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A Prospective Comparitive Study of Ketamine-Propofol versus Fentanyl-Propofol for Monitored Anesthesia Care of Patients Undergoing Endoscopic Retrograde Cholangiopancreaticography

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Abstract

Introduction: *Endoscopic Retrograde Cholangiopancreatography (ERCP) is a diagnostic and therapeutic procedure that involves the manipulation of an endoscope through the duodenum. Anaesthesia for this procedure should be balanced to minimize movement during the procedure and maintain airway patency to prevent obstruction and respiratory failure. This study was conducted to evaluate the efficacy of a propofol-ketamine infusion compared to a propofol-fentanyl infusion to provide adequate anaesthesia while undergoing an ERCP and to assess the safety of propofol-ketamine infusion during the procedure.*

Materials and Methods: *A total of 60 patients were selected and randomly divided into two groups of 30 each. Group A received a propofol-ketamine infusion and group B received a propofol-fentanyl infusion. The efficacy of the combination was assessed in terms of hemodynamic stability, depth of sedation, patient satisfaction, and airway complications during the procedure.*

Results: *There is no significant difference in the hemodynamic variables between the two groups. Propofol consumption is more in group B (209.7 ± 20.254) as compared to group A (183.7 ± 25.118). Patients in Group A required minimal airway intervention for desaturation. Patient satisfaction is better in group A as compared to group B. In group A the recovery time was 4 ± 1.066 as compared to 5.3 ± 1.061 in group B which is statistically significant.*

Conclusion: *The propofol-ketamine infusion provides better patient satisfaction, early recovery time, and minimal airway obstruction when compared to propofol-fentanyl infusion.*

Key words: *Endoscopic retrograde cholangiopancreatography, Propofol-ketamine, Propofol-fentanyl.*

Abbreviations: *ASA- American society of anaesthesiology; BMI- body mass index; BP-blood pressure; ECG- electrocardiogram; ERCP-Endoscopic Retrograde Cholangiopancreatography ; HR- Heart rate; IM-intramuscular; IV-intravenous; Kg- kilogram ; MAP- mean arterial pressure; Mg- milligram; ml-millilitre; Mcg-microgram; Min-minute; Spo2-oxygen saturation.; SD-standard deviation.*

1. INTRODUCTION

Endoscopic Retrograde Cholangiopancreatography (ERCP) is a diagnostic and therapeutic procedure that involves the manipulation of an endoscope through the duodenum to examine and treat ailments of the bile and pancreatic ducts. This is an uncomfortable procedure requiring sedation, analgesia or even general anesthesia