INTRODUCTION

Constipation is an unusual subject in intensive care journals and textbooks. Nevertheless, it is a complication commonly identified among critically ill patients. These are more prone to constipation for a number of factors, including: confinement to the bed, use of sedatives and opioids, neuromuscular blockers, vasopressors, inflammatory mediators, shock, dehydration and electrolyte disturbances, among others.(1-2)

The incidence of constipation in patients in intensive care units (ICUs) vary widely in literature, between 5% and 83%.(1-5) This can be attributed to lack of definition of such patients. Besides the already known consequences of constipation, in recent years it was observed that this complication may also be related to worse prognosis of critically ill patients. This review endeavors to describe the main available scientific evidence showing that constipation is a prognostic marker and a clinical representation of intestinal dysfunction, in addition to eventually interfering in the prognosis with treatment. Ogilvie syndrome, a major cause of morbidity and mortality in intensive care units was also reviewed. Considering the above cases it was concluded that more attention to this disorder is required in intensive care units as well as development of protocols for diagnosis and management of critically ill patients.

Keywords: Constipation; Colonic pseudo-obstruction; Critical care; Intensive care; Gastrointestinal motility

ABSTRACT

Constipation is a common complication identified among critically ill patients. Its incidence is highly variable due to lack of definition of such patients. Besides the already known consequences of constipation, in recent years it was observed that this complication may also be related to worse prognosis of critically ill patients. This review endeavors to describe the main available scientific evidence showing that constipation is a prognostic marker and a clinical representation of intestinal dysfunction, in addition to eventually interfering in the prognosis with treatment. Ogilvie syndrome, a major cause of morbidity and mortality in intensive care units was also reviewed. Considering the above cases it was concluded that more attention to this disorder is required in intensive care units as well as development of protocols for diagnosis and management of critically ill patients.

Keywords: Constipation; Colonic pseudo-obstruction; Critical care; Intensive care; Gastrointestinal motility

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Intestinal constipation in intensive care units

vomiting, restlessness, intestinal obstruction and perforation and others, still poorly elucidated. Recent studies have identified constipation as an independent prognostic factor in the evolution of critically ill patients and demonstrated that treatment can result in better prognosis.

**Intestinal constipation as a marker of severity**

In addition to previously known implications of constipation, studies published in the last decade have shown that constipation can be associated with poor outcome of patients admitted to intensive care units (Chart 1). In 2003, Mostafa et al. studied 48 patients consecutively admitted over a period of 3 months in a mixed intensive care unit, receiving enteral nutrition, mechanical ventilation and with an expected ICU stay of at least 3 days. They observed a statistically significant relationship between weaning failure from mechanical ventilation and constipation. For patients with an over-3-day stay, without a bowel movement, frequency of weaning failure was 17 of 40 patients, while among 8 patients without constipation there was no weaning failure from mechanical ventilation (p <0.05). Van der Spoel et al. in 2006 published a study confirming some findings of the Mostafa study, showing an increase in the duration of mechanical ventilation among patients who remained constipated for more than 6 days in the ICU. Mechanical ventilation time in the early evacuation group (within the first 6 days in the ICU) was 10.9 days versus 19.2 days for the late evacuation group (only after 6 days in ICU), p = 0.018. Moreover, this study showed shorter stay of patients who had early evacuation (12.6 days x 21.4 days, p = 0.017) and positive correlation between days with no evacuation and no increase in the Sequential Organ Failure Assessment (SOFA) score. Another interesting result is that approximately 50% of patients had not evacuated by the 6th day after admission to the ICU. It is noteworthy that this study had a protocol for treatment of constipation, including administration of lactulose and phosphate enemas to patients that after the 3rd day of stay had not evacuated.

In an observational study conducted in Brazil, Nassar et al. studied constipation in patients with 3 or more days in an intensive care unit. Constipation was defined as failure to eliminate feces for 3 consecutive days. The study included 106 patients and incidence of constipation in this cohort was 69.9%. In this study, constipation was not related to any of the prognostic variables studied, namely: renal replacement therapy, days free of mechanical ventilation, length of ICU stay, ICU mortality and hospital mortality. Two other interesting findings of this study were in multivariate analysis, the association between early initiation of enteral nutrition and low incidence of constipation and no association between use of opioids and a higher incidence of this complication.

