Original Article

The effect of intraoperative low-dose ketamine versus dexmedetomidine infusion on postoperative bowel recovery in patients undergoing gastrointestinal malignancy surgeries: Placebo-controlled, randomized trial

Sabari K. Kumar, Satyajeet Misra[1], Bikram K. Behera[1], Neha Singh[1], Dillip K. Muduly[2], Anand Srinivasan[3]

Department of Anaesthesiology, Vinayaka Mission's Kirupananda Variyar Medical College and Hospitals, Salem, Tamil Nadu, Departments of [1]Anesthesiology and Critical Care, [2]Surgical Oncology and [3]Pharmacology, All India Institute of Medical Sciences, Bhubaneswar, Odisha, India

Abstract

Background and Aims: No studies have compared the effects of ketamine and dexmedetomidine on bowel recovery. We evaluated the effects of intraoperative low-dose ketamine or dexmedetomidine infusion on postoperative bowel recovery in patients undergoing gastrointestinal (GI) malignancy surgeries.

Material and Methods: This placebo-controlled, randomized study was carried out in 84 American Society of Anesthesiologists II patients, aged 18–70 years, of either gender, undergoing elective open GI malignancy surgeries. Patients received intraoperative infusion of ketamine @ 0.1 mg kg^{-1} h^{-1} (KET), dexmedetomidine @ 0.25 μg kg^{-1} h^{-1} (DEX), or normal saline (placebo). Primary outcome was the time to first flatus and/or stool. Secondary outcomes included time to extubation, total analgesic requirement, postoperative pain scores, time to feeds, duration of intensive care unit (ICU) and hospital stay, and the incidence of adverse events. Continuous data were analyzed by the one-way analysis of variance (ANOVA) or the Kruskal–Wallis test. Categorical data were analyzed by the Chi-square test or the Fisher's exact test.

Results: Median time to passage of flatus and/or stool was 3 [interquartile range (IQR) 2–3] days in the KET group, 2 [IQR 2–3] days in the DEX group, and 2 [IQR 2–3] days in the placebo group ($P = 0.53$ for placebo vs. KET, 0.81 for placebo vs. DEX, and 0.99 for KET vs. DEX). Pain scores and analgesic consumption were significantly less in the intervention groups versus placebo ($P < 0.001$). No difference was seen in other secondary outcomes.

Conclusion: Low-dose ketamine or dexmedetomidine did not result in early bowel recovery despite lower pain scores and opioid consumption in patients undergoing open GI malignancy surgeries.

Keywords: Bowel recovery, dexmedetomidine, gastrointestinal, ketamine, malignancy, surgery

Key Message:

a. What is known: Ketamine and dexmedetomidine may promote bowel recovery by improving analgesia and decreasing opioid usage.
b. Main findings: This randomized controlled trial found no evidence of earlier bowel recovery with ketamine or dexmedetomidine versus placebo despite lower pain scores and analgesic consumption in the ketamine and dexmedetomidine groups.

Address for correspondence: Dr. Satyajeet Misra,
Department of Anesthesiology and Critical Care, AIIMS Bhubaneswar, Odisha, India.
E-mail: misrasatyajeet@gmail.com

Access this article online

Quick Response Code:

Website: https://journals.lww.com/joacp

DOI: 10.4103/joacp.joacp_322_23

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Kumar SK, Misra S, Behera BK, Singh N, Muduly DK, Srinivasan A. The effect of intraoperative low-dose ketamine versus dexmedetomidine infusion on postoperative bowel recovery in patients undergoing gastrointestinal malignancy surgeries: Placebo-controlled, randomized trial. J Anaesthesiol Clin Pharmacol 2025;41:145-50.

