Study Protocol

Effect of dexmedetomidine on recovery of postoperative gastrointestinal function in patients with adhesive bowel obstruction: A single-center randomized clinical trial

Protocol version: 1.0 (September 10, 2022)

Trial registration: ChiCTR2200063569 (registered on September 12, 2022 at www.chictr.org.cn)

Ethics approval: Approved by the Ethics Committee of Shaoxing People's Hospital (Approval No. 2022-124)

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1. Administrative information

1.1 Title

Effect of dexmedetomidine on recovery of postoperative gastrointestinal function in patients with adhesive bowel obstruction: A single-center randomized clinical trial

1.2 Trial registration

This trial was prospectively registered on September 12, 2022, at the Chinese Clinical Trial Registry (ChiCTR2200063569).

1.3 Protocol version

Version 1.0, dated September 10, 2022.

2. Introduction

2.1 Background and rationale

Adhesive bowel obstruction (ABO) is a common surgical emergency, often resulting from intraperitoneal adhesions after previous abdominal surgery. Surgical intervention is frequently required, but anesthesia and surgical trauma can exacerbate intestinal dysfunction, delay gastrointestinal (GI) recovery, and prolong hospital stay. Intestinal mucosal barrier injury, inflammatory response, and oxidative stress play pivotal roles in the pathogenesis of ABO and postoperative GI dysfunction.

Dexmedetomidine (Dex), a highly selective alpha-2 adrenoceptor agonist, possesses sedative, analgesic, and anti-inflammatory properties. Preclinical studies have shown that Dex attenuates intestinal ischemia-reperfusion injury and protects intestinal barrier integrity. However, clinical evidence regarding its effect on GI functional

recovery in patients undergoing surgery for acute ABO remains limited.

2.2 Objectives

Primary objective: To investigate whether intraoperative intravenous infusion of dexmedetomidine shortens the time to first flatus (a surrogate marker of GI motility recovery) in patients undergoing laparoscopic surgery for acute adhesive bowel obstruction.

Secondary objectives:

1. To evaluate the effect of Dex on other GI function parameters (time to first oral feeding, time to first feces, I-FEED score).
2. To assess the effect of Dex on biomarkers of intestinal permeability (FABP2, LPS), inflammation (IL-6, TNF-α), and oxidative stress (MDA, SOD).
3. To determine whether Dex reduces intraoperative anesthetic and opioid consumption and postoperative opioid requirement.
4. To compare the incidence of postoperative nausea and vomiting (PONV) and hemodynamic adverse events between groups.
5. To evaluate the effect of Dex on postoperative hospital stay.

2.3 Hypothesis

We hypothesize that intraoperative administration of dexmedetomidine, compared with placebo, will accelerate postoperative GI function recovery in patients undergoing laparoscopic surgery for acute ABO, and that this effect is associated with attenuation of intestinal mucosal injury, inflammatory response, and oxidative stress.

3. Methods

3.1 Trial design

This is a prospective, randomized, double-blind, placebo-controlled, parallel-group, single-center superiority trial with a 1:1 allocation ratio.

3.2 Study setting

The trial is conducted at the Department of Anesthesiology and General Surgery, Shaoxing People's Hospital, Shaoxing, Zhejiang, China. Patient enrollment began on September 15, 2022, and was completed on December 15, 2023.

3.3 Eligibility criteria

Inclusion criteria:

· Adult patients aged 18–75 years
· American Society of Anesthesiologists (ASA) physical status II or III
· Body mass index (BMI) 18–35 $kg \cdot m^{-2}$
· Diagnosed with acute adhesive bowel obstruction requiring laparoscopic surgery
· Planned to undergo laparoscopic surgery for adhesive bowel obstruction, which may include adhesiolysis with or without enterectomy
· Provision of written informed consent

Exclusion criteria:

· Bradycardia (heart rate < 50 bpm) or third-degree atrioventricular block
· Tertiary hypertension (systolic blood pressure ≥ 180 mmHg or diastolic blood pressure ≥ 110 mmHg)
· Recent use (within 7 days) of probiotics, antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs), opioid analgesics, or glucocorticoids
· History of cancer, neurological disease, language or hearing impairment preventing communication
· Pregnancy or lactation
· Known allergy to dexmedetomidine or any anesthetic agent used in the protocol

