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Research Article

Cisatracurium Compared to Atracurium for the Prevention of Postoperative Delirium in Colorectal Cancer Surgery: Protocol of a Double-Blind, Randomized, Clinical Trial

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ABSTRACT

Background: Non-depolarizing neuromuscular blocking agents have been shown to play a role in postoperative delirium (POD) and postoperative cognitive dysfunction (POCD). Cisatracurium is known for its higher potency, lower induction dose, anti-inflammatory activity, lower histamine release, and better hemodynamic stability compared to atracurium, all of which may benefit postoperative cognitive function. This study aims to assess the preventive effects of cisatracurium compared with atracurium on POD incidence in patients undergoing colorectal surgery.

Methods: This single-center, randomized, controlled trial will be conducted at a tertiary care hospital of Sina (Tehran, Iran) from November 2025, assessing the preventive effects on POD of 0.2 mg/kg cisatracurium compared to 0.5 mg/kg atracurium induction dose with subsequent similar drug maintenance on a total of 200 patients undergoing mass resection surgery of colorectal cancers. Patients will be randomly assigned to a 1:1 allocation to each group. The primary outcome will be the prevalence of POD, assessed twice daily from the night after surgery until day 5, using the intensive care delirium screening checklist (ICDSC). The secondary aims are clinically relevant outcomes, including POCD, as measured by the Montreal Cognitive Assessment (MoCA), postoperative pain using a visual analogue scale (VAS), POD severity using the ICDSC, and duration of hospitalization.

Conclusion: This paper provides the protocol for the study comparing the activity of two neuromuscular blocking agents in preventing POD in colorectal cancer surgeries based on the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guideline.

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Introduction

Delirium manifests as disturbances in the patient's level of consciousness (i.e., wakefulness and awareness), the content of consciousness (i.e., orientation, thought process, and thought pattern), and attention, with a fluctuating pattern over a short period. It is accompanied by increased or decreased psychomotor activity, known as hyperactive or hypoactive delirium, respectively, and cognitive impairments (e.g., memory, language, visuospatial function, or perceptual deficits) [1-2], and if left untreated, it is associated with long-term cognitive impairment and increased mortality [3]. Delirium is most commonly observed in postoperative patients and those in the intensive care unit (ICU) [4]. Postoperative delirium (POD), which occurs hours to days after surgery due to the effects of anesthesia and inflammation in response to surgical stress, is most frequently reported following complex surgeries such as cardiac (32%) and abdominal procedures (30%) [5-7]. In contrast, postoperative cognitive dysfunction (POCD), a recently updated nomenclature of delayed neurocognitive recovery, which occurs after the acute phase of surgery, can impair patients' quality of life, increase healthcare costs, and eventually lead to mortality [8].

Previously, various studies have focused on the prevention of POD, mainly on pharmacological (e.g., dexmedetomidine, olanzapine, risperidone, and melatonin) [9] and non-pharmacological (e.g., physical activity, reorientation, clinical adjustment, and sensory stimulation) [10] approaches. This extensive focus on prevention rather than treatment stems from the inefficiency of treatment approaches compared to prevention strategies, as well as the lack of a gold-standard treatment for POD, which has led to techniques that alleviate the symptoms of established POD rather than treating the disease [11]. This matter underscores the importance of prevention in postoperative patient care, focusing on modifiable risk factors such as perioperative medication, preoperative cognitive training, nutrition, postoperative pain, and sleep [12]. A reasonable approach to preventing POD is to address the underlying mechanisms that drive it.

While predisposing factors contributing to POD, such as advanced age, pre-existing cognitive impairment, and comorbidities like cancer, hypertension, diabetes, heart failure, or chronic kidney disease, are known, the underlying mechanism is not yet fully understood [13, 14]. Surgical trauma and hypoperfusion due to operative blood loss can lead to the release of inflammatory mediators such as C-reactive protein (CRP), interleukin (IL) 6, and tumor necrosis factor (TNF)-α, which in turn damage endothelial cells and increase the blood-brain barrier permeability [15].