Submitted: 24-Jul-2023 **Revised:** 30-Oct-2023
Accepted: 24-Dec-2023 **Published:** 08-May-2024

Introduction

Patients undergoing major gastrointestinal (GI) malignancy surgeries face a wide range of problems like perioperative immunosuppression, postoperative ileus, infection, and impaired wound healing, which may delay bowel recovery, and this can impact the overall outcome.[1-3] Therefore, an optimal balance is required between anti- and pro-inflammation that might result in bowel recovery, and anesthetics which favor this balance may thus be desirable.[4]

Infusions of ketamine and dexmedetomidine are commonly used intraoperatively for their opioid-sparing and anti-inflammatory properties. Owing to these properties, ketamine and dexmedetomidine have been used as part of enhanced recovery after surgery (ERAS) protocols for faster recovery, but studies have mostly investigated an opioid-sparing effect.[5-8] There is limited evidence of the effect of either ketamine or dexmedetomidine infusion on postoperative bowel recovery following GI malignancy surgeries. Furthermore, there are no head-to-head comparisons of these two drugs on bowel recovery and other safety profiles, which may guide clinicians to choose any one drug over the other.

Against this background, the primary aim of this study was to assess the effect of low-dose intraoperative infusion of ketamine or dexmedetomidine on bowel recovery in terms of time to passage of first flatus/and or stool. We hypothesized that patients receiving either low-dose ketamine or dexmedetomidine infusion will have earlier bowel recovery versus placebo. Secondary aims were to assess time to extubation after surgery, visual analog scores (VAS) for postoperative pain, total opioid and local anesthetic requirement, postoperative nausea and vomiting (PONV), time to tolerance of solid diet, duration of intensive care unit (ICU) and hospital stay, and the incidence of adverse events.

Material and Methods

This parallel-arm, placebo-controlled, randomized study was conducted after Institutional Ethics Committee approval (IEC/AIIMS BBSR/PG THESIS/2017-18/33). Informed written consent was obtained from each patient enrolled in the study. The study was prospectively registered in the Clinical Trial Registry of India (CTRI number: CTRI/2018/02/011880) before patient enrollment. Study start date was 02.19.2018, and the date of last patient recruitment was 10.22.2019.

Adult patients of either gender, belonging to American Society of Anesthesiologists II, aged 18–70 years, and posted for elective open GI malignancy surgery (gastric and colorectal cancers) under general anesthesia were enrolled into the study. Patients refusing to provide consent, those undergoing emergency or re-do surgeries, patients with coagulopathies (since this would be a contraindication to placement of an epidural catheter), uncontrolled diabetics, patients with heart blocks or arrhythmias, patients with intracranial disease, patients who could not be extubated >6 h of surgery, and those who had known contraindications or allergy to study drugs were excluded from the study. In addition, we excluded patients undergoing laparoscopic surgeries, obese patients (body mass index >30 kg m^{-2}), as well as patients with preoperative biochemical abnormalities like hypokalemia (serum potassium <3.5 mmol l^{-1}) or hypoalbuminemia (serum albumin <4 g dl^{-1}) since these could affect bowel and other postoperative recovery profiles.

Following enrollment, patients were randomized into one of three groups by a computer-generated random number sequence as follows: group KET (n = 28): patients received intravenous (IV) infusions of ketamine @ 0.1 mg kg^{-1} h^{-1} (1 mg ml^{-1} in 50 ml); group DEX (n = 28): patients received IV infusions of dexmedetomidine @ 0.25 µg kg^{-1} h^{-1} (4 µg ml^{-1} in 50 ml); and group placebo (n = 28): patients received varied IV infusions of normal saline.

All infusions were begun after tracheal intubation but before skin incision and were continued until skin closure. Allocation concealment was carried out with opaque sealed envelopes, which were opened when the patients were received in the preoperative holding area. The drugs for infusions were prepared and administered by an anesthesia resident from the adjoining theater who was not part of the study. Primary and secondary outcome measures were recorded by anesthesia providers or nurses unaware of the group allocation.

As per the institutional protocol, mechanical bowel preparation was carried out for patients scheduled for colorectal malignancy surgeries and for highly invasive gastric malignancies, the day before surgery. Routine mechanical bowel preparation was avoided for other gastric malignancy surgeries. Unrestricted access to clear fluids was allowed until 2 h before surgery. Premedication was not administered.

Inside the theater, monitoring of patients was carried out with pulse oximetry, five-lead electrocardiogram (ECG), and noninvasive blood pressure before induction of anesthesia, and end-tidal carbon dioxide ($ETCO_2$) and nasopharyngeal temperature monitoring after tracheal intubation. Invasive blood pressure monitoring and/or central vein cannulations were performed as indicated on per case basis. Anesthesia was standardized in all patients and consisted of placement

of thoracic or lumbar epidural catheter under local anesthesia with the patient awake, followed by IV induction with propofol (2–3 mg kg^{-1}), fentanyl (2 μg kg^{-1}) and vecuronium bromide (0.15 mg kg^{-1}).

Anesthesia was maintained with isoflurane in a mixture of 50% air in oxygen and titrated to a bispectral index (BIS) (BIS Quatro; Covidien, Mansfield, MA, USA) of 50–60. Fluids were standardized in all patients and consisted of IV lactated Ringer's solution given at a loading volume of 4 ml kg^{-1} followed by a maintenance regimen of 4–6 ml kg^{-1} h^{-1}. Packed red blood cells were transfused if the hemoglobin was less than 8 g dl^{-1}. Ventilation was adjusted to maintain an $ETCO_2$ of 35–45 mmHg during the procedure.

A bolus dose of IV paracetamol (1000 mg in 100 ml) and 5 ml of 0.125% bupivacaine were administered via the epidural catheter after tracheal intubation and before skin incision in all patients. Intraoperative rates of the epidural bupivacaine infusions were left to the discretion of the attending anesthesiologist. Fentanyl 1 μg kg^{-1} bolus was repeated if there was a >20% increase in either heart rate and/or systolic blood pressure. Intraoperative core temperature was maintained in all patients within 35°C–37°C using warm fluids and forced air warming blankets. At the end of the surgery, isoflurane was discontinued and neuromuscular blockade was antagonized with IV neostigmine (50 μg kg^{-1}) and glycopyrrolate (10 μg kg^{-1}) when there were spontaneous respiratory efforts. The time to extubation was noted in minutes from administration of neostigmine to removal of the tracheal tube.

Patients were shifted to surgical ICU and were shifted to the ward once they met the institutional criteria. Postoperatively, 1000 mg of paracetamol was administered IV every eighth hour for the first 24–36 h. Epidural infusions of 0.125% bupivacaine were continued at 4 ml h^{-1} and increased by 1 ml h^{-1} after administering a 5 ml bolus if VAS was >4, till a maximum of 6 ml h^{-1}. Fentanyl 1 μg kg^{-1} was additionally given IV if VAS was still >4. VAS was measured every second hour on days 0 and 1. Epidural infusions were continued 48–72 h postoperatively. Total intraoperative and postoperative opioids and local anesthetic consumption were recorded until the first 48 h. Postoperatively, patients received a restrictive fluid administration of lactated Ringer's solution @ 1.5–2 ml kg^{-1} h^{-1} till satisfactory feeds were achieved by the oral or feeding jejunostomy route. Blood sugars were titrated in all patients between 140 and 180 mg dl^{-1}.

Vasopressor support (noradrenaline) was initiated if patients' systolic blood pressure was <90 mmHg despite fluid challenges (aliquots of 250 ml). PONV was recorded for the first 48 h as a binary (present/absent) response. Other adverse events recorded were the incidence of bradycardia (heart rate <50 beats min^{-1} with or without the need for vasoactive drugs), and postoperative agitation, combative behavior, or hallucination (with or without need for treatment) during the duration of ICU stay.

Previous studies have shown that a 1-day difference in time to passage of flatus could be considered significant.[9,10] Accordingly, allowing for a standard deviation (SD) of 1 day, a total sample size of 84 was calculated (28 in each group) to detect a difference of at least 1 day in the time to passage of flatus and/or stool. The study was powered to 90%, allowing an alpha error of 5%. $P < 0.05$ (2-tailed) was considered significant. The normality of the data was analyzed by Shapiro–Wilk test. Continuous data were expressed as mean (SD) or median [interquartile range (IQR)] depending on the normality and analyzed with the one-way analysis of variance (ANOVA) with Tukey *post hoc* test for pairwise comparisons or the Kruskal–Wallis test followed by *post hoc* Bonferroni correction for pairwise comparisons, respectively. Categorical data were expressed as percentages and analyzed by Chi-square test or the Fisher's exact test. Data analysis was carried out by the statistical software R (R Studio Version 3.6, Vienna, Austria).

Results

A total of 95 patients were assessed for eligibility and 84 patients were enrolled after they were found to meet the inclusion criteria over a 1.9-year period [Figure 1; CONSORT diagram; CONSORT- Consolidated Standards of Reporting Trials]. Baseline characteristics are presented in Table 1. There was no significant difference in the duration of surgery or intraoperative fluid requirement which could potentially impact the outcomes.

The median time to passage of flatus and/or stool was 3 [IQR 2–3] days in the KET group, 2 [IQR 2–3] days in the DEX group, and 2 [IQR 2–3] in the placebo group. The difference in the primary outcome between the groups was not significant ($P = 0.53$ for placebo vs. KET; 0.81 for placebo vs. DEX; and 0.99 for KET vs. DEX).

The median VAS was significantly lower in the intervention groups versus placebo on postoperative day 0: 2 [IQR 2–3] in the KET group, 2 [IQR 2-2] in the DEX group, and 3 [IQR 3–4] in the placebo group ($P < 0.001$ for placebo vs. both KET and DEX). On postoperative day 1, however, VAS was lower only in the DEX group versus placebo ($P < 0.001$), but not between KET and placebo groups ($P = 0.13$). VAS was comparable between the KET and DEX groups on postoperative day 0 ($P = 0.39$), but a significantly lower VAS was seen in the DEX versus KET groups on postoperative day 1 ($P < 0.001$).

Table 1: Baseline characteristics of the three groups

Parameters	Group KET (*n*=28)	Group DEX (*n*=28)	Group placebo (*n*=28)
Age(years)	48 [40–63.2]	59 [53–63]	54.5 [48.7–66]
Male: female	15:13	20:8	21:7
Duration of surgery (min)	224.6 (71.2)	193.4 (62.5)	212.5 (68.4)
Intraoperative fluids (ml)	1992.9 (476.8)	1907.1 (682.5)	1960.7 (610)

ANOVA=analysis of variance, DEX=dexmedetomidine, KET=ketamine. Values are median [interquartile range], mean (standard deviation), or number of patients. P is not significant between the groups for the duration of surgery and intraoperative fluids. One-way ANOVA with Tukey post hoc test was used for testing the difference in the duration of surgery and the fluid requirements among the three groups

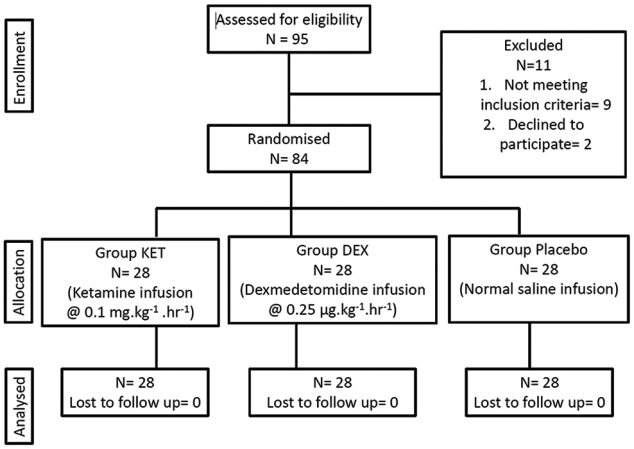

Figure 1: CONSORT flow diagram showing enrollment of patients in the study CONSORT- Consolidated Standards of Reporting Trials

