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Effect of Gastric Residual Evaluation on Enteral Intake in Extremely Preterm Infants
A Randomized Clinical Trial

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➕ Supplemental content

IMPORTANCE Evaluating prefeed gastric residuals is considered routine care but has little supporting evidence.

OBJECTIVE To determine the effect of omitting prefeed gastric residual evaluation on nutritional outcomes in extremely preterm infants.

DESIGN, SETTING, AND PARTICIPANTS This single-center randomized clinical trial compared the omission of gastric residual evaluation with prefeed gastric residual evaluation. Infants were recruited from a level 4 neonatal intensive care unit and were enrolled from October 17, 2013, to October 8, 2016, and then followed up for 6 weeks after birth. Eligible participants were infants born at 32 or fewer weeks' gestation with a birth weight of 1250 g or less; they were enrolled within 72 hours after birth and within 24 hours after feeding initiation. All participants (N = 143) were included in the modified intent-to-treat analysis, which was conducted from March to July 2018.

INTERVENTIONS The residual group underwent prefeed gastric residual evaluation; the no residual group did not. Feeding decisions were made according to nutritional guidelines, and infants received only human milk.

MAIN OUTCOMES AND MEASURES The primary outcome was weekly enteral nutrition intake in mL/kg for 6 weeks after birth.

RESULTS Of 143 infants, 74 (51.7%) were randomized to undergo gastric residual evaluation (residual group) and 69 (48.3%) to omitted gastric residual evaluation (no residual group). The residual group comprised an even number of male and female infants (37 [50.0%]) with a mean (SD) gestational age of 27.1 (2.4) weeks and a mean (SD) birth weight of 888.8 (206.6) grams, whereas the no residual group had more male infants (36 [52.17%]), a mean (SD) gestational age of 27 (1.2) weeks, and a mean (SD) birth weight of 915.2 (180) grams. The no residual group had feedings that advanced more quickly compared with the residual group (mean weekly increase, 20.7 mL/kg/d vs 17.9 mL/kg/d; P = .02) and consumed more feedings at weeks 5 (137.2 [95% CI, 128.6-145.8]; P = .03) and 6 (141.6 [95% CI, 133.2-150.0]; P = .03). Among the secondary outcomes, the no residual group had higher mean estimated log weights (7.01 [95% CI, 6.99-7.02] vs 6.98 [95% CI, 6.97-7.00]; P = .03), had fewer episodes of abdominal distention (0.59 [95% CI, 0.34-1.01] vs 1.79 [95% CI, 1.27-2.53]; P = .001), and were discharged 8 days earlier (4.21 [95% CI, 4.14-4.28] vs 4.28 [95% CI, 4.19-4.36]; P = .01). Odds for necrotizing enterocolitis (0.58 [95% CI, 0.18-0.19] vs 0.026 [95% CI, 0.006-0.109]), death (0.004 [95% CI, 0.0003-0.046] vs 0.012 [95% CI, 0.001-0.131]), late-onset sepsis (0.970 [95% CI, 0.67-1.40] vs 1.38 [95% CI, 0.97-1.94]), and ventilator-associated pneumonia (0.084 [95% CI, 0.033-0.214] vs 0.056 [95% CI, 0.019-0.168]) were similar between groups.

CONCLUSIONS AND RELEVANCE Among extremely preterm infants, the omission of gastric residual evaluation increased the delivery of enteral nutrition as well as improved weight gain and led to earlier hospital discharge; these results may translate into evidence-based practice.

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P roviding sufficient enteral nutrition to critically ill pa-
tients reduces complications and improves health
outcomes.[1-3] Unfortunately, the feeding goals of pa-
tients who receive feedings through oro-nasogastric feeding
tubes are rarely met, with the most important barrier being
large gastric residuals.[4,5] Evaluating gastric residuals has been
considered standard care for decades without substantial sup-
porting evidence. Large gastric residuals have traditionally been
assumed to represent (1) feeding intolerance; (2) a risk for as-
piration and ventilator-associated pneumonia (VAP); or (3) in
extremely preterm infants, an early sign of necrotizing entero-
colitis (NEC), a devastating disease affecting up to 7% to 14%
of infants born at very low birth weight (VLBW).[6-9] However,
little evidence exists to indicate that evaluating gastric residu-
als improves patient outcomes and whether omitting this
evaluation may cause harm.[10,11] In addition, variation in the
definition of large gastric residuals; lack of evidence-based
management for abnormal gastric residuals; and potential
variation in gastric residual volume owing to feeding tube type
and size as well as patient position and aspiration technique
further limit the clinical usefulness of evaluation.[12-14]

Prefeed gastric residuals are evaluated by more than 97%
of neonatal intensive care unit (NICU) nurses,[15] but evidence
suggests this evaluation may be unnecessary.[11,16] Omitting gas-
tric residual evaluation has been shown to improve enteral nu-
trition delivery in adults and children without increasing feed-
ing intolerance or VAP.[10,16,17] Moreover, in several small studies,
preterm infants who did not undergo gastric residual evalua-
tion had improved nutritional outcomes.[11,18,19] However, to our
knowledge, this study is the first adequately powered ran-
domized clinical trial to determine the risks and benefits of
omitting gastric residual evaluation in VLBW infants, the popu-
lation at greatest risk for adverse nutritional outcomes of gas-
tric residual evaluation. Not only are these infants innately vul-
nerable but they also require frequent feedings (every 2-3
hours) and, because of their prematurity and level of acuity,
require a feeding tube for weeks to months.[20,21] Thus, the pri-
mary objective of this randomized clinical trial was to deter-
mine the effect of omitting prefeed gastric residual evalua-
tion on the amount of enteral nutrition provided to premature
VLBW infants for 6 weeks after birth. We hypothesized that
infants who did not undergo gastric residual evaluation would
have increased weekly enteral intake. Secondary objectives in-
cluded determining the effect of omitting gastric residual evalu-
ation on nutritional and infant outcomes as well as on risk of
gastric content aspiration and VAP.

Methods

Study Participants

From October 17, 2013, to October 8, 2016, infants were re-
cruited from a level 4 NICU and enrolled in the study if eli-
gible. They were eligible for inclusion if they were born at 32
or fewer weeks' gestation, had a birth weight of 1250 g or less,
were younger than 72 hours, and were receiving some feed-
ings by 72 hours after birth. Infants were ineligible if they had
congenital or chromosomal abnormalities, including com-

Key Points

Question What is the effect of omitting evaluation of prefeed
gastric residuals on nutritional outcomes in extremely preterm
infants?

Findings In this randomized clinical trial of 143 premature, very
low-birth-weight infants, those who did not undergo gastric
residual evaluation advanced feeds more quickly and consumed
more enteral nutrition at weeks 5 and 6 after birth.

Meaning Among extremely preterm infants, the omission of
gastric residual evaluation was safe and increased the delivery of
enteral nutrition.

plex congenital heart disease or a gastrointestinal condition.
Infants were withdrawn from the study if stage II or greater
NEC or spontaneous intestinal perforation occurred. This study
was approved by the University of Florida Institutional Re-
view Board, and the research protocol is available in Supple-
ment 1. Parental written informed consent was obtained by the
research team within 72 hours of life and within 24 hours of
initiating feeds. This study followed the Consolidated Stan-
dards of Reporting Trials (CONSORT) reporting guideline.

After parents or guardians signed the informed consent
forms, infants were randomized to 1 of 2 groups by a computer-
generated sequence with random-length permuted blocks of
sizes (4, 6, or 8) to maintain an approximate balance of assign-
ment to each treatment group. Infants were randomized to
either gastric residual evaluation (residual group) or omitted
gastric residual evaluation (no residual group) (**Figure**).
Randomization was concealed until the intervention was
assigned.

Study Intervention

All infants were enrolled by the research team. The residual
group underwent prefeed gastric residual evaluation, and the
no residual group did not. Gastric content aspiration was not
used to verify feeding tube placement for infants in the no re-
sidual group. Instead, a combination of 2 insertion depth mea-
surement strategies and verification of the calculated depth
prior to every feeding was used.[22,23] Because nurses re-
corded information regarding gastric residual volume, nei-
ther the clinical team nor the research staff were blinded to the
intervention. However, all feeding decisions, including time
of initiation, rate of advancement, and human milk fortifica-
tion, were made according to the NICU nutritional guide-
lines. Other clinical decisions, including initiation and dura-
tion of parenteral nutrition (PN), length of central line access,
withholding of feedings, and the need for abdominal radio-
graphs and laboratory analyses, were also based on the NICU
nutritional guidelines. The clinical team made all of the clini-
cal decisions except those regarding gastric residual evalua-
tion. Infants received only human milk (mother's own milk or
pasteurized donor human milk).