Withdrawal criteria (post-randomization exclusion):

· Occurrence of serious adverse effects during surgery (defined as severe allergic reactions, unexplained hemodynamic instability requiring vasopressor support beyond protocol, or any event deemed by the attending anesthesiologist to necessitate deviation from the study protocol)
· Failure of blood sample collection or laboratory testing
· Intraoperative blood loss > 500 mL
· Conversion from laparoscopic to open surgery

These criteria were set a priori to exclude patients with intraoperative events that could profoundly and independently affect gastrointestinal recovery and inflammatory responses, thereby confounding the assessment of the intervention's effect.

3.4 Interventions

3.4.1 Dexmedetomidine group

Patients receive a loading dose of dexmedetomidine 0.5 $\mu g \cdot kg^{-1}$ infused intravenously over 15 minutes immediately before induction of anesthesia, followed by a continuous maintenance infusion of 0.3 $\mu g \cdot kg^{-1} \cdot h^{-1}$ until 30 minutes before the anticipated end of surgery.

3.4.2 Control group

Patients receive an equivalent volume of 0.9% normal saline infused at the same rate and duration as the dexmedetomidine group.

3.4.3 Perioperative management

All patients receive standard monitoring (ECG, SpO_2, NIBP, invasive arterial blood pressure). Anesthesia induction: propofol 2 $mg \cdot kg^{-1}$, sufentanil 0.2–0.5 $\mu g \cdot kg^{-1}$, rocuronium 1.2 $mg \cdot kg^{-1}$. Anesthesia maintenance: propofol 2–5 $mg \cdot kg^{-1} \cdot h^{-1}$ and remifentanil 0.2–0.4 $\mu g \cdot kg^{-1} \cdot min^{-1}$ titrated to maintain bispectral index (BIS) values between 45 and 55. Muscle relaxation is maintained with intermittent cisatracurium

0.1 mg·kg⁻¹. All patients receive prophylactic antibiotics (cefuroxime 1.5 g and metronidazole 0.5 g) 30 minutes before skin incision. Intraoperative fluid management follows a standardized protocol. Hemodynamic management: ephedrine 5–10 mg i.v. for MAP < 65 mmHg; atropine 0.5 mg i.v. for HR < 50 bpm.

Postoperative analgesia: patient-controlled intravenous analgesia (PCIA) with sufentanil 2 μg·kg⁻¹ (control group) or sufentanil 2 μg·kg⁻¹ plus dexmedetomidine 2 μg·kg⁻¹ (Dex group), diluted in 0.9% saline to a total volume of 200 mL. Pump settings: loading dose 3 mL, background infusion 6 mL·h⁻¹, bolus 4 mL, lockout 15 min. Rescue analgesia: additional sufentanil 5 μg i.v. if VAS > 4.

3.5 Outcomes

3.5.1 Primary outcome

· Time to first flatus (hours) from the end of surgery, defined as the first passage of flatus reported by the patient.

3.5.2 Secondary outcomes

· Time to first oral feeding (hours)
· Time to first feces (hours)
· I-FEED (Intake, Feeling nauseated, Emesis, Exam, Duration of symptoms) scores assessed daily from postoperative day (POD) 1 to POD7
· Plasma biomarkers:
  · Intestinal permeability: lipopolysaccharide (LPS), intestinal fatty acid binding protein 2 (FABP2)
  · Inflammation: interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α)
  · Oxidative stress: malondialdehyde (MDA), superoxide dismutase (SOD)
· Intraoperative consumption of propofol (mg·kg⁻¹·h⁻¹) and remifentanil (μg·kg⁻¹·h⁻¹)
· Postoperative sufentanil consumption (μg·kg⁻¹) within 48 hours post-surgery
· Incidence of postoperative nausea and vomiting (PONV) within 48 hours
· Postoperative hospital stay (days)
· Intraoperative hemodynamic parameters: proportion of MAP ≤ 65 mmHg, MAP ≥ 105 mmHg, HR ≤ 50 bpm, HR ≥ 120 bpm (based on 5-minute interval recordings)

