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COMPARISON OF DEXMEDETOMIDINE VERSUS KETOFOL FOR MODERATE SEDATION IN ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP): A RANDOMIZED CONTROLLED TRIAL

The protocol is approved by the ethical review committee of SIUT (CRP #: 234).

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Introduction

The utilization of endoscopic retrograde cholangiopancreatography (ERCP) for both diagnosis and treatment of pancreaticobiliary diseases has witnessed a significant surge in recent times.[1,2] Conscious sedation is routinely administered during ERCP procedures to enhance patient comfort and facilitate gastroenterologist interventions.[3,4] However, it is essential to acknowledge that sedation in ERCP carries the potential for adverse intraoperative events.[5,6] Various pharmacological agents, including midazolam, propofol, ketamine, and dexmedetomidine, are available, offering rapid induction and smooth recovery.[3-8]

Dexmedetomidine, a relatively recent addition to the pharmacological arsenal, has gained prominence as an alternative sedative in conscious sedation. It acts as a potent and highly selective α-2 adrenergic receptor agonist, demonstrating sympatholytic, sedative, amnestic, and analgesic properties.[9] Dexmedetomidine stands out for its unique ability to provide conscious sedation and analgesia without inducing respiratory depression. However, it is crucial to note the potential side effects, such as bradycardia and hypotension.[10]

Ketamine, characterized as an N-methyl D-aspartate receptor antagonist, offers sedative, analgesic, and amnestic effects without causing respiratory depression. On the other hand, propofol, a sedative-hypnotic agent, boasts a rapid onset and fast recovery time.[6]

The ERCP procedure, vital for diagnosing and managing biliary and pancreatic disorders, has become increasingly prevalent. Recognized as a complex, protracted, and uncomfortable procedure, ERCP necessitates adequate sedation and analgesia to mitigate agitation and discomfort, which have been identified as potential factors contributing to ERCP failure. Despite the escalating demand for ERCP, there remains a dearth of local and international studies comparing the efficacy of these two pharmacological agents in patients undergoing ERCP, leading to clinical equipoise. Sedation in gastrointestinal endoscopy not only alleviates patient discomfort but also enhances operator performance. This study aims to address this gap by providing current, locally relevant statistics, offering insights into the comparative effectiveness of dexmedetomidine and ketamine-propofol combination during ERCP procedures. The outcomes of this study could contribute to the refinement of management protocols, optimizing the balance between patient comfort and procedural success.

Methodology

Study design:

Randomized controlled trial.

Study setting:

Sindh Institute of Urology and Transplantation (SIUT), Karachi, Pakistan.

Study duration:

December 2021 to June 2022

Sample selection

Inclusion criteria

- Aged 20-60 years
- Any gender
- Scheduled for elective ERCP
- American Society of Anesthesiologists (ASA) classification I or II

Exclusion criteria

- Allergic to dexmedetomidine, Ketofol, or related medications
- BMI over 36 kg/m2 (morbidly obese)
- History of stroke, renal impairment, chronic obstructive pulmonary disease, asthma, chronic liver disease, hypothyroidism, and congestive cardiac failure
- Pregnant, or breastfeeding women
- Patients who reported chronic use of sedative medications or substance abuse
- Known contraindications to ERCP
- Already enrolled in another clinical trial study

Sample size

The sample size for the study will be 62, i.e., 31 in each group. The sample size will be calculated by using the Open Epi software where alpha will be taken as 5%, power of the test 1-beta 90, mean time to good recovery as 11.4±0.5 versus 12.5±1.8 [10].

Data collection procedure

A brief history of demographic data will be taken from each patient. Preoperative assessment included history, general physical examination, systemic examination, and routine laboratory investigations.

Patients will be randomly divided into two groups using computer randomization. All patients will be taken to the procedure room and venous access will be secured on a non-dominant hand by 20G IV cannula, intravenous (I/V) fluid (ringer lactate or normal saline) will be started by 8 ml/kg/h,

and oxygen support will be provided by nasal cannula at 4 liters per minute. Standard monitors will be attached for heart rate (HR), noninvasive blood pressure (systolic and diastolic), mean arterial blood pressure (MAP), and peripheral oxygen saturation SpO2. Injection midazolam 0.05 mg/kg will be also given I/V to every patient in both groups to decrease the anxiety of patients.