Based upon these data, constipation may be linked to prognosis of critically ill patients. However, a new question arises: would intestinal constipation be only a marker of severity or the clinical manifestation of an organ dysfunction that must be diagnosed and treated in

<table>
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<td>van der Spoel, 2006</td>
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<td>Nassar, 2009</td>
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<td>No difference between groups in relation to ventilation-free days in 28 days.</td>
<td>No difference</td>
<td>No difference</td>
</tr>
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N – number of patients; SOFA – Sequential Organ Failure Assessment; ICU – intensive care unit; APACHE – Acute Physiologic Chronic Health
order to modify prognosis of these patients?

**Constipation: a marker of severity or organ dysfunction to be treated?**

In a new study published in 2007, van der Spoel et al. again address the issue of constipation. The purpose this time was to establish whether lactulose and polyethylene glycol are effective purgatives when compared to placebo and also whether patients who used these medications for treatment of constipation showed some prognostic benefit. This study, double-blind, randomized, controlled, with 308 individuals, included patients who did not evacuate until the 3rd day of ICU and were diagnosed with multiple organ dysfunction receiving hemodynamic support and mechanical ventilation. The authors showed the effectiveness of lactulose and polyethylene glycol to promote evacuation when compared to the placebo group. There was no statistical difference between the lactulose and polyethylene glycol (PEG) groups regarding effectiveness in promoting bowel movement. There were also shorter ICU stays in the group that made use of lactulose when compared with the placebo group (156 hours x 196 hours, \( p = 0.016 \)) and a tendency to reduce length of the PEG group (190 hours x 196 hours, \( p = 0.6 \)). In patients who evacuated by the 6th day of hospitalization, length of ICU stay was a mean of 148 hours against 261 hours in the group who evacuated after the 6th day (\( p = 0.01 \)). Multivariate analysis identified the Acute Physiologic Chronic Health Evaluation II (APACHE II) score and time for fecal production (time between ICU admission and the first evacuation) as the independent predictors of mortality.\(^2\)

**How could intestinal constipation affect prognosis of critically ill patients?**

Constipation could potentially affect prognosis of critically ill patients in many ways. They can be classified as: mechanical, nutritional and infectious causes.

**Mechanical causes**

Abdominal distension may hinder action of the diaphragm, reducing lung compliance and increased respiratory effort.\(^2\) In some patients, it may be related to increased intra-abdominal pressure (IAP).\(^9\) IAP increases reduce lung compliance; increases pleural and intrathoracic pressure, and may cause edema and atelectasis. Patients presenting intra-abdominal hypertension syndrome may require a higher positive end expiratory pressure (PEEP) to offset the effects of increased IAP. That is why, intestinal constipation could be related to increased duration of mechanical ventilation.\(^8,10-11\)

**Nutritional causes**

Intestinal constipation may represent one facet of a major condition, dysfunction of intestinal motility. Patients who develop constipation often concomitantly present with gastroparesis and ileoparesia that delay the onset and hinder progression of nutritional support. These patients may delay or even not meet the nutritional target intended for the enteral route. Inadequate nutrient intake leads to a worse prognosis because it reduces muscle strength and overall functional capacity\(^12\) lessens the capacity to synthesize new tissue and wound healing\(^13-14\) increase the number of infections\(^15\) as well as increases length of stay and morbidity and mortality.\(^16-17\)

**Bacterial translocation**

The digestive system, besides its function to absorb nutrients, plays an important role in defending the organism. The intestinal barrier protects the organism against thousands of anaerobic microorganisms, gram-positive, gram-negative and antigens coming from food. This barrier comprises the Peyer plaques which constitute approximately 70% of the organism’s lymphoid tissue and also isolated lymphocytes. Through a series of systems functioning together, the intestinal barrier maintains homeostasis.\(^18\) M cells of the intestinal mucosa serve as an access-portal to antigens allowing them to reach the antigen-presenting cells, particularly dendritic cells of the Peyer plaques. The intestinal mucosa epithelial cells may also, by means of endocytosis and binding of MHC class proteins, present the processed antigen on intraepithelial lymphocytes or lamina propria lymphocytes, or directly on dendritic cells of Peyer’s plaques. Among the intestinal mucosa cells and structures that maintain the physical and functional integrity of mucosal as tight junctions were found.\(^19\) The dendritic cells can, by their dendrites, contact antigens through these structures.\(^20\) By means of all these paths, the lymphoid system maintains organic integrity.