Study Outcomes

The primary outcome for this study was weekly enteral
nutrition measured in mL/kg for 6 weeks after birth. Pre-

Figure. Consort Diagram

NEC indicates necrotizing enterocolitis; SIP, spontaneous intestinal perforation.
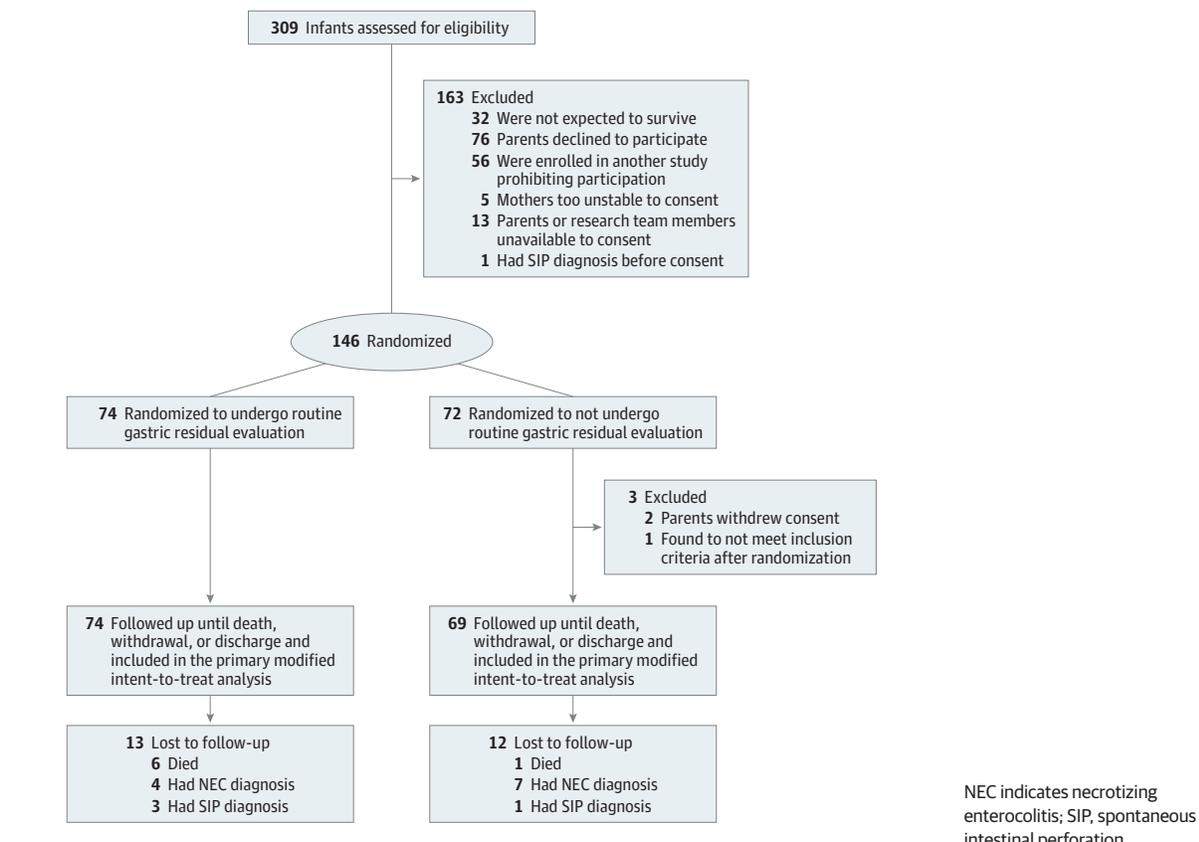
specified secondary outcomes included days to full feeds (120 mL/kg/d), hours of PN, hours with a central line, evidence of PN–associated liver disease (PNALD) (ie, level of direct bilirubin [DB] and level of alkaline phosphatase; DB and alkaline phosphate levels were assessed with clinically ordered laboratory tests), growth indices (weekly weight, head circumference, and length), days to discharge, evidence of feeding intolerance (episodes of emesis and episodes of increased abdominal circumference by >2 cm during the 6-week trial), episodes of presumed (treated with antibiotics for ≥5 days) or culture-proven late-onset sepsis (occurring ≥3 days of life), and evidence of stage II or greater NEC. Other health outcomes, including incidence of intraventricular hemorrhage, death, bronchopulmonary dysplasia (BPD), and duration of respiratory support, were compared between groups. Secondary outcomes also included occult fecal blood, fecal calprotectin and S100A12 levels, as well as motilin and gastrin levels but these were not included in this study.

Evidence of gastric content aspiration and incidence of VAP were assessed through (1) evidence of VAP on a chest radiograph as read by a pediatric radiologist, (2) positive tracheal cultures when done in accordance with clinical care, and (3) if the infant was ventilated, tracheal aspirate samples collected weekly during routine endotracheal tube suctioning and sent to the hospital laboratory for analysis of pepsin level.

Sample Size and Statistical Analysis

In a preliminary study, 40 VLBW infants had a mean (SD) enteral intake at 14 days of 72 (65) mL/kg/d. To detect a 50% improvement (Cohen d = 0.55), 104 infants were required to achieve 80% power at 2-sided P = .05 for the primary outcome of weekly enteral intake. Given the 143 infants available for analysis, an effect size of 0.31 (Cohen f) provided 80% power to detect the treatment-by-week interaction within the 2 (treatment) by 6 (time) generalized linear mixed model (GLMM) used.[24,25] The sample size was planned to accommodate dropouts, including deaths (estimated at 15%) and development of NEC (estimated at 7%).

