



# HHS Public Access

Author manuscript

*J Perinatol.* Author manuscript; available in PMC 2010 February 23.

Published in final edited form as:

*J Perinatol.* 2009 May ; 29(5): 372–375. doi:10.1038/jp.2008.234.

## TRANSPYLORIC TUBE FEEDING IN VERY LOW BIRTHWEIGHT INFANTS WITH SUSPECTED GASTROESOPHAGEAL REFLUX: IMPACT ON APNEA AND BRADYCARDIA

**WF Malcolm, M.D.,**

Department of Pediatrics, Duke University, Durham, NC

**PB Smith, M.D., M.H.S.,**

Department of Pediatrics, Duke University, Durham, NC

**S Mears, NNP,**

Duke University Medical Center, Durham, NC

**RN Goldberg, M.D., and**

Department of Pediatrics, Duke University, Durham, NC

**CM Cotten, M.D., M.H.S.**

Department of Pediatrics, Duke University, Durham, NC

### Abstract

**OBJECTIVE**—Our aim was to assess safety and efficacy of transpyloric tube feeding as a therapeutic option to reduce apnea and bradycardia in hospitalized very low birthweight infants with clinical signs suggestive of gastroesophageal reflux.

**PATIENTS AND METHODS**—This was a retrospective single center cohort study of VLBW infants hospitalized from 2001–2004 with signs of GER who received transpyloric enteral tube feedings. Apnea (>10 sec) and bradycardia (<100 bpm) episodes were compared before and after the initiation of transpyloric feedings. The Wilcoxon signed-rank test was used to compare differences between cardio-respiratory episodes before and after treatment at 1-day and combined 3-day intervals. Events recorded to assess safety of transpyloric feedings included death, sepsis, and necrotizing enterocolitis.

**RESULTS**—72 VLBW infants with a median birth weight of 870 grams (range 365–1435g) and gestational age of 26 weeks (23–31weeks) were identified. Median weight at initiation of transpyloric feedings was 1297 grams (820–3145g) and infants received transpyloric feeds for median duration of 18 days (1–86days). After initiation of transpyloric feedings, a reduction in apnea episodes from 4.0 to 2.5 ( $P=0.02$ ) and a decrease in bradycardia episodes from 7.2 to 4.5 ( $P<0.001$ ) was observed when comparing total number of episodes for the 3 days before and after

Users may view, print, copy, and download text and data-mine the content in such documents, for the purposes of academic research, subject always to the full Conditions of use:[http://www.nature.com/authors/editorial\\_policies/license.html#terms](http://www.nature.com/authors/editorial_policies/license.html#terms)

Corresponding Author: William F Malcolm, MD, Assistant Professor, Dept of Pediatrics/Neonatology, Box 3179, Duke University Medical Center, Durham, NC 27710, Office- (919) 681-6026, Pager- (919) 970-7474, Fax- (919) 681-6065, malco002@mc.duke.edu.

**Financial Disclosure:** Dr Malcolm was funded by a diversity supplement through the National Institute of Child Health and Human Development Cooperative Multicenter Neonatal Research Network (grant 3 U10 HD040492-06S1) and the Gerber Foundation

treatment. Five (6.9%) of the infants developed necrotizing enterocolitis while receiving transpyloric feedings. None of the infants receiving human milk ( $P=0.07$ ) and 36% of those receiving hydrolysate based formula ( $P<0.01$ ) during transpyloric feeds developed NEC. No infants had late-onset culture proven sepsis. Seven (9.7%) infants died prior to hospital discharge.

**CONCLUSIONS**—Transpyloric feedings, especially when limited to human milk, may safely reduce episodes of apnea and bradycardia in preterm infants with suspected gastroesophageal reflux. Prospective randomized studies are needed to determine the biologic impact of bypassing the stomach, as well as the safety and efficacy of this intervention. Results of such studies could modify the current prevailing safety concerns regarding transpyloric feeding in this population.

