

BMJ Open Effects of hydromorphone-based intravenous patient-controlled analgesia with and without a low basal infusion on postoperative hypoxaemia: study protocol for a randomised controlled clinical trial

Yumei Ma ¹, Zhuomin Deng,² Xiangying Feng,³ Jialin Luo,³ Yang Meng,¹ Jingjing Lin,¹ Xiaoxiao Mu,¹ Xuan Yang,¹ Huang Nie¹

To cite: Ma Y, Deng Z, Feng X, *et al.* Effects of hydromorphone-based intravenous patient-controlled analgesia with and without a low basal infusion on postoperative hypoxaemia: study protocol for a randomised controlled clinical trial. *BMJ Open* 2022;**12**:e064581. doi:10.1136/bmjopen-2022-064581

► Prepublication history for this paper is available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2022-064581>).

Received 12 May 2022
Accepted 30 October 2022



© Author(s) (or their employer(s)) 2022. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

Correspondence to
Huang Nie; niehuang@163.com

ABSTRACT

Introduction When patients receive patient-controlled intravenous analgesia (PCIA), no basal infusion is always recommended, as the addition of a basal infusion increases the occurrence of postoperative opioid-induced respiratory depression. However, few studies have investigated whether low basal infusions increase the incidence of postoperative hypoxaemia relative to no basal infusion. We intend to conduct a clinical trial to test the hypothesis that PCIA with a low basal infusion does not increase the occurrence of postoperative hypoxaemia relative to PCIA with no basal infusion.

Methods and analysis This single-centre parallel randomised controlled clinical trial will be conducted with 160 patients undergoing gastrointestinal tumour surgery. The assigned nurse will set analgesic pumps (low or no basal infusion PCIA) according to block-based randomisation sequence. Other investigators and all participants will be blinded to intervention allocation. All patients will be monitored continuously with the ep pod, a wireless wearable device, recording of oxygen saturation (SpO₂) and daily ambulation duration for 48 hours postoperatively. Three follow-up evaluations will be conducted to assess the analgesic effect (Numeric Rating Scale (NRS) pain score) and opioid-related side effects (Overall Benefit of Analgesic Score (OBAS)). The primary outcome will be the area under the curve for hypoxaemia (defined as SpO₂<95%) per hour. The secondary outcomes will be the areas under the curve for hypoxaemia defined as SpO₂<90% and <85% per hour, hydromorphone consumption, OBASs at 24 and 48 hours postoperatively, NRS scores at 4, 24 and 48 hours postoperatively, and the ambulation time per hour over 48 hours.

Ethics and dissemination The study has been approved by the Xijing Hospital Ethics Committee (KY20212163-F-1). Written informed consent will be obtained from all patients or their authorised surrogates. All data will be managed with confidentiality. Findings will be disseminated at international conferences and in peer-reviewed journals.

Trial registration number ChiCTR2100054317.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Continuous monitoring of the vital signs of patients receiving patient-controlled intravenous analgesia for 48 hours will reflect the primary outcome of postoperative hypoxaemia more objectively than traditional monitoring.
- ⇒ The use of a portable wireless wearable monitoring system will ensure high-quality data because of its high patient compliance relative to traditional monitoring.
- ⇒ We will evaluate opioid side effects using overall benefit of analgesic scores obtained with a simple multidimensional quality assessment instrument for the measurement of patients' benefits from postoperative pain therapy.
- ⇒ The limitation is that this study will be conducted at a single centre, which may weaken the external validity of the results.

BACKGROUND

Opioids remain the mainstream drugs used for acute postoperative pain control, but their potential side effects include nausea and vomiting, itching and even respiratory depression. Opioid-induced respiratory depression is usually preceded by sedation and, if left untreated, can progress to cardiac arrest and death.¹ In a review of 357 acute pain claims dating to 1990–2009 from the Anesthesia Closed Claims Project database, 92 cases were found to be postoperative opioid-induced respiratory depression (POIRD), and about 55% of patients who experienced POIRD died.² Ninety-seven percent of these cases were judged to have been preventable with better monitoring.²

In settings without continuous postoperative monitoring, such as traditional surgical

wards, the incidence of respiratory depression is about 1%, although it varies depending on the definition and analgesic modality used.^{3–8} With continuous monitoring, including oximetry and capnography, the incidence of respiratory depression is as high as 12%.⁹ Recently, technologies for continuous monitoring with pulse oximetry and the wireless notification of clinical staff via paging systems have become commercially available.^{10–12} Such continuous pulse oximetry monitoring will feasibly provide more detailed information on the frequency and severity of POIRD.

