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Original Research Article

Comparison of etomidate and propofol for moderate sedation during ERCP: A randomized clinical study

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ABSTRACT

Introduction: Endoscopic retrograde cholangio - pancreatography (ERCP) is the solution to many biliary problems from a diagnostic solution to complex therapeutic interventions. Etomidate is considered safe as an induction agent in hemodynamically unstable patients and can be considered as an alternative to propofol. In this study, we compared etomidate with propofol during ERCP in respect of hemodynamic stability and early recovery of patients.

Materials and Methods: The study was randomized, double blinded, comprising of 60 patient i.e 30 patients in each group undergoing therapeutic ERCP. In the procedure room, standard monitoring was done. All patients received loading dose of dexmedetomidine 10 min before initiation of the procedure. After 10 min group P(Propofol) patients received inj propofol bolus dose (2mg/kg/min)) and then infusion of propofol at 100- 150mcg/kg/min group E(Etomidate) patients received inj etomidate (0.3mg/kg/min) and then infusion of etomidate started at 8- 10mcg/kg/min. Depth of sedation was measured by using Ramsay sedation score.

Results: Requirement of rescue analgesia was more in group E (P=0.002) and recovery was also prolonged in group E (P=0,001). Changes in heart rate and mean arterial pressure from baseline was more in group P than group E. Patient and gastroenterologist satisfaction score was more in group P as compared to group E.

Conclusion: Etomidate can be a good alternative in hemodynamically unstable patient in comparison to propofol although etomidate group patients required more rescue analgesia and had prolonged recovery.

1. Introduction

Endoscopic Retrograde Cholangiopancreatography (ERCP) is a challenging procedure, as it requires moderate sedation, mostly done outside the operation theatre, position of patient is mostly prone, lengthy procedure and both shared the same airway.[1] The patient's clinical stability during the procedure was of utmost importance.[2] It should ensure complete immobility, sufficient analgesia, and it should avoid any complications such as perforation or peritonitis during the procedure.[3] Airway reflexes should be maintained and patent while giving drugs for moderate sedation and proper monitoring should be done throughout.[4] ERCP procedures (diagnostic or therapeutic) include bile or pancreatic duct as papillotomy and dilatation of ampulla of vater, some procedure was lengthy also as implantation of the stent, stone removal, and lithoytripsy. According to the duration of the procedure, the method of anesthesia was decided whether required moderate sedation, deep sedation, or general anesthesia.[1] Dexmedetomidine, a newer drug that is used for conscious sedation. It is a potent α-2 adrenergic agonist. It is sympatholytic, duration of action is short, can be used for sedation, amnesia, analgesia and to relieve procedure-related anxiety.[5] It has a unique and peculiar property of conscious sedation in which the patient appears to be asleep but can easily arousable with no respiratory depression and blood pressure response is also dose- dependent.[6] Etomidate is a non-

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barbiturate, carboxylated imidazole hypnotic that induces anesthesia in the central nervous system through its action on $GABA_A$ receptors[7] and it is considered safe for unstable cardiovascular patients who are at high risk even for moderate sedation. Propofol is a non-opioid, non-barbiturate, sedative-hypnotic with fast onset and short duration of action with prompt recovery. But it has some unenviable properties like cardiovascular and respiratory depression.[8] Another drug, Ketamine (used as a rescue drug) is an NMDA receptor antagonist, phencyclidine derivatives which produce dissociative sedation. It causes amnesia and analgesia but its use as a single sedative agent is not advocated due to its emergence reactions.[9]

In our study, we compared the etomidate and propofol as regards of hemodynamic, sedation, recovery time, patient and gastroenterologist satisfaction and complications during the procedure.

2. Methods and Materials

The study was approved by Ethical Committee of Mahatma Gandhi Medical College and Hospital before its start. It was a randomized double-blinded study comprising 60 patients i.e.,30 patients in each group of ASA grade I-III, aged 18-70 years, weight 45-90 kg and posted for an elective procedure. Written and informed consent was obtained from all patients who were undergoing the procedure. Patients who had adrenocortical insufficiency were using sedative or opioid for analgesia, had allergy to any of the study drug, history of heart failure (ejection fraction $<$ 50%) patients, or of severe respiratory disease were not included in the study. A detailed pre- anesthetic check-up was done before the procedure which included a general and systemic examination and all routine laboratory tests including hemogram, coagulogram, and biochemical indices. The gasteroenterologist, anaesthesiologist and their assistant all were blinded to the grouping.

In the procedure room, standard 5 leads ECG, non-invasive blood pressure and pulse oximetry, heart rate (HR) was attached and continuous monitoring of vital parameters was done. Venous access of 20G cannula was secured on the dorsum of the non-dominant hand. Oxygen was administered by using nasal catheter at a rate of 5 l/min throughout the procedure. ERCP was done in the prone position in all patients without tracheal intubation as our institution protocol.

Baseline parameters were noted after the positioning of the patient in every 5 min throughout the procedure. Then, before initiation of the procedure all patients received a loading dose of dexmedetomidine 1mcg/kg iv over 10 min. After 10 min patients received 2mg midazolam, 1 mg butorphanol, loading dose of etomidate (E) i.e. 0.3mg/kg and infusion of etomidate started at 8-10 mcg/kg/min in group E and in propofol (P) group loading dose of 1.5mg/kg and infusion started at 100-150mcg/kg/min. The level of sedation was assessed at 1-3min interval and the procedure was started when Ramsay sedation score (RSS) of 4 was achieved and time to achieve RSS of 4 was noted. All emergency drugs and equipments were available in the procedure room. An HR less than 50 bpm or a decrease of 20% from the baseline was considered as bradycardia, whereas an HR more than 110 bpm or an increase of 20% from the baseline level was considered as tachycardia. If mean arterial pressure (MAP) becomes less than 60 mmHg or get lowers down by 20% from the baseline was regarded as hypotension and if MAP increases over 150 mmHg or more than 20% from the baseline was regarded as hypertension. The patient was considered desaturated when SpO_2 level dropped below 92% for more than 10 seconds. Ketamine was given when the patient restrains three or more times during the procedure or patient or endoscopist became uncomfortable while performing the procedure. It was given in top- up incremental dose of 10 mg until the patient again reached RSS 3-4 and endoscopist became comfortable. When myoclonus occurred in group E patient, immediately 50-100 mg bolus of propofol was given and was taken on the infusion of propofol for anesthesia maintenance for the remaining procedure.

The patient's satisfaction was assessed by (1=unacceptable, 2=extremely uncomfortable, 3=slightly uncomfortable, 4= no discomfort). The gastroenterologist's satisfaction was assessed immediately after ERCP as (1=poor, 2=fair, 3=good, 4=excellent(R). Complications that were observed during the procedure were respiratory depression, allergies, coughing, gagging, nausea, and vomiting.

In the recovery room, all patients were observed before discharge for Modified Aldrete Score (MAS) and vital parameters recorded in every 5min by Anaesthesiologist along with any adverse effects. When patient achieved MAS of 9-10, were discharged from the recovery room.

2.1. Statistical analysis

The data was coded and entered into a Microsoft Excel spreadsheet. The analysis was done using SPSS version 20 (IBM SPSS Statistics Inc., Chicago, Illinois, USA) Windows software program. Descriptive statistics included computation of percentages, means, and standard deviations. The independent t-test (for quantitative data within two groups), paired t-test (for quantitative data to compare before and after observations) and repeated measures analysis of variance (ANOVA) [for quantitative data within three groups] was used for quantitative data comparison of all clinical indicators. Chi-square test used for qualitative data whenever two or more than two groups were used to compare. Level of significance was set at $P \leq 0.05$.

3. Results

There was no statistically significant differences in either the demographic data or the baseline vitals in both the groups. It was noted that in both the groups systolic blood pressure (SBP) (Figure 1) significantly decreased after dexmedetomidine infusion and remained decreased significantly from baseline till the time of probe insertion but in group P decrease in SBP is more at 5 min, 10 min and 15 min whereas, in group E SBP remain more stable as compare to group P.

In diastolic blood pressure (Figure 2) also significant change after dexmedetomidine infusion in both the group but in group P it fall more at 5 min, 10 min, and 15 min but remained close to baseline in group E and same changes occurred with mean arterial pressure (MAP) (Figure 3). Because of changes in heart rate, group E remained more stable as compared to group P.

Patient satisfaction score (Figure 4) was high in group P as 8 patients had no discomfort while in group E only 2 patients had no discomfort. 20 patients in group P and 22 patients in group E had slight discomfort during the procedure. Gastroenterologist satisfaction (Figure 5) was also excellent in group P in comparison of group E

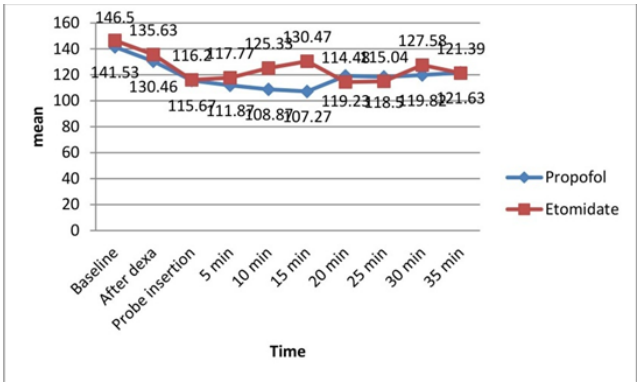

Fig. 1: Thechange in Systolic Blood pressure from baseline

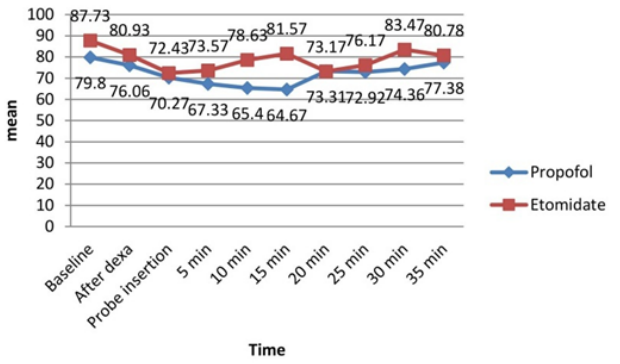

Fig. 2: The change in DBP from baseline

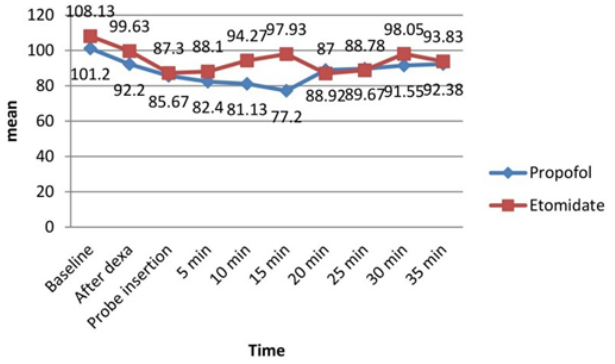

Fig. 3: Change in MPB from baseline

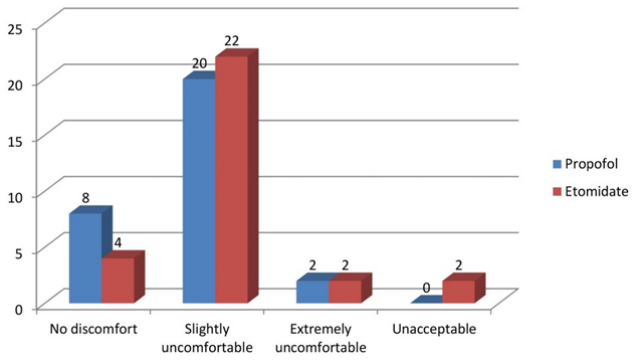

Fig. 4: Patient satisfaction was more or less similar in both groups

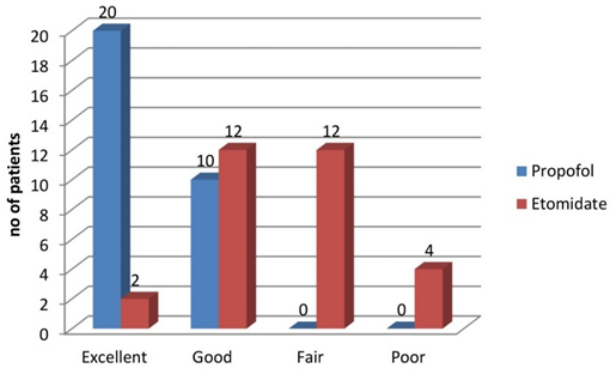

Fig. 5: Gastroenterologist satisfaction was also excellent in group P as compared to group E

4. Discussion

In our study, we compared etomidate and propofol on hemodynamic stability, fastest recovery and patient and gastroenterologist satisfaction score during the procedure. In our institute, ERCP was done in the prone position without tracheal intubation in all patients and this position is also favorable to a gastroenterologist for performing the procedure. But, as we all know that prone position inhibits breathing by obstructing the airway and makes