This leads to infiltration of inflammatory mediators and activation of microglia and astrocytes, causing neuronal dysfunction, impaired synaptic communication, and ultimately, the cognitive and behavioral changes seen in POD and POCD [16].

Another possible explanation is intraoperative neurotransmitter dysregulation [17]. Studies have previously shown that dysregulation of acetylcholine plays a role in POD development [18-19]. For example, a study by Moellman et al. found that patients on medications with higher anticholinergic burden had increased rates of POD [20]. Additionally, melatonin, another neurotransmitter, has been associated with POD, as patients with lower melatonin levels tend to develop the condition [21]. Various studies have examined how melatonin supplementation might prevent POD [22]. Interventions targeting neurotransmitter receptors, such as γ-aminobutyric acid (e.g., remimazolam), 5-hydroxytryptamine (e.g., ondansetron), N-methyl-D-Aspartate (e.g., ketamine), and dopamine (e.g., antipsychotics) receptors, have also been tested for POD prevention [23-24]. More recently, research into the effects of histaminergic medication on postoperative cognition has yielded mixed results: some H1-receptor blockers show partial benefit, while H2-receptor blockers may have adverse effects [25-27]. These mixed findings could be due to the non-selective nature of antihistamine drugs, which can exhibit anticholinergic activity and thus contribute to the development of POD and POCD [28].

Atracurium is a non-depolarizing neuromuscular blocking agent (NMBA) used to induce and maintain anesthesia for endotracheal intubation and muscle relaxation [29]. It functions as a nicotinic receptor blocker by competing with acetylcholine at the neuromuscular junction, with an onset of about 2-3 minutes and a duration of approximately 45 minutes after induction [30]. Cisatracurium, an isomer of atracurium, has three times the potency of atracurium and a longer duration of action, lasting about 60 minutes, requiring a lower dose for anesthesia, thus potentially having fewer complications [31]. Cisatracurium also has a better side-effect profile because it does not release histamine or cause hemodynamic instability compared to atracurium [32]. Meanwhile, animal studies have shown that septic rats receiving cisatracurium demonstrated lower serum levels of inflammatory markers such as TNF-α, IL-1β, IL-6, and procalcitonin [33]. Also, cisatracurium is often preferred in certain procedures, such as cardiac surgeries and surgeries involving patients at risk of drug reactions [34].

A retrospective study by Cao et al. showed better early postoperative cognitive function, as measured by the Mini-Mental Status Exam (MMSE), in patients receiving cisatracurium [35]. This calls for further randomized trials to assess the preventive differences between these two NMBAs in POD, due to their differences in

anticholinergic activity, histamine release, hemodynamic stability, and anti-inflammatory activity.

Objectives

The primary aim of this study is to determine the effect of cisatracurium compared to atracurium in preventing POD in adult patients undergoing colorectal cancer surgery.

The secondary aim is to assess clinically relevant outcomes, including postoperative cognitive function, total length of hospitalization, postoperative pain, and delirium severity, between the cisatracurium and atracurium groups.

Methods

Patient and Public Involvement

No patients or members of the public were directly involved in the design of this trial protocol. The research question and outcome measures were developed based on clinical priorities and gaps identified in the scientific literature.

Trial Design

This trial is a randomized, parallel-group, observer-, patient-, and analyst-blinded study with two arms, featuring a 1:1 allocation ratio, each consisting of 100 patients, conducted at Sina Hospital. The Consolidated Standards of Reporting Trials (CONSORT) flow diagram is available in (Figure 1). The implementation of this study will follow the CONSORT guidelines [36].

Trial setting

This single-center study will be conducted at Tehran University of Medical Sciences, at the University Hospital of Sina (Tehran, Iran). The study was designed in adherence to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist for interventional trials [37]. Data collection began on 2025-10-15 and is ongoing, with an estimated end on 2026-04-01.

Eligibility criteria

Inclusion criteria:

1. Patients diagnosed with colorectal cancer
2. Candidates for elective surgery of metastatic or non-metastatic R0 (complete microscopic) mass resection
3. Adult patients older than 40 years
4. ASA score grade I-III [38]

Exclusion criteria:

1. Patients with delirium the night before surgery
2. Emergency surgery candidates
3. Candidates needing multiple surgeries or who need to go back to the operating room after the initial surgery
4. Previous history of any drug reactivity (including asthma and anaphylaxis)
5. Patients with severe audiovisual problems who are unable to complete the cognitive and delirium assessments
6. Addiction or substance abuse

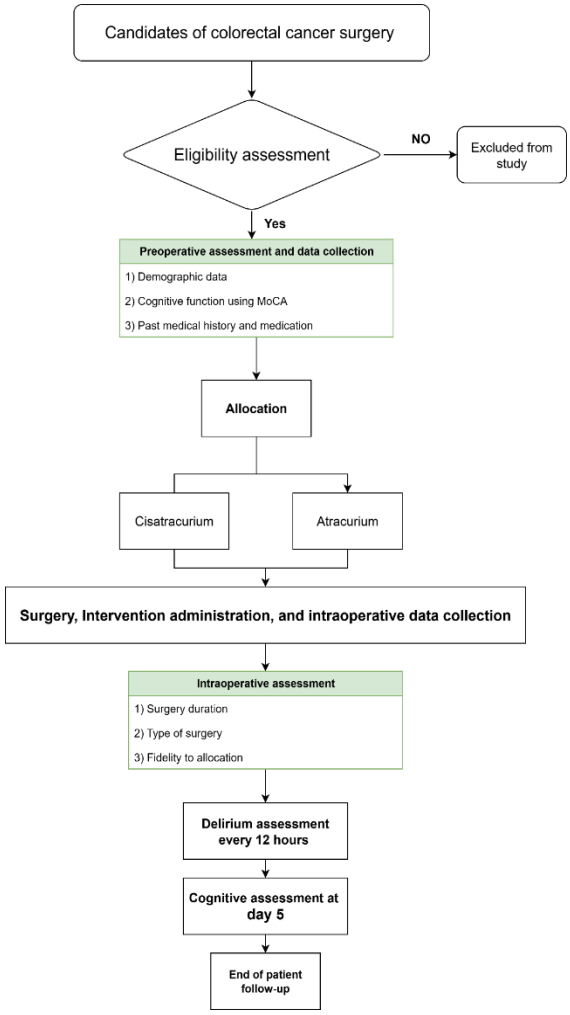

Figure 1- Consolidated Standards of Reporting Trials flow diagram

To ensure standardization and safety in administering the trial interventions, all clinical personnel involved in delivering the study interventions must meet the following eligibility criteria:

Anesthesiologists administering the study drugs (atracurium or cisatracurium) or managing intraoperative anesthesia must have at least 3 years of independent post-residency practice. Surgeons performing the procedures must be accompanied by at least one colorectal surgery fellow or subspecialist. Personnel assisting with the preparation or administration of study drugs must be familiar with the interventions and follow study protocols.

Intervention, Comparator, and Routine Anesthetic Care

All patients are advised not to eat or drink from midnight before the surgery. Surgeries will be performed during the morning shift (8 AM–4 PM). After being admitted to the operating room, the anesthetist will perform routine assessments, including monitoring heart rate, electrocardiography, blood pressure, pulse oximetry, and partial pressure of end-tidal carbon dioxide (ETCO2). Patients will receive pre-oxygenation with 100% oxygen using facemasks to ensure a higher oxygen reserve during intubation.

Anesthesia induction will then begin with 0.03 mg/kg midazolam and 2-3 µg/kg fentanyl as premedication, followed by 2 mg/kg of propofol. For neuromuscular blockade, patients will receive either the intervention (cisatracurium) or the active control (atracurium), based on their randomization groups.

Intervention (Cisatracurium besylate):

- A bolus dose of 0.2 mg/kg will be administered intravenously for induction. Maintenance doses of 2 mg will be given every 45 minutes from a vial with a concentration of 2 mg/ml (1 cc).

Comparator (Atracurium besylate):

- A bolus dose of 0.5 mg/kg will be administered intravenously for induction. Maintenance doses will be given every 45 minutes, with 10 mg administered from a vial with a concentration of 10 mg/ml (1 cc).

Once adequate neuromuscular blockade is achieved, tracheal intubation will be performed by an anesthesiologist not involved in the study's allocation or assessments. Mechanical ventilation will be administered with a tidal volume of 6 ml/kg and a ventilation rate of 12-16 breaths per minute to maintain an $ETCO_2$ of 30-40. Anesthesia will be maintained with a 10-20 mg/kg/hr propofol infusion based on the Bispectral Index Score (BIS). BIS electrodes will be placed on the forehead, and the depth of anesthesia will be kept between 40 and 60. Toward the end of surgery, muscle relaxant reversal will be administered with 0.5 mg/kg neostigmine and 0.02 mg/kg atropine. To prevent postoperative nausea, 4 mg of ondansetron will be given.

The surgical team may need to modify the intervention to achieve additional muscular relaxation. When necessary, an extra dose of 2 mg of cisatracurium or 10 mg of atracurium (1 cc of each from the blinded vials) will be given. To promote adherence to the protocols, all staff members will undergo mandatory, standardized training on the protocol provided by the primary investigator. The use of any other medications needed for the participant's routine care, including intraoperative or postoperative medications, is allowed. To monitor fidelity, an anesthesiologist who is not involved in outcome assessment or patient care will observe the administration to ensure the protocol is followed correctly. Analgesia will be managed with a remifentanil perfusion of 0.5 µg/kg/min during surgery. Postoperative pain management with 1 g intravenous acetaminophen administration every 6 hours after surgery and 2-3 mg intravenous morphine every 3 hours after surgery if the patient's pain using the visual analogue scale (VAS) is ≥ 5 to address inadequate pain control.

Outcomes

The primary outcome is POD incidence from postoperative days 0 to 5, measured twice daily with the Intensive Care Delirium Screening Checklist (ICDSC), diagnosed when, at least in a single measurement, the ICDSC score is ≥ 4 [39].

The secondary outcomes measured are listed below:

1. POD severity is measured by ICDSC, which ranges from 0 to 8.
2. Postoperative cognitive function was assessed on postoperative day 5 using the Montreal Cognitive Assessment (MoCA) [40].
3. The duration of hospital stay was measured in days hospitalized after surgery.
4. Pain severity between the two groups will be compared using the VAS [41].

Harms

Harms will be systematically assessed and documented for all randomized participants from the first dose of the study drug through the end of anesthesia and into postoperative recovery. All participants will be actively monitored for known pharmacological side effects of neuromuscular blocking agents and their reversal drugs, including anaphylaxis/hypersensitivity reactions (e.g., bronchospasm, hypotension, tachycardia, flushing, urticaria), cardiovascular effects (e.g., bradycardia, tachycardia, hypotension, hypertension), and prolonged neuromuscular blockade.

Participant Timeline

Candidates for colorectal surgery will be enrolled in the study on the night before their scheduled surgery. After obtaining the participant's written consent, baseline characteristics and cognitive function (using the MoCA) will be recorded, and the intervention group will be assigned using predetermined randomization. Patients will receive the assigned intervention during anesthesia, and intraoperative data will be collected. Post-surgery, outcomes including pain (using the Visual Analogue Scale, VAS), sedation (using the Richmond Agitation-Sedation Scale, RASS), POD (using the ICDSCS) every 12 hours for 5 days, and postoperative cognitive function (using the MoCA) on the fifth day after surgery will be documented (Table 1).

Sample Size

Due to the lack of an explicit randomized trial that directly compares cisatracurium with atracurium on POD as the primary outcome in colorectal/abdominal surgery, our assumptions draw on two major factors, namely (i) RCTs in colorectal/abdominal surgeries that establish baseline POD incidence (≈32–56%) [42] and (ii) comparative studies of the two neuromuscular blockers showing hemodynamic stability and lower histamine-related effects with cisatracurium, alongside registry data linking neuromuscular blockade exposure and reversal to POD risk. Specifically, RCTs in elderly colorectal/abdominal populations report POD rates of ~32–56% (e.g., melatonin vs placebo; intraoperative BP targets), which we use to set the control-arm risk for sample-size planning.

