A Prospective Randomized Trial of Feeding Methods in Very Low Birth Weight Infants

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ABSTRACT. Objective. To test the hypothesis that very low birth weight infants fed by continuous nasogastric gavage (CNG) would achieve full enteral feedings (100 kcal/kg/d) at an earlier postnatal age and have less feeding intolerance (FI) than infants fed by intermittent bolus gavage (IBG).

Methods. Eighty infants were stratified by birth weight (700 to 1000 g and 1001 to 1250 g) and randomized into CNG or IBG feeding groups. CNG infants were comparable with IBG in birth weight, gestational age, sex, race, and day of onset of feeding (5.7 ± 2.1 days vs 5.6 ± 2.2 days, respectively). Feedings were given as undiluted Similac Special Care formula (Ross Laboratories, Columbus, OH) via a specific protocol designed for each 50 to 100 g birth weight category. Feedings were advanced isoenergetically by a maximum of 25 mL/kg/d until an endpoint of 100 kcal/kg/d for at least 48 hours was reached. An infant whose feedings were withheld for >12 hours based on predetermined criteria was considered to have an episode of FI.

Results. Infants in the CNG group reached full enteral feeding at 17.1 ± 8.9 days compared with 15.5 ± 5.5 days in the IBG group; these were not statistically different. Secondary outcome variables such as days to regain birth weight (CNG, 12.6 ± 5 days vs IBG, 12.5 ± 3.7 days), days to reach discharge weight of 2040 g (CNG, 60 ± 13.4 days vs IBG, 62 ± 13.6 days), and number of episodes of FI were not significantly different between feeding methods. FI was primarily associated with birth weight ≤1000 g (71%) vs 1001 to 1250 g (38%).

Conclusion. Feeding methods are associated with similar outcomes when feeding regimens are comparable. Pediatrics 1997;100(4). URL: http://www.pediatrics.org/cgi/content/full/100/4/e4; premature infants, feeding methods, feeding intolerance, gastric residual.

Abbreviations. CNG, continuous nasogastric gavage; IBG, intermittent bolus gavage; NEC, necrotizing enterocolitis; GR, gastric residual; FI, feeding intolerance.

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http://www.pediatrics.org/cgi/content/full/100/4/e4
sequentially numbered opaque sealed envelopes using a table of random numbers. CNG feedings were delivered via an indwelling 5F polyvinyl nasogastric catheter with a continuous infusion pump (IVAC Medsystem III, San Diego, CA). IBG feedings were given by gravity every 3 hours for 15 to 30 minutes via an indwelling 5F nasogastric catheter similar to that used for CNG. Positioning of the nasogastric tube was not routinely confirmed by radiographs. Catheters in both groups were changed every 3 days per standard nursery protocol. Nonnutritive sucking was continued in both groups of infants to lessen behavioral distress. Gastric residual (GR) was measured with the same catheter every 2 hours in the CNG group and every 3 hours (prefeed) in the IBG group as currently practiced in our nursery. 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.

Parenteral nutrition, including lipid emulsion, was started on days 2 to 3 and continued until each infant tolerated full enteral feedings. All infants were fed undiluted 20 cal/oz Similac Special Care formula (Ross Laboratories, Columbus, OH). Feeding protocols were designed for each 50 to 100 g weight category as shown in Table 1. Patients were started on 12 to 16 mL/kg/d and the feedings were advanced by a maximum of 25 mL/kg/d. Feedings were advanced at a similar increment of mL/kg/d for 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 100 kcal/kg/d for at least 48 hours. Nipple feedings were initiated when infants reached a weight of 1500 g; feedings were then advanced by the neonatologist as tolerated by the infant.

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 CNG group as a GR 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 the hourly rate when the rate was 3 to 5 mL/h, or more than half when the rate was >5 mL/h. In the IBG group, the residual was defined as excessive when the amount of formula was more than half of the preceding feeding. Except in rare instances, GR was refed in either group.

