Propofol-Dexmedetomidine versus Propofol-Ketamine for Anesthesia of Endoscopic Retrograde Cholangio-Pancreatography (ERCP)

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Abstract

The ideal method for anesthetic management during ERCP varied between deep sedation and general anesthesia with preference for general anesthesia over sedation.

Aim of the study:

To compare the effect of propofol-dexmedetomidine versus ketamine-propofol combination in patients undergoing ERCP as regard intra-procedural hemodynamic parameters (HR and MAP), total propofol consumption and recovery criteria that involved post-procedural hemodynamic parameters (HR and MAP), post-procedural pain, PONV, cognitive dysfunction Respiratory adverse events and measurement and recording of recovery time.

Material and methods:

Patients ERCP, age 20-50ys old, ASA II-III, were randomly allocated in two groups each of which was 30. **Group-I** received dexmedetomidine loading 1µg/kg slow IV over 15min then infused at a rate of 0.5µg/kg/h by syringe pump. **Group II** received Ketamine 1mg/kg slow IV over 15min then infused at a rate of 0.5mg/kg/h by syringe pump. **Both groups** received propofol**;** 1-2mg/kg induction – then 5mg/kg/h IV infusion, 0.5mg/kg boluses guided by hemodynamic parameters, atracurium 0.5mg/kg intubating dose followed by 0.1mg/kg every 20min. Cuffed ETT was inserted and CMV. By the end of the procedure, patients turned supine and reversed by administration of neostigmine (0.05mg/kg) + atropine (0.01mg/kg). Extubation was performed after fulfillment of the criteria of extubation.

Conclusion:

Dexmedetomidine-propofol combination was better than ketamine-propofol combination as regard; hemodynamic parameters (intra- and post-procedural), PONV, cognitive functions and recovery time. Incidence of pain had no clinical significant value between both groups. Total propofol consumption had no clinical significant difference between both groups.

Recommendation:

Dexmedetomidine - propofol combination as TIVA technique for ERCP requires further studies with recommendation to include; different types of patients; geriatric, critically ill and increasing the sample size of patients.

Keyword: ERCP- TIVA- PONV- PPH-SOD

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List of Abbreviations

Abbreviations	*Full term*
ABP	Arterial Blood Pressure
ACLS	Advanced Cardiac Life Support.
ACTH	Adreno-Cortico- Trophic Hormone.
ADH	Anti-Diuretic Hormone.
ALT	Alanine Amino-Transferase
ALT	Alanine Amino-Transferase.
ASA	American Society of Anesthesiologists.
ASGE	American Society of Gastro-Enterology.
AST	Aspartate Amino-Transferase
AV	AV: Atrio-Ventricular.
α.....	Alpha
BP	Blood Pressure.
β	Beta
c-AMP.....	cyclic-Adenosine Mono-Phosphate.
CBF	Cerebral Blood Flow.
CMRO2	Cerebral Metabolic Rate for O2 consumption.
CNS	Central Nervous System
COP.....	Cardiac Output
CSF	Cerebro-Spinal Fluid
CT	Computed Tomography
ECG	Electro-Cardio-Graphy
EEG.....	Electro-Encephalo-Graphy
ERCP	Endoscopic Retrograde Cholangio-Pancreatography.
ETT	Endo-Tracheal Tube.
EUS	Endoscopic Ultra-Sound.
GA	General Anesthesia**.**
GABA	Gamma Amino-Butyric Acid.

List of Abbreviations

Abbreviations	*Full term*
GI	Gastro-Intestinal.
GIT.....	Gastro-Intestinal Tract.
h.....	Hour
H2.....	Histamine receptor type 2.
HBF.....	Hepatic Blood Flow.
HPS	Hepato-Pulmonary Syndrome.
HR.....	Heart Rate.
HRS.....	Hepato-Renal Syndrome.
ICP	Intra-Cranial Pressure.
IgG	Immuno-globulin G.
IM.....	Intramuscular.
INR.....	International Normalized Ratio.
IOP.....	Intra-Ocular Pressure.
IV.....	Intravenous.
IVC.....	Inferior Vena Cava.
LFTs.....	Liver Function Tests.
Log	Logarithm.
LT.....	Left.
MAP.....	Mean Arterial Pressure.
MELD.....	Mortality in End Stage Liver Disease without liver transplantation.
MRCP.....	Magnetic Resonance Cholangio-Pancreatography.
MRI.....	Magnetic Resonant Image.
NMDA	N-methyl-D-Aspartate.
NPO.....	NPO: Nothing Per Os.
NSAID	Non Steroidal Anti-Inflammatory Drugs.
PACU.....	Post-Anesthesia Care Unit.
PADS	Post-Anesthesia Discharge Scoring System.

