15-Feb-26

COVER LETTER

To
Protocol Registration and Results System (PRS) Team
ClinicalTrials.gov
U.S. National Library of Medicine

Subject: Clinical Trial Registration Submission

Dear Sir/Madam,

I am submitting our study titled **"Comparison of Dexmedetomidine and Dexamethasone for the Prevention of Postoperative Nausea and Vomiting in Patients Undergoing Laparoscopic Cholecystectomy: A Randomized Controlled Trial"** for registration on ClinicalTrials.gov.

This is a prospective, double-blind, randomized controlled trial to be conducted at Patel Hospital, Karachi, Pakistan. The study aims to compare the effectiveness of intravenous dexmedetomidine and dexamethasone in preventing postoperative nausea and vomiting in adult patients undergoing elective laparoscopic cholecystectomy.

The protocol follows Good Clinical Practice guidelines. Ethical approval will be obtained from the Ethical Review Committee of Patel Hospital and CPSP. Written informed consent will be obtained from all participants.

We kindly request registration of this trial and assignment of a ClinicalTrials.gov Identifier. Please let us know if further information is required.

Sincerely,
Dr. Marium Rafiq
Principal Investigator
Patel Hospital, Karachi, Pakistan

15-Feb-26

TITLE:
COMPARISON OF DEXMEDETOMIDINE AND DEXAMETHASONE FOR THE PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY; A RANDOMIZED CONTROLLED TRIAL

INTRODUCTION:

Currently, laparoscopic cholecystectomy (LC) is the gold standard for treating gallstones. It provides faster recovery, less pain postoperatively, shorter hospital stays, and a lower morbidity rate and suffering following surgery [1]. However, postoperative nausea and vomiting (PONV) is one of the most distressing symptoms that are commonly observed after laparoscopic cholecystectomy under general anesthesia [2]. PONV incidence ranges from 12-38% and sometimes as high as 70% in patients who underwent laparoscopic cholecystectomy but did not receive prophylactic antiemetic therapy. Most PONV cases are reported during the first 24 hours after laparoscopic cholecystectomy [3,4]. The most predictive factors for a higher risk of postoperative nausea and vomiting include age (less than 50 years), female gender, history of motion sickness and/or PONV, the use of opioids, exposure to volatile anesthetics, long duration surgeries, prolonged anesthesia, carbon dioxide retention, and the type of surgical procedure. Surgical techniques that manipulate the stomach and GI tract by creating pneumoperitoneum or the Trendelenburg position cause raise in intraabdominal pressure leading to an increased risk of postoperative nausea and vomiting (PONV) such as laparoscopic surgeries [5].

For the prevention and treatment of PONV, a number of pharmacological agents have been used. Dexmedetomidine is a potent and highly selective α2-adrenoceptor agonist, exhibits sedative, hypnotic, analgesic, sympatholytic and antiemetic properties [6,7]. Dexamethasone is an economical corticosteroid drug with excellent anti-inflammatory and antiemetic properties with negligible side effects [8,9]. Different studies reported the antiemetic effects of dexmedetomidine and dexamethasone for prevention of PONV after laparoscopic cholecystectomy. A study by Singh M, et al. reported the significantly low PONV score in the dexmedetomidine group as compared to dexamethasone group (2.9±1.6 Vs. 4.0±1.6) [3]. A study by Khadka B, et al. reported the 23.25% and 27.9% PONV in the dexmedetomidine and dexamethasone group respectively [10]. Another study by Bakri MH, reported the 21.0% and 28.0% PONV in the dexmedetomidine and dexamethasone group respectively [11].

Despite continuing advancement in anesthetic and surgical techniques, both the incidence and severity of postoperative nausea and vomiting is continuously increasing after laparoscopic procedures [12].

Therefore, different drugs have been used and compared for better outcomes. However, no gold standard has been established yet. Recently, the effect of dexmedetomidine on PONV has been the focus of clinical researchers. Nevertheless, controversy about the effectiveness of dexmedetomidine as compared to dexamethasone for PONV is still ongoing, for different results reported in associated literature. **No such research work has been done in Pakistan.** Therefore, to fill this gap, this study has been designed to determine the relative effectiveness of dexmedetomidine and dexamethasone in preventing postoperative nausea and vomiting following laparoscopic cholecystectomy in our population.

OBJECTIVES:

- ❑ To compare the postoperative nausea and vomiting score between patients receiving dexmedetomidine and dexamethasone after laparoscopic cholecystectomy.