Feedings were discontinued for 3 hours if residual was excessive and there were no other clinical findings. Guidelines for withholding feedings for longer periods included two or more of the following: excessive GR, increase in abdominal girth measured at the umbilicus by 2 cm or more in 6 hours, guaiac positive stools, dilated loops of bowel, abnormal abdominal roentgenograms, possible sepsis, apnea, and bradycardia occurring more than 3 times per 8 hour shift (cessation of breathing for more than 20 seconds and heart rate <80 beats/min). Any infant whose feedings were withheld for more than 12 hours was considered to have an episode of feeding intolerance (FI). NEC was defined by modified Bell's criteria.

Daily, weight, intake and output, number of stools, number of guaiac positive stools, number of hours that feedings were withheld, episodes of apnea, and bradycardia were recorded. All stools were tested for blood and abdominal circumference was measured every 8 hours routinely and more often depending on clinical status.

**TABLE 1. Feeding Protocol**

<table>
<thead>
<tr>
<th>Day</th>
<th>Birth Weight</th>
<th>CNG* (mL)</th>
<th>IBG (mL)</th>
<th>CNG (mL)</th>
<th>IBG (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>700–1000 g</td>
<td>1001–1250 g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.3–0.5</td>
<td>1.0–1.5</td>
<td>0.5–0.7</td>
<td>1.5–2.0</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>0.8–1.0</td>
<td>2.5–3.0</td>
<td>1.8–2.5</td>
<td>5.5–7.0</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1.3–1.8</td>
<td>4.0–5.5</td>
<td>3.0–3.8</td>
<td>9.0–11.5</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>1.6–2.5</td>
<td>5.0–7.5</td>
<td>4.3–5.2</td>
<td>13.0–15.5</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>2.6–3.6</td>
<td>8.0–11.0</td>
<td>6.3–7.5</td>
<td>19.0–26.0</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>4.0–5.6</td>
<td>13.0–19.0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* CNG indicates continuous nasogastric gavage mL per feed per hour.
† IBG indicates intermittent bolus gavage mL per feed every 3 hours.

**Statistical Analysis**

Based on the data of Krishnan et al, we hypothesized that CNG feedings would result in a 35% decrease in the number of days required to reach full enteral feedings (primary outcome) compared with IBG feedings. The sample size, based on an α of .05 and a β error of .20, was calculated to be 70 patients. For continuous measures, the two groups were compared using the unpaired Student’s t test adjusting for unequal variances if necessary. Categorical measures were compared using the χ² test or Fisher’s exact test when the expected cell sizes were not adequate to meet the test assumptions. All results are reported as mean ± standard deviation.

**RESULTS**

Ninety-one patients were eligible for the study and 89 were enrolled. Of the 2 patients who were not enrolled, 1 had developed NEC and the other was fed before consent could be obtained. Of the 89 enrolled, 9 (4 CNG and 5 IBG) were not included in the data analysis for the following reasons: of the 4 CNG patients, 2 were diagnosed as having severe congenital syphilis, 1 had been switched to breastfeeding, and 1 required surgery for intestinal malrotation. Of the 5 IBG patients, the protocol had not been followed in 3 patients, 1 patient had been switched to breastfeeding, and 1 was transferred to another hospital before completing the protocol. There were no deaths among the 89 infants and no other adverse outcomes.

Demographic data of the 80 patients (39 CNG, 41 IBG) who completed the study are provided in Table 2. There were 40 patients who weighed ≥1000 g at birth and 40 who weighed between 1001 and 1250 g at birth. No significant differences were seen between the CNG and IBG groups at the onset of the study. Feedings were initiated in the CNG group at 5.7 ± 2.1 days and in the IBG at 5.6 ± 2.2 days.

Infants regained their birth weight (CNG, 12.6 ± 5 days vs IBG, 12.5 ± 3.7 days), reached successful feeding criteria of 100 kcal/kg/d (CNG, 17 ± 8.9 days vs IBG, 15.5 ± 5.5 days), and reached discharge weight of 2040 g (CNG, 60 ± 13.4 days vs IBG, 62 ± 13.6 days) at similar time periods regardless of the feeding methods. There were also no significant differences between CNG and IBG methods when the results were examined within each weight category (Table 3), although the smaller infants took longer than their larger counterparts to reach full enteral feeds (18.7 ± 5.9 vs 12.8 ± 4.6, P < .0001) and discharge weight (68 ± 9.8 vs 48.7 ± 6.6 P < .0001). In addition, there were no differences between the groups in the number of days spent on the ventilator (CNG, 8.9 ± 10.9 days vs IBG, 9.4 ± 9.8 days).