List of Abbreviations

Abbreviations	*Full term*
PEEP.....	Positive End Expiratory Pressure.
PEP	Post-ERCP Pancreatitis.
PONV.....	Post-Operative Nausea and Vomiting.
PPH.....	Porto-Pulmonary Hypertension.
PSA	Procedural Sedation Analgesia.
PT.....	Prothrombin Time.
P-value.....	Probability value.
QT-c.....	QT interval corrected to heart rate.
R	Rectus.
RA	Regional Anesthesia.
RT	Right
S.....	Sinister
SA.....	Sino-Atrial.
SD.....	Standard Deviation.
Sec	Second
SOD.....	Sphincter of Oddi Dysfunction.
SPO2	Oxygen saturation in pulsating blood flow.
SPSS.....	Statistical Program for Social Science.
TIPS	Trans-jugular Intra-hepatic Porto-systemic Shunt.
TIVA.....	Total Intravenous Anesthesia.
UOP.....	Urine Output.
US.....	Ultra-Sonography.
V/Q.....	Ventilation/ Perfusion.
VAS.....	Visual Analogue Scale.
Vd.....	Volume of distribution.

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INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) plays a crucial role in the diagnosis and treatment of pancreaticobiliary pathologies and its use has increased in recent years. It is performed orally via an endoscope. It takes longer time and more complex to perform than other parallel procedures. It is extremely painful and irritating procedure when conducted without anesthesia. To ensure immobility, sufficient analgesia and the avoidance of coughing, gagging or nausea, patients should be deeply sedated or anesthetized and monitoring should be performed while undergoing ERCP procedures ***(1).***

In general, most of endoscopic procedures are done under moderate sedation. The target level of sedation and the agent chosen will depend on *the characteristics of endoscopic procedures* (the degree of invasiveness, level of procedure-related discomfort or pain, the need of patients to lie relatively motionless and the duration of the procedure), *patient's factors* (age, co-morbidities, anxiety and patient preference) and *the need for patients cooperation.* Deep sedation or GA should be considered for patients who have been difficult to manage with moderate sedation and are anticipated to be poorly responsive to sedative; this includes patients who have a long term use of narcotics, benzodiazepines, alcohol, or neuropsychiatric medications ***(1).***

In fact, most complications in GI endoscopy are related to sedation; include cardiopulmonary events such as hypoxemia, hypoventilation, airway obstruction, apnea, arrhythmia, hypotension, and vasovagal episodes ***(2)***. ***Raymonds and his colleagues (2006) (3)*** supported a continued preference for GA rather than conscious sedation for ERCP especially when a complex and painful interventions are planned in prone position.

Dexmedetomidine, is a stereoisomer of medetomidine, was approved by Food and Drug Administration at the end of 1999 for use in human as a short term medication (< 24h). It is a highly selective α2-agonist; eight times higher specificity for receptors compared to clonidine ***(4)***. Dexmedetomidine has a perioperative sedative, analgesic and anxiolytic properties similar to benzodiazepines but it has less side effects and better hemodynamics ***(4).*** Dexmedetomidine provides analgesia with ceiling effect at doses > 0.5µg/kg thus this effect is not dose-dependent ***(5).*** Patients receiving dexmedetomidine experienced modest, dose-dependent impairment of short term memory. Dexmedetomidine is not a powerful anti-emetic. Dexmedetomidine has been shown to cause much less respiratory depression than other sedatives. However, co-administration of dexmedetomidine with other anesthetic agents, sedatives, hypnotics, or opioids is likely to cause additive effects ***(4).*** Dexmedetomidine attenuates, but not completely abolishes, stress-induced sympatho-adrenal responses protecting the patients from noxious sympathetic stimulation and hemodynamic changes which is one of anesthetic goals ***(6).*** It is necessary to monitor ABP even after discontinuation of dexmedetomidine as its infusion has induced long lasting decrease in mean arterial blood pressure (MAP) in healthy volunteers with a maximum decrease of 14% for 0.25µg/kg and 16%for 0.5µg/kg at 60min after discontinuation ***(7).*** No study has described the long term use of dexmedetomidine but adaptive changes and withdrawal syndrome like those seen with clonidine can be expected from dexmedetomidine ***(6).***