OPERATIONAL DEFINITION:

- Nausea is a subjective unpleasant sensation with awareness of urge to vomit.
- Vomiting is a spasmodic contraction of abdominal wall & diaphragm muscles with forceful expulsion of gastric contents.

- **POSTOPERATIVE NAUSEA AND VOMITING (PONV):**
  It will be assessed by using Postoperative nausea and vomiting (PONV) scaling score:

PONV score	Patient response
0	Without PONV
1	Nausea without vomiting
2	Nausea with vomiting (<3 times/day)
3	Vomiting ≥ 3 times/day

ASSOCIATED FACTORS: will be assess in terms of following:

- Diabetes Mellitus: documented history of diabetes and on treatment
- Hypertension: documented history of hypertension and on treatment
- Smoking status:
  - ✓ **Smoker:** individual having smoked 100 or more cigarettes in life and smoked in last month too will be taken as smoker

- ✓ **Ex-smoker:** individual having smoked 100 or more cigarettes in life and not smoked in last month will be taken as Ex-smoker

HYPOTHESIS:

- There is difference in postoperative nausea and vomiting scores between patients receiving dexmedetomidine and dexamethasone after laparoscopic cholecystectomy.

MATERIAL AND METHODS:

STUDY DESIGN: Double blind randomized controlled trial

STUDY SETTING: The study will be conducted in the operating room, post anesthesia care unit (PACU) and in the wards at Patel Hospital, Karachi.

DURATION OF STUDY: Minimum six months after approval of synopsis by the Ethical Review Committee, Patel Hospital and College of Physicians and Surgeons Pakistan (CPSP).

SAMPLE SIZE: The sample size calculation was done using the Open EPI software for "Sample size For Comparing Two Means" by using findings of Singh M, et al. who reported the significantly low PONV score in the dexmedetomidine group as compared to dexamethasone group (2.9±1.6 Vs. 4.0±1.6) [3], by taking confidential interval 95% and power 80%, the sample size stands to be n=68 (34 in each group).

- Group A (Dexmedetomidine Group): 34 patients
- Group B (Dexamethasone Group): 34 patients

SAMPLING TECHNIQUE: Non-Probability Consecutive Sampling.

SAMPLE SELECTION:

- ➢ **INCLUSION CRITERIA:**
- ❑ Both male and female patients will be included
- ❑ Patient between the age of 18 to 60 years.
- ❑ Patient undergoing elective Laparoscopic Cholecystectomy.
- ❑ Patients with American Society of Anesthesiologists (ASA) physical status I and II.

- **EXCLUSION CRITERIA:**

- Patient not willing to participate in study.
- Patients with a history of allergy to dexmedetomidine and dexamethasone.
- Patients having motion sickness and history of PONV in past anesthesia experience.
- Patients receiving antiemetic drugs during the last 48 hours before laparoscopic cholecystectomy.
- Patients with body mass index ≥ 30 kg/m2
- Patients with emergency laparoscopic cholecystectomy.
- Laparoscopic cholecystectomy lasts for more than one hour.
- Laparoscopic cholecystectomy converting to open cholecystectomy.

DATA COLLECTION PROCEDURE:

This study will be performed after the permission of Research evaluation unit (REU) of College of Physicians and Surgeons Pakistan (CPSP) and written informed consent for the study will be obtained from the patient one day before the procedure. Trial registration number will be obtained after the approval of synopsis.

Patients admitted at Patel Hospital, Karachi for elective Laparoscopic cholecystectomy and who fulfill the inclusion criteria will be included in the study. Before inclusion the purpose, procedure, risks and benefits of the study will be explained. Confidentiality will be ensured. Demographic details of each patient including name, gender, age, smoking status, history of comorbid conditions like diabetes mellitus and hypertension (confirmed on medical records) will be obtained. Weight will be measured on a digital scale in kg without shoes and in hospital gown. Height of each patient will be measured by using stadiometer, in meters without shoes and cap. BMI of each patient will be calculated by using BMI formula (BMI=weight in kg/height in meter^2).

Patients will be allocated into two groups by computer generated randomization table with two-armed blocks of four.

The group allocation will be concealed in sealed opaque envelopes that will only be opened by the respective anesthesia resident who will be preparing and administering the drug just before the procedure.