All infants were included in the modified intent-to-treat analysis. Data analysis was performed from March to July 2018. Descriptive statistics were generated to characterize groups. Given the range of measurement levels (eg, continuous and censored), several statistical methods appropriate for outcome variable distribution were used. Statistical assumption tenability and model fit were evaluated for each model; when appropriate, remediation, such as Box-Cox family of transformation, non-normal link function, or inclusion of a scale measurement, was used. Adjacent categories were merged for categorical variables with small cell sizes. Variables clinically relevant to outcomes were evaluated for inclusion as covariates within models. Covariates were retained if they were statistically significant or if their removal reduced model fit as

evaluated by the Bayes Information Criterion. Inclusion of relevant covariates within a randomized design reduces error variance, thereby increasing the power to detect treatment differences, and enables exploring the heterogeneity of response to treatment through evaluating interaction with treatment. The trial was not powered to detect those interactions, but they provide information to better understand the effect of omitting gastric residual evaluation. A description of the statistical methods and associated outcome variables appears below.

Generalized linear mixed model analysis was used for outcomes consisting of repeated measures. With the exception of DB, unstructured-type (when each variance and each covariance is estimated uniquely from the data) within-participant covariance matrix forms best fit the data as assessed using Bayes Information Criterion. Effects included in models consisted of main effects for treatment (gastric residual: no or yes) and week (1-6), the treatment-by-week interaction, and selected covariates relevant to specific outcomes. Treatment-by-covariate interactions with $P > .05$ were removed from the model. Simple main effects, which deconstruct interacting effects, were examined for statistically significant interaction effects involving treatment.

Generalized linear model (GLM) analysis was used for outcomes consisting of single noncensored values compared between groups. Effects tested consisted of main effects for treatment, selected covariates relevant to the specific outcome modeled, and treatment-by-covariate interactions. Interactions with $P > .05$ were removed from the model.

Days to full feeds (120 mL/kg/d), hours of PN, hours with a central line, days to discharge, and respiratory support were compared using techniques suitable for censored data. By default, those accelerated failure time regression models transform the response with the natural logarithm before fitting specified models for γ, log-logistic, and log-normal distributions.[26,27] Data were censored at the end of the 6-week trial.

Differences in maximum alkaline phosphatase level and mean pepsin value were tested using a Wilcoxon 2-sample test, with exact P value estimates owing to residual-value non-normal distribution.[26]

An interim analysis, executed after half the planned accrual had been followed for 6 weeks, was performed to assess whether continued randomization was ethical. After evaluating the results, the data monitoring committee recommended the completion of planned accrual.

Results

In total, 143 infants were included in the study; 309 infants were eligible for inclusion, and 163 were excluded or parents refused consent. Of the 143 infants, 74 (51.7%) were randomized to undergo gastric residual evaluation (residual group) and 69 (48.3%) were randomized to omitted gastric residual evaluation (no residual group) (Figure). The residual group comprised an even number of male and female infants (37 [50.0%]) with a mean (SD) gestational age of 27.1 (2.4) weeks and a mean (SD) birth weight of 888.8 (206.6) grams, whereas the no re-

sidual group had more male infants (36 [52.17%]), a mean (SD) gestational age of 27 (1.2) weeks, and a mean (SD) birth weight of 915.2 (180) grams.

Eighteen infants (26.1%) in the no residual group had 1 or more gastric residuals evaluated, either inadvertently or when ordered, for symptoms of gastrointestinal dysfunction. Four infants (5.8%) were withdrawn for NEC, and no infant had gastric residuals evaluated for more than 1 day. The 2 groups were similar in sex, delivery mode, multiple birth, exposure to antenatal steroids, Apgar or SNAP (Score for Neonatal Acute Physiology) II score, and feeding type (mother's own milk vs donor human milk). However, infants in the no residual group compared with the residual group were nearly twice as likely to be African American (39 of 69 infants [56.5%] vs 22 of 74 infants [29.7%]; **Table 1**).

Primary Outcome

Results of the GLMM comparing enteral nutrition between groups over the 6-week study are presented in **Table 2**. The change in enteral nutrition over time differed between groups. Both groups increased over time, but the no residual group exhibited a steeper increase compared with the residual group (mean weekly increase, 20.7 mL/kg/d vs 17.9 mL/kg/d; $P = .02$). As seen in the simple main effects results, least square means for the groups were similar in weeks 1 through 4 but higher for the no residual group at weeks 5 (137.2 [95% CI, 128.6-145.8] vs 123.9 [95% CI, 115.2-132.6]; $P = .03$) and 6 (141.6 [95% CI, 133.2-150.0] vs 128.4 [95% CI, 119.9-136.9]; $P = .03$).

Secondary Outcomes

Results of the groups' days to full feeds, hours on PN, and hours with a central line appear in **Table 3**. Product-limit curves are similar between groups, with P values for homogeneity of strata ranging from 0.3 to 0.8 (eFigure in Supplement 2). The accelerated failure time regression models comparing mean time to outcome demonstrated no statistically significant differences, ranging from $P = .59$ for days to 120 mL/kg/d to $P = .97$ for days requiring invasive ventilation. After natural log transformation to normalize the distribution of residual values, mean log-transformed DB and odds for occurrence of an elevated DB (>2 mg/dL) were similar between groups (Table 3). Maximum alkaline phosphate levels were similar between the residual group and no residual group (median interquartile range [IQR], 481 [371-664] vs 495.5 [393-650.5]; $P = .95$).

Infants in the no residual group had higher least square means values for estimated mean log weight (7.01 [95% CI, 6.99-7.02] vs 6.98 [95% CI, 6.97-7.00]; $P = .03$); however, head circumference (25.85 [95% CI, 25.62-26.08] vs 25.94 [95% CI, 25.71-26.17]; $P = .56$) and length (36.78 [95% CI, 36.44-37.11] vs 36.41 [05% CI, 36.08-36.74; $P = .59$) were similar between groups (Table 2). The no residual group had fewer episodes of abdominal distention (0.59 [95% CI, 0.34-1.12] vs 1.79]95% CI, 1.27-2.53]; $P = .001$) but more emesis episodes (5.01 [95% CI, 3.87-6.50] vs 2.46 [95% CI, 1.70-3.56]; $P = .002$), and the number of abdominal radiographs were similar between groups (3.81 [95% CI, 3.24-4.64] vs 4.34 [95% CI, 3.66-5.34]; **Table 4**).

Variables indicative of VAP were similar between groups, including odds for a positive tracheal aspirate and number of

Table 1. Baseline Characteristics of Infants

Variable	Frequency, No. (%)	
	Residual Group (n = 74)	No Residual Group (n = 69)
Gestational age, mean (SD), wk	27.1 (2.4)	27.0 (1.2)
Birth weight, mean (SD), g	888.8 (206.6)	915.2 (180.0)
Race		
White	49 (66.2)	28 (40.58)
African American	22 (29.7)	39 (56.5)
Asian	0	1 (1.45)
Other	3 (4.1)	1 (1.45)
Ethnicity		
Hispanic	10 (13.51)	6 (8.70)
Sex		
Male	37 (50.0)	36 (52.17)
Female	37 (50.0)	33 (44.14)
Mode of delivery		
Cesarean	55 (74.32)	54 (78.26)
Vaginal	19 (25.68)	23 (33.33)
Multiple births	18 (24.32)	15 (21.75)
Received antenatal steroids	68 (91.89)	56 (81.16)
5-m Apgar score, mean (SD)	6.58 (2.26)	6.39 (2.39)
SNAP-II score, mean (SD)	20.58 (12.58)	21.25 (12.51)
Type of feeding		
% MOM, mean (SD)	55.04 (39.90)	49.89 (38.52)

Abbreviations: MOM, mother's own milk; SNAP, Score for Neonatal Acute Physiology.

positive aspirates (0.084 [95% CI, 0.033-0.214] vs 0.056 [95% CI, 0.019-0.168]) (Table 4). Pepsin levels were similar between the residual and no residual groups (median [IQR], 1.00 [0.2-5.7] vs 0.90 [0-2.0]; P = .27). No instances of VAP were found on chest radiograph. Odds for BPD (0.512 [95% CI, 0.305-.858] vs 0.680 [95% CI, 0.414-1.120]; P = .43) and use of respiratory support (6.02 [95% CI, 2.79-12.96] vs 2.45 [95% CI, 1.34-4.47]; P = .53; Table 4) were similar between the residual and no residual groups. Least square means for estimated log days requiring invasive ventilation were also similar (1.96 [95% CI, 1.70-2.23] vs 1.97 [95% CI, 1.69-2.25]; P = .97; Table 3).

The product-limit survival curves for days to discharge were similar (eFigure in Supplement 2), but when gestational age entered into the model, infants in the no residual group were discharged 8 days earlier than those in the residual group (4.21 [95% CI, 4.14-4.28] vs 4.28 [95% CI, 4.19-4.36]; P = .01; Table 3). Odds for NEC (0.58 [95% CI, 0.18-0.19] vs 0.026 [95% CI, 0.006-0.109]), death (0.004 [95% CI, 0.0003-0.046] vs 0.012 [95% CI, 0.001-0.131]), and late-onset sepsis (0.970 [95% CI, 0.67-1.40] vs 1.38 [95% CI, 0.97-1.94]), and VAP (0.084 [95% CI, 0.033-0.214] vs 0.056 [95% CI, 0.019-0.168]) were similar between groups (Table 4).