However, in some situations antigens and microorganisms may break this barrier, a process called bacterial translocation.\(^21\) Inflammatory mediators can increase intestinal permeability without necessarily damaging the mucosa. Cytokines may act as modulators of these structures and may thus increase permeability to antigens that promote onset of an intestinal inflammatory cascade.\(^18\) Some *in vitro* studies have shown that TNF-α, IFN-γ, IL-4, IL-3 increase permeability of the intestinal barrier. The mechanism is not yet fully understood, however,
Intestinal constipation can also result from severe Ogilvie's syndrome or colonic pseudo-obstruction syndrome. A dilation of the cecum and right colon in the absence of mechanical obstruction occurs in this syndrome. It was described in 1948 by William Ogilvie in two patients with colon paresis caused by retroperitoneum neoplasms with invasion of the celiac plexus. Its incidence is not well established in literature. It is an important cause of morbidity and mortality in ICU patients, and in presence of intestinal perforation, mortality can exceed 50%. It is caused by imbalance of the autonomic activity with parasympathetic suppression and increased sympathetic activity. Interruption of the autonomic nerves activity, from S2 to S4 leaves the distal colon sluggish and the proximal colon functioning. This may be caused by electrolyte disturbances, mostly hypokalemia, hypocalcemia and hypomagnesemia. The clinical condition may be represented by: abdominal distention (100%), abdominal pain (80%) and nausea/vomiting (60%). Patients reported passage of flatus and/or stool in 40% of cases. There may be bowel sounds in 70% of cases. Distension develops for 3 to 7 days, but can occur in less than 24 hours. The differential diagnosis includes mechanical obstruction and megacolon due to *Clostridium difficile*. Colonic distension should be confirmed by simple abdominal X-ray and mechanical obstruction should be discarded by computed tomography (Figures 1 and 2). The treatment assesses signs of impending or already installed perforation. Once these warning signs are discarded, a conservative management in the first 24 to 48 hours may be the best choice. During this period, possible causes should be re-dressed, and relief, measures undertaken such as a gastric probe. If improvement is not achieved neostigmine (2 to 2.5 mg intravenously over 3 to 5 minutes) may be used and the patient monitored, with atropine available at the bedside. The patient must be constantly monitored and under surveillance for at least 30 minutes after infusion of neostigmine. If desired effects are not achieved with these measures, or in case of recurrence, decompression via colonoscopy may be attempted and, ultimately
surgery or percutaneous decompression.\(^{(31,34)}\)

![Figure 1- Computed tomography (panoramic) of the abdomen of patient with Ogilvie syndrome showing acute colon distension, including cecal dilatation of 13.6 cm.](image)

Figure 1- Computed tomography (panoramic) of the abdomen of patient with Ogilvie syndrome showing acute colon distension, including cecal dilatation of 13.6 cm.

![Figure 2 – Computed tomography showing colon-dilatation in patient with Ogilvie Syndrome.](image)

Figure 2 – Computed tomography showing colon-dilatation in patient with Ogilvie Syndrome.

**Treatment of intestinal constipation**

Some experimental studies illustrate the possible relationship between treatment of intestinal constipation and bacterial translocation. Ozaslan et al. evaluated 50 Wistar mice that were divided into 10 controls, 20 submitted to ligature of the common biliary duct plus enteral administration of 2ml/day lactulose and 20, only submitted to common biliary duct ligature. The primary objective was to detect presence of *Escherichia coli* in mesenteric lymph nodes and cecum of these animals. As a result, a reduction in bacterial translocation in the group receiving lactulose (2 / 20 when compared with 8 / 20, \(p = 0.06\)) was found. There was also a reduction of translocation of other gram-negative bacteria (\(p <0.01\)).\(^{(35)}\)

Another study that also supports the above was performed in 45 guinea pigs divided as follows: 15 in the surgical control group, 15 in the group of surgery trauma receiving 0.9% saline by gavage and 15 in the group receiving surgery trauma lactulose by gavage. The purpose was to identify bacterial translocation to mesenteric lymph nodes. A statistically significant reduction from enteric translocation to lymph nodes in the lactulose group was detected. Furthermore, in the mecum of the lactulose group animals, an increased count of lactobacilli and a reduced number of gram-negative and anaerobic bacteria was detected as well as an increased thickness of the intestinal mucosa.\(^{(36)}\)

Several laxative medications are available that can be classified according to their action mechanism:

- Bulk-forming laxatives (psyllium, polycarbophil, methylcellulose)
- Lubricating agents (mineral oil)
- Stimulants:
  - surfactants (Ducusate, biliary acids);
  - diphenylmethane derivatives (phenolphthalein, bisacodyl, sodium picosulphate);
  - ricinoleic acid (castor oil);
  - anthraquinones (senna, cascara sagrada, aloe, rhubarb);
- osmotic agents (salts of magnesium and phosphate, lactulose, sorbitol, polyethylene glycol);
- glycerin suppositories;
- phosphonate and glycerine enemas.

