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Constipation and duration of mechanical ventilation in the Pediatric ICU

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Keypoints

Constipation is common in critically ill children. It is associated with longer periods of mechanical ventilation.

Constipation is easy to identify and treat.

Abstract

Introduction

Constipation is common in critically ill children in pediatric intensive care units (PICU). In this study, we explore the association between constipation and longer periods of mechanical ventilation in the PICU.

Material and methods

We performed a retrospective cohort study of patients in the PICU on invasive mechanical ventilation for more than 2 days, exploring the association between constipation, defined as no bowel movements in > 3 days, and duration of mechanical ventilation.

Results

A total of 258 patients met inclusion criteria. Nearly half the patients suffered from constipation and those who did, and survived admission, required 2 additional days of invasive ventilation.

Conclusions

Constipation was associated with longer dependence on mechanical ventilation in critically ill children. Given this association, and possible links with other PICU complications, constipation should be prevented in mechanically ventilated PICU patients.

Keywords

constipation, mechanical ventilation, laxatives.

Introduction

A number of factors have been associated with duration of mechanical ventilation in patients in the pediatric intensive care unit (PICU). Many of these elements are related to patient characteristics (such as severity of illness) as well as treatment effects (use of neuromuscular blockade, sedation, vasopressors etc.) (1-3). Although not routinely mentioned in this context in pediatric critical care, constipation has been associated with worse clinical outcomes in the adult ICU population, including longer duration of mechanical ventilation (4-6). One PICU study has identified risk factors for constipation in the PICU, but failed to demonstrate an association between constipation and hospital LOS, or a statistically significant link to longer invasive ventilator support (7). Impaired bowel motility is felt to be commonplace in the PICU and constipation, defined as no bowel movements is > 3 days, has been described in 46% of PICU patients (5, 7, 8). A number of risk factors have been identified for constipation in critically ill adults and children, many of which are modifiable (6, 7). For example, reduced or alternative

sedative or analgesic agents use may reduce constipation (6, 8). In addition, the use of laxatives and prokinetic agents can reduce the frequency of constipation and medications blunting the gastrointestinal effects of opioids have also shown initially promising results (8-10). There is thus a high incidence of a potentially treatable condition that may add to PICU morbidity, including longer periods of mechanical ventilation. We conducted a retrospective cohort study of mechanically ventilated patients to look at the association between constipation and prolonged mechanical ventilation. We hypothesize that constipation, a potentially remediable complication of care, is associated with a longer duration of mechanical ventilation and thus exposure to potential greater PICU morbidity.

Material and Methods

We received approval from the Yale University Health Investigation Committee. We conducted a cohort study of patients < 21 years old admitted to the PICU between June 1, 2013 and December 31, 2017 for more than 3 days who received invasive ventilator support for ≥2 days. Post-operative abdominal and cardiac surgical patients, those with devastating traumatic or anoxic brain injuries (GCS 3) and patients with tracheostomy tubes were excluded from the study. We identified these patients using Virtual Pediatric ICU Performance System (VPS) database and subsequently reviewed the electronic medical record of patients to confirm eligibility. Data gathered included demographic information such as age (in months), gender, weight, admission diagnosis and severity of illness. The following clinical data was recorded: daily intake and output/fluid balance, type and route of nutritional therapy, number of bowel movements per day, length of invasive ventilation (in days) and length of PICU stay (in hours). The use of narcotics and sedatives (infusion/scheduled or prn), diuretics, and the use of laxatives (docusate, bisocodyl, polyethylene glycols, lactulose, glycerin suppositories and enemas) and prokinetic (metaclopromide and erythromycin) medications were documented. The primary outcome of interest was the duration of mechanical ventilation. The unit of analysis was each episode of mechanical ventilation. The primary predictor of interest was the presence of constipation defined as no bowel movements in 72 hours without clinical or radiographic evidence of ileus. Potential confounders were severity of illness, age, and opioid use. Continuous variables were expressed as medians (interquartile range) and compared between those with and without constipation using Mann-Whitney U test. Categorical variables were expressed using counts (percentages) and compared using chi-square test. Duration of mechanical ventilation was modelled using negative binomial regression truncated at 2 days given the eligibility criteria, adjusting for intra-individual correlation. Because the duration of mechanical ventilation could not be fully determined in patients who died, presence of constipation was interacted with mortality to assess the effect of mortality. Associations were expressed as incidence rate ratios (IRR; 95% confidence interval [CI]). Sample size was based on available patients during the study period. Statistical analyses were performed using Stata 15.1 (StataCorp, College Station, TX). Statistical significance was evaluated at a 2-sided level of significance of 0.05, except for the interaction, which was assessed at 0.10.