Discussion

We found that infants who did not undergo gastric residual evaluation received considerably more enteral nutrition without an increase in adverse health outcomes. When gastric residual evaluation was omitted, infants advanced feedings more quickly and consumed more enteral nutrition at

weeks 5 and 6 after birth. These findings are consistent with those in other studies that found increased enteral intake when gastric residual evaluations were omitted. In their randomized clinical trial of 61 preterm VLBW infants, Torrazza et al[11] found that, when gastric residual evaluations were omitted, infants reached full feedings (150 mL/kg/d) nearly 6 days earlier. Although not statistically significant, these findings may be clinically important in preterm infants at substantial risk for complications associated with suboptimal enteral nutrition.[11] In another study after a practice change that omitted gastric residual evaluation, infants at 34 weeks' gestation or younger reached full feedings (150 mL/kg/d) 1 day earlier.[18] When prefeed abdominal circumferences were evaluated in place of gastric residuals in a study, VLBW infants experienced fewer feeding interruptions (0 vs 2; P < .001) and required less time to reach full feeds (10 vs 14 days; P < .001).[19] Conversely, Singh et al,[28] in a randomized clinical trial of infants with a birth weight between 1500 g and 2000 g, found no difference in days to reach full feeds (120 mL/kg/d).

Evidence is lacking that large gastric residuals indicate feeding intolerance[16,29] and, in infants born extremely preterm, may be normal owing to gastrointestinal immaturity and reduced motility.[30] We found that, when gastric residual evaluation was omitted, infants experienced fewer episodes of abdominal distension and, although not statistically significant, required fewer abdominal radiography. Similarly, Shulman et al,[31] in a prospective study of 50 preterm infants, found no association between feeding intolerance (longer time to full feedings and/or decreased feedings) and large gastric residuals (>50% and/or >2 mL/kg), and gastric residuals up to

Table 2. Repeated Measures Outcomes Analyzed Using Generalized Linear Mixed Model Analysis

Variable	P Value	Estimate (95% CI)[a]	
		Residual Group	No Residual Group
Weekly feedings, mL/kg/d			
Birth weight	.03	NA	NA
GA	<.001	NA	NA
GA × week	<.001	NA	NA
Week	.006	NA	NA
Treatment	.048	NA	NA
Treatment × week	.02	NA	NA
Simple main effects			
Week 1	.27	25.7 (21.8 to 29.5)	22.6 (18.6 to 26.5)
Week 2	.12	83.2 (72.9 to 93.4)	94.7 (84.3 to 105.2)
Week 3	.28	109.2 (98.5 to 120.0)	117.7 (106.9 to 128.5)
Week 4	.15	119.4 (109.5 to 129.4)	129.6 (119.7 to 139.6)
Week 5	.03	123.9 (115.2 to 132.6)	137.2 (128.6 to 145.8)
Week 6	.03	128.4 (119.9 to 136.9)	141.6 (133.2 to 150.0)
Estimated log direct bilirubin			
Week	<.001	NA	NA
GA	<.001	NA	NA
Birth weight	<.001	NA	NA
Treatment			
Transformed values	.98	−0.777 (−0.892 to −0.661)	−0.778 (−0.895 to −0.661)
Untransformed values[b]	NA	0.690 (0.563 to 0.819)[b]	0.671 (0.542 to 0.799)[b]
Occurrence of elevated (>2 mg/dL) direct bilirubin			
GA	.07	NA	NA
Birth weight	.008	NA	NA
Treatment	.53	0.040 (0.017 to 0.092)	0.057 (0.025 to 0.131)
Estimated log transformed weight			
Birth weight	<.001	NA	NA
GA	<.001	NA	NA
Week	<.001	NA	NA
GA × treatment	.047	NA	NA
Treatment			
Transformed values	.03	6.98 (6.97 to 7.00)	7.01 (6.99 to 7.02)
Untransformed values[b]	NA	1129.7 (1111 to 1148)[b]	1145.3 (1126 to 1164)[b]
Head circumference			
Week	.02	NA	NA
Birth HC	<.001	NA	NA
GA	<.001	NA	NA
Birth HC × week	<.001	NA	NA
GA × week	<.001	NA	NA
Treatment	.56	25.94 (25.71 to 26.17)	25.85 (25.62 to 26.08)
Length			
Birth length	<.001	NA	NA
GA	<.001	NA	NA
Week	<.001	NA	NA
Birth length × treatment	.008	NA	NA
GA × treatment	.005	NA	NA
Treatment	.59	36.41 (36.08 to 36.74)	36.78 (36.44 to 37.11)

Abbreviations: GA, gestational age; HC, head circumference; NA, not applicable.

