1**). Also, no significant differences were present between groups for the number of infants who were removed from the study.

There was no significant difference in weight gain between the two groups. The mean weekly increment was 151.6 grams (range 108.9 - 194.3) in the continuous group, versus 152.4 (range 102.2 - 202.6) in the bolus group.

We found no significant differences between groups in the time taken to achieve full feeds (8 oral feedings per day). Full oral feeding (means and range) was achieved at 31 (19 - 43) days of life in the continuous group, versus 29 (18 - 40) days in the bolus group.

Table 1. Basic demographic and clinical characteristics of patients at study entry.

	Continuous (n = 51)	Bolus (n = 52)
Gestational age (wk) and (SD)	32.3 (1.2)	32.3 (1.1)
Males, n (%)	23 (45)	26 (50)
Birth weight (g) and (SD)	1670 (352)	1735 (347)
Type of feeding		
Human milk, n (%)	34 (67)	37 (71)
Formula, n (%)	17 (33)	15 (29)
IRDS, n (%)	15 (29)	13 (25)
Intracranial hemorrhage, n (%)	1 (2)	3 (6)
Coffeine	33 (65)	28 (54)
Need of oxygen	10 (20)	13 (25)
Excluded (%)	3 (5.9)	4 (7.7)

Also, no significant differences in the number of "incident-days" were found. The continuous group showed a mean of 3.5 (range 0 - 9) "incident-days". The bolus group showed a mean of 2.7 (range 0 - 6.5) days (**Table 2**). Calculated as total number of incidents, there were also no differences in the number of incidents between the two study groups (data not shown).

None of the infants in either group developed necrotizing enterocolitis.

4. DISCUSSION

We conducted a randomized controlled trial in preterm infants to study the clinical effects of continuous versus bolus nasogastric tube feeding.

No significant changes between the two types of feeding were found on the number of incident-days, time needed to reach full oral feeding, weight gain and total time of admission.

Our study has a number of strengths. We carefully calculated the power needed to find a significant difference in the number of incidents. Preceding the study, we clearly defined the clinical parameters to use in measuring the effects. Also, we used an intention to treat analysis for evaluation of possible differences.

Drawbacks of the study are the absence of blinding for the patients, doctors, nurses, and other caregivers involved, and absence of a placebo-control group. It was felt that blinding would be too difficult to perform for practical reason, as would be the use of placebo feeding. An extra team of caregivers would have been needed, which, for practical and financial reasons, was not feasible.

However, we feel that the results are robust, since only few patients failed randomization and results are those of intention to treat analyses.

Several studies in the past have given different results. Schanler *et al.* found no differences between groups in the number of days on which feedings were interrupted for feeding intolerance, as assessed by gastric residual volume [13]. We did not measure gastric residual volume in our study, since it was not seen as a useful parameter. Apart from the exclusions indicated, no feeding interruptions for intolerance occurred. Toce *et al.* found no difference between groups in the average number of hours spent nil per os per day for feeding intolerance [14]. Similarly, Akintorin found no difference in the number

Table 2. Results.

	Continuous (n = 51)	Bolus (n = 52)
"Incident-days"	3.5 (0 - 9)	2.7 (0 - 6.5)
Postnatal age at reaching full oral feedings (days)	31 (19 - 43)	29 (18 - 40)
Mean weekly increment of weight (grams)	151.6 (108.9 - 194.3)	152.4 (102.2 - 202.6)

Data presented as means (range).

of infants who experienced feeding intolerance, defined as feeds held longer than 12 hours [15]. More recently, Dsilna *et al.* found no difference in feeding intolerance defined as the number of occasions the infant was diagnosed with suspected necrotizing enterocolitis (Bell Stage I) followed by interruption of enteral feeds for at least 8 hours [8]. A meta-analysis could not be performed because modes of measuring feeding intolerance were not comparable. Schanler reported that infants fed by the continuous feeding method gained weight slower than infants fed by the intermittent bolus feeding method [13]. Toce, however, did not find a difference in weight gain (grams per kg per day) between the two groups [14]. Similarly, Macdonald *et al.* and also Silvestre *et al.* both found no difference in weight gain (grams per week) between the two groups [11,16].

The most recent Cochrane analysis reported that overall, the seven included trials, involving 511 infants of less than 1500 grams, found no differences between the two feeding methods in time to achieve full enteral feeds [12].

In the subgroup analysis of those studies comparing continuous versus intermittent bolus nasogastric milk feedings, the findings remained unchanged. There was no significant difference in somatic growth and incidence of NEC between the two feeding methods. One study noted a trend toward more apneas during the study period in infants fed by the continuous tube feeding method compared to those fed by intermittent feedings delivered predominantly by orogastric tube placements. In subgroup analysis based on weight groups, one study suggested that infants less than 1000 grams, and 1000 - 1250 grams birth weight, gained weight faster when fed by the continuous nasogastric tube feeding method compared to intermittent nasogastric tube feeding. A trend was observed toward earlier discharge for infants less than 1000 grams birth weight fed by the continuous tube feeding method compared to intermittent nasogastric tube feeding.

In conclusion, in line with other studies, we found no differences in either weight gain, time to achieve full oral feedings, or number of incidents between premature babies fed by either continuous or bolus nasogastric tube feeding methods.

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