Peripherally acting opioid receptor antagonists in pediatric patients

Madam,

We read with great interest the original article published by Michelet et al. in the July–September issue of this journal.[1] The authors by their personal experience and analysis have elaborated in an extremely lucid way the factors affecting recovery of postoperative bowel function after pediatric laparoscopic surgery, both elective and emergencies. The authors identify the extent of surgery, complications due to surgery, emergency surgeries, postoperative morphine consumption, and the postoperative use of nonsteroidal antiinflammatory drugs along with paracetamol as the factors associated with time for recovery of bowel function.

The last two factors, i.e., reducing the use of morphine and using multimodal nonopioid-based analgesia are in the domain of the anesthesiologist. With this letter, we want to take the discussion a little further.

Reversing the effect of opioid can be a solution but using opioid antagonist naloxone will reverse the analgesia conferred due to μ-receptor agonism as it crosses blood–brain barrier. Due to this problem, peripherally acting...
opioid receptor antagonists were developed, viz., alvimopan and methylnaltrexone. Both the drugs do not cross blood–brain barrier and thus reverse the effect at the intestinal level. Alvimopan is an orally available, peripherally acting µ-receptor antagonist which is approved by US Food and Drug Administration for use after bowel surgeries. The number of doses is limited to 15, with the first dose of 12 mg to be administered preoperatively followed by 12 mg twice daily for 7 days. Risk Evaluation and Mitigation Strategy is implemented with the use of perioperative alvimopan due to the cardiovascular adverse effects associated with its chronic use seen in patients taking it for opioid-induced constipation.[2] Unfortunately, alvimopan is neither approved nor studied in pediatric patient population.

Like alvimopan, methylnaltrexone is a peripherally acting opioid receptor antagonist which is administered subcutaneously and studied extensively in opioid-induced constipation in cancer patients. It is used at a dose of 0.15 mg/kg and is administered subcutaneously till the constipation is relieved.[3] Unlike alvimopan, methylnaltrexone has been used effectively in pediatric patients (oncology and surgical patients) and has been found to be effective in relieving opioid-induced constipation.[4] It is used in the same dose as in adult patients. Other nonsurgical factors that needs to be addressed are electrolyte imbalance (optimum serum potassium and magnesium levels) and use of laxatives to facilitate bowel movement. Drugs such as neostigmine and lignocaine have also been used successfully in treating ileus/obstruction in pediatric patients but randomized and high-volume studies are lacking in the literature.[5]

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Conflicts of interest
There are no conflicts of interest.

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References
1. Michelet D, Andreu-Gallien J, Skhiri A, Bonnard A, Nivoche Y, Dahmani S. Factors affecting recovery of postoperative bowel function after pediatric laparoscopic surgery. J Anaesthesiol Clin Pharmacol 2016;32:369-75.
2. Kraft M, Maclaren R, Du W, Owens G. Alvimopan (Entereg) for the management of postoperative ileus in patient undergoing bowel resection. P T 2010;35:44-9.
3. Thomas J, Karver S, Cooney GA, Chamberlain BH, Watt CK, Slatkin NE, et al. Methylnaltrexone for opioid-induced constipation in advanced illness. N Engl J Med 2008;358:2332-43.
4. Rodrigues A, Wong C, Mattussi A, Alexander S, Lau S, Dupuis LL. Methylnaltrexone for opioid-induced constipation in pediatric oncology patients. Pediatr Blood Cancer 2013;60:1667-70.
5. Traut U, Brügger L, Kunz R, Pauli-Magnus C, Haug K, Bucher HC, et al. Systemic prokinetic pharmacologic treatment for postoperative adynamic ileus following abdominal surgery in adults. Cochrane Database Syst Rev 2008;1:CD004930.

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