

CLINICAL INVESTIGATION

Bowel Frequency in Critically Ill Children

Karen D. Dominguez, PharmD and Matthew E. Borrego, PhD

Department of Pharmacy Practice, College of Pharmacy, University of New Mexico Health Sciences Center, Albuquerque, New Mexico

BACKGROUND Bowel frequency in healthy children has been determined, but it is not well documented in critically ill children. The objectives of this prospective observational study were to determine if critical illness alters stool frequency in children and to identify risk factors that may increase or decrease stool frequency.

METHODS Stool frequency was assessed in children admitted to the pediatric intensive care unit (PICU) over a five month period. The median daily number of bowel movements during admission to the PICU was compared to the patient's estimated number of bowel movements prior to illness. Stepwise linear regression was performed to determine which factors best predicted stool frequency in critically ill children.

RESULTS Daily stool frequency was significantly reduced ($P < 0.001$) during PICU stay (median = 0.5; interquartile: 0, 0.8) compared to preadmission stool frequency estimates (median = 2; interquartile: 1, 2.5). Covariates associated with an increase in stool frequency included male gender and length of stay in the PICU. Conversely, the administration of opioids decreased stool frequency.

CONCLUSIONS Bowel frequency was reduced by 75% in children admitted to the PICU. The use of opioids was associated with decreased bowel frequency. Male gender and increased PICU stay was associated with increased bowel frequency.

KEYWORDS: bowel frequency, constipation, critical illness, opioid, pediatrics

J Pediatr Pharmacol Ther 2004;9:187-191

INTRODUCTION

Bowel frequency in healthy children has been well documented.¹⁻⁴ However, there are no published data regarding the effects of critical illness or its treatment on stool frequency in this population of children. Several factors associated with critical illness (e.g., restricted oral intake, limited physical activity, electrolyte abnormalities, medications) may cause a decrease in stool output in children.⁵ Even though disorders of gastrointestinal tract motility in critically ill patients seem to occur frequently, the pathophysiology is not well studied and both decreased motility and diarrhea can occur.^{6,7}

A study of adult patients admitted to a medi-

cal/surgical ICU for at least three days reported that 83% of patients were constipated.⁸ The same study also noted that a greater number of consti-

ABBREVIATIONS: PICU, pediatric intensive care unit

pated patients failed mechanical ventilation weaning. It would be helpful to determine if critical illness alters stool frequency in children and to identify risk factors that may increase or decrease stool frequency. In the event that stool frequency decreases, these results could assist in developing a definition for constipation in this population. The results may also aid in the identification of risk factors for constipation and those Pediatric Intensive Care Unit (PICU) patients who may benefit from a prophylactic regimen. The purpose of this prospective observational study was to determine if critical illness alters stool frequency in children and to identify factors related to critical illness that may contribute to stool frequency.

Address reprint requests to: Karen D. Dominguez, PharmD, College of Pharmacy, MSC09 5360, 1 University of New Mexico, Albuquerque, NM 87131-0001, e-mail: kdominguez@salud.unm.edu

© 2004 Pediatric Pharmacy Advocacy Group

MATERIALS AND METHODS

All patients admitted to the PICU for more than 48 hours during a five-month study period were eligible for inclusion. Patients with a gastrointestinal disease or any disorder that would alter or otherwise make assessment of stool output difficult (e.g., anatomic malformation, neuropathic condition, intestinal nerve or muscle disorder, connective tissue disorder, or recent gastrointestinal surgery) were excluded.

The number of each patient's daily bowel movements during admission to the PICU was compared to the patient's estimated number of daily bowel movements prior to illness. These estimates were obtained from the parents as part of routine admission data collection by the PICU nurses. Daily bowel movements during admission to the PICU were also compared to published values for bowel frequency in healthy children.¹ Stool frequency was routinely recorded as part of the daily PICU assessment. Data were collected for factors related to critical illness that might alter stool frequency. These included patient demographic information (i.e., age, gender, race, diagnosis, height, weight), fluid and nutritional intake, metabolic disorders (i.e., hypercalcemia, hypokalemia) and medication use (i.e., receipt of one or more doses of an opioid, laxative, prokinetic gastrointestinal agent, or systemic catecholamine). The opioid primarily used in our PICU was fentanyl. The gastrointestinal medications primarily used included metoclopramide to facilitate enteral feeding, histamine receptor antagonists for stress ulcer prophylaxis and docusate sodium and prune juice when a laxative was needed. At the time of the study, erythromycin, antacids, and other laxatives were not used routinely; hence, data for these agents were not collected. Four pharmacy students involved with the research project collected the data using a uniform data collection tool. Bowel frequency data were obtained from the PICU flowsheet.