When patients receive patient-controlled intravenous analgesia (PCIA), no basal infusion is always recommended over PCIA with basal infusion to reduce the occurrence of adverse events, including POIRD. However, most studies leading to this recommendation were conducted with high basal infusions in the gynaecological surgical context^{13–18}; whether PCIA with low basal infusion has similar effect remains unknown. Lehmann *et al*¹⁹ conducted a randomised trial to compare low and high basal infusions of hydromorphone PCIA; they found that the high-dose group consumed significantly more hydromorphone, but that self-reported pain intensities were comparable between groups. In other research, the use of hydromorphone PCIA with low basal infusions had also yielded satisfactory outcomes.^{20–22} Bai *et al*²² discovered that patients in a basal infusion plus bolus group experienced significantly less-intense static and dynamic pain than did those in a bolus-only group, suggesting that the analgesic effect of low-basal infusion PCIA is superior to that of no-basal infusion PCIA. However, whether low basal infusion increases the incidence of POIRD relative to no basal infusion has not been investigated.

We aim to perform continuous postoperative oxygen saturation (SpO₂) monitoring using a wireless wearable device to determine the degree of postoperative hypoxaemia in patients receiving PCIA with and without low basal hydromorphone infusions. We will test the hypothesis that low-basal infusion PCIA is not inferior to no-basal infusion PCIA in terms of the occurrence of postoperative hypoxaemia in the first 48 hours after gastrointestinal tumour surgery, with hypoxaemia defined first as <95% integrated SpO₂ and second as <90% or <85% SpO₂.

METHODS AND ANALYSIS

Aims and hypotheses

The primary aim of this study will be to investigate the occurrence of hypoxaemia during the first 48 postoperative hours in patients receiving PCIA with and without low basal infusions. The secondary aims will be to compare the effects of PCIA with and without low basal infusion on hydromorphone consumption, analgesia, adverse events and postoperative ambulation.

Study design

This single-centre parallel randomised controlled trial will be conducted with 160 patients undergoing

gastrointestinal tumour surgery at the First Affiliated Hospital of the Air Force Military Medical University (Xijing Hospital, Xi'an, China). Participants will be allocated randomly at a 1:1 ratio to receive postoperative PCIA with and without a low basal hydromorphone infusion. All participants will be monitored using a wearable wireless device (ePM/ep pod; Mindray Medical International, Shenzhen, China) for 48 hours from the start of PCIA, and approximately three follow-up assessments will be conducted in the hospital to assess opioid-related side effects. The study design is presented in figure 1.

Recruitment

Inclusion criteria

1. Patients scheduled for elective gastrointestinal tumour resection under general anaesthesia who will receive postoperative PCIA.
2. Age >18 years.
3. Body mass index (BMI) 18.5–30 kg/m².
4. American Society of Anesthesiologists grades I–III.
5. Voluntary participation and provision of written informed consent.

Exclusion criteria

1. SpO₂ <90% or chronic severe respiratory disease (chronic obstructive pulmonary disease, obstructive sleep apnoea syndrome).
2. History of chronic pain, analgesic or sedative abuse, or known opioid allergy.
3. Kidney disease (serum creatinine concentration >140 (males) or 130 (females) μmol/L and oliguria/anuria) or renal replacement therapy (eg, dialysis).
4. Hepatic disease (liver enzyme concentrations twice the normal values).
5. Pregnancy or breastfeeding status.
6. Operation time >5 hours.
7. Plan for postoperative transfer to the intensive care unit.
8. Participation in another clinical trial in the previous 3 months.

Withdrawal criteria

1. Treatment measures taken due to complications or disease changes that render continued study participation unsuitable.
2. Unblinding due to the implementation of emergency measures.
3. Participant request.

Randomisation and blinding

A 1:1 randomisation sequence will be generated using the R software (The R Foundation for Statistical Computing, Vienna, Austria) with randomly sized blocks of 2 and 4 and sealed in envelopes. Enrolled participants will be randomised to the test and control groups, with PCIA treatment modalities indicated on paper slips sealed in sequentially numbered opaque envelopes kept by a secretary not otherwise involved in the trial. The participants and investigators will be blinded to group allocation. The