3.6 Participant timeline

· Screening and enrollment: Preoperative assessment, informed consent
· Baseline: Demographic data, ASA status, BMI, preoperative I-FEED score; blood sampling (before Dex loading dose)
· Intraoperative: Anesthetic and opioid consumption, hemodynamic recordings, surgical data
· POD1, POD3, POD7: Blood sampling for biomarker assays
· Daily until discharge: I-FEED score assessment, recording of GI function recovery events, PONV
· Discharge: Postoperative hospital stay

3.7 Sample size calculation

Sample size was estimated using G*Power 3.0.10 (University Kiel, Germany) based on the primary outcome (time to first flatus). From a pilot study, the mean (SD) time to first flatus was 70 (17.8) hours in the control group and 61 (14.6) hours in the Dex group. To detect this difference with a two-sided significance level (α) of 0.05 and a power (1-β) of 0.85, a sample size of 60 patients per group was required. Assuming a 1:1 allocation ratio and accounting for a 25% withdrawal or loss to follow-up, the total sample size was set at 150 patients.

3.8 Recruitment

Consecutive eligible patients admitted to Shaoxing People's Hospital with acute adhesive bowel obstruction scheduled for laparoscopic surgery are approached by a research coordinator. Written informed consent is obtained from each patient or their legal representative.

4. Assignment of interventions

4.1 Randomization

A computer-generated randomization sequence with a 1:1 allocation is prepared by an independent statistician. The sequence is concealed using sequentially numbered, opaque, sealed envelopes. Envelopes are opened by a dedicated research nurse not involved in patient care or outcome assessment, who prepares the study drug (dexmedetomidine or normal saline) in an unlabeled syringe.

4.2 Blinding

Patients, surgeons, postoperative care providers, outcome assessors, and statisticians are blinded to group assignment. The anesthesiologists administering the intraoperative infusion are aware of group allocation due to the nature of the intervention; however, anesthesia depth is guided by objective BIS monitoring to standardize anesthetic management and minimize performance bias. The randomization code is broken only after the final statistical analysis is completed.

5. Data collection and management

5.1 Data collection methods

· Demographic and baseline clinical data are collected from electronic medical records.

· Intraoperative data (drug doses, fluids, urine output, blood loss, hemodynamic measurements) are recorded by attending anesthesiologists.

· Postoperative GI function outcomes (flatus, feces, oral feeding, I-FEED scores) are assessed daily by trained research nurses blinded to group allocation.

· Blood samples are collected at designated time points, processed, and stored at -80°C until batch analysis.

· ELISA assays are performed by laboratory personnel blinded to group assignment.

5.2 Data management

All data are entered into a password-protected electronic database (Microsoft Excel, SPSS). Double-data entry is performed for verification. Range checks and consistency checks are applied. The final dataset will be archived for at least 5 years after publication.

5.3 Statistical methods

Statistical analyses are performed using SPSS version 21.0 and GraphPad Prism 7.0. Normality of continuous data is assessed using the Shapiro–Wilk test and visual inspection of Q–Q plots.

· Normally distributed continuous data: presented as mean (SD), compared using independent-sample t-test (two groups) or repeated-measures ANOVA (serial measurements).
· Non-normally distributed continuous data: presented as median (25th, 75th percentiles), compared using Mann–Whitney U test.
· Categorical data: presented as n (%), compared using χ^2 test or Fisher's exact test as appropriate.
· All tests are two-tailed, and $P < 0.05$ is considered statistically significant. No interim analysis is planned.

6. Ethics and dissemination

6.1 Research ethics approval

This study was approved by the Ethics Committee of Shaoxing People's Hospital (Approval No. 2022-124) on September 5, 2022. The trial is conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

6.2 Informed consent

Written informed consent is obtained from all participants or their legal representatives before enrollment. The consent form explains the purpose of the study, procedures, potential risks and benefits, confidentiality, and the right to withdraw at any time without penalty.

6.3 Confidentiality

All patient-identifiable information is removed and replaced with unique study codes. Data are stored on password-protected hospital servers accessible only to authorized study personnel.