The median daily number of bowel movements during the entire admission to the PICU was compared to the patient's estimated number of bowel movements prior to illness using Wilcoxon matched pairs signed ranks test. Median stool output determination and nonparametric analyses were required because of skewed data. A z-test for two population means was used to compare mean stool frequency during illness to a calculated weighted mean of published stool frequency

Table 1. Patient Demographics (n = 58)

Variable	Median (Interquartile Range)
Age (mo)	25.4 (3.5, 92)
Weight (kg)	11.7 (5.4, 27.3)
Height (cm)	88.0 (64, 116)
Gender (male)	52%
Race	
Hispanic	45%
White	41%
American Indian	7%
Black	3%
Asian	2%
Other	2%
Primary Diagnosis Category	
Respiratory disease	34%
Cardiac disease or surgery	29%
Neurologic disease	12%
Non-respiratory infection	7%
Other	17%

for healthy children.^{1,9} The published article reports the number of patients, mean and standard deviation of stool frequency for six different age categories in a total of 662 healthy children. Due to our small sample size, comparisons of mean and standard deviations for each respective age category was not possible so a calculated (from the data provided in the published article) weighted mean stool frequency of all the healthy children was used in the comparison.

Step-wise linear regression was performed to determine which factors related to critical illness best predicted stool frequency. The following variables were included: age, gender, height, weight, diagnosis, length of PICU stay, total intake, enteral intake, intravenous intake, total output, urine output, hypokalemia (i.e., serum potassium < 3.5 mEq/L at any time during PICU stay), hypercalcemia (i.e., serum calcium > 11 mg/dL at any time during PICU stay), and use of opioids, dopamine, prune juice, docusate, or metoclopramide. An *a priori* level of significance for all analyses was defined as $P \leq 0.05$.

The study was approved by the University of New Mexico Health Science Center Human Research Review Committee. Informed consent was not required.

RESULTS

Fifty-eight patients were enrolled in the study. Demographic data are presented in Table 1. The median daily stool frequency during PICU admission was 0.5 compared to the median estimated daily stool frequency prior to PICU admission of

Table 2. Bowel Frequency and Factors That May Alter Bowel Frequency (n = 58)

Variable	Median (Interquartile Range)
Estimated stool frequency prior to admission (d)	2 (1.0, 2.5)
Stool frequency during PICU stay (d)	0.5 (0, 0.8)
Length of PICU stay (d)	5 (4.0, 8.0)
Intake (mL/kg/d)	88.4 (62.6, 117.5)
Output (mL/kg/d)*	65.6 (45.5, 97.2)
Urine output (mL/kg/hr)	2.1 (1.6, 3.5)
Enteral intake (mL/kg/d)	14.1 (0, 32.9)
Drug Use During PICU Stay	
Opiates	91%
Dopamine	34%
Prune juice (laxative)	14 %
Docusate	7%
Metoclopramide	5%
Electrolyte abnormality	
Hypokalemia (< 3.5 mEq/L)	47%
Hypercalcemia (> 11 mg/dL)	7%

*Output included urine, stool, gastric fluid suctioning, chest tube output, gastrostomy, jejunostomy and other ostomy output.

2.0 (Table 2). This 75% reduction in stool frequency was statistically significant ($z = 5.699$, $P < 0.0001$). In addition, there was a statistically significant decrease ($z = 9.14$, $P < 0.0001$) in stool frequency in our sample of ill children (0.7 ± 0.8) compared to previously published values for healthy children (1.7 ± 0.8).¹

Factors that may alter bowel frequency in the critically ill patient are presented in Table 2, and nutritional intake data is shown in Table 3. The median length of stay in the PICU was 5 days (range: 2 to 35). Almost all of the patients received fentanyl and the majority received enteral feeds at some time during the PICU stay.

Male gender, length of PICU stay, and use of opioids were the significant predictors of stool frequency (Table 4). Increased length of stay and male gender were significantly predictive ($P = 0.014$ and $P = 0.016$, respectively) of increased bowel movements. The use of opioids was significantly predictive ($P = 0.041$) of decreased bowel movements. In an attempt to explain why male gender was a significant positive predictor of stool output, differences between males and females were assessed. There were no differences between genders for any demographic variables (i.e., age, diagnosis, height, weight, length of stay), fluid and nutrition intake, presence of metabolic disorders (i.e., hypercalcemia, hypokalemia) or medication use (i.e., narcotics, laxatives, metoclopramide, systemic catecholamines).