In one of his studies, van der Spoel et al. tested the efficacy of lactulose and polyethylene glycol comparing one to the other and the placebo in a group of critically ill patients. In this study a similar efficacy was described for both drugs and both were statistically superior to placebo in promoting bowel movement.\(^{(2)}\) Lactulose is described in other protocols for treatment of intestinal constipation.\(^{(4)}\) Senna, an anthraquinone, is also described in a treatment protocol.\(^{(7)}\) Enemas are generally reserved for patients unresponsive to enteral drug administration.\(^{(2,4,7)}\) There is no evidence described for the advantage of phosphonate enemas or enemas glycerine.
In terms of prevention, the relationship between constipation and use of opioids is well known, especially morphine. Opioids can cause intestinal constipation primarily through direct action on specific receptors in the myenteric plexus.\(^{(37)}\) Daily interruption of sedation and of non-medicinal comfort measures may reduce use of these drugs, thus reducing incidence of constipation among patients who require sedation and analgesia. Opioid antagonists, such as oral naloxone\(^{(38)}\) or oral methylnaltrexone,\(^{(37)}\) can also be used to mitigate the effects on intestinal motility. Furthermore, the fact that constipation may cause pain demands attention because if pain is not identified it may increase consumption of opioids and sedatives to ameliorate patient comfort and contribute to perpetuation of the condition.

**Clinical implications**

The reasons given in this review suggest that intestinal constipation in addition to being a marker of prognosis can be an organic dysfunction to be diagnosed and treated. Although it is not known whether there is a causal relationship between occurrence and generation of more dysfunction, perhaps treatment may contribute to a better prognosis of critically ill patients in intensive care units.

There are no clear guidelines for management of constipation in intensive care units. Based upon experience of important studies on the subject, a few points are suggested

1. Intensive care units should establish protocols for the identification, quantification and treatment of constipation.\(^{(1,7)}\)

2. Diagnosis of intestinal constipation of critically ill patients should be based on frequency of stools because it is easier to record and understanding for medical and nursing staff. If possible, also record the estimated amount and appearance.\(^{(7)}\) The Bristol scale (Bristol Stool Form Scale) is used to standardize the appearance of feces. Its use has been already described in diagnostic protocols and treatment of constipation in critically ill patients. This scale presents pictures and description of the appearance of stool and a number that represents the classification category of stools.\(^{(7,39)}\)

3. The team responsible for the care of the patient should be aware of onset and early progression of diet, using wherever possible the enteral route. Diets meeting the patient’s need of fibers are also useful to prevent development of constipation.\(^{(5,7)}\)

4. The team must be aware of conditions that favor occurrence of intestinal constipation, such as prolonged immobilization, use of opioids, excessive sedation, neuromuscular blockers, dehydration, electrolyte imbalance, shock, and others, always attempting to minimize exposure to these conditions and begin specific therapy when intestinal constipation is foreseen or in the presence of risk factors.\(^{(7)}\)

In summary, intestinal constipation is a common complication in critically ill patients. Among causes of constipation, Ogilvie syndrome must be emphasized. Constipation can be related to prognosis of critically ill patients and thus represents a clinical manifestation of intestinal dysfunction. As such it has to be diagnosed and treated. More studies are required on the subject to warrant drafting of guidelines for diagnosis and management of this complication.

**RESUMO**

A constipação intestinal é uma complicação comumente identificada entre pacientes graves. Sua incidência é bastante variável devido à carência de uma definição aplicável a estes pacientes. Além das consequências já conhecidas da constipação, nos últimos anos tem-se percebido que essa complicação também pode estar relacionada ao pior prognóstico de pacientes críticos. Ao longo desta revisão procurou-se descrever as principais evidências científicas disponíveis mostrando ser a constipação um marcador prognóstico e uma das representações clínicas da disfunção intestinal, além da possibilidade de interferir no prognóstico com o tratamento. Revisou-se também a síndrome de Ogilvie, importante causa de morbidade e mortalidade nas unidades de terapia intensiva. Conclui-se, por todo o exposto, ser necessária mais atenção a esse distúrbio nas unidades de terapia intensiva, com elaboração de protocolos de diagnóstico e manejo em pacientes graves.

**Descritores:** Constipação intestinal; Pseudo-obstrução colônica; Cuidados críticos; Cuidados intensivos; Mobilidade gastrointestinal

**REFERENCES**