Propofol is a non-barbiturate sedative hypnotic, its popularity as a procedural sedation analgesia (PSA) agent is growing rapidly due mainly to its favorable pharmacokinetic profile as the lipid solubility confers a quick onset and short recovery time. It has also the advantages of functioning as an

anti-emetic, anticonvulsant, antipruritic and amnestic agent. Although it is extremely effective and potent, propofol use is limited by a relatively high incidence of dose-dependent hypotension and respiratory depression ***(8)***.

Ketamine is a phencyclidine derivative. It is unique in that it is a dissociative anesthetic. It provides excellent amnesia and analgesia and preserves muscle tone, maintaining airway reflexes and spontaneous respiration. Despite its obvious advantages over other agents, some practitioners are hesitant to use ketamine alone secondary to its propensity to cause vivid and frightening emergent reactions; additionally significant adverse effects including; sympathomimetic effects and vomiting and excessive salivation even when administered in sedating doses ***(9).***

It is postulated that combining propofol-ketamine may preserve sedation efficacy while minimizing their respective adverse effects. This is due partly to the fact that many of the aforementioned potential adverse effects are dose-dependent and when used in combination the doses administered of each can be reduced. Also, the CVS effects of each are opposing in action, thus theoretically balancing each other out when used together. The theoretical advantages of this combination produce more stable hemodynamic and respiratory profile that were tested and found to be true in group of healthy volunteers receiving GA ***(10)***. Effectiveness of the two agents in combinations has been recently demonstrated and this new combination could allow a novel induction agent with favorable effect on hemodynamic. To date, this combination is known as ketofol has not yet been standardized as an induction agent ***(11).***

OBJECTIVES AND AIM OF THE WORK

This study was performed to compare the effects of propofol/ dexmedetomidine versus propofol/ketamine combinations for anesthesia of patients undergoing ERCP as regard intra-procedural hemodynamic parameters in the form of heart rate (HR) and mean arterial pressure (MAP), total propofol consumption by the end of the procedure, as well as, recovery criteria that included post-procedural hemodynamic parameters in the form of HR and MAP, pain, post-procedural nausea and vomiting, cognitive functions and post-procedural respiratory adverse events; in the form of apnea, labored breathing and desaturation arterial; O2 saturation (SPO2) < 94% on room air. Recovery time was also recorded and compared between both groups.

DEXMEDETOMIDINE

Alpha-2 agonists have several beneficial actions during the perioperative period. They decrease sympathetic tone, with attenuation of neuroendocrine and hemodynamic responses to anesthesia and surgery reduce anesthetic and opioid requirements and cause sedation and analgesia. They allow psychomotoric function to be preserved while letting the patient rest comfortably. With this combination of effects, α2 agonists may offer benefits in the prophylaxis and adjuvant treatment of perioperative myocardial ischemia. Furthermore, their role in pain management and regional anesthesia is expanding ***(12).***

Dexmedetomidine, a stereoisomer of medetomidine, was approved by the FDA at the end of 1999 for use in human as a short term medication (< 24h) for analgesia and sedation in the ICU. Its unique properties render it suitable for sedation and analgesia during the whole perioperative period ***(13)***.

Physiology of the α2 receptor:

Adrenergic receptors were originally differentiated into α and β receptors on the basis of the rank order of potency of various natural and synthetic catecholamines in different physiologic preparations. It was believed that activation of either α- or β- adrenergic receptors produced excitatory affects in some tissues and inhibitory effects in others. Later a subclass of α adrenoceptors was discovered that regulates the release of neurotransmitters. From this it was inferred that the receptors are located at a pre-synaptic site. However, classification of the receptors on the basis of anatomic location alone is a problematic, because α2 receptors have been also been found at the post-synaptic and extra-synaptic sites. Pre-synaptic α2