Patients received either Dexmedetomidine or Ketofol for sedation. All syringes and infusion sets will be covered by silver paper and these infusions will be labeled as infusion 1 or 2. In patients who receive Dexmedetomidine, a 2ml ampule of 100 ug/ml will be diluted in 18 ml of normal saline, making a total volume of 20 ml. Patients received dexmedetomidine as a bolus over 10 minutes in a dose of 1ug/kg followed by an infusion at the rate of 0.5ug/kg/hr and it will be labeled as “infusion 1”. In the Ketofol group, 2 ml ketamine (50mg/ml) and 10 ml of propofol 1% (10mg/ml) will be diluted in 8ml of normal saline. This mixture will be 20 ml each, making 5mg/ml of ketamine and propofol. Patients will receive 1mg/kg over 10 minutes followed by 50ug/kg/min of infusion, labeled as “infusion 2”.

During infusion, vitals were recorded at 0,1,3,5, and 10-minute intervals from the start, and the Ramsay Sedation scale score (RSS) was recorded every 1 minute. Both infusions were started as per the randomization of groups. The mean difference in time to achieve adequate sedation and time to good recovery were noted as outcomes in each group. In addition, complications during the procedure and recovery were also noted. Adequate sedation was defined as the time from initiation of infusion to achieve an RSS score of 4. While Modified Aldrete’s score (MAS) was used to assess the recovery. Time from discontinuation of the infusion to achieve an MAS score of 9 was labeled as a good recovery.

Statistical analysis

Statistical Package for Social Sciences (SPSS) version 26 will be used for the purpose of statistical analysis. Mean ±Standard Deviation (SD) will be computed for quantitative variables such as age, time to achieve RSS, and time to achieve MAS. Frequency and percentages will be calculated for gender, ASA status, diabetes, hypertension, smoking, cough during procedure, gagging during procedure, apnea during procedure, apnea during recovery, and post-operative nausea and vomiting. Comparison will be done to see the association of baseline characteristics, complications during procedure, and complications during recovery on the outcome. Chi-Square test will be applied. Moreover, the mean difference of time to achieve RSS and time to achieve MAS will be explored using independent t-test. The p-value of ≤ 0.05 will be considered as significant.

References

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CONSENT FORM

Research Title: Comparison of Dexmedetomidine versus Ketofol for Moderate Sedation in Endoscopic Retrograde Cholangiopancreatography (ERCP): A Randomized Controlled Trial

Principle Investigator: Dr. Syed Muhammad Abbas

Institute: Sindh Institute of Urology & Transplantation (SIUT)

1. Introduction: You are being requested to voluntarily participate in a research project described below. Please read the consent form that describes nature of the study. If you have any queries, please feel free to contact the study researcher or the study staff.

2. Purpose of the study: This study is being conducted to compare the efficacy of dexmedetomidine versus ketofol for moderate sedation in patients undergoing ERCP.

3. Confidentiality: All information collected during this study will be kept confidential. Your personal information will not be disclosed to anyone outside the research team, and your data will be anonymized to protect your privacy.

4. Risks & benefits: There are potential risks and benefits associated with both Dexmedetomidine and Ketofol. Participants may experience side effects such as drowsiness, low blood pressure, or respiratory depression. However, these effects will be closely monitored by the medical team. The benefits include effective sedation for a successful ERCP procedure.

Contact Information:

If you have any questions or concerns about the study, you can contact Dr. Syed Muhammad Abbas at +92 333 1318838.

You are welcome to contact the investigator if you have any questions.

Authorization Statement

Date: _____

I have read the conditions about the study. I know that being in this study is voluntary.
I am willing to give the blood samples for laboratory investigation for the research.

Participant Name: _____ Age: _____ Participant Signature:_____
Contact #: _____