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Development of a novel opioid-free anesthesia protocol for laparoscopic surgery

Submission date
27/11/2023

Recruitment status
No longer recruiting

Registration date
02/12/2023

Overall study status
Completed

Last Edited
24/04/2025

Condition category
Surgery

[_] Prospectively registered
[_] Protocol
[X] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Background and study aims
During the last decade, anesthesiologists have focused on opioid-free anesthesia (OFA). However, mitigating the hemodynamic response to the surgical stimulus required multimodal anesthesia that combines locoregional analgesia techniques to block nociceptive afferent neurons. This study aims to evaluate the efficacy and safety of OFA protocol employing transabdominal plane block and rectus sheath block in association with magnesium sulfate and NSAIDs in ensuring adequate intraoperative and postoperative pain control in laparoscopic abdominal surgery.

Who can participate?
Consecutive patients aged 18 years old and over who planned for laparoscopic scheduled abdominal surgery and underwent general anesthesia at Villa Sofia Hospital of AOOR Villa Sofia-Cervello in Palermo, Italy

What does the study involve?
Each patient will undergo a preoperative evaluation to evaluate anesthesiologist risk according to the ASA and sign the informed consent to be involved in the study at least 24 hours before the scheduled surgery.

Primary outcomes are postoperative pain control evaluated with a rating scale at each time-point and episodes of postoperative pain (defined as any episode with a numeric rating scale greater than or equal to 3) within 24 hours after extubation.

The secondary outcome is a composite of postoperative adverse events within the first 24 hours after extubation with mobilization recovery time and in-hospital length of stay.

Sample size
The sample size calculation was based on the postoperative rating scale score from the literature. The anticipated percentage of scores >3 postoperatively was 40%. A 50% reduction in the OFA group is considered to be clinically relevant. A sample size calculation determined that 90 patients per group were needed in the study. We aimed to recruit an additional 20% of patients for drop-out or loss to follow-up.

What are the possible benefits and risks of participating?
The benefits include a possible better control of postoperative pain and a reduction in postoperative side effects such as nausea, vomiting, constipation, itching, and drowsiness. No particular risks are foreseen in executing this anesthetic protocol; however, none are greater than those linked to a standard anesthetic protocol.

Where is the study run from?
Department of Neuroscience and Emergency with Trauma Center, A.O.O.R. Villa Sofia Cervello (Italy)

When is the study starting and how long is it expected to run for?
April 2019 to February 2023

Who is funding the study?
University Hospital Policlinico "Paolo Giaccone" of Palermo (Italy)

Who is the main contact?
Dr Giuseppe Accurso, Department of Anaesthesia, Intensive Care and Emergency, Policlinico Paolo Giaccone, Palermo, giuseppe.accurso@policlinico.pa.it (Italy)

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Opioid-free anesthesia with magnesium sulphate (OFAM) and regional parietal blocks (RPB) vs opioids inclusive anesthesia (OIA) in laparoscopic surgery. Postoperative pain control and adverse events during the first 24 hours after surgery.

Study objectives
Compare the efficacy and safety of opioid-free anesthesia (OFA) protocol with bilateral transversus abdominis plane (TAP) block versus the conventional analgesic plan with opioids. The anticipated percentage of numerical rating scale (NRS) scores >3 postoperatively was 40%. We considered a 50% reduction in the OFA group to be clinically relevant.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 13/06/2019, Palermo2 Ethics Committee (Viale Strasburgo 233, Palermo, 90100, Italy; +39 0917801111; urp@ospedaliriunitipalermo.it), ref: n° 118 AOR/29-04-2019

Study design
Monocenter interventional unblinded randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment, Safety, Efficacy

Health condition(s) or problem(s) studied
Intraoperative and postoperative pain control in laparoscopic abdominal surgery

Interventions
Intervention groups
Preoperative management:
Based on ideal body weight (IBW), patients will be premedicated with 6 ml/kg crystalloids in 30 minutes, i.m. 75 mcg clonidine, and i.v. 0.05 mg/kg midazolam in bolus. Loco-regional anesthesia of the abdominal wall is performed by expert operators: first, single-shot ultrasound-guided (USG) bilateral TAP block with the administration of 25-30 ml of ropivacaine (0.3%) for each side, in an overall volume of 50-60 ml, according to patient body mass index (BMI); finally, single-shot USG-bilateral RSB with the administration of 10 ml of ropivacaine (0.3%), for each side, in an overall volume of 20 ml, according to patient BMI. The efficacy and extension of the blocks will then be tested with a prick test after ten minutes. Five minutes before induction, a bolus of 30 mg/kg magnesium sulfate in 100 ml of 0.9% NaCl solution will be administered; after that, an intravenous infusion of 8 mg/kg/h magnesium sulfate 5% will be started.