DISCUSSION

Critical illness can produce changes in intesti-

nal motility resulting in either decreased motility or diarrhea.⁷ The cause of bowel dysfunction in critically ill patients is presumed to be multifactorial. Any disruption in regulation of the intestinal nervous system, hormonal interactions or smooth muscle contraction can cause changes in intestinal motility. Suggested mechanisms for this alteration include the release of endotoxins during sepsis, abdominal ischemia from cardiovascular dysfunction or use of catecholamines, lack of intestinal stimulation during periods of decreased enteral intake, and use of medications that either inhibit or stimulate gastrointestinal tract motility.^{6,7} This study demonstrated a 75% decrease in bowel movement frequency during a median PICU stay of five days. A study of adult patients also suggests a decrease in bowel movement frequency during critical illness.⁸ While changes in baseline bowel frequency were not reported, constipation occurred in 85% of patients. Studies of nutritional support during critical illness noted that constipation occurred in 15.7% of adult patients and 79% of pediatric patients.^{10,11}

Stool output is assessed daily in critically ill patients, in part, to determine if constipation is present and if pharmacological treatment is warranted. The North American Society for Pediatric Gastroenterology and Nutrition has developed guidelines for the evaluation and treatment of constipation in children.⁵ They define constipation as a delay or difficulty in defecation, present for two or more weeks, sufficient to cause significant distress for the patient. This definition seems overly stringent for hospitalized children. Another approach would be to define constipation in this

Table 3. Nutrition Intake

Type of Nutrition	Patients* (n = 58)	Days in PICU** (n = 435)
Parenteral	9% (n = 5)	11% (n = 47)
Enteral	59% (n = 34)	47% (n = 203)
None	36% (n = 21)	43% (n = 185)

*Patients receiving nutrition at any time during PICU stay. Some patients received both parenteral and enteral nutrition on the same day; hence the sum of the percentages exceeds 100.

**Total patient days nutrition received in PICU.

population using a threshold numerical value for daily bowel movements (e.g., constipation is present when bowel movement frequency is less than one per day). This approach was taken by Mostafa and colleagues who defined constipation in critically ill adults as no bowel movement for three consecutive days.⁸ This criteria may also be inappropriate because stool frequency varies widely in children.¹⁴ Our study suggests that a reasonable definition of constipation in the critically ill child would be a 75% reduction from the child's non-hospitalized bowel frequency, over a period of three to five days.

Male gender and increased length of PICU stay were predictive of increased bowel movements. It is unclear why male gender was a predictive variable in the step-wise regression analysis. Mostafa et al. reported no statistically significant differences in gender between constipated and non-constipated critically ill adult patients.⁸ In an attempt to explain why male gender was a significant predictor of increased stool output, differences between males and females in other variables (e.g., length of PICU stay, opioid use) were assessed, but none were found.

The use of metoclopramide or laxatives (i.e., prune juice or docusate) was not predictive of stool output. However the use of opioids was predictive of decreased bowel movements. Based on the pharmacological actions of opioids this is not surprising. Opioids can decrease gastrointestinal neural activity, which causes decreased propulsion in the small and large intestines, increased fluid absorption, and increased anal sphincter tone, all of which leads to constipation and incomplete bowel evacuation. Some of these effects are due to activation of opioid receptors in the central nervous system but they are primarily due to activation of intestinal opioid receptors.¹² The mechanism of opioid-induced constipation is complex and involves decreased neural output via inhibition of acetylcholine release and in-

creased fluid absorption via stimulation of mucosal sensory receptors.¹²

A complicating factor in this study is the limited amount of enteral intake, which may be an important reason for decreased bowel movements. The median intake of any enteral nutrition was only 14 mL/kg/day. Enteral intake for otherwise healthy children can range from about 80-150 mL/kg/day, depending on the type of formula. While caloric requirements during critical illness may vary, 14 mL/kg/day of any infant formula is very low. Total parenteral nutrition is usually initiated in the PICU when nutrition has not been provided for a few days and enteral nutrition is undesirable. About 9% of patients received parenteral nutrition. While not investigated in this study, it is possible that stool frequency would decrease in children receiving intravenous nutrition compared to enteral nutrition.