[a] All estimates are least square means except for occurrence of elevated bilirubin, which are odds.

[b] Untransformed values provided for clinical reference only.

2 to 3 mL/kg have not been shown to indicate feeding intolerance (less feedings at 14 days of life) in preterm infants.[32]

Contrary to results in previous studies, we found no differences in length of time PN or a central line was required nor

Table 3. Outcomes Analyzed Using Survival Analysis

Variable	P Value	LSM (95% CI) Residual Group	No Residual Group
Days to full feeds, 120 mL/kg/d[a]			
GA	.006	NA	NA
Treatment			
Transformed values	.59	2.47 (2.29-2.65)	2.51 (2.38-2.63)
Untransformed values[b]	NA	18.1 (16.3-20.0)[b]	15.9 (14.1-17.8)[b]
Hours of parenteral nutrition[c]			
Birth weight	<.001	NA	NA
Weekly median % of MOM	.003	NA	NA
Treatment			
Transformed values	.64	5.67 (5.55-5.78)	5.71 (5.59-5.82)
Untransformed values[b]	NA	358.8 (312.2-405.4)[b]	356.8 (310.6-403.1)[b]
Hours with a central access[c]			
Birth weight	<.001	NA	NA
Weekly median % of MOM	.001		
Treatment	.95	5.81 (5.69-5.93)/402.6 (352.4-452.8)[b]	5.81 (5.70-5.93)/398.6 (350.2-447.0)[b]
Transformed values	.95	5.81 (5.69-5.93)	5.81 (5.70-5.93)
Untransformed values[b]	NA	402.6 (352.4-452.8)[b]	398.6 (350.2-447.0)[b]
Days requiring invasive ventilation[d]			
GA	<.001	NA	NA
Treatment	.97	1.96 (1.70-2.23)/14.3 (11.2-17.4)[b]	1.97 (1.69-2.25)/13.3 (10.1-16.5)[b]
Days to discharge[a]			
GA	<.001	NA	NA
GA × treatment	.03	4.28 (4.19-4.36)	4.21 (4.14-4.28)
Treatment			
Transformed values	.01	4.28 (4.19-4.36)	4.21 (4.14-4.28)
Untransformed values[b]	NA	86.4 (80.7-92.1)[b]	79.1 (73.17-84.5)[b]

Abbreviations: GA, gestational age; LSM, least square means; MOM, mother's own milk; NA, not applicable.

[a] Gamma distribution modeled.

[b] Untransformed values provided for clinical reference only.

[c] Log-logistic distribution modeled.

[d] Log-normal distribution modeled.

in the incidence of PNALD or metabolic bone disease. When feedings are interrupted or decreased, PN is required in greater amounts and/or for longer periods, thereby increasing the risk for PNALD, prolonged need for central lines, and metabolic bone disease.[33-35] Torrazza et al[11] found that infants who did not undergo gastric residual evaluation required nearly central line 6 days less and more than 1 day less on PN, although these findings were not statistically significant. Two additional small studies reported that, when gastric residual evaluation was omitted, infants required fewer days of PN, but differences in timing of feeding initiation and inclusion of infants older than 32 weeks' gestation may have affected results. Neither study included the number of days that a central line was required or the incidence rate of PNALD.[18,19]

In addition, we found that infants who did not undergo gastric residual evaluation were discharged home 8 days earlier. These findings are consistent with research in adults and children indicating that improved enteral nutrition reduces both intensive care unit and hospital stay,[4,36,37] but previous research in preterm infants has not indicated differences in length of NICU stay.[19] Furthermore, when gastric residual evaluation were omitted, improved weight gain in infants was observed but no substantial differences in either head circumference or length. When feedings are interrupted or decreased owing to large gastric residuals, growth may be negatively affected.[38] Because of the association between adequate growth and improved neurodevelopmental outcome in extremely preterm infants, these findings may be particularly important.[39-41]

Large gastric residuals have traditionally been considered an early symptom of NEC,[6] but we found no differences in incidence of NEC between the residual and no residual groups. Two retrospective case-control studies have suggested gastric residual volume may be higher in infants who develop NEC,[6,8] but our findings are consistent with other studies of preterm infants in which omission of gastric residual evaluation was not associated with an increased incidence of NEC.[11,18,19,28]

Large gastric residuals have traditionally been believed to increase the risk of emesis and aspiration, thus increasing the risk of VAP, but evidence to support this assumption is lacking.[10,42] Preterm infants are at an increased risk for VAP

Table 4. Outcomes Analyzed Using Generalized Linear Model Analysis

Variable	P Value	Estimate (95% CI)[a]	
		Residual Group	No Residual Group
No. of emesis episodes			
Race	.26	NA	NA
Treatment × race	.008	NA	NA
GA	.002	NA	NA
Weekly median % of MOM	<.001	NA	NA
Treatment	.002	2.46 (1.70-3.56)	5.01 (3.87-6.50)
Simple main effect			
African American	.006	2.62 (1.97-3.49)	4.16 (3.54-4.89)
Non–African American	<.001	2.22 (1.83-2.68)	6.18 (5.33-7.16)
No. of episodes of abdominal distension			
Race	<.001	NA	NA
Weekly median % of MOM	.03	NA	NA
Treatment	.001	1.79 (1.27-2.53)	0.590 (0.344-1.012)
No. of abdominal radiographs			
GA	<.001	NA	NA
Weekly median % of MOM	.08	NA	NA
Treatment	.25	4.34 (3.66-5.34)	3.81 (3.24-4.64)
Positive tracheal aspirate occurrence			
GA	<.001	NA	NA
Weekly mean % of MOM	.03	NA	NA
Treatment		NA	NA
1	.17	0.055 (0.029-0.107)	0.088 (0.051-0.152)
≥2		0.015 (0.007-0.033)	0.024 (0.012-0.047)
Brochopulmonary dysplasia			
Overall	.001	NA	NA
GA	<.001	NA	NA
Treatment	.43	0.512 (0.305-0.858)	0.680 (0.414-01.12)
Respiratory support[b]			
GA	<.001	NA	NA
Treatment	.053	6.02 (2.79-12.96)	2.45 (1.34-4.47)
IVH stage (modeling probability of higher stage)			
Overall	.06	NA	NA
GA	.03	NA	NA
Treatment		NA	NA
Stage 2	.62	3.95 (1.74-8.96)	3.07 (1.39-6.78)
Stage 3 or 4		0.365 (0.167-0.796)	0.284 (0.126-0.638)
No. of late-onset sepsis episodes[c]			
Poisson model			
Length of stay	<.001	NA	NA
Treatment	.08	1.38 (0.97-1.94)	0.97 (0.67-1.40)
Zero-inflation model			
GA	.002	NA	NA
Occurrence of NEC[c]			
GA	.02	NA	NA
Estimated log weekly mean % of MOM	.08	NA	NA
Treatment	.25	0.026 (0.006-0.109)	0.058 (0.018-0.190)
Death within 6 weeks[c]			
GA	<.001[d]	NA	NA
Treatment	.60[d]	0.012 (0.001-0.131)	0.004 (0.0003-0.046)

Abbreviations: GA, gestational age; IVH, intraventricular hemorrhage; MOM, mother's own milk; NA, not applicable; NEC, necrotizing enterocolitis.

[a] All estimates are odds except for IVH stage and number of positive tracheal aspirate samples (which are odds ratios) and number of late-onset sepsis episodes, number of emesis episodes, number of abdominal distensions, and number of abdominal radiographs (which are least square means).

[b] Whether or not infant required respiratory support.

[c] Death, late-onset sepsis, and NEC were mutually exclusive.

[d] Exact conditional P value.

owing to the use of uncuffed endotracheal tubes, reduced immune competency, decreased lower esophageal sphincter tone, and decreased gastrointestinal motility.[43]

Previous research suggests that evaluating gastric residuals does not protect against VAP in adults and children,[4,16,44] but the present study, to our knowledge, is the first to address the effect of omitting gastric residual evaluation on the incidence of VAP in extremely preterm infants. Using objective determinants of VAP, including tracheal pepsin levels, positive endotracheal cultures, and radiographic evidence, we did not find increased incidence of VAP when gastric residual evaluations were omitted. Although VAP has been associated with morbidity, including increased risk for BPD in preterm infants,[45,46] we found no difference in incidence of BPD, need for respiratory support, or days requiring invasive ventilation between the 2 groups in this study.

Strengths and Limitations

Strengths of this study include omitting the evaluation of aspiration of gastric residuals to verify feeding tube placement, thereby limiting any potential disruption in digestion. In addition, all infants were fed only human milk to minimize the differences in gastric emptying and feeding intolerance that may occur with formula feedings.[47]

This trial has several limitations. Because information on gastric residual evaluation is included in medical records and monitored by clinicians, blinding was impossible. Therefore, a change in clinician behavior resulting from group assignment could not be completely excluded. In addition, the study was not powered to address safety concerns, including the risk for NEC.

Conclusions

The results of this trial suggest that evaluating gastric residuals is unnecessary and may decrease the delivery of enteral nutrition to extremely preterm infants. Limiting gastric residual evaluation to infants with symptoms of gastrointestinal dysfunction (including abdominal distension or tenderness, emesis, and clinical decompensation or bloody stools) may increase enteral nutrition delivery in this vulnerable population. These findings can be translated into evidence-based practice in the care of VLBW infants.

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