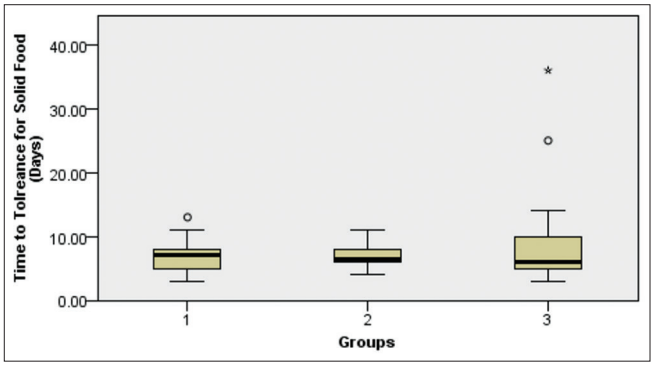

Figure 2: Box–Whisker plot for time to tolerance for oral feeds. Median is depicted by a dark black line in the box, with the box denoting the interquartile range; outliers are denoted by the * or ° symbols. Group 1- ketamine; Group 2- dexmedetomidine; Group 3- placebo

The mean total perioperative fentanyl consumption was significantly lower in the intervention groups versus placebo: 185.7 (SD 80.3) µg in the KET group and 175 (SD 77.5) µg in the DEX group versus 276.7 (SD 90.7) µg in the placebo group ($P < 0.001$ for placebo vs. both KET and DEX groups; $P = 0.87$ between KET and DEX). The mean total perioperative epidural bupivacaine used was significantly lower in the intervention groups versus placebo: 259.3 (SD 39.8) mg in the KET group and 250.5 (SD 31.7) mg in the DEX group versus 310.5 (SD 45.3) mg in the placebo group ($P < 0.001$ for placebo vs. both KET and DEX; $P = 0.68$ between KET and DEX). There was no difference in the median time to tolerance of solid food ($P = 0.4$ for all intergroup comparisons) [Figure 2]. No significant differences were found in the other secondary outcome parameters [Table 2]. No adverse events like psychomimetic episodes in the KET group or bradycardia in the DEX group were noted.

Discussion

In this study, we failed to find any beneficial effect of intraoperative low-dose infusion of ketamine or dexmedetomidine versus placebo on bowel recovery in patients undergoing open GI malignancy surgeries. The benefits of lower opioid requirements and better analgesia seen with ketamine and dexmedetomidine did not translate into improved postoperative bowel recovery. Safety profiles of the drugs, however, were favorable.

Postoperative ileus is common after major GI surgery and results in PONV, abdominal distention, absence of passage of flatus or stool, gas and fluid accumulation, and poor tolerance to enteral feeds.[1,2] Delayed bowel recovery due to postoperative ileus increases morbidity and hospital stays and adds to the overall health-care costs.[1] Apart from bowel handling, various other factors like perioperative use of opioids and inflammation, sympathetic overactivation, and so forth play a major role in delayed bowel recovery.[1,2] This is the basis or ERAS principles, which aim to promote anesthetic adjuvants with opioid-sparing and immunomodulatory properties like ketamine and dexmedetomidine as part of accelerated care pathways to promote gut motility.

Perioperative infusion doses of ketamine ranged from 1 to 5 µg kg^{-1} min^{-1} or from 0.06 to 0.3 mg kg^{-1} h^{-1}.[11] Our findings are similar to McKay and Donais,[12] who failed to find any effect of low-dose ketamine (1.5 mg kg^{-1} bolus followed by infusion of 2.5 µg kg^{-1} min^{-1}) on bowel recovery in patients undergoing open abdominal surgeries. It has been suggested that the incidence of psychomimetic effects increases with continuous doses of ketamine >2.5 µg kg^{-1} min^{-1}.[5] Unlike other studies, however,[12,13] we did not find any adverse effects like postoperative hallucinations in our patients. This

Table 2: Secondary outcomes

Parameters	Group KET (*n*=28)	Group DEX (*n*=28)	Group placebo (*n*=28)	*P*
Time to extubation (min)	15 [10–21]	13.5 [9.5–22.5]	17.5 [10–12]	0.27
Number of patients with PONV	3	2	8	0.21
Number of patients needing vasopressor support	15	12	15	0.70
Duration of ICU stay (days)	1 [1–1]	1 [1–1]	1 [1–2]	0.50
Duration of postoperative hospital stay (days)	9 [7–11.5]	7.5 [7–9.2]	7 [6–13.5]	0.60