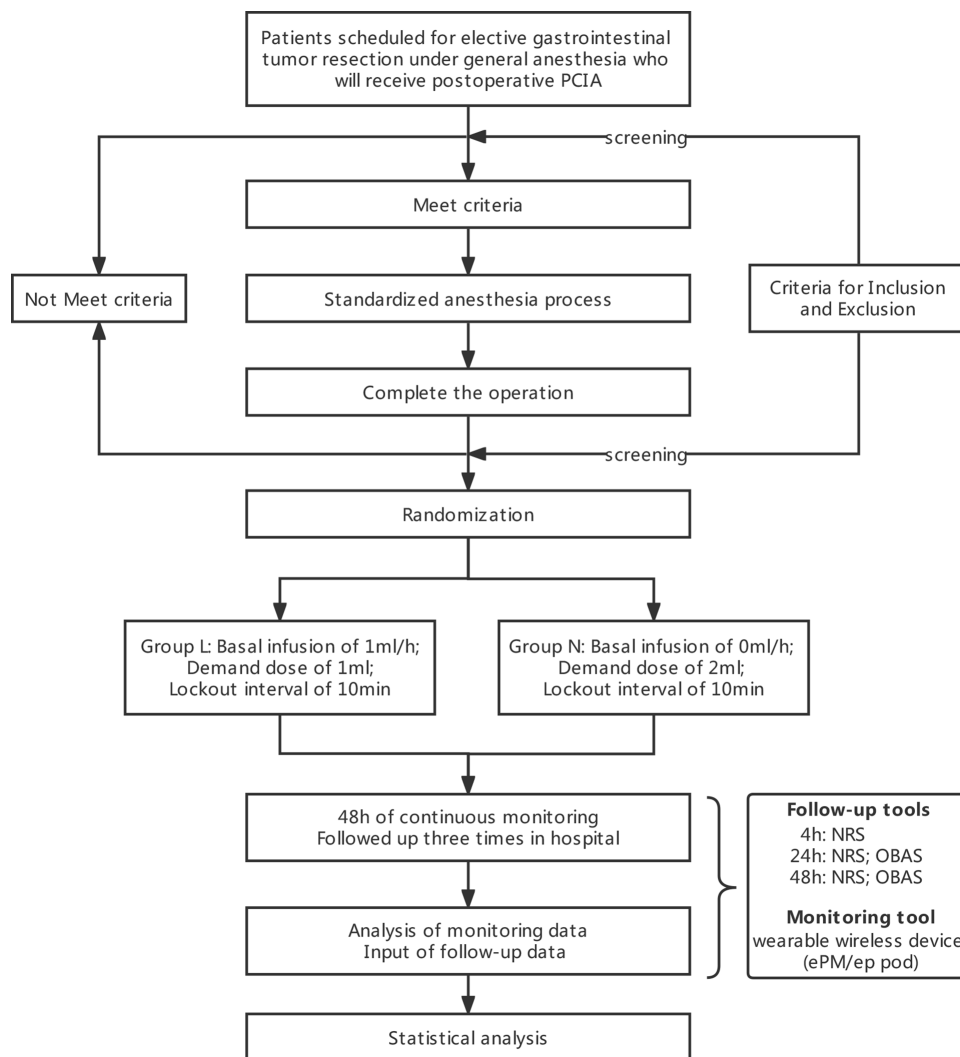


Figure 1 Flow of the trial. NRS, Numeric Rating Scale; OBAS, Overall Benefit of Analgesic Score; PCIA, patient-controlled intravenous analgesia.

assigned anaesthetic nurse, who will not otherwise participate in the trial, will open each envelope before the end of each operation and set the analgesic pump accordingly. The investigators will not be involved in intraoperative management; they will conduct only postoperative follow-up.

Procedures and interventions

The researcher will explain the purpose of and risks associated with the trial to eligible subjects, and provide them with education about PCIA and wireless wearable devices. All those who agree to participate in the trial will sign an informed consent form (example is available in online supplemental file 1).

After the placement of standard monitors and radial arterial catheters as necessary, the attending anaesthesiologist will routinely administer preoperative medication, such as dexamethasone (4–8 mg). Anaesthesia will be induced with propofol (1–2 mg/kg) or etomidate (0.15–0.3 mg/kg), sufentanil (0.3–0.5 µg/kg), midazolam (0.02 mg/kg) and rocuronium (0.6 mg/kg), and maintained with remifentanyl (0.1–0.2 µg/kg/min)

and sevoflurane (1%–2%) in an oxygen or propofol target-controlled infusion (3–6 µg/mL). Palonosetron (0.25 mg) will be used routinely to prevent nausea and vomiting after induction. The anaesthesia depth will be guided by Narcotrend (Narcotrend Group, Hannover, Germany) monitoring, with the Narcotrend index maintained at 40–60. After intubation, the end-tidal carbon dioxide concentration will be maintained at 35 ± 5 mmHg. Rocuronium (0.1–0.2 mg/kg) will be added intermittently to maintain muscle relaxation and will not be given in the 30 min before the end of the operation. In the absence of contraindication, the patients will be given intravenous non-steroidal anti-inflammatory drug injections 15–20 min before surgical incision. According to our enhanced recovery after surgery protocol, local infiltration will be performed before incision and at the end of surgery. Hydromorphone (10 µg/kg) will be given intravenously 30 min before the end of surgery. Anaesthesia reversal will be achieved with the intravenous administration of neostigmine (30–50 µg/kg) and atropine (20 µg/kg) after the



Figure 2 Simulated patient monitoring with the ePM/ep pod series monitor (includes a demonstration of a training). (A) The bedside component (ePM) displays the patient's vital signs, received wirelessly. (B). The ep pod can monitor three-lead electrocardiography output, SpO₂, respiratory rate and daily ambulation duration. (C) The bp pod non-invasively records the patient's blood pressure. *Note: Mindray Medical International has authorised the copyright of the figure, in which the people depicted are not patient and were taken with the participants knowledge. The person in the demonstration of training is not our patients. SpO₂, oxygen saturation.

operation. The patients will be transferred to recovery room for monitoring and then back to the ward after about 1 hour.