FI was diagnosed in 28 patients, 14 in each group.

**TABLE 2. Demographic Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>CNG (n = 39)</th>
<th>IBG (n = 41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (g)*</td>
<td>1005 ± 168</td>
<td>995 ± 142</td>
</tr>
<tr>
<td>Gestation (wk)*</td>
<td>28.8 ± 1.9</td>
<td>28.9 ± 2.1</td>
</tr>
<tr>
<td>Small for gestational age</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>20</td>
<td>19</td>
</tr>
<tr>
<td>Race (black)</td>
<td>36</td>
<td>38</td>
</tr>
<tr>
<td>Apgar (1 min)*</td>
<td>5.6 ± 2.0</td>
<td>4.9 ± 1.8</td>
</tr>
<tr>
<td>Apgar (5 min)*</td>
<td>7.6 ± 1.1</td>
<td>7.0 ± 1.9</td>
</tr>
</tbody>
</table>

* Mean ± SD.
are in contrast to those reported in abstract by Krish-
achieve full feedings nor in time to regain birth
ences between CNG and IBG methods in days to
100 kcal/kg/d. There were also no significant differ-
decreased amount of time to achieve full feedings of
continuous nasogastric feedings would result in a
most likely because 20 of the 28 infants with FI
was associated with time to reach full enteral feed-
tive and not controlled for energy intake. Our results
was primarily supplied by parenteral nutrition. FI
in the time to regain birth weight as caloric intake
those without FI. The presence of FI was not a factor
the ventilator longer when compared (Table 4) with
14 infants with FI in the CNG group, 4 had suspect
suspect NEC and 2 had Bell’s Stage 2 or greater; 1 of
required surgery and the other was treated
suspect NEC and 2 had Bell’s Stage 2 or greater; 1 of the 2
required surgery and the other was treated medically.
Infants with FI were smaller at birth, and were on
the ventilator longer when compared (Table 4) with
those without FI. The presence of FI was not a factor
in the time to regain birth weight as caloric intake
was primarily supplied by parenteral nutrition. FI
was associated with time to reach full enteral feed-
ings as well as with time to reach discharge weight
most likely because 20 of the 28 infants with FI
weighed less than 1000 g at birth.

DISCUSSION

This study did not confirm our hypothesis that
continuous nasogastric feedings would result in a
decreased amount of time to achieve full feedings of
100 kcal/kg/d. There were also no significant differ-
ces between CNG and IBG methods in days to
achieve full feedings nor in time to regain birth
weight or to reach discharge weight. These findings
are in contrast to those reported in abstract by Krish-
nan and Satish; however, their study was retrospec-
tive and not controlled for energy intake. Our results
extend the findings of Silvestre et al who defined
full enteral feedings as 75 kcal/kg/d and discharge
weight as 1800 g; in their study there were also no
differences between feeding methods in growth and
macronutrient retention. Infants were approximately
100 g heavier than in our study and were started on
enteral feedings while the umbilical catheter was still
in place. Toce et al used a 20 cal/oz isoenenergetic
regimen and showed improvement in weight gain in
only one subgroup of infants (1000 to 1249 g); there
were no differences in infants >1250 g nor in the 10
infants who were <1000 g; all were off the ventilator
when feeding protocols were begun. Urrutia and
Poole reported, in an abstract, similar results be-
tween feeding methods in infants <1500 g. Symington
et al also found no differences between the
feeding methods but recommended continuous feed-
ing as less expensive because the catheters in the
intermittent group were removed after every feed-
ing. In our study, catheters were replaced every 3
days in both groups of patients; hence cost of cathe-
ters was not a serious issue. Bolus feeding on the
other hand, was considered superior to continuous
feeding by Schanler et al, but the study was not
controlled and FI was defined solely on the basis of
GR.

