ORIGINAL ARTICLE

Stool Output as a Prognostic Marker in Sepsis: A Prospective Study

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Abstract

Background: Although constipation occurs frequently in patients admitted in the ICU, its impact on their outcome has not been extensively studied. The aim of this study is to investigate the occurrence of constipation and its implications in patients admitted with a diagnosis of sepsis.

Materials and methods: This is a prospective observational study of adult patients admitted with sepsis to a tertiary care, referral ICU, over the period of 3 months between January and March 2019, and who stayed for three or more days. Patients with gastrointestinal bleed/disorders and those who undergone major gastrointestinal surgery and failure to start feed within 72 hours of ICU admission were excluded.

Results: Among the 61 septic patients, constipation occurred in 16 (26.2%) of the patients. Constipated and nonconstipated patients were equally matched in terms of gender ($p = 0.082$) or comorbidities. Acute Physiology and Chronic Health Evaluation II (APACHE II) score ($p = 0.001$), duration of mechanical ventilation ($p = 0.053$), and ICU mortality ($p = 0.011$) were higher in the constipation group.

Conclusion: Monitoring the frequency of bowel movements in critically ill patients admitted with sepsis and the avoidance of constipation can decrease duration of mechanical ventilation and mortality rate in ICU.

Keywords: Bowel movements, Constipation, Laxatives in critically ill, Prognosis in sepsis.

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Introduction

Defecation is a basic body function that tends to be overlooked in most hospitalized patients. The American Gastroenterological Association has defined constipation as three bowel movements per week or less, a sense of incomplete evacuation, hard stools, difficulty in passing stools, or the need for manual maneuvers for evacuation.[1] Several factors are responsible for the increased frequency of constipation among the patients admitted to intensive care, such as shock, the use of sedatives and opioid agents, electrolyte imbalances, and diet changes.[2] Epidemiological studies have shown that the incidence of constipation in the ICU ranges from 5 to 83%.[3–5] The etiology of constipation also varies across studies. Time to the first defecation has been found to correlate with severity of illness, vasoactive agents, administration of morphine, cisapride and lactulose, duration of mechanical ventilation, and ICU length of stay.[5,6] An Indian study has also observed a similar association between mechanical ventilation and the absence of daily bowel movements.[7]

Materials and Methods

Study Subjects

This is a prospective study conducted at a tertiary care, referral ICU over a 3-month period between January 2019 to March 2019. The study included all adult, septic patients who stayed for three days in ICU or longer. Sepsis was defined according to the Surviving Sepsis Campaign International Guidelines.[8] Patients with gastrointestinal bleed/disorders or those who undergo major gastrointestinal surgery and failure to start feeding within 72 hours of ICU admission were excluded. The study was approved by the ethics committee of the hospital.

Study Protocol

Data were collected from patients' charts and the electronic medical records, including age, gender, the reason for admission, APACHE II score, time to initiation of enteral feeding, length of stay in ICU, ICU mortality, hospital mortality or discharge, and comorbid conditions.

Statistical Analysis

All continuous variables are presented as mean and range. Categorical variables are presented as a percentage and compared with $\chi 2$ or Fisher Exact Test, with one degree of freedom. The Statistical Package for the Social Sciences (SPSS) 16.0. (SPSS, Chicago, Ill) was used for statistical analysis. A p-value below 0.05 was considered statistically significant.

Results

During the study period, there were 71 patients admitted with a diagnosis of sepsis, of whom 61 patients fulfilled the inclusion criteria. Patients were divided into two groups: group I, with 45 patients who did not have constipation and group II, with 16 patients who did have constipation. In group I, there was 29 male patients (64.4%) and 16 females (35.5%), with an APACHE II score of 15 [range (15, 21)]. In group II, there were 14 males (87.5%) and two females (12.5%) with an APACHE II of 30 [range (25, 35)].

No patients were given laxatives, oral opioid analgesics or stool softeners during the first three days in ICU. An association

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test was performed between the two groups and documented in Table 1. There was no difference in gender (14 vs 2 males, 29 vs 16 females), OR: 0.25; 95% CI: 0.05–1.28 and $p = 0.082$ (Table 1). Patients' comorbidities were compared and also documented in Table 1. There was no difference in comorbidities between the obstructive sleep apnoea ($p = 0.774$), cor pulmonale ($p = 0.774$), obesity ($p = 0.437$), and hypothyroidism ($p = 0.29$) (Table 1). ICU mortality was significantly lower in group I (18% vs 50%; OR: 4.62; 95% CI: 1.33–16.02, $p < 0.011$).

The clinical outcome variables are documented in Table 2. APACHE II score ($p < 0.001$) and duration of invasive mechanical ventilation ($p < 0.053$) were found to be higher in group II. Other variables such as duration of non-invasive ventilation ($p = 0.222$), ICU length of stay ($p = 0.158$) and hospital length of stay ($p = 0.340$) were similar between the two groups. Logistic regression analysis showed that a high APACHE II score was the only independent risk factor leading to constipation ($p < 0.002$), as shown in Table 3.