At the end of each operation, the assigned anaesthetic nurse will prepare the PCIA infusion device according to the patient's group assignment. The PCIA drug regimen for both groups will be 10 mg hydromorphone in 100 mL saline. Patients in the low basal infusion group (group L) will receive a basal infusion of 1 mL/hour with a demand dose of 1.0 mL and a lockout interval of 10 min. Those in the no basal infusion group (group N) will receive no basal infusion, with a demand dose of 2.0 mL and a lockout interval of 10 min.

The patients will be connected to the PCIA system on arrival in the recovery room. They will be monitored via the ePM/ep pod (figure 2) for 48 hours or until hospital discharge, if occurring sooner. This wireless system is composed of patient-worn and bedside components for the accurate continuous monitoring of three-lead electrocardiography output, the SpO₂, the respiratory rate and the daily ambulation duration. It non-invasively measures blood pressure hourly. The data will be recorded continuously on the bedside component and downloaded to a laptop. The investigator in charge of postoperative follow-up will visit patients three times daily, including during weekends and evenings, to ensure compliance with monitoring. The duration of oxygen therapy during the study period will also be recorded. All participants will be prescribed flurbiprofen (50 mg, three times daily) for 3 days postoperatively. When the analgesic effect is not satisfactory, extra hydromorphone will be given as rescue analgesia, and this administration will be recorded. Patients experiencing postoperative nausea and vomiting will be given 5 mg tropisetron intravenously, and this administration will be recorded. All patient requests to withdraw from the trial or stop using PCIA will also be recorded.

Outcome measurement

Primary outcome

The primary outcome is the integrated area under curve (AUC) for hypoxaemia (defined as SpO₂ <95%) per hour during the ≤48 hours period of continuous measurement in hospital. This outcome characterises the hypoxaemia duration and severity. Many criteria for hypoxaemia have been used in related studies; we defined hypoxaemia as SpO₂ <95% for the assessment of the primary outcome and examined SpO₂ <90% and <85% as secondary outcomes.^{23–25}

SpO₂ data will be downloaded weekly. For cleaning, 1 min segments of these data will be extracted, and segments with SpO₂ <60% will be excluded as outliers. Then, intervals between two consecutive SpO₂ measurements >1 min will be defined as gaps. The total proportion of all gaps per patient will be determined to show the quality of the recorded monitoring data. We will use the Gaussian kernel in Matlab R2016b (MathWorks, Natick, Massachusetts, USA) to process the original data and interpolate missing values. Then, smoothed SpO₂ time curves will be generated (figure 3). Finally, AUCs will be calculated as the sum of the product of the hypoxaemia duration (in hours) and its difference from the hypoxaemia threshold of 95% (as a percentage), divided by the number of monitoring hours.

Secondary outcomes

1. AUC for hypoxaemia defined as SpO₂ <90% per hour, calculated as described above.
2. AUC for hypoxaemia defined as SpO₂ <85% per hour, calculated as described above.
3. Hydromorphone consumption over 48 postoperative hours (or hospitalisation duration, if <48 hours).
4. Overall Benefit of Analgesia Scores²⁶ (OBASs, reflecting the analgesic effect, opioid side effects and patient satisfaction; table 1) at 24 and 48 hours postoperatively.