DEX=dexmedetomidine, ICU=intensive care unit, KET=ketamine, PONV=postoperative nausea and vomiting. Values are median [interquartile range] or number of patients. Chi-square test was used for categorical variables (PONV, postoperative vasopressor support), while the Kruskal–Wallis test with post hoc Bonferroni correction was used for other continuous variables

may be because the infusion dose of ketamine in our study was ~1.67 μg kg^{-1} min^{-1}.

Infusion doses of dexmedetomidine in various studies ranged from 0.2 to 07 μg kg^{-1} h^{-1}.[11] While some studies reported a beneficial effect of dexmedetomidine on postoperative bowel recovery,[14-17] other studies have failed to find such a beneficial effect.[18-20] This may be due to different doses used, patient populations with different pharmacokinetics (obese patients), nature of surgeries (bowel handling vs. no bowel handling), and possibly, an antimotility effect of dexmedetomidine itself,[18] which may occur with doses as low as 0.2 μg kg^{-1} h^{-1}.[21]

The main limitation of our study was that we included patients undergoing both gastric and colorectal cancers, which may have affected the results. It has been shown that incidence of postoperative ileus varies according to the site of resection, with an incidence of 19.2% for small bowel resections versus 14.9% for large bowel resections.[1,22] Another limitation was that the doses of the drugs studied were not equipotent. This was borne by the fact that VAS on postoperative day 1 was lower in the dexmedetomidine group versus ketamine group. It has also been shown that epidural analgesia promotes bowel recovery due to sympatholysis.[23] All patients in our study received epidural analgesia. Thus, the effect of any drug in addition to an epidural technique which itself promotes bowel recovery may be minimal. Finally, the rates of infusion of the drugs were varied as they were weight based which may have affected blinding.

To conclude, intraoperative infusion of low-dose ketamine or dexmedetomidine in patients undergoing open GI malignancy surgeries did not result in a faster bowel recovery versus placebo, despite lower postoperative pain scores and analgesic requirements. Further trials may look at different doses of these two drugs to see the effect on bowel recovery.

Acknowledgements

We acknowledge Professor Madhabananda Kar, HOD (Surgical Oncology) for his support and guidance throughout the study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Luckey A, Livingston E, Taché Y. Mechanisms and treatment of postoperative ileus. Arch Surg 2003;138:206-14.
2. Berger NG, Ridolfi TJ, Ludwig KA. Delayed gastrointestinal recovery after abdominal operation-role of alvimopan. Clin Exper Gastroenterol 2015;8:231-5.
3. Wehner S, Straesser S, Vilz TO, Pantelis D, Sielecki T, de la Cruz VF, *et al*. Inhibition of p38 mitogen-activated protein kinase pathway as prophylaxis of postoperative ileus in mice. Gastroenterology 2009;136:619-29.
4. McBride WT, Armstrong MA, McBride SJ. Immunomodulation: An important concept in modern anaesthesia. Anaesthesia 1996;51:465-73.
5. Schmid RL, Sandler AN, Katz J. Use and efficacy of low-dose ketamine in the management of acute postoperative pain: a review of current techniques and outcomes. Pain 1999;82:111-25.
6. Hoskote H, Jenkins S. The role of intravenous ketamine for Enhanced Recovery after Surgery (ERAS) protocol for acute postoperative pain management after laparoscopic hysterectomy. Int J Pain Relief 2020;4:12-22.
7. Ge DJ, Qi B, Tang G, Li JY. Intraoperative dexmedetomidine promotes postoperative analgesia and recovery in patients after abdominal hysterectomy: A double-blind, randomized clinical trial. Sci Rep 2016;6:21514.
8. Kaye AD, Chernobylsky DJ, Thakur P, Siddaiah H, Kaye RJ, Eng LK, *et al*. Dexmedetomidine in Enhanced Recovery After Surgery (ERAS) protocols for postoperative pain. Curr Pain Headache Rep 2020;24:21.
9. Taguchi A, Sharma N, Saleem RM, Sessler DI, Carpenter RL, Seyedsadr M, *et al*. Selective postoperative inhibition of gastrointestinal opioid receptors. N Eng J Med 2001;345:935-40.
10. Asao T, Kuwano H, Nakamura J, Morinaga N, Hirayama I, Ide M. Gum chewing enhances early recovery from postoperative ileus after laparoscopic colectomy. J Am Coll Surg 2002;195;30-2.
11. Scott MJ, McEvoy MD, Gordon DB, Grant SA, Thacker JKM, Wu CL, *et al*. American Society for enhanced recovery (ASER) and perioperative quality initiative (POQI) joint consensus statement on optimal analgesia within an enhanced recovery pathway for colorectal surgery: Part 1-from the perioperative period to PACU. Perioperative Med 2017;6:8.
12. McKay WP, Donais P. Bowel function after bowel surgery: morphine with ketamine or placebo; a randomised controlled trial pilot study. Acta Anaesthesiol Scand 2007;51:1166-71.