CNG 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. Others have suggested that IBG
may be more beneficial because of lower risk of
precipitation into the delivery system or because of
ease of administration because it does not require as
much equipment; however, this may be compen-
sated by the nursing time required to deliver a bolus
feeding. IBG, on the other hand, has been associated
with increasing gastroesophageal reflux, abdominal
distention, apnea, and bradycardia attributable to
increased vagal stimulation and aspiration because
of poor gastric motility. Increased cyclic surges of
ghormones are found in infants fed intermittently;
however, higher peak levels of insulin, gastrin, and
other gut hormones are maintained by continuous
feedings. The clinical significance of these findings
in improving nutrition could not be established as
weight gain was not different between intermittent
and continuous groups.

In general, the literature suggests 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 meta-
bolically stable.

Our hypothesis that infants fed by CNG would
achieve caloric feedings earlier than their IBG coun-
termates was based on our assumption that CNG
infants would have less FI. Unlike the findings of
Silvestre et al the number of infants in our study
who developed FI were the same regardless of
method of feeding. Although the study sample was
not based on the incidence of FI, the sample size was
adequate to show some important differences be-
tween infants who developed FI and those who did
not: infants with FI were more likely to weigh <1000

**TABLE 3.** Analysis of Outcome Based on Weight Groups

<table>
<thead>
<tr>
<th>Days to</th>
<th>700–1000 g</th>
<th>1001–1250 g</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNG</td>
<td>IBG</td>
<td>CNG</td>
</tr>
<tr>
<td>n = 17</td>
<td>n = 23</td>
<td>n = 22</td>
</tr>
</tbody>
</table>

- Regain birth weight* 12.8 ± 6.3 12.9 ± 3.9 12.5 ± 4.0 12.0 ± 3.4
- Full enteral feeds* 19.7 ± 6.7 18 ± 5.4 13 ± 5.2 12.4 ± 3.9
- Reach discharge weight* 68 ± 7.2 68 ± 11.6 49 ± 9.0 48 ± 3.0

* Mean ± SD.

**TABLE 4.** Comparison of Infants With and Without Feeding Intolerance (FI)

<table>
<thead>
<tr>
<th>FL (n = 28)</th>
<th>No FL (n = 52)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (g)*</td>
<td>953 ± 124</td>
<td>1026 ± 164</td>
</tr>
<tr>
<td>700–1000 g (%)</td>
<td>20 (71)</td>
<td>20 (38)</td>
</tr>
<tr>
<td>Gestation (wk)*</td>
<td>28.4 ± 2.0</td>
<td>29.2 ± 2.1</td>
</tr>
<tr>
<td>Initiate feeds (days)*</td>
<td>6.3 ± 1.9</td>
<td>5.3 ± 2.2</td>
</tr>
<tr>
<td>Reach full feeds (days)*</td>
<td>23.1 ± 8.8</td>
<td>13.1 ± 3.4</td>
</tr>
<tr>
<td>Regain birth weight (days)*</td>
<td>13.0 ± 5.3</td>
<td>12.4 ± 3.9</td>
</tr>
<tr>
<td>Reach discharge weight (days)*</td>
<td>69.3 ± 13.6</td>
<td>57.1 ± 11.0</td>
</tr>
<tr>
<td>Intermittent mandatory ventilation (days)</td>
<td>13.7 ± 11.2</td>
<td>7.1 ± 9.2</td>
</tr>
</tbody>
</table>

* Mean ± SD.
and require ventilator support for longer periods of time than their non-FI counterparts. As a result, infants with FI reached full enteral feeds and discharge weights significantly later than those without FI.

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. On the other hand, none of the infants who had excessive residual without other signs or symptoms developed NEC or FI. Hence, excessive residual, per se, is not an indication for withholding feedings for prolonged periods.

In summary, the method of feeding is not associated with differences in outcome when similar energy intakes are provided and when guidelines for discontinuation of feedings are followed. The final choice of method of feeding remains that of clinical judgment based on the tolerance and the clinical condition of the infant.

REFERENCES