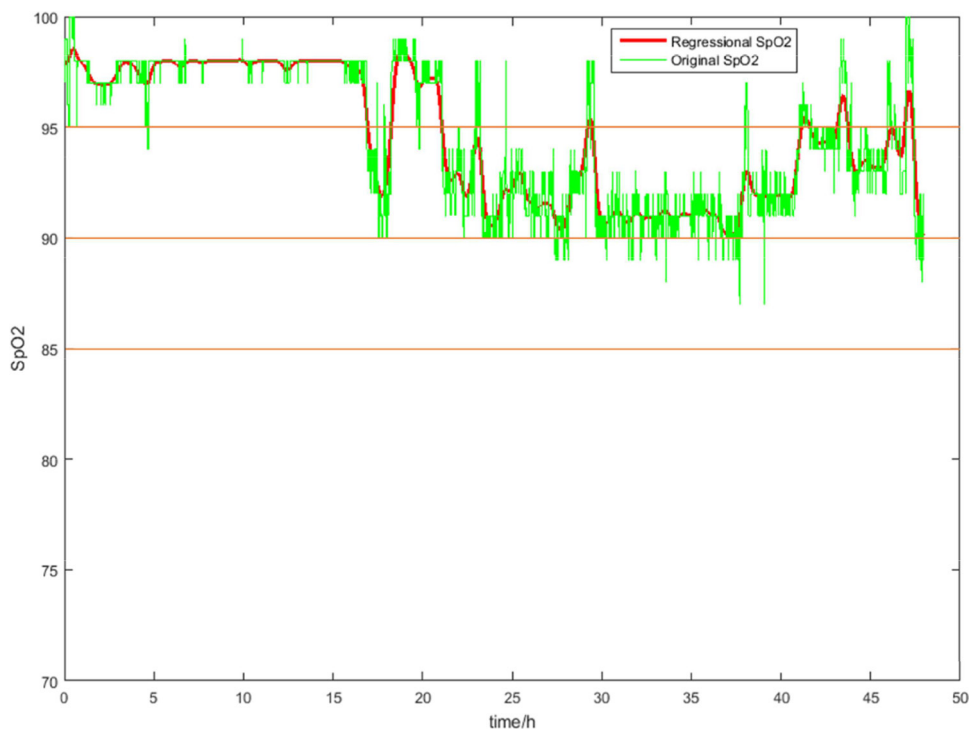


Figure 3 Example SpO₂ time curve. The orange lines show the hypoxaemia thresholds. SpO₂, oxygen saturation.

5. Numeric Rating Scale (NRS) scores for pain (0 (no pain at all)–10 (worst pain imaginable)) at rest and during movement at 4, 24 and 48 hours postoperatively.
6. Ambulation time per hour during the 48 postoperative hours (or hospitalisation duration, if <48 hours).

Sample size

AUCs for hypoxaemia (SpO₂ <95%) per hour obtained previously using this definition have exhibited a skewed distribution.²³ Using the PASS 2015 software (NCSS, Kaysville, Utah, USA), we determined that a minimum of 144 patients will be required to have 80% power to prove that the 95% lower limit of the one-sided confidence interval (CI) will be above the non-inferiority limit of 1.25 for the ratio of means between two groups (coefficient of variation, 0.5), to prove the non-inferiority of low-basal infusion PCIA relative to no-basal infusion PCIA in terms of hypoxaemia. Considering a drop-out rate of 10%, at least

160 patients (80 per group) will need to be included in the study.

Data collection

We have designed a case report form (CRF) for researchers' data recording for this study. Two data managers supervised by an independent quality monitor will enter all CRF data into an Epidata V.3.1 (EpiData Association, Odense, Denmark; <http://www.epidata.dk>) database. At enrolment, one researcher will collect data on participants' demographic characteristics, medical histories, tobacco and alcohol consumption, relevant preoperative laboratory test results, and preoperative clinical condition through patient interviews and from electronic medical records. Procedure-related clinical information will be collected from the surgical anaesthesia clinical information system. SpO₂ and activity data collected by the ePM/ep pods will be exported periodically. The researcher responsible for visitation will collect

Table 1 Overall benefit of analgesia score items

Item	Score
1 Please rate your current pain at rest on a scale between 0 and 4	0=minimal pain to 4=maximum imaginable pain
2 Please grade any distress and bother from vomiting in the past 24 hours	0=not at all to 4=very much
3 Please grade any distress and bother from itching in the past 24 hours	0=not at all to 4=very much
4 Please grade any distress and bother from sweating in the past 24 hours	0=not at all to 4=very much
5 Please grade any distress and bother from freezing in the past 24 hours	0=not at all to 4=very much
6 Please grade any distress and bother from dizziness in the past 24 hours	0=not at all to 4=very much
7 How satisfied are you with your pain treatment during the past 24 hours	0=not at all to 4=very much
Total score	Sum of responses to items 1–6 + (4 – item 7 response)

NRSs and OBASs at 4, 24 and 48 hours, and data on hydromorphone consumption recorded by the analgesia pumps on the completion of treatment. Information on the use of extra analgesia and antiemetic drugs will be recorded. Before discharge, the patients will be surveyed (using a 0–100 scale) about their satisfaction with postoperative monitoring by a wearable device.

Management of withdrawals

Participants will be informed during recruitment of their right to withdraw from the study at any time without prejudice. Based on experience, we considered the expected drop-out rate in estimating the sample size. The statistical analysis will be performed on an intention-to-treat (ITT) basis to account for data lost due to participant withdrawal.

Data analysis

The primary analysis will be ITT. A sensitivity analysis will be performed on a per-protocol set basis. All analyses will be carried out using SAS V.9.1 (SAS Institute) with a two-sided significance level of 0.05. Descriptive statistical analysis will be performed to compare the patients' baseline data (eg, age, sex, BMI, surgery type) between groups. The Kolmogorov-Smirnov test will be applied to continuous variables. Normally distributed data will be expressed as means±SD, and non-normally distributed data will be expressed as medians with IQRs. Count variables will be presented as frequencies with percentages or ratios.