A limitation of the study involves the use of parental recall to estimate usual bowel frequencies prior to PICU admission. The estimated frequency may not be accurate; however, a study of children with defecation disorders documented fair agreement between parental recall and recorded defecation frequency.¹³ Given this potential limitation, bowel frequency was also compared to published values in normal children and a statistically significant decrease was also found. Another limitation involves the collection of the bowel frequency data during ICU admission from the flowsheet. The flowsheet data recorded by the nurses were not formally assessed for accuracy. The patients in this study represent only the sickest children at a time when their illness is most severe. These children eventually were transferred to the sub-acute care unit or general pediatric ward when their illnesses were improved. Since patients were not followed after transfer from the PICU, it is unknown when their bowel frequency returned to normal.

In conclusion, bowel frequency was altered in our sample of critically ill children. Male gender and increased length of PICU stay predicted an increase in stool frequency. The use of opioids was a predictor of decreased stool frequency. Overall, there was a 75% decrease in stool frequency compared to preadmission estimates. It may be reasonable to diagnose constipation in critically ill children with at least a 75% reduction of their usual bowel frequency over a period of several days during hospitalization and to initiate laxative

Table 4. Variables that Best Predicted Stool Frequency*

Variable	Regression Coefficient	Standard Error of Coefficient	Standardized Regression Coefficient (β)	F value	P value
Male gender	0.522	0.209	0.317	6.246	0.016
Length of PICU stay	0.037	0.015	0.330	6.547	0.014
Opiate use	-0.744	0.354	-0.272	4.409	0.04

*Stepwise linear regression ($r = 0.516$, $r^2 = 0.266$).

The following variables were included in the model, but were not statistically significant: hypercalcemia, hypokalemia, diagnosis, race, weight, age, intake, output, urine output, intravenous intake, enteral nutrition intake, prune juice, dopamine, metoclopramide, docusate.

therapy in all children receiving scheduled opioid medications. Unfortunately, the ideal laxative regimen is unknown. Studies assessing the efficacy of both prophylactic and treatment regimens in critically ill patients are needed.

DISCLOSURE: The authors declare no conflicts or financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employment, gifts, and honoraria.

ACKNOWLEDGMENTS: This work was presented in part in poster format at the American College of Clinical Pharmacy Annual Meeting, Albuquerque, October 20-23, 2002.

REFERENCES

- Fontana M, Bianchi C, Cataldo F, Conti Nibali S, Cucchiara S, Gobio Casali L, Iacono G, Sanfilippo M, Torre G. Bowel frequency in healthy children. *Acta Paediatr Scand* 1989;78:682-4.
- Weaver LT, Steiner H. The bowel habit of young children. *Arch Dis Child* 1984;59:649-52.
- Bloom DA, Seeley WW, Ritchey ML, McGuire EJ. Toilet habits and continence in children: an opportunity sampling in search of normal parameters. *J Urol* 1993;149:1087-90.
- Hyams JS, Treem WR, Etienne NL, Weinerman H, MacGilpin D, Hine P, et al. Effect of infant formula on stool characteristics of young infants. *Pediatrics* 1995;95:50-4.
- Baker SS, Liptak GS, Colletti RB, Croffie JM, Di Lorenzo C, Ector W, Nurko S. Constipation in infants and children: evaluation and treatment. A medical position statement of the North American Society for Pediatric Gastroenterology and Nutrition. *J Pediatr Gastroenterol Nutr* 1999;29:612-6.
- Ritz MA, Fraser R, Tam W, Dent J. Impacts and patterns of disturbed gastrointestinal function in critically ill patients. *Am J Gastroenterol* 2000;95:3044-52.
- Thompson JS. The intestinal response to critical illness. *Am J Gastroenterol* 1995;90:190-200.
- Mostafa SM, Bhandari S, Ritchie G, Gratton N, Wenstone R. Constipation and its implication in the critically ill patient. *Br J Anaesth* 2003;91:815-19.
- Bland JM, Kerry SM. Weighted comparison of means. *BMJ* 1998;316:129.
- Montejo JC. Enteral nutrition-related gastrointestinal complications in critically ill patients: a multicenter study. The nutritional and metabolic working group of the Spanish Society of Intensive Care Medicine and Coronary Units. *Crit Care Med* 1999;27:1652-3.
- Taylor RM, Preedy VR, Baker AJ, Grimble G. Nutritional support in critically ill children. *Clin Nutr* 2003;22:365-9.
- Kurz A, Sessler DI. Opioid-induced bowel dysfunction: pathophysiology and potential new therapies. *Drugs* 2003;63:649-71.
- van der Plas RN, Benninga MA, Redekop WK, Taminiau JA, Büller HA. How accurate is the recall of bowel habits in children with defaecation disorders? *Eur J Pediatr* 1997;156:178-81.