Table 1- Study period and timetable

	Enrollment	Allocation	Post-allocation	Close-out
Time point (hours)	T_{-1}	T_0	T_{1-10}	T_{11}
Eligibility screen	X			
Informed consent	X			
Allocation	X			
Surgery		X		
Intervention				
Cisatracurium/Atracurium		X		
Assessments				
MoCA	X			
Demographic, past medical history, and medication	X			
Intraoperative data		X		
Postoperative lab values			X	X
Postoperative pain (VAS)			X	X
ICDSC			X	X

T-1 = The night before surgery, T0 = Surgery, T1 = 6 hours after the end of surgery, T2-11= Every 12 hours until day 5

Therefore, primary calculations of the sample size for POD incidence were calculated using the G*Power tool, with an $\alpha = 0.05$ and power = 0.85; a two-tailed z-test of proportions with a prevalence of 0.35 in the atracurium group and a 0.20 clinically important absolute risk reduction in the cisatracurium group; a sample of 166 was required. Given a 20% dropout rate, the total sample size was calculated to be 200 patients.

To assess the prior of an absolute 20% risk reduction, after inclusion of the first 40 patients, an interim analysis on the blinded data was done for the incidence of first-day POD, showing a prevalence of 35% (7/20) in one group (unknown) and 5% (n=1/20) in the other group (unknown), showing a higher absolute risk reduction than the prior; thus, no increase in the sample size was deemed required. This analysis was done by the research committee on blinded data to ensure an adequate sample size. To reduce type I error, the sample size was not reduced based on the newer 30% absolute risk reduction calculations.

Recruitment

A designated member of the research team will review the operating room schedules daily for all upcoming elective surgeries that meet the inclusion criteria. This will enable early identification of potential participants. Before obtaining written consent, patients will receive clear, concise brochures explaining the trial in plain language. The explanation will focus on the common use of both drugs, the importance of the research question, and the minimal additional burden involved. A screening log will be maintained to record all screened patients, their eligibility status, and the primary reasons for non-inclusion or refusal. Based on a previous feasibility study of the same colorectal surgery population, a recruitment rate of 4.7 per week is expected, allowing the team to reach the necessary sample size in six months within the study's deadline, including a two-month contingency [22].

Randomization and Blinding

The random allocation sequence will be generated online by a statistician who is not involved in participant recruitment, enrollment, or clinical management. The sequence will be created using Research Randomizer Version 4.0 (Urbaniak, G. C., & Plous, S.), without stratification, and the randomization list will be kept confidential and inaccessible to any investigators or personnel involved in the trial's conduct. The anesthesiologist responsible for administering the interventions will be blinded to the allocation and will not have access to the allocation sequence. A single unblinded researcher prepared the study drugs in each envelope throughout the study and coded the envelopes according to the randomization sequence. This investigator was not involved in patient enrollment, anesthesia implementation, intervention, data collection, or assessments. The researchers involved in patient inclusion, outcome assessment, and statistical analysis are blinded to the interventions. This protocol protects

other researchers gathering baseline, intraoperative, and postoperative data; anesthesiologists; data analysts; participants; and any other personnel involved in patient care (e.g., surgeons, nurses) from the risk of divulgence of the randomization.

Data Collection

1) Delirium assessment:

Primarily, patients' attention will be assessed using the RASS [43]. RASS is a 10-point scale with excellent interrater reliability and validity [44], showing high sensitivity (70%) and specificity (93%) for delirium detection, and will be administered before delirium assessments [45]. If patients are highly sedated (RASS = -4, 5) due to severe inattention, delirium assessment will not be performed. POD will be evaluated using the ICDSC by trained researchers blinded to the patient's intervention group. The ICDSC is an 8-point instrument with high validity and reliability, with a sensitivity of 83% and specificity of 87% in diagnosing delirium [46-47]. The first delirium assessment will be performed 6 hours after surgery to prevent confusing POD with emergence agitation. Starting the next day, assessments will be conducted twice daily, between 7 and 8 AM and 7 and 8 PM, until the fifth day post-surgery. All assessments will be carried out by medical doctors who are formally trained in the use of the RASS and ICDSC. At any time during evaluation, if the ICDSC score is ≥ 4, the patient is considered POD-positive.

2) Cognitive assessment:

Patients' preoperative cognitive function will be measured using the MoCA test on the day before surgery and reassessed 5 days after surgery to evaluate postoperative cognitive function. Assessments will be conducted by the primary investigator, who is formally certified in the use of the MoCA. If an ongoing POD remains until day 5, the patient is no longer eligible for postoperative MoCA assessment, and this will be recorded [8].

3) Lab data, preoperative cognitive function, intraoperative data, and pain:

Patients' daily lab results, including complete blood count (CBC), erythrocyte sedimentation rate (ESR), CRP, electrolytes, and hospitalization, will be recorded starting the day before surgery. Postoperative pain will be assessed using an 11-point scale (0 = no pain, 10 = worst pain) with the VAS. Intraoperative data, such as the type of surgery, duration, intraoperative morphine dose administered, and surgery-related complications, will be documented by the anesthetist.

Retention and Data Management

To reduce loss to follow-up, the research team will incorporate outcome assessments into routine clinical care. Research staff will perform daily visits for delirium screening, building rapport, and reminding participants of the study's importance. All data will be recorded on paper and then transferred to a Google Sheet. To ensure accurate data entry, validation will be completed by a different researcher by cross-checking the paper forms. Before starting statistical analysis, any out-of-range data will be identified and verified against patients' medical records. Primary analysis (ITT): The primary outcome will be analyzed under the intention-to-treat principle.

Statistical Methods

SPSS software (version 27, SPSS Inc., Chicago, IL, USA) and R software (version 4.1.2, R Core Team, Vienna, Austria) will be used for all statistical analyses.

1) Analysis of baseline characteristics:

The success of randomization will be evaluated by comparing baseline demographic and clinical characteristics between the two treatment groups. Data normality will be assessed using the Shapiro-Wilk test. Continuous data will be presented as mean ± standard deviation for normally distributed data and median (interquartile range) for skewed data. Categorical variables will be summarized as frequency (percentage). Continuous variables will be compared between the intervention and control groups using Student's t-test. Little's MCAR test will guide our missing-data strategy; a non-significant result ($p \geq 0.05$) will indicate that the data are consistent with Missing Completely at Random, whereas a significant result ($p < 0.05$) will signal deviation from MCAR and the need for additional diagnostics or alternative imputation approaches [48].

2) Primary outcome analysis:

POD prevalence (i.e., at least one positive ICDSC score) will be compared between groups using an unadjusted chi-square test. The inferential analysis will involve a logistic regression model that adjusts for the covariates (if needed). Postoperative delirium (POD) over postoperative days 1–5 will be analyzed using multilevel logistic regression (generalized linear mixed models) on day-level data. In the initial model, we will include the intervention group, time, and the intervention × time interaction as fixed effects, with a random intercept for patients to account for within-subject correlation. Subsequent models will additionally adjust for relevant clinical and demographic covariates.

3) Secondary outcome analysis:

For delayed neurocognitive recovery, a linear regression model will be used, with postoperative MoCA score as the outcome and the intervention, time, and intervention × time interaction as fixed factors, adjusted for. In the subsequent model, other relevant clinical and demographic covariates will be adjusted for. A generalized linear model with an ordinal outcome will be used to assess pain (VAS) and POD severity (ICDSC) measured 6 hours after surgery, with time and the intervention × time interaction as fixed factors; in the subsequent model, other relevant clinical and

demographic covariates will be adjusted for. A P value < 0.05 will be considered statistically significant for the primary outcome analysis. Analyses of secondary outcomes will be regarded as exploratory and interpreted with caution, focusing on effect sizes and 95% confidence intervals rather than strict statistical significance. All analyses will follow an intention-to-treat approach, including all enrolled patients. Although the primary aim of this study is not model selection, we will evaluate model performance to ensure reproducible and robust results. Competing models will be compared using changes in -2 log-likelihood and corresponding chi-square tests with appropriate degrees of freedom, as well as changes in pseudo-R^2 indices where applicable.

Monitoring

A formal Data Monitoring Committee (DMC) will not be established for this trial. This decision is based on two principles. The intervention under investigation in this study (cisatracurium) is a neuromuscular blocking agent that is a well-established drug with comparable risks and fewer cardiovascular side effects compared to atracurium [49]. Given the low-risk nature of the intervention, safety monitoring will be an ongoing responsibility of the clinical anesthesia team. All serious adverse events will be documented and reported to the relevant IRB according to their guidelines.

Ethics

The protocol and informed consent were reviewed by the Sina Hospital ethics committee (IRB) and were approved (ethics code: IR.TUMS.SINAHOSPITAL.REC.1404.055). Substantive modifications to the study protocol, including sample size, interventions, assessment duration, and study design, will be reported to the IRB ethics committee and implemented only after their approval. The trial was registered at IRCT (registration code: IRCT20250902067095N1). The conduct of this study will adhere to the Declaration of Helsinki. Patients scheduled for colorectal cancer surgery will be screened for eligibility on the night of surgery, and written informed consent will be obtained. The primary investigator, who is familiar with all aspects of the study, will inform participants of the possible risks and benefits of cisatracurium and atracurium, as well as the random assignment of participants, procedures, and the duration of assessments. If accepted, the patient and the researcher will sign the written consent in duplicate. Upon enrollment, each participant will be assigned a unique de-identified code to replace their name in all data collection forms, databases, and samples. Confidentiality will be maintained when sharing information and publishing results, with only aggregated, de-identified data being released.

Discussion

This randomized, double-blind, controlled study aims to assess the preventive effects of cisatracurium on POD compared with atracurium. To our knowledge, this is the first trial comparing these two medications on postoperative cognition. The significance of this study is that it compares two NMBAs routinely used during surgery, as they possess anticholinergic activities with different potencies, potentially leading to POD and POCD [31]. In addition to their differences in anticholinergic activity, cisatracurium has been shown to reduce histamine release and improve hemodynamic stability. Previous studies have demonstrated the detrimental effects of hemodynamic instability on postoperative cognition [50], as well as studies showing the efficacy of antihistaminergic drugs in preventing POD [51]. With previous studies showing a beneficial influence of cisatracurium on postoperative MMSE [35], their differences in potency and neurotransmitter activity prompt an investigation into the actual effects of cisatracurium on postoperative cognitive function.

This study has several potential limitations. Including patients older than 40 years, who have a medium risk of developing delirium, may dilute the effects of our comparison and result in a non-significant difference. This choice was made in accordance with the Network for Investigation of Delirium: Unifying Scientists (NIDUS) for delirium research, to include patients with a medium risk of developing delirium, as some interventions may not prevent delirium in high-risk patients [52]. Another limitation is the limited generalizability of our study's results to other types of surgery, as abdominal procedures may require higher doses of NMBAs than other procedures. For this issue, we set a predetermined maintenance dose of NMBAs, while the surgery team presumably needed a higher level of muscular relaxation. The additional doses of NMBAs will not be given using a quantitative depth-of-blockade measurement method (e.g., Train of Four), potentially resulting in variable depths of blockade due to differences in patient metabolism. We have limited our study to patients who are candidates for resection of a colorectal mass. This population encompasses various surgeries (including total or partial colectomies, sigmoidectomy, proctectomy, or any combination of them) that may have different effects on patients' postoperative conditions, including pain, inflammation, and recovery. To address this limitation, we will collect the location of the mass, the type of surgery, the use of a laparoscope, and the duration of surgery.

Conclusion

Through this study, we aim to assess the differences between two widely used NMBAs in preventing POD

and hypothesize that cisatracurium will reduce the prevalence of POD compared to atracurium.

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Author contributions

KF, PP, and PK conceived of the study. KF, ER, MN, FE, and MAM developed the protocol. KF handled ethical approval and trial registration. KF, HV, and RB planned the statistical analysis. KF, RSM, and MRK wrote the original manuscript. PP, PK, MN, MAM, HV, and FE reviewed and edited the protocol. All authors contributed to preparing this manuscript, reviewed it, and approved the final version.

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