The Mann-Whitney U test will be used to examine the difference between groups in the total duration of hypoxaemia defined as SpO₂ <95% per hour. If this difference is significant, we will calculate the ratio of means between groups with a 95% CI and compare that with the non-inferiority limit of 1.25. Subgroup analyses will be performed according to baseline variables such as age, BMI, initial SpO₂ and surgery type.

The Mann-Whitney U test will be used to compare AUCs for hypoxaemia defined as SpO₂ <90% and 85% per hour. According to the results of the Kolmogorov-Smirnov test, the hydromorphone consumption and the ambulation time per hour will be compared using Student's t-test or Mann-Whitney U test. Similarly, we will use repeated-measures analysis of variance or generalised linear mixed model for within-group comparison of OBASs and NRS scores from different time points after operation.

Patient and public involvement

No patient or member of the public will be involved in the design or implementation of this study.

Ethics and dissemination

The Xijing Hospital Ethics Committee, which conforms to Chinese legislation and the Declaration of Helsinki, approved the procedures of this study no. KY20212163-F-1, 22 November 2021. Written informed consent will be obtained from all patients or their authorised surrogates. All data will be managed with confidentiality. The study

has been registered with the Chinese Clinical Trial Registry (<http://www.chictr.org.cn>; no. ChiCTR2100054317). The investigators will disseminate the trial findings in peer-reviewed scientific journals and conference presentations.

DISCUSSION

Gastrointestinal cancer is very prevalent worldwide, especially in China. Among the approximately 4.5688 million new cancer cases in 2020, colorectal and gastric cancer cases ranked second and third, respectively.²⁷ Surgery is the first-line intervention for gastrointestinal cancer, but postoperative pain control remains unsatisfactory despite the application of multimodal analgesia approaches.²⁵ PCIA with opioids such as morphine and hydromorphone remains the mainstream modality for postoperative analgesia. Compared with morphine use, the use of hydromorphone is associated with a lower risk of adverse events due to its less active metabolite hydromorphone-3-glucuronid.^{28 29} However, little clinical research has been conducted to explore the optimal use of hydromorphone PCIA for patients who have undergone gastrointestinal cancer surgery, especially in China.

Previous studies have suggested that the use of a supplemental basal infusion with PCIA confers no advantage, and could increase the incidence of complications, including POIRD.^{13–18} In a meta-analysis of 14 randomised controlled trials, George *et al*³⁰ found that the addition of a background infusion to demand-dose PCIA with opioids was associated significantly with an increased rate of respiratory depression, but reported moderate heterogeneity for this outcome and advised that the finding be interpreted with caution due to the small sample and wide range of respiratory depression definitions. In addition, the opioids studied in most of the studies included in the meta-analysis were morphine. Although there is no clear definition of high and low basal infusion rates for PCIA, the recommended dose was 1–3 mg/hour for morphine when the basal infusion was introduced into clinical practice,³¹ and later the common rate was 1–2 mg/hour for morphine in opioid-naïve patients.³² McKenzie³¹ cautioned that using 1–3 mg/hour morphine could compromise the safety of patient-controlled analgesia in overly sedated patients. Parker *et al*³³ compared morphine doses of 0.5, 1 and 2 mg/hour with no basal infusion for patients who had undergone gynaecological surgery and found that the addition of continuous infusion did not reduce demands or the supplemental bolus doses. In several recent studies, adding a basal infusion to PCIA yielded satisfactory results. White *et al*³⁴ demonstrated that a background morphine infusion with PCIA following colorectal cancer surgery provided better pain management, reduced opioid consumption and minimised complications relative to a bolus-only protocol. Sinatra *et al*³⁵ also investigated the benefits of basal morphine infusion doses <1 mg/hour with PCIA. Bai *et al*²² used 0.12 mg/hour infusion of hydromorphone (equivalent to 0.8 mg/hour intravenous morphine) for

patients with the mean weight of about 60 kg who had undergone single-port video-assisted thoracoscopic surgery, which resulted in lower pain scores than in a no basal infusion group. Based on the results of those studies, we consider basal morphine infusion rates ≤ 1 mg/hour to be low and those >1 mg/hour to be high. These findings above raise the questions of whether hydromorphone PCIA with a low basal infusion as a multimodal analgesic strategy increases postoperative hypoxaemia in patients undergoing gastrointestinal tumour surgery and whether low-basal infusion PCIA will have a better analgesic effect than a bolus-only protocol in these patients. Our trial is designed to explore these questions.