Results

A total of 272 patients were screened for the study of whom 258 were eligible for inclusion. Of those included, 119 met the criteria for constipation (46%). There was no statistically significant difference in ethnicity between the two groups. Most of those enrolled were males (61%), comprising 57% of those with constipation and 65% of those without, although differences between the groups were non-significant. Infants 12 months old or younger represented 48% of all patients and 25% of these was diagnosed with constipation. More than 90% of patients in both groups received enteral nutrition. A higher percentage of those without constipation had a principal

diagnosis respiratory failure (63%) compared to those with constipation (39%). Finally, PIM 2 scores were slightly lower in the constipation group. (Table 1)

Patient Characteristics	- constipation	+ constipation	P value
ETHNICITY			*0.33*
Non-hispanic white	55	43	
Non-hispanic African-American	24	31	
Hispanic	39	32	
Other	21	13	
GENDER			*0.25*
male	90	68	
AGE (months)			*<0.001*
≤ 12	94	30	
13-60	26	44	
61-120	6	16	
>121	13	29	
WEIGHT /kg (median/IQR)	5.9 (3.9 – 11.9 kg)	15.8 (10.2-34.8)	*<0.001*
DIAGNOSIS			*<0.001*
Respiratory failure	88	46	
Neurologic injury	13	29	
Cardiovascular	14	13	
Sepsis	4	6	
Oncologic	5	6	
Trauma	0	3	
Metabolic/GI/GU	12	6	
Surgical	3	10	
Dx bronchiolitis	58	21	
PIM 2 (median/IQR)	-4.05 (-2.41 to – 4.88)	-3.52 (-2.06 to -4.74)	*0.26*
TOTAL	**139**	**119**	

Table 1. Characteristics of Patients with and without constipation

Constipation (IRR: 1.36; 95% CI: 1.05, 1.76), death (IRR: 2.62; 95% CI: 1.08, 6.38) and their interaction (IRR: 0.40; 95% CI: 0.14, 1.11) were associated with duration of mechanical ventilation. Among survivors, constipation was associated with 2.0 (95% CI: 0.3, 3.8) excess days of mechanical ventilation. Among non-survivors the association was not statistically significant at -6.9 (95% CI: -20.3, 6.5) days. (Figure 1)

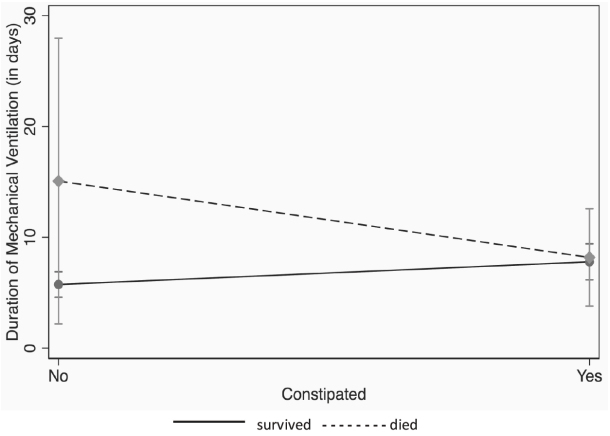

Figure 1. Association of duration of mechanical ventilation with constipation and death

The only factors associated with constipation were age (older) and the use of laxative agents. Only 39% of patient received this treatment prior to the onset of constipation, 22% after the onset and 37% received none at all.

Discussion

This is the first study to show a significant association between constipation and duration of mechanical ventilation in a PICU population. In this report, mechanically ventilated patients with constipation who survived PICU admission were at greater risk for longer episodes of mechanical ventilation than those without constipation. Since constipation may be a modifiable condition and prolonged mechanical ventilation is associated with greater complications, the finding of this study has direct, clinical implications. In our cohort, patients with constipation were older and weighed more that those without, consistent with factors identified in univariate analysis in another large cohort (3). In addition, those with constipation were less likely to have a diagnosis of respiratory

failure (39% versus 63%) and had slightly lower PIM 2 scores, although this latter factor did not achieve statistical significance. Consistent with the nutrition protocol at our institution, > 90 % of patients in both groups received enteral nutrition. Only age was associated with constipation on multivariable analysis. The association between constipation and longer periods of mechanical ventilation found in our study builds on a prior PICU investigation suggesting a similar link that did not achieve statistical significance (7). Other previously described risk factors for longer duration of mechanical ventilation in the PICU include treatment factors such as the antecedent use of non-invasive ventilation, early institution of sedation infusions as well as volume overload (2, 3). Regardless of the cause, prolonged mechanical ventilation is associated with PICU complications, including ventilator-associated pneumonia and increased mortality (3, 11, 12). The incidence of constipation in the critically ill is increasingly recognized. It may occur in as many as 83% of adult ICU patients and affect nearly half of those in the PICU (5, 7). It is noteworthy that the incidence of constipation found in our study (46%) was the same as detected in the only other published report looking at this issue in critically ill children (7). Rates as high as 51% have been describe in the PICU (13). Constipation may be caused by extrinsic factors, such as decreased mobility, dietary imbalance, and dehydration; organic disease, or; iatrogenic or treatments factors (e.g. narcotic or vasopressor use) (14). PICU patients may be exposed to all of these risk factors and also suffer from interactions between them. For example, abdominal distension, may lead to discomfort and agitation in children, which may in turn lead to more narcotics and sedative use, higher doses of vasopressors and worsening constipation (7). Ultimately, constipation and abdominal distension may contribute to lung restriction (15-17). In this clinical context, its association with longer episodes of mechanical ventilation is easy to conceive. Fittingly, constipation is no longer viewed as a mild or inconvenient complication of critical illness (14, 18, 19). In adults, it may prevent the attainment of enteral nutritional goals, trigger ICU delirium and, along with general gastrointestinal dysmotility disorders, is associated with important clinical outcomes including: lengthier mechanical ventilation, increased ICU length of stay, and mortality (6, 20, 21). Constipation has a number of potentially harmful clinical consequences in children in addition to prolonging mechanical ventilation. For instance, dysmotility may cause increasing intra-abdominal pressure, mucosal injury leading to bacterial translocation and increased PICU mortality (7, 21). This problem can be particularly concerning in at-risk risk groups, like oncology patients (22). Moreover, as a component of feeding intolerance, constipation may delay and interrupt the provision of enteral nutrition, a therapy shown to have mortality benefit for mechanically ventilated PICU patients (7, 23). Early enteral nutrition, advancing to near-estimated caloric and protein requirements remains the recommended nutritional regimen for critically ill children (24). Age alone was associated with constipation in our study, which was not powered to identify risk factors. There has been regrettably little study of this issue, with one report identifying higher doses of sedation and analgesia on univariate analysis and use of vasoconstrictors on multivariate study as modifiable risk factors for PICU constipation (7). Children with constipation and other forms of intolerance have also been noted to have had delays in enteral nutrition relative to those without. In adult studies, negative fluid balance, and delayed enteral feeds were also noted as risk factors that could be altered (6, 20). A number of strategies have been proposed to combat constipation, the foremost being vigilance and anticipation for at-risk patients (8, 25). The positive association between the use of promotility agents and constipation in our study likely reflects a therapy that was begun *after* the onset of constipation (in almost a quarter of patients), rather than prophylactically, as called for in the recently adopted feeding protocol. The prophylactic use of these agents is advocated in adult patients (10, 26). In addition, the use of enteral nutrition feeding protocols, including

early initiation of enteral feeds, monitoring and routine use of promotility agents, enhances tolerance and helps advance enteral nutrition in children and adults (13, 27, 28). There is no strong evidentiary support for any particular prokinetic or laxative agent (29). Multiple agents, and combinations of agents may be effective, including the range of stimulants, osmotics agents, softeners and, more recently, opioid antagonists (9, 10, 26, 29-31). This study has a number of limitations. To begin, there is no universally accepted definition of constipation (31). However, the definition employed in our study (> 3 days without a bowel movement) has been used in both the adult and pediatric critical care literature and permits us to focus on the clinical implications of this phenomenon (5, 7, 18). Second, as a retrospective review, we could only define associations and not demonstrate causality. It is, therefore, possible that the relationship actually functions in reverse, that mechanical ventilation leads to constipation. One presumes, however, that limiting the duration of mechanical ventilation is already a goal of care. We would suggest that associations between mechanical ventilation and constipation have already been made in the adult ICU and that such links makes sense physiologically. Furthermore, since constipation may lead to other PICU complications and has relatively benign and effective therapies, there is little harm and potential benefit in assuming the causality is as we suggest. Third, we did not distinguish between laxatives and prokinetics used, nor between different dosages, rendering it difficult to assess the particular impact of each. The same is true for narcotic use. Finally, as noted above, we were underpowered to look at other modifiable risk factors for constipation, such as opioid use, fluid balance, diuretics, etc., which could be clinically relevant.

Conclusion

Constipation affected nearly half of the patients in our study. A modifiable condition, it was associated with lengthier episodes of mechanical ventilation in critically ill pediatric patients. Given this association and possible links with other PICU complications, constipation should be prevented in mechanically ventilated PICU patients.

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