Discussion

Constipation in ICU patients is still poorly understood and its incidence rate is inconsistent across the world. The observational trial conducted by Mostafa et al., in 2003 which included 48 patients shows that weaning failure from mechanical ventilation and over-3-day stay is significantly associated with constipation.[9] Another observational study by Van der Spoel et al. showed an association between the duration of mechanical ventilation and constipation.[5] Fecal stasis resulting from constipation can induce overgrowth of gram-negative bacteria in the digestive tract, translocation of bacteria and endotoxins leading to detrimental effects.[10]

Another study demonstrated that opioid therapy is a significant risk factor and recommends that stimulant or osmotic laxatives should be routinely considered for this patient population.[11] Nassar Jr et al., found that initiating enteral feeding earlier may lead to an earlier return of bowel movements.[4] Laxative prophylaxis was also seen to successfully prevent constipation in ICU patients. Furthermore, bowel movement occurring 5 days or later is associated with fewer ventilator days observed by Masri et al.[12] A study by Guerra et al. showed an association between a lack of bowel movements during hospitalization and longer hospitalization time.[13] Enteral nutrition has been shown to keep the gastrointestinal mucosal structure and function intact in both *in vitro* and clinical studies.[14] Although the incidence rate varies widely across various studies, constipation appears to be a very common problem, including in the present study, where about 26% of patients were affected during their ICU stay.

Diabetes mellitus is known to lead to various gastrointestinal complications including impaired gastric contraction and emptying and dysmotility of the small bowel, colon, and rectum, thus predisposing to constipation.[15] Similarly, chronic kidney disease has been known to cause constipation on account of dietary restrictions (e.g., limited intake of fibers and fluids),

Table 1: Association between nonconstipation and constipation with comorbidities and severity of illness

Characteristics		*Nonconstipation n = 45 (%)*	*Constipation n = 16 (%)*	*OR (95% CI)*	*p-value*
Gender	Male	29 (64.4)	14 (87.5)	Reference	
	Female	16 (35.5)	2 (12.5)	0.25 (0.05–1.28)	0.082
ICU mortality		8 (17.8)	8 (50.0)	4.62 (1.33–16.02)	0.011
Diabetes		32 (71.2)	8 (50.0)	0.40 (0.12–1.31)	0.127
Hypertension		26 (57.7)	6 (37.5)	0.43 (0.13–1.41)	0.163
IHD		9 (20.0)	2 (12.5)	0.57 (0.10–2.98)	0.502
COPD		5 (11.1)	2 (12.5)	1.14 (0.19–6.57)	0.881
CKD		10 (22.3)	3 (18.7)	0.80 (0.19–3.40)	0.771
OSA		2 (4.5)	1 (6.5)	1.43 (0.12–16.9)	0.774
Cor pulmonale		2 (4.5)	1 (6.5)	1.43 (0.12–16.9)	0.774
Obesity		1 (2.3)	1 (6.5)	2.93 (0.17–49.0)	0.437
Hypothyroid		3 (6.6)	0 (0.0)	–	0.29

Table 2: Relationship between groups and ICU outcome variables

Variables	*Constipation*		*p-value*
	Yes	*No*	
APACHE (median, (range))	30 (25, 35)	15 (15, 21)	0.001
Duration MV (median, (range))	6 (3, 19)	3 (1, 10)	0.053
Duration NIV (median, (range))	4 (3, 10)	3 (2, 5)	0.222
Duration ICU (median, (range))	12.5 (3.25, 27.5)	6 (4, 7)	0.158
Duration Hospital (median, (range))	17 (3.25, 27.5)	7 (6, 11)	0.340

APACHE: acute physiology and Chronic Health Evaluation; MV: mechanical ventilation; NIV: non-invasive ventilation; ICU: intensive care unit

Table 3: Regression analysis to find the effect of comorbidity and severity of illness on constipation

Variables	*p-value*
Diabetics	0.751
Hypertension	0.331
IHD	0.151
COPD	0.262
CKD	0.596
OSA	1.000
Obesity	1.000
Thyroid	0.999
APACHE	0.002

chronic medication use (e.g., phosphate binders), and a high prevalence of comorbidities such as diabetes mellitus in this population.[16] Other common comorbid conditions associated with constipation include chronic obstructive pulmonary disease and hypothyroidism.[17,18] Obesity per se does not cause constipation but such individuals may have other risk factors leading to constipation, such as lack of physical exercise and a poor quality diet with an inadequate intake of fibers and vegetables in general.[19] There are no studies showing a link between the other common comorbidities such as hypertension, ischemic heart disease, OSA and cor pulmonale, and constipation. This study shows that none of the common comorbidities were associated with constipation.

The present study also found that severity of illness as denoted by a higher APACHE II score, duration of mechanical ventilation, and ICU mortality was significantly associated with constipation in sepsis patients. Constipation leading to failure to wean off mechanical ventilation and increased ICU mortality has been seen in other studies as well.[5,6,9,20]

The limitations of this study were that it is an observational study in a single-center, and the sample size was too small to show the power of the study. Multicenter studies with a larger sample size are required to study the risk factors for constipation and its prevention.

Conclusion

Patients who are critically ill, especially those on mechanical ventilation for longer periods, are prone to constipation and this can have a detrimental effect on the outcome. Hence, prevention and treatment of bowel dysfunction could lead to better prognosis and ICU outcomes in sepsis.

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