Intraoperative management:
A continuous intravenous infusion of 90 mg ketorolac (2 ml/h) in a solution of 48 ml NaCl 0.9%

will be administered 1 hour after the surgical incision.
The continuous intravenous infusion of magnesium sulfate will be stopped 5 minutes before the end of the surgery, and an i.v. A 1 g acetaminophen bolus will be administered over 15 minutes.

Postoperative management:
1 g of acetaminophen i.v. A bolus will be administered if the numerical rating scale (NRS) score > 3 in the 24 from the end of the surgery.

Control Group
Preoperative management:
Midazolam 0.05 mg/kg i.v.

Intraoperative management:
Target-controlled infusion (TCI) i.v. (3 to 5 ng/ml corresponding to 0.1 to 0.25 μg·kg−1·min−1 of Remifentanil. I.v. bolus 1 g acetaminophen plus i.v. Ondansetron (4 mg) was administered 30 minutes before the end of surgery.

Postoperative management:
Continuous infusion (2 ml/h) with an elastomeric pump of 90 mg ketorolac and 0.1 mg/kg/h morphine will be administered in the 24-hour postoperative period.
A flipping-a-coin method will be performed for randomization (heads = control, tails = treatment) to determine the assignment of each participant.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Pain measured using a Numerical Rating Scale (NRS) in the postoperative period at the end of surgery (T0) and at 6 (T1)-12 (T2)-18 (T3)-24 (T4) hours

Key secondary outcome(s))
Composite of postoperative adverse events such as hypoxemia, defined as a SpO2 level of less than 95% with a need for oxygen supplementation; postoperative ileus, defined as an absence of flatus or stools; postoperative nausea and vomiting with the need for rescue antiemetic medication, unplanned intensive care unit (ICU) admission, mobilization recovery time and in-hospital length of stay measured using patient study records within the first 24 hours after extubation

Completion date
01/02/2023

Eligibility

Key inclusion criteria
Consecutive patients older than 18 years old who planned for laparoscopic scheduled abdominal surgery and will undergo general anesthesia

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Mixed

Lower age limit
18 years

Sex
All

Total final enrolment
379

Key exclusion criteria
1. Age below 18 years old
2. Pregnant women
3. Confirmed diagnosis of hypermagnesemia, hyponatremia, hypocalcemia, hyperkalemia
4. Acidosis states
5. Acute or chronic kidney disease
6. Hypothyroidism
7. Hypoadrenocorticism
8. Neuromuscular disorders
9. Bradycardia
10. Bradyarrhythmia
11. Atrioventricular block
12. Pacemaker
13. Heart failure associated with hypotension and reduced cardiac function
14. Shock

Date of first enrolment
01/10/2020

Date of final enrolment
31/12/2022

Locations

Countries of recruitment
Italy

Study participating centre
Department of Neuroscience and Emergency with Trauma Center, A.O.O.R. Villa Sofia Cervello.
Piazza Salerno 1
Palermo
Italy
90100

Sponsor information

Organisation
Azienda Ospedaliera Universitaria Policlinico "Paolo Giaccone" di Palermo

ROR
https://ror.org/05p21z194

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Azienda Ospedaliera Universitaria Policlinico "Paolo Giaccone" di Palermo

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated or analyzed during the current study will be available upon request from Giuseppe Accurso, giuseppe.accurso@policlinico.pa.it. These data will be shared after the publication of the paper upon request. The data are anonymous and in MS EXCEL format.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		23/04/2025	24/04/2025	Yes	No
Participant information sheet			01/12/2023	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Statistical Analysis Plan			01/12/2023	No	No