We plan to choose the hydromorphone infusion rate of 0.1 mg/hour as the low basal infusion group in this study; this rate is likely less than 0.12 mg/hour of Bai *et al*²² when body weight is considered. In our trial, the demand doses will be set at 0.1 and 0.2 mg in the low basal group and no basal group (both lockout intervals as 10 min), respectively, which means the maximum possible doses in 1 hour are 0.7 and 1.2 mg in an ideal scenario. However, patients rarely reach the maximum hourly dose in clinical practice, as we have observed in previous pretrials. This study aims to explore whether postoperative hypoxaemia differs between the PCIA modalities; we will not focus on whether different PCIA doses result in different degrees of hypoxaemia. We will compare hydromorphone consumption between groups when the trial is finished. In Parker *et al* study, similar to our study design and parameter settings, the results showed morphine consumption during 72 postoperative hours was comparable between groups.³³

The strength of this study is that we will use a wireless wearable continuous monitor to collect data on patients' vital signs postoperatively, which will enable the accurate determination of the degree of postoperative hypoxaemia. Unlike traditional monitoring, the wireless wearable device can monitor patients continuously without affecting their daily activity or sleep. The postoperative hypoxaemia data acquired from patients in this study will better reflect the real clinical situation. If the results support our hypotheses, this randomised clinical trial will provide important evidence for the clinical application of low basal infusion PCIA for postoperative acute pain management in patients undergoing gastrointestinal tumour surgery.

Trial status

At the time of manuscript submission, the study had been launched, and a few patients had participated in it. Recruitment began on 14 December 2021. Enrolment will continue until 160 patients have been enrolled in the trial; it is expected to be completed in December 2022.

Author affiliations

¹Department of Anesthesiology and Perioperative Medicine, Fourth Military Medical University Xijing Hospital, Xian, Shaanxi, China

²PMLS Upstream Marketing Department, Mindray Medical International Ltd, Shenzhen, Guangdong, China

³Department of General Surgery, Fourth Military Medical University Xijing Hospital, Xian, Shaanxi, China

Acknowledgements We thank Medjaden for scientific editing of this manuscript. We also thank Nong Yan for his professional guidance and assistance with the data processing plan. We thank the reviewers for their constructive comments, which helped us to improve the quality of the paper.

Contributors All authors made substantial contributions to the intellectual content of this paper. Yumei Ma and HN conceived and designed the study. XF, Jialin Luo, Yang Meng, Jingjing Lin and XM participated in the study design and are the principal investigators in charge of multi-institutional coordination. ZD is responsible for equipment and technical support. XY is responsible for ethical supervision. Yumei Ma and HN will contribute to data analysis.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iD

Yumei Ma <http://orcid.org/0000-0001-9814-2952>

REFERENCES

- Pöpping DM, Zahn PK, Van Aken HK, *et al*. Effectiveness and safety of postoperative pain management: a survey of 18 925 consecutive patients between 1998 and 2006 (2nd revision): a database analysis of prospectively raised data. *Br J Anaesth* 2008;101:832–40.
- Lee LA, Caplan RA, Stephens LS, *et al*. Postoperative opioid-induced respiratory depression: a closed claims analysis. *Anesthesiology* 2015;122:659–65.
- Shapiro A, Zohar E, Zaslansky R, *et al*. The frequency and timing of respiratory depression in 1524 postoperative patients treated with systemic or neuraxial morphine. *J Clin Anesth* 2005;17:537–42.
- Rowbotham DJ. Advances in pain. *Br J Anaesth* 2001;87:1–2.
- Schug SA, Torrie JJ. Safety assessment of postoperative pain management by an acute pain service. *Pain* 1993;55:387–91.
- Sidebotham D, Dijkhuizen MR, Schug SA. The safety and utilization of patient-controlled analgesia. *J Pain Symptom Manage* 1997;14:202–9.
- Walder B, Schafer M, Henzi I, *et al*. Efficacy and safety of patient-controlled opioid analgesia for acute postoperative pain. A quantitative systematic review. *Acta Anaesthesiol Scand* 2001;45:795–804.
- Paul JE, Buckley N, McLean RF, *et al*. Hamilton acute pain service safety study: using root cause analysis to reduce the incidence of adverse events. *Anesthesiology* 2014;120:97–109.
- Overdyk FJ, Carter R, Maddox RR, *et al*. Continuous oximetry/capnometry monitoring reveals frequent desaturation and bradypnea during patient-controlled analgesia. *Anesth Analg* 2007;105:412–8.
- Posthuma LM, Downey C, Visscher MJ, *et al*. Remote wireless vital signs monitoring on the ward for early detection of deteriorating patients: a case series. *Int J Nurs Stud* 2020;104:103515.