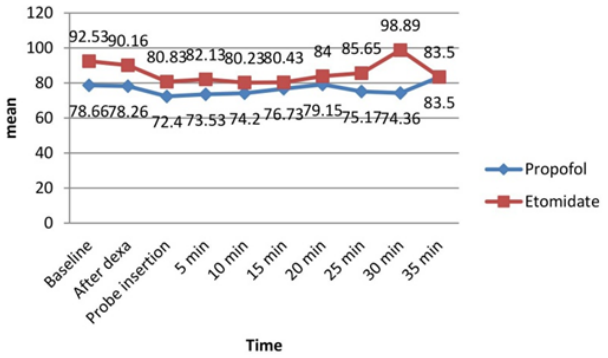

Fig. 6: The change in heart rate from baseline

intubation difficult for anaesthesiologist and it also hampers the venous return. Therefore, one must watch for hypoxia and hypotension under moderate sedation without tracheal intubation. We all know that ERCP is a complex procedure which requires moderate sedation or general anesthesia[10] for patients stability in the prone position and to relieve anxiety, discomfort, and pain. While considering all we had to maintain patient's airway reflexes and maintain cardiovascular and respiratory stability.[11] Before the initiation of the procedure patients in both the groups received dexmedetomidine for sedation and analgesia.

Among gastroenterologist, propofol is considered as a better induction agent with fast onset and early recovery with fewer side effects so it has more acceptance for short procedures.[12–14] Propofol was administered by using target-controlled infusion system as it is quite safe and effective for ERCP like short procedures.[15] In guidelines of sedation and anesthesia in GI endoscopy it was mentioned that sudden and transient hypotension occurred in 4% to 7% of cases using propofol sedation and hypoxia occurred in 3% to 7% of cases.[16]

Etomidate may be viewed as an alternative to propofol for the i.v. induction agent especially for the hemodynamically unstable patient. It s onset of action is rapid, reaches its peak level within 1 minute and duration is of 3-5 minutes. According to Miller's Anaesthesia "The properties of etomidate i.e., hemodynamic stability, minimal respiratory depression, cerebral protection and pharmacokinetics enabling rapid recovery after a single dose.[17] It lacks the effect on sympathetic nervous system and baroreceptor so may due to this it is more hemodynamically stable.[18]

Patients are more prone to develop hypotension and bradycardia suffering from obstructive jaundice than as compared to non-jaundice patient during induction and maintenance of anesthesia.[19,20] These patients had decreased sensitivity for the sympathetic and vagal components of the baroreflex.[21] Reich et al. Suggested that "etomidate can be used as an alternative to propofol to induce patients older than 50 years of age with ASA physical status >III to avoid severe hypotension."[22]

The common side effect of etomidate as myoclonus, which occurred in 20% to 45% of the patients in the Falk review.[23] Miner et al. compared etomidate and propofol in their randomized clinical trial and noted a 20% incidence of myoclonus.[24] Jin-Chao Song et.al noted myoclonus in only one patient in their study.[10] In our present study, two patients suffered myoclonus during the procedure, both required 50 mg i.v propofol bolus and a brief period of mask ventilation was done and then the patient was shifted to propofol infusion for the rest of the procedure. Premedication with midazolam in all patients reduces the incidence of myoclonus.[25,26] The incidence of myoclonus was less in our study as compared to other studies because we used midazolam (2mg i.v.) and dexmedetomidine 1mcg/kg in each patient and we delivered etomidate at a rate of 8-10 mcg/kg/hr which is very slow compared to other studies and this slow delivery speed might have reduced the incidence of myoclonus.

In group P two patients had nausea and vomiting whereas in group E no patient had such complaint. In Vinson's study it was noted that 4% of patients (5 of 134) had nausea and vomiting.[27] The second well- known side effect of etomidate is its adrenocortical suppression property.[28] One limitation was not able to measure the adrenocortical hormone level as it was not cost-effective for every patient. Etomidate was used in ASA I-III in our study while Komatsu evaluated it in class III-IV.

We concluded that etomidate is more hemodynamically stable as compare to propofol and can be safely used in ASA I-III patients. So, etomidate can be a better alternative to propofol in such patients.

5. Source of Funding

None.

6. Conflict of Interest

The authors declare no conflict of interest. The study complies with current ethical consideration.

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