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Efficacy of Propofol Combination with either Ketamine, Dexmedetomidine or Midazolam for Sedation during Upper Gastrointestinal Endoscopic Procedures: A Prospective, Randomized, Comparative Study

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Ain Shams University
Faculty of Medicine
Ethical Committee of Scientific research

Informed consent form for parents or guardians of patients who are invited to participate in the research

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Introduction and aim of the work:

Gastrointestinal endoscopy can be categorized as upper or lower endoscopy depending on whether the upper GI tract (esophagus, stomach, duodenum, jejunum) or lower GI tract (rectum, colon, and terminal ileum) is examined ***(Kim, 2023).***

Upper Gastrointestinal (UGI) disorders vary from esophagitis, barrett's esophagus, peptic ulcer, esophageal and/or gastric varices, gastro-duodenal erosions to gastrointestinal tumors which include esophageal and gastric tumors ***(Niimi et al., 2017).*** Such disorders may be asymptomatic or associated with symptoms such as indigestion, abdominal pain, hematemesis, acute or chronic anemia, dysphagia and excessive vomiting ***(Akdamar et al., 1986).*** Sometimes, unexpected symptoms appear suddenly with life-threatening complications ***(Stewart et al., 2014).*** These disorders require upper gastrointestinal endoscopy as a diagnostic and therapeutic procedure that allows doctors to image, assess, and treat GI illnesses ***(Kim, 2023).***

To compare the efficacy of ketamine-propofol, dexmedetomidine-propofol and midazolam-propofol combinations as procedural sedative agents for adult patients undergoing elective upper gastrointestinal endoscopic procedures.

Place of work:

Internal medicine endoscopy unit in Ain Shams University Hospitals, Cairo, Egypt.

Number and Selection of participants:

- 75 patients undergoing elective upper gastrointestinal endoscopic procedures (25 patients per group) will be needed

Plan of the work:

Consented and enrolled 75 patients will be randomly assigned to one of the following three groups:

1. **Group (D):** which is Dexmedetomidine-Propofol group (n = 25)
2. **Group (K):** which is Ketamine-Propofol (Ketofol) group (n = 25)
3. **Group (M):** which is Midazolam-Propofol group (n = 25)

A. <u>Preoperative settings</u>:

All patients will be fasting for 8 hours. All patients will have their medical and anesthetic history taken with a full physical examination. Revision of radiological images and routine investigations including CBC, coagulation profile, electrolytes, kidney, and liver profiles will be done.

B. <u>Intraoperative settings</u>:

-Standard ASA monitoring as electrocardiogram (ECG) for heart rate (beats/min), pulse oximetry for (SpO_2 as a percentage) and non-invasive blood pressure (NIBP) (mmHg), to record baseline data and follow up throughout the procedure.

- A nasal prong will be connected to the patient with an oxygen flow rate of 3 liter/min. Then, a 20 G peripheral venous cannula will be inserted and intravenous (iv) Ringer's solution 8 ml/kg/hr will be started.
- Diluted 4mg ondansetron will be given slowly iv as an antiemetic premedication.
-After positioning the patient in the left lateral position, all UGI endoscopic procedures will be performed by an accredited gastroenterologist, neither the endoscopist nor the patient know the study drugs. Anesthetic care will be provided by an accredited specialist anesthesiologist. After confirming the readiness of the endoscopist, all patients will undergo deep sedation under monitored anesthetic care (MAC) according to the assigned group:

➔ **Patients assigned to (Group D) will be injected as follows:**

Dexmedetomidine infusion syringe (50mls)**:** will be filled with 2mls of dexmedetomidine (200µg) diluted in 48 ml of 0.9% normal saline to make a final volume of 50mls and a final dexmedetomidine concentration of 4µg/ml. It will be infused as 1µg /kg/hr iv.

Propofol infusion syringe (50mls)**:** will be filled with 20mls of 1% propofol (200mg) diluted in 30mls 0.9% normal saline to make a final volume of 50mls and a final propofol concentration of 4mg/ml. It will be iv administered as 0.5 mg/kg slow iv for 10 minutes, then infused at a rate of 0.5mg/kg/hr.

➔ **Patients assigned to (Group K) will be injected as follows:**

Ketamine infusion syringe (50mls)**:** will be filled with 2mls of ketamine (100mg) diluted in 48mls 0.9% normal saline to make a final volume of 50mls to reach a final ketamine concentration of 2mg/ml. It will be administered as a bolus dose of 0.25 mg/kg iv then infused at a rate of 0.25mg/kg/hr.

Propofol infusion syringe (50mls): will be filled with 20mls of 1% propofol (200mg) diluted in 30mls 0.9% normal saline to make a final volume of 50mls and a final propofol concentration of 4mg/ml. It will be iv administered as 0.5 mg/kg slow iv for 10 minutes, then infused at a rate of 0.5mg/kg/hr.

➔ **Patients assigned to (Group M) will be injected as follows:**

Midazolam infusion syringe (50mls): will be filled with 10mls of Midazolam (50mg) diluted in 40mls 0.9% normal saline to make a final volume of 50mls to reach a final midazolam concentration of 1mg/ml. It will be administered as a bolus dose of 0.05 mg/kg iv over 2 minutes then infused at a rate of 0.025mg/kg/hr.

Propofol infusion syringe (50mls): will be filled with 20mls of 1% propofol (200mg) diluted in 30mls 0.9% normal saline to make a final volume of 50mls and a final propofol concentration of 4mg/ml. It will be iv administered as 0.5 mg/kg slow iv for 10 minutes, then infused at a rate of 0.5mg/kg/hr.

All patients will be targeted to reach a level of deep sedation defined as Ramsay sedation scale (RSS) score of ≥ 4. RSS will be assessed every 5 minutes throughout the procedure till its end. In the case of RSS score is < 4 or if the patient shows limb movement at any time within the procedure, rescue propofol doses of 20 mg iv increments will be given.

-Upper gastrointestinal diagnostic and therapeutic endoscopy will be performed by Pentax^{R} Medical EPK-i5000 High Resolution Video Process. Therapeutic gastroscopy will include variceal band ligation, and endoscopic haemostasis as injection of bleeding peptic ulcers with adrenaline or bleeders control via either argon plasma coagulation (APC) or heater probe coagulation.

-Any hemodynamic instability will be managed as per the standard guidelines. Any incidence of bradycardia (HR<50 beats/min), tachycardia

(HR > 20% of baseline values), or hypotension (MAP < 60 mmHg) will be managed by requesting the endoscopist to cease the procedure till atropine 0.01 mg/kg is given to treat bradycardia, or an extra bolus dose of propofol to increase the depth of sedation and analgesia to treat tachycardia. However, if hypotension is encountered, it will be treated by giving 250 ml of I.V. crystalloids bolus and if no improvement I.V. ephedrine 6 mg will be given.

C. Postoperative settings:

After the procedure is over and the drug infusions are stopped, patient will be transferred to the PACU and connected to Standard monitoring as electrocardiogram (ECG), pulse oximetry and non-invasive blood pressure (NIBP) (mmHg), to record data upon arrival to PACU and to calculate his modified Aldrete score at which patient will be discharged when his score is ≥9.

Benefits expected from the study:

To compare the efficacy of ketamine-propofol, dexmedetomidine-propofol and midazolam-propofol combinations as procedural sedative agents for adult patients undergoing elective upper gastrointestinal endoscopic procedures.

Conducting the consent:

The consent will be conducted to the legal guardian or the patient by the investigator, Doctor Hazem Mohamed Sabry Abdelaziz in the Anaesthesia and Intensive Care Department, Ain Shams University Hospital. Literate individuals will be left to read the consent followed by its explanation by the mentioned investigator, while illiterate individuals will have the consent read and explained to them as well.

Risks and complications:

- Any incidence of respiratory (e.g. apnea, desaturation)
- Hemodynamic compromise (e.g hypotension, bradycardia, tachycardia, arrhythmia, cardiac arrest)
- Any other adverse effects (e.g. nausea, vomiting, allergy, seizure, recovery agitation, and delayed recovery) will be managed accordingly and documented.

Reimbursements in cases of risks and complications:

Should your patient get physically injured as a result of research-related procedures, Doctor Hazem Mohamed Sabry Abdelaziz will provide first-aid medical treatment.

Alternatives to participating:

In case of refusing to participate in this research, your patient will be followed up and will receive his treatment as planned.

Confidentiality:

You will deal in complete confidentiality, and no one has right to read your patient medical information except the main researcher. After the research is complete, you will be informed regarding your patient `s research results and also further information regarding your patient `s health status.

Right to refuse or withdraw:

Any participant doesn`t have to take part in this research if he/she or want. They may also stop participating at anytime. If you have read this form and have decided to let your patient to participate in this study, please understand that your patient's participation is voluntary and you have the right to withdraw your consent or discontinue participation at any time without penalty or loss of benefits to which your patient is otherwise entitled. Your decision whether or not to participate in this

study will not affect your patient's medical care. Individual privacy will be maintained in all published and written data resulting from the study.

Contact Information:

Questions, Concerns, or Complaints: If you have any questions, concerns or complaints about this research study, its procedures, risks and benefits, or alternative courses of treatment, you should ask the investigator, Hazem Mohamed Sabry Abdelaziz at mobile number: 01006948041. If you have any problems or concerns about the study, you can also call Prof. Gihan Seif El-Nasr Mohamed the main supervisor at mobile phone number: 01001832723.

You do not have to sign this consent form. But if you do not, your patient will not be able to participate in this research study.

Certificate of consent:

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I ask have been answered to my satisfaction. I consent voluntary to participate in this research and understand that I have the right to withdraw from the research at any time without in any way affecting my patient`s medical care.

- Name of participant:
- Signature of legal guardian:
- Or participant:
- Identity number or finger print: .....
- Date:

I have accurately read or witnessed the accurate reading of the consent to the potential participant. The individual has had the opportunity to ask questions I confirm that the individual has given consent freely.

- Name of researcher: Hazem Mohamed Sabry Abdelaziz
- Signature of researcher:
- Date:

This proposal has been reviewed and approved by Ethical Committee of Scientific research, which is a committee whose task is to make sure that research participants are protected from harm.

If you wish to find more about Ethical Committee of Scientific research.
Contact:
Name:
Address:
Telephone number: