

CONSTIPATION IS INDEPENDENTLY ASSOCIATED WITH DELIRIUM IN CRITICALLY ILL VENTILATED PATIENTS

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Dear Editor,

Delirium is a central nervous system (CNS) dysfunction reported in up to 80% of intensive care unit (ICU) patients associated with negative short and long-term outcomes (1,2). Gastrointestinal motility disorders are frequent in ICU patients leading to frequent delayed passage of stools (3). Because there is a bi-directional communication between the CNS and the digestive tract (4), we believed it relevant to test the hypothesis that constipation and delirium are related in ICU patients.

The aims of this study were 1) to determine if delayed passage of stools was independently associated with the development of delirium in mechanically ventilated patients and 2) to identify which delay in the passage of stools had the best discrimination capacity to predict delirium. For that purpose, we performed a prospective observational cohort study between May 1, 2013 and April 31, 2014. The study was previously approved by the hospital's Institutional Review Board. Patients with mechanical ventilation (MV) duration of 2 days or more were eligible for the study if they were 18 years of age or older, were expected to be free of delirium, had been placed under MV less than 24 hours before admission to the ICU, and had an ICU of 4 days or more. Constipation management was not protocolized. All patients received a selective decontamination of the digestive tract with a solution containing polymyxin

E, tobramycin and amphotericin B. Patient sedation status was evaluated using the Richmond Agitation Sedation Scale (RASS) and the protocol did not include a systematic daily interruption. The presence of delirium was assessed using the Confusion Assessment Method for the ICU (CAM-ICU) (5). Delirium status was determined twice daily by a trained ICU nurse or a research-physician. Delirium was defined as two consecutive days testing positive on the CAM-ICU. Stool production was assessed daily by nurses in our ICU who routinely used a semi quantitative tool for scoring.

During the 12 months of the study, 1052 patients were admitted at our ICU, 168 were assessed for delirium, and delirium was documented in 105 (62.5%) patients (Supplementary Fig.1). Baseline characteristics did not differ significantly between patients with and without delirium (Supplementary Table 1). The median delay until first bowel movement was 5 days, while the median delay until the diagnosis of delirium was 7 days. Delay in passage of stools, duration of MV before being assessable for delirium and duration of treatment with benzodiazepines were the variables found to be independently associated with delirium (Table 1). The area under receiver-operating characteristic curve of delay in passage of stools (0.76) was significantly higher than duration of treatment with benzodiazepines (0.65, $p= 0.03$) and duration of MV (0.64, $p= 0.04$) (Supplementary Fig 2) and the most discriminative cut-off point was 5 days for delay in passage of stools.

In conclusion, this is the first report to suggest that there is an independent association between constipation and delirium in ventilated ICU patients and that the likelihood of delirium increased after the fifth day of an ICU stay without bowel movements

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Table 1: Unadjusted and adjusted analysis for variables associated with delirium

Variables	Unadjusted analysis			Adjusted analysis		
	HR	95% CI	P value	HR	95% CI	P value
Delay in passage of stools (1-day increment)	1.05	0.99-1.10	0.06	1.14	1.06-1.12	<0.01
Delay in nutrition (1-day increment)	0.98	0.99-1.02	0.69			
Delay in laxatives (1-day increment)	1.01	0.96-1.06	0.67			
Abdominal distension	1.23	0.87-1.90	0.23			
Age > 60 years	1.23	0.84-1.80	0.29			.
Male	1.16	0.79-1.72	0.45			
Severity						
SAPS II (1-point increment)	1.01	0.99-1.02	0.35			
SOFA score on day 1 of MV (1-point increment)	1.01	0.96-1.06	0.82			
Charlson comorbidity index score (1-point increment)	1.05	0.96-1.14	0.31			
Baseline risk factors ICU delirium						
History of hypertension	0.89	0.60-1.3	0.56			.
At-risk drinking	1.08	0.70-1.67	0.76			
Home use of benzodiazepines	1.64	1.08-2.50	0.02	1.27	0.83-1.94	0.28
Current smoking	1.21	0.78-1.86	0.39			
Liver cirrhosis, n (%)	1.10	0.42-1.61	0.56			
Treatments in the ICU						

Duration of MV (1-day increment)	1.30	1.22-1.40	<0.01	1.47	1.32-1.64	0.01
Corticosteroid administration	0.99	0.62-1.35	0.63			.
Duration of benzodiazepines (1-day increment)	1.06	1.01-1.12	0.02	1.09	1.01-1.18	0.03
Duration of morphine (1-day increment)	1.02	0.99-1.10	0.12			
Duration of propofol (1-day increment)	1.01	0.95-1.05	0.93			
Potential contributors to ICU delirium, n (%)						
Severe sepsis or septic shock	0.98	0.59-1.30	0.51			
hyponatremia < 125 mmol/L	1.03	0.55-1.93	1.65			
One episode or more of hypoglycaemia < 2.2 mmol/L	0.60	0.19-1.91	0.39			
One episode or more of SpO2 <89% during at least 30 mn	0.88	0.65-1.20	0.42			
Length of ICU stay before first chair (1-day increment)	1.02	0.93-1.12	0.69			

SAPS, Simplified Acute Physiologic Score; SOFA, Sequential Organ Failure Assessment; CAM-ICU, Confusion Assessment Method for the Intensive Care Unit; MV, mechanical ventilation.