

LETTER

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Gut microbiota plays a pivotal role in opioid-induced adverse effects in gastrointestinal system

Rongpeng Xu¹, Liying Miao², Chun Yang³ and Bin Zhu^{1*}

Dear Editor,

Recently, we read with great interest the article by Yan et al. [1], in which the authors reviewed the effect of opioids on gastrointestinal function in ICU patients. This review deepens our understanding of the opioid analgesia in ICU patients; however, the mechanisms of gastrointestinal dysfunction induced by opioids need to be further elucidated.

As noted by the authors, 63–86% of ICU patients were treated with opioids, associated with a significantly higher incidence of gastrointestinal dysfunction [1]. More importantly, opioid-induced bowel dysfunction is associated with poor outcomes in critically ill patients. The authors suggest that opioids in the enteric nervous system inhibit neuronal excitability and cause neurotransmitter release imbalance via binding to opioid receptors, leading to gastrointestinal dysfunction [1]. This might partially explain that opioid antagonists are intended to treat opioid-induced constipation. However, current studies have found that the effects of opioid antagonists on gastrointestinal function are contradictory [1]. Meanwhile, the use of opioid antagonists can also cause serious adverse reactions, such as reversing the protective effect of opioids on inflammatory lung injury [2]. Thus, it is of great importance to further study the mechanism of gastrointestinal dysfunction caused by opioids and to find novel treatment targets.

It is well recognized that opioids could alter the composition and function of gut microbiota [1]. In addition, it should be noted that dysbiosis of gut microbiota can cause intestinal wall edema and abnormal production of microbial metabolites, resulting in gastrointestinal dysmotility and intestinal absorption dysfunction [3]. Interestingly, opioids can modulate 5-hydroxytryptamine (5-HT) metabolism, and dysfunctional 5-HT signaling may underlie the mechanisms of gastrointestinal disorders. Meanwhile, studies have shown that gut microbiota can regulate 5-HT synthesis [4]. Furthermore, opioids have obviously inhibitory effects on the central nervous system and can affect intestinal function through the gut brain axis, and that gut microbiota is an important part of the gut brain axis [5]. These suggest that the gut microbiota is critical in opioid-induced gastrointestinal dysfunction.

Given the extensive use of opioids for analgesia in ICU patients, it should be paid attention to explore the specific mechanism of gastrointestinal dysfunction caused by opioids. Dysbiosis of gut microbiota might play an important role in the mechanism of opioid-induced gastrointestinal adverse effects. Further detailed studies should focus on the effectiveness of probiotics, prebiotics and fecal microbiota transplantation in this important clinical issue.

Authors' response

Yun Yan⁴, Yu Chen⁴ and Xijing Zhang⁴

⁴Department of Critical Care Medicine, Xijing Hospital, The Fourth Military Medical University, Xi'an, China

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*Correspondence: icuzb@qq.com

¹ Department of Critical Care Medicine, The Third Affiliated Hospital of Soochow University, Changzhou 213000, China

Full list of author information is available at the end of the article



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We thank Xu et al. for their comments and interest in our review about the effect of opioids on gastrointestinal (GI) function in ICU patients [1]. Xu et al. expressed the effect of opioids on the alternation of the GI microbiota and the regulation of GI by the central nervous system through the gut microbiota.

Although we aimed to comprehensively and mainly focus on the direct effect of opioids in GI dysmotility in our review, we agree with the important role of gut microbiota on the GI and patients' prognosis. And the benefit of gut microbiota on the GI function had been proved by probiotics, prebiotics and fecal microbiota transplantation [6]. However, the ICU-acquired gut microbiota dysbiosis included patient-related factors and modern ICU intervention [7]. The use of proton pump inhibitors, antibiotics, artificial nutrition and vasoactive agents may affect the gut microbiota [8]. Moreover, the previously reported significantly gut microbiota dysbiosis were stroke, transient ischemic attack, and chronic kidney disease [8]. Meanwhile, most of the articles regarding opioids' effect on the microbiome was with morphine, and data about the impact of other types of opioids was little [6]. Additionally, the shift and the overgrowth of opioid-induced gut microbiota more resulted from the dysmotility of GI [6]. Whether the change of gut microbiota caused by opioids had an important role in mediating the GI function was uncertain. And the proportion of cause and consequence of microbiota dysbiosis on the GI injury in the ICU patients was unclear.

GI injury in ICU patients is multifactorial, and the management of critically ill patients with GI dysfunction is complex. We recognize that there are many mechanisms involved in the effect of opioids on the GI. We recognize the necessity of further studies that focus on the effect of opioids on the GI to provide more evidence on the clinical. Moreover, ICU patients are populations with complex conditions and higher heterogeneity. It should clarify whether the inhibition of opioids or the disturbance of opioid-induced gut microbiota on the GI function had a significantly important role in the ICU patients, and then optimize the drug administration for those who had a high risk of GI injury or already had GI injury.

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Author details

¹Department of Critical Care Medicine, The Third Affiliated Hospital of Soochow University, Changzhou 213000, China. ²Department of Nephrology, The Third Affiliated Hospital of Soochow University, Changzhou 213000, China. ³Department of Anesthesiology and Perioperative Medicine, The First Affiliated Hospital of Nanjing Medical University, Nanjing 210029, China.

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