Group A patients will receive an intravenous (IV) single dose of 1 μg/kg of dexmedetomidine, and Group B patients will receive an IV single dose of 8 mg dexamethasone after induction of anesthesia. During the procedure, patients and the data collector will be blinded to group allocation. The study drugs

will be prepared and administered to the patients by the anesthesia resident. The anesthetist providing the respective study drugs will not take part in collecting data postoperatively nor in the data analysis. Anesthesia management will be the same for both groups using standard protocols. LC will be performed according to standard protocol.

On arrival in operation theatre, standard monitoring will be applied to the patient including pulse oximeter, noninvasive blood pressure, and capnograph. After denitrogenation with 100% oxygen for 3 minutes, anesthesia will be induced with IV nalbuphine 0.1mg/kg and propofol 2mg/kg, followed by IV atracurium 0.5 mg/kg to facilitate endotracheal intubation. Patients will be ventilated with a tidal volume (VT) of 6–8 ml/kg, respiratory rate (RR) of 10–12 breaths/min, and inspiratory to expiratory ratio of 1:2. Ventilatory parameters (VT, RR) will be adjusted to maintain ETCO2 tension between 35-45 mm of Hg. Anesthesia will be maintained with a fraction of inspired oxygen (FIO2) of 0.6 using a mixture of oxygen and air with volume-controlled ventilation and isoflurane (MAC of 1.0). Atracurium will be given intermittently to maintain neuromuscular blockade. During anesthesia, all patients will receive 1 g IV paracetamol and IV lactated Ringer's solution at a rate of 10 ml/kg. They will be maintained at 2 ml/kg/h during recovery until they are able to tolerate oral fluids.

All patients will be positioned in a standard reverse Trendelenburg position (rT) during surgery with head up 30º and left lateral tilt 15º. Pneumoperitoneum will be established with carbon dioxide, and the intra-abdominal pressure will be maintained around 12 mmHg.

Upon completion of surgery, neostigmine and glycopyrrolate (2.5/0.5mg) will be given slowly IV to restart spontaneous breathing, which will be followed by tracheal extubation. Patients will be sent to the recovery room and later to their respective wards.

Postoperatively, the score of PONV will be evaluated using the PONV scaling score by the anesthesia resident blinded to both the intervention and control group at the following intervals: on arrival in the PACU (T0), at 4 h (T1), at 12 h (T2) and finally at 24 h (T3) postoperatively.

The rescue antiemetic drug (ondansetron 8mg) IV will be received by the patients reporting a high PONV score (2-3). All results will be collected and filled in proforma accordingly by the anesthesia resident.

DATA ANALYSIS PROCEDURE:

After collection of data the analyses will be conducted by using Statistical Package for Social Science (SPSS) software, Version 25.

To check the normality of quantitative data Shapiro Wilk test will be applied. Mean and standard deviation (SD) or median and interquartile range (IQR) as appropriate will be calculated for quantitative variables like age (years), weight (kg), height (m) and BMI (kg/m^2).

For qualitative variables like gender, ASA status, history of diabetes and hypertension frequency and percentages will be computed. For comparison of PONV score between groups independent T-test or Mann Whitney U test will be applied. Effect modifiers like age, gender, ASA status, History of hypertension, diabetes and BMI will be stratified to observe the effect of these on outcome. Post stratification independent T-test or Mann Whitney U test will be applied and p-value ≤ 0.05 will be considered significant.

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PROFORMA

MR No: _____

GROUP:

☐ Group A (Dexmedetomidine Group)

☐ Group B (Dexamethasone Group)

PATIENT DETAILS:

- Name: _____
- Gender: ☐ Male ☐ Female
- Age (Years): _____
- Height (m): _____
- Weight (kg): _____
- BMI (kg/m^2): _____
- Smoking: ☐ Yes ☐ No
- ASA Status: ☐ I ☐ II
- H/O diabetes Mellitus: ☐ Yes ☐ No
- H/O Hypertension: ☐ Yes ☐ No
- Postoperative nausea and vomiting (PONV) scaling score:

PONV score	Patient response
0	Without PONV
1	Nausea without vomiting
2	Nausea with vomiting (<3 times/day)
3	Vomiting ≥ 3 times/day

- on arrival in the PACU (T0) PONV score: _____
- at 4 h (T1) postoperatively PONV score: _____
- at 12 h (T2) postoperatively PONV score: _____
- at 24 h (T3) postoperatively PONV score: _____