### Keywords

GERD; Feeding Methods; Infant; Premature; Apnea

---

### Introduction

The clinical diagnosis of gastroesophageal reflux (GER) is common among preterm infants having apnea and bradycardia. Earlier studies of preterm infants suggested an association between GER and apnea [1–3]; however, more recent studies using combined pH and multichannel intraluminal impedance monitoring have challenged these findings. [4–8] While a temporal relationship between GER and apnea of prematurity remains an ongoing debate, therapeutic interventions including anti-reflux medications and transpyloric tube (TPT) feeding are frequently used in this population with little evidence to support their use. [9–11]

TPT feeding in preterm infants bypasses the stomach and, theoretically, reduces the potential for GER that occurs secondary to lower esophageal sphincter relaxation or delayed gastric emptying. A recent Cochrane review of nine randomized controlled trials of transpyloric versus gastric feeding in preterm infants concluded that there was no evidence for improved “feeding tolerance” or growth with TPT feeds, but found an increased risk for “gastrointestinal disturbance” requiring cessation of feeds. [12] There was no increased risk for necrotizing enterocolitis (NEC), spontaneous intestinal perforation, aspiration pneumonia, or mortality reported, when allocation bias was controlled. The trials included in the review evaluated TPT feeding as an initial feeding strategy versus gastric feeding for improved growth and feeding tolerance, whereas TPT feeding has not been evaluated as a treatment method for reducing GER episodes or episodes of autonomic instability, such as apnea and bradycardia, occurring in very preterm infants suspected of having GER.

Our objectives in this study were to assess 1) whether or not TPT feedings reduced cardio-respiratory episodes, and 2) the safety of this intervention in a population of VLBW infants with suspected GER.

### METHODS

This was a review of all very low birthweight (VLBW,  $BW<1500$  g) infants hospitalized at Duke University Medical Center from January 1, 2001 to December 31, 2004 with signs of

GER with gastric feedings, who then received TPT feedings. We identified patients by reviewing the discharge summaries of all VLBW infants having a hospital charge for a TPT from unit stock or for placement of a TPT in the Department of Radiology. Determination of each infant's GER diagnosis and need for TPT feeding was by the neonatal attending on service. Our unit protocol for treating GER reserves the use of TPT feeding for those infants whose episodes of suspected GER are excessive or severe and who have failed trials of other GER treatments, including: positional changes, changes to the feeding schedule, elemental formulas, and anti-reflux medications, including antacids and metoclopramide.

Transpyloric enteral feeding tubes were placed fluoroscopically by a pediatric radiologist or advanced by the bedside nurse and confirmed by abdominal radiograph. An 8-French, polyurethane, non-weighted feeding tube was inserted by nasoduodenal route regardless of placement method. Feedings were then given continuously by pump.

Episodes of apnea > 10 seconds and bradycardia < 100 beats per minute were recorded by the bedside nurse as alerted by bedside impedance monitoring. We compared cardio-respiratory episodes before and after the initiation of TPT feedings at 1-day and combined 3-day intervals. The Wilcoxon signed-rank test was used to compare differences between daily cardio-respiratory episodes before and after TPT feedings were initiated.

Safety was monitored by noting episodes of death, sepsis, necrotizing enterocolitis, or spontaneous intestinal perforation. Sepsis was determined by positive blood culture, excluding untreated coagulase negative staphylococcus. NEC was defined by radiographic (Bell's Stage IIA or greater) or surgical evidence. Descriptive statistics were used to summarize safety results, while Fisher's exact and Kruskal-Wallis tests were used to compare factors of those that developed NEC and those that did not.

Infant socio-demographic, perinatal, and neonatal course history were also documented. This study was approved by Duke University's Institutional Review Board.

## RESULTS

72 VLBW infants with a median birth weight of 870 grams (range 365–1435g) and gestational age of 26 weeks (23–31weeks) were included (Table 1). The median weight at initiation of transpyloric feedings was 1297 grams (820–3145g) and age of 59 days (10–177days). Infants received feeds by this route for a median duration of 18 days (1–86days).