13. Webb AR, Skinner BS, Leong S, Kolawole H, Crofts T, Taverner M, *et al*. The addition of a small-dose ketamine infusion to tramadol for postoperative analgesia: A double-blinded, placebo-controlled, randomized trial after abdominal surgery. Anesth Analg 2007;104:912-7.
14. Wang X, Liu W, Xu Z, Wang F, Zhang C, Wang B, *et al*. Effect of dexmedetomidine alone for intravenous patient-controlled analgesia after gynecological laparoscopic surgery: A consort-prospective, randomized, controlled trial. Medicine 2016;95:e3639.
15. Cho JS, Kim HI, Lee KY, An JY, Bai SJ, Cho JY, *et al*. Effect of intraoperative dexmedetomidine infusion on postoperative bowel movements in patients undergoing laparoscopic gastrectomy: a prospective, randomized, placebo-controlled study. Medicine 2015;94:e959.
16. Lu Y, Fang PP, Yu YQ, Cheng XQ, Feng XM, Wong GT, *et al*. Effect of intraoperative dexmedetomidine on recovery of gastrointestinal function after abdominal surgery in older adults: a randomized clinical trial. JAMA Network Open 2021;4:e2128886.
17. Behera BK, Misra S, Jena SS, Mohanty CR. The effect of perioperative dexmedetomidine on postoperative bowel function recovery in adult patients receiving general anesthesia. Minerva Anestesiol 2022; 88:51-61.
18. Cheung CW, Qiu Q, Ying ACL, Choi SW, Law WL, Irwin MG. The effects of intra-operative dexmedetomidine on postoperative pain, side-effects and recovery in colorectal surgery. Anaesthesia 2014;69:1214-21.
19. Tufanogullari B, White PF, Peixoto MP, Kianpour D, Lacour T, Griffin J, *et al*. Dexmedetomidine infusion during laparoscopic bariatric surgery: the effect on recovery outcome variables. Anesth Analg 2008;106:1741-8.
20. Beloeil H, Garot M, Lebuffe G, Gerbaud A, Bila J, Cuvillon P, *et al*. Balanced opioid-free anesthesia with dexmedetomidine versus balanced anesthesia with remifentanil for major or intermediate noncardiac surgery. Anesthesiology 2021;134:541-51.
21. Memis D, Dökmeci D, Karamanlioglu B, Turan A, Türe M. A comparison of the effect of gastric emptying of propofol or dexmedetomidine in critically ill patients: Preliminary study. Eur J Anaesthesiol 2006;23:700-4.
22. Livingston EH, Passaro EP. Postoperative ileus. Dig Dis Sci 1990;35:121-32.
23. Guay J, Nishimori M, Kopp SL. Epidural local anesthetics versus opioid-based analgesic regimens for postoperative gastrointestinal paralysis, vomiting, and pain after abdominal surgery: A Cochrane review. Anesth Analg 2016;123:1591-602.