- 11 Weller RS, Foard KL, Harwood TN. Evaluation of a wireless, portable, wearable multi-parameter vital signs monitor in hospitalized neurological and neurosurgical patients. *J Clin Monit Comput* 2018;32:945–51.
- 12 Weenk M, Koeneman M, van de Belt TH, *et al.* Wireless and continuous monitoring of vital signs in patients at the general ward. *Resuscitation* 2019;136:47–53.
- 13 Mackie AM, Coda BC, Hill HF. Adolescents use patient-controlled analgesia effectively for relief from prolonged oropharyngeal mucositis pain. *Pain* 1991;46:265–9.
- 14 Parker RK, Holtmann B, White PF. Effects of a nighttime opioid infusion with PCA therapy on patient comfort and analgesic requirements after abdominal hysterectomy. *Anesthesiology* 1992;76:362–7.
- 15 White PF, Parker RK. Is the risk of using a "basal" infusion with patient-controlled analgesia therapy justified? *Anesthesiology* 1992;76:489.
- 16 Doyle E, Robinson D, Morton NS. Comparison of patient-controlled analgesia with and without a background infusion after lower abdominal surgery in children. *Br J Anaesth* 1993;71:670–3.
- 17 Morad A, Winters B, Stevens R, *et al.* The efficacy of intravenous patient-controlled analgesia after intracranial surgery of the posterior fossa: a prospective, randomized controlled trial. *Anesth Analg* 2012;114:416–23.
- 18 van Beers EJ, van Tuijn CFJ, Nieuwkerk PT, *et al.* Patient-controlled analgesia versus continuous infusion of morphine during vaso-occlusive crisis in sickle cell disease, a randomized controlled trial. *Am J Hematol* 2007;82:955–60.
- 19 Lehmann KA, Paral F, Sabatowski R. [Postoperative pain therapy with hydromorphone and metamizole. A prospective randomized study in intravenous patient-controlled analgesia (PCA)]. *Anaesthesist* 2001;50:750–6.
- 20 Duan G, Yang G, Peng J, *et al.* Comparison of postoperative pain between patients who underwent primary and repeated cesarean section: a prospective cohort study. *BMC Anesthesiol* 2019;19:189.
- 21 Huang C-Y, Li S-X, Yang M-J, *et al.* A comparative study of three concentrations of intravenous nalbuphine combined with hydromorphone for post-cesarean delivery analgesia. *Chin Med J* 2020;133:523–9.
- 22 Bai Y, Sun K, Xing X, *et al.* Postoperative analgesic effect of hydromorphone in patients undergoing single-port video-assisted thoracoscopic surgery: a randomized controlled trial. *J Pain Res* 2019;12:1091–101.
- 23 Belcher AW, Khanna AK, Leung S, *et al.* Long-acting patient-controlled opioids are not associated with more postoperative hypoxemia than short-acting patient-controlled opioids after noncardiac surgery: a cohort analysis. *Anesth Analg* 2016;123:1471–9.
- 24 Cashman JN, Dolin SJ. Respiratory and haemodynamic effects of acute postoperative pain management: evidence from published data. *Br J Anaesth* 2004;93:212–23.
- 25 Sun Z, Sessler DI, Dalton JE, *et al.* Postoperative hypoxemia is common and persistent: a prospective blinded observational study. *Anesth Analg* 2015;121:709–15.
- 26 Lehmann N, Joshi GP, Dirkmann D, *et al.* Development and longitudinal validation of the overall benefit of analgesia score: a simple multi-dimensional quality assessment instrument. *Br J Anaesth* 2010;105:511–8.
- 27 Cao W, Chen H-D, Yu Y-W, *et al.* Changing profiles of cancer burden worldwide and in China: a secondary analysis of the global cancer statistics 2020. *Chin Med J* 2021;134:783–91.
- 28 Murray A, Hagen NA. Hydromorphone. *J Pain Symptom Manage* 2005;29:57–66.
- 29 Smith H, Bruckenthal P. Implications of opioid analgesia for medically complicated patients. *Drugs Aging* 2010;27:417–33.
- 30 George JA, Lin EE, Hanna MN, *et al.* The effect of intravenous opioid patient-controlled analgesia with and without background infusion on respiratory depression: a meta-analysis. *J Opioid Manag* 2010;6:47–54.
- 31 McKenzie R. Patient-controlled analgesia (PCA). *Anesthesiology* 1988;69:1027.
- 32 Grass JA, Grass Jeffrey A. Patient-controlled analgesia. *Anesth Analg* 2005;101:S44–61.
- 33 Parker RK, Holtmann B, White PF. Patient-controlled analgesia. *JAMA* 1991;266:1947–52.
- 34 White I, Ghinea R, Avital S, *et al.* Morphine at "sub-analgesic" background infusion rate plus low-dose PCA bolus control pain better and is as safe as twice a bolus-only PCA regimen: a randomized, double blind study. *Pharmacol Res* 2012;66:185–91.
- 35 Sinatra R, Chung KS, Silverman DG, *et al.* An evaluation of morphine and oxymorphone administered via patient-controlled analgesia (PCA) or PCA plus basal infusion in postcesarean-delivery patients. *Anesthesiology* 1989;71:502–7.