### Efficacy Assessments

A reduction in apnea episodes from 4.0 for the combined 3 days prior to treatment to 2.5 episodes for the combined 3 days after initiation of TPT feedings ( $P = 0.02$ ) was observed (Figure 1). In the immediate day before and after initiating TPT feeds, the number of apnea episodes decreased from 2.4 to 2.0 ( $P=0.10$ ). We observed a decrease in total bradycardia episodes from 7.2 to 4.5 ( $P < 0.001$ ) in the 3-day intervals before and after TPT placement and a reduction from 4.6 to 3.2 ( $P < 0.01$ ) in the immediate day before and after the initiation of TPT feeds.

## Safety Assessments

Five (6.9%) of the 72 infants developed NEC while receiving TPT feedings, similar in number when compared to those developing NEC before initiating (9.7%) or after discontinuing (8.3%) TPT feeds (Table 2). The infants that developed NEC during TPT feedings were similar to those that did not develop NEC with respect to birth weight, gestational age, gender, race, age and weight at time of initiating TPT feeding (Table 3). None of the infants receiving human milk during TPT feeding developed NEC ( $P=0.07$ ) and 36% of those receiving hydrolysate based formula developed NEC ( $P<0.01$ ).

Seven (9.7%) of the infants died prior to hospital discharge. Two infants died after developing NEC while receiving TPT feeds. Five others died from complications of extreme prematurity and whose death was not temporally related to TPT feeds, including one each from complications of bronchopulmonary dysplasia, severe hydrocephalus, pulmonary hypertension, pulmonary hypoplasia, and one who died from congenital heart disease. No infant had an episode of sepsis or spontaneous intestinal perforation while receiving TPT feedings.

## DISCUSSION

A definite causal relationship between GER and episodes of apnea and bradycardia remains elusive. It is likely that clinicians overdiagnose GER, attempting to explain a reason for the cardio-respiratory episodes related to immaturity of multiple physiologic functions. While it may be difficult to determine whether or not the cardio-respiratory instability elicited the reflux response, or the reflux of milk into the hypopharynx elicited the cardio-respiratory response, clinicians often seek therapeutic options to reduce these episodes in very low birthweight infants. Agreeing on the best therapeutic approach to this situation, however, has been challenging and has included alterations in optimal nutrition, use of medications with known risks, and even surgery. [13] We have included use of TPT feeding in our approach to the infant with apparent GER and recalcitrant cardio-respiratory instability.

Using the preterm infant as his own control, we found that TPT feeding reduces both apnea and bradycardia when compared to gastric feeds. It is possible that TPT feeds reduce GER episodes by allowing the milk to bypass the stomach thereby reducing obstructive apnea associated with milk refluxed to the proximal esophagus and hypopharynx. However, it may be that TPT feeding simply decreases the gastric distension associated with poorer respiratory function in bolus fed preterm infants. [14] The impact of TPT feeding on acid and non-acid reflux episodes and associated cardio-respiratory events in preterm infants has not been evaluated by randomized controlled trial.

One of the problems of diagnosing and treating GER in preterm infants is the lack of standard practice guidelines. The North American Society for Pediatric Gastroenterology and Nutrition Clinical Practice Guidelines for the evaluation and management of infants and children with suspected GER are not intended to be utilized for the management of neonates less than 72 hours old, premature infants or infants with neurological impairments. [15] Thus, neonatologists often start empiric treatment, though behavioral symptoms and cardio-

respiratory signs are often poorly predictive of GER and effective medical treatments have not been determined. [16–17]

Misra et al. also described a reduction in GER-associated apnea with TPT feeding in a small number of preterm infants and suggested using bedside-placed TPTs as a diagnostic tool for GER in this population. [18] Regardless of the mechanism for reducing apnea, we feel that this feeding method should be considered as a temporary treatment option in preterm infants with “excessive or severe” apnea or bradycardia events. Its effectiveness in improving these events should be evident within 24–72 hours.

A current systematic review comparing gastric versus TPT feeds in preterm infants have cautioned of a possible increased risk of mortality and feeding intolerance with TPT feeds. The increased mortality, however, disappeared when allocation bias was controlled. There were no differences in NEC, spontaneous perforation, sepsis or aspiration pneumonia. [12] While 7% of the babies in our study population developed NEC while receiving TPT feeds, this was similar to the number who developed NEC before or after receiving TPT feedings. Of note, 40% of the infants in our study received maternal breastmilk (non-donor) during TPT feedings and none of those infants developed NEC, while 15% of the infants received hydrolysate based formula during TPT feeds and over one third of them developed NEC.

This study is limited by the retrospective nature of the data collection and the unblinded evaluation of the bedside nurse to the intervention of TPT feedings. The number of recorded events in this study is likely lower than the true incidence, as bedside impedance monitoring and clinical nursing notation usually underestimates actual events. Lastly, while maturation may account for a decrease in cardio-respiratory events, it is unlikely that a maturational improvement would be significant when comparing both one and three day intervals in a preterm infant who is two months old. A randomized controlled trial would be necessary to properly determine efficacy of this intervention.

## CONCLUSION

Transpyloric tube feedings are effective in reducing apnea and bradycardia in preterm infants with suspected GER. This method of feeding appears to be safe enough to warrant a clinical trial in a select population of preterm infants having excessive or severe apnea or bradycardia episodes suspected to be related to GER, particularly if the source of nutrition is human milk. Pivotal prospective studies of treatment methods for GER in preterm babies with clear inclusion criteria and outcome measures are needed to make more uniform evidence-based clinical practice recommendations.

## Abbreviations

<b>VLBW</b>	very low birthweight (<1500g)
<b>GER</b>	astroesophageal reflux
<b>TPT</b>	transpyloric tube
<b>NEC</b>	necrotizing enterocolitis

## References

1. Herbst JJ, Minton SD, Book LS. Gastroesophageal reflux causing respiratory distress and apnea in newborn infants. *J Pediatr.* 1979; 95:763–768. [PubMed: 39984]
2. Spitzer AR, Boyle JT, Tuchman DN, Fox WW. Awake apnea associated with gastroesophageal reflux: A specific clinical syndrome. *J Pediatr.* 1984; 104:200–205. [PubMed: 6694012]
3. Menon AP, Schefft GL, Thach BT. Apnea associated with regurgitation in infants. *J Pediatr.* 1985; 106:625–629. [PubMed: 3981319]
4. Peter CS, Sprodowski N, Bohnhorst B, Silny J, Poets CF. Gastroesophageal reflux and apnea of prematurity. No temporal relationship. *Pediatrics.* 2002; 109:8–11. [PubMed: 11773535]
5. Barrington KJ. Apnea at discharge and gastro-esophageal reflux in the preterm infant. *J Perinatol.* 2002; 22:8–11.
6. Molloy EJ. Does gastroesophageal reflux cause apnea in preterm infants? *Biol Neonate.* 2005; 87:254–61. [PubMed: 15711034]
7. Wenzl TG, Schenke S, Peschgens T, Silny J, Heimann G, Skopnik H. Association of apnea and nonacid gastroesophageal reflux in infants: Investigations with the intraluminal impedance technique. *Pediatr Pulmonol.* 2001; 31:144–149. [PubMed: 11180691]
8. Di Fiore JM, Arko M, Whitehouse M, Kimball A, Martin RJ. Apnea is not prolonged by acid gastroesophageal reflux in preterm infants. *Pediatrics.* 2005; 116:1059–1063. [PubMed: 16263989]
9. Kimball AL. Gastroesophageal reflux medications in the treatment of apnea in premature infants. *J Pediatr.* 2001; 138:355–60. [PubMed: 11241042]
10. Clark RH. Reported medication use in the neonatal intensive care unit: data from a large national data set. *Pediatrics.* 2006; 117(6):1979–1987. [PubMed: 16740839]
11. Malcolm WF, Gantz M, Martin RJ, Goldstein RF, Goldberg RN, Cotten CM, et al. Use of medications for gastroesophageal reflux in extremely low birth weight infants at discharge. *Pediatrics.* 2008; 121(1):22–27. [PubMed: 18166553]
12. McGuire W. Transpyloric versus gastric tube feeding for preterm infants. *Cochrane Database Systematic Review.* 2007; (3)
13. Guillet R, Stoll BJ, Cotten CM, Gantz M, McDonald S, Poole WK, et al. Association of H2-blocker therapy and higher incidence of necrotizing enterocolitis in very low birthweight infants. *Pediatrics.* 2006; 117(2):137–42.
14. Blondheim O, Abbasi S, Fox WW, Bhutani VK. Effect of enteral gavage feeding rate on pulmonary functions of very low birth weight infants. *J Pediatr.* 1993; 122:751–5. [PubMed: 8496756]
15. Rudolph CD, Mazur LJ, Liptak GS, Baker RD, Boyle JT, Colletti RB, et al. Pediatric gastroesophageal reflux clinical practice guidelines. *J Pediatr Gastroenterol Nutr.* 2001; 32(supplement 2)
16. Snel A, Barnett CP, Cresp TL, Haslam RR, Davidson GP, Malbert TH, et al. Behavior and gastroesophageal reflux in the premature neonate. *J Pediatr Gastroenterol Nutr.* 2000; 30:18–21. [PubMed: 10630434]
17. Hibbs AM. Metoclopramide for the treatment of gastroesophageal reflux disease in infants: a systematic review. *Pediatrics.* 2006; 118(2):746–52. [PubMed: 16882832]
18. Misra S, Macwan K, Albert V. Transpyloric feeding in gastroesophageal-reflux-associated apnea in premature infants. *Acta Paediatrica.* 2007; 96(10):1426–29. [PubMed: 17850402]

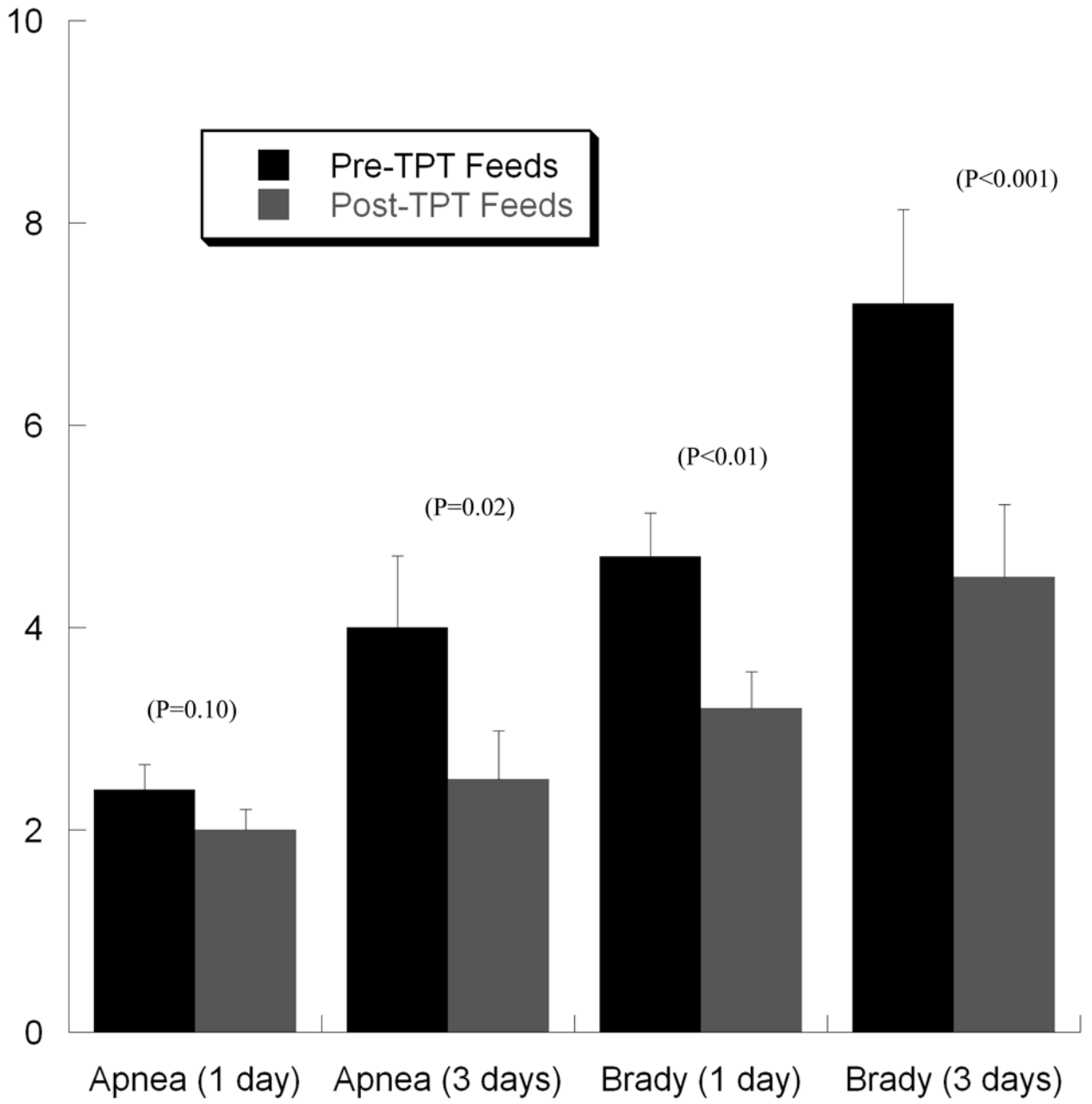


Figure 1.

**Table 1**

Demographics for study population (n=72)

Gestational Age at birth (weeks)	26 (range 23–31)
Birth weight (grams)	870 (365–1435)
Age at start of TPT feeds (days)	59 (10–177)
Post-conceptual age at start of TPT feeds (weeks)	34 (29–48)
Weight at start of TPT feeds (grams)	1297 (820–3145)
Duration of TPT feeds (days)	18 (1–86)
Race: Black	36 (50%)
White	31 (43%)
other	5 (7%)
Male Gender	45 (62%)
Received human milk (non-donor) at start of TPT feeds	29 (40%)
Received milk-based preterm formula at start of TPT feeds	16 (22%)
Received hydrolysate formula at start of TPT feeds	11 (15%)
Received amino acid formula at start of TPT feeds	16 (22%)
CLD (O2 at 36 weeks)	25 (35%)
IVH (Grade 3 or 4) or PVL	15 (21%)

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript



**Table 2**

Infants developing NEC during TPT feeds

Patient	NEC (n=5) during TPT feed		Age at TPT start (days)	Wt at TPT start (g)	Nutrition during TPT feeds		NEC outcome
	(GA, BW)				Formula:	(kcal/oz)	
1	(26wks, 1055g)		51	1440	Hydrolysate based	24	Medically treated
2	(27wks, 1095g)		47	1110	Hydrolysate based	24	Surgery, death
3	(26wks, 770g)		71	1293	Hydrolysate based	20	Surgery, death
4	(29wks, 1205g)		33	1450	Hydrolysate based	20	Surgery, short gut
5	(27wks, 915g)		85	1229	Amino acid based	22	Medically treated

**Table 3**

Comparison of infants developing NEC vs. no NEC during TPT feeds

	NEC infants N = 5	Non-NEC infants N = 67	P value
BW (grams)	1055	854	0.17
GA (weeks)	27	26	0.41
Wt at start of TPT feeds (grams)	1293	1300	0.95
Age at start of TPT feeds (days)	51	59	0.95
(%) Male	80	59	0.64
(%) African-American	80	46	0.56
(%) Receiving human milk	0	44	0.07
(%) Receiving preterm formula	0	22	0.24
(%) Receiving hydrolysate formula	80	11	<0.01
(%) Receiving amino acid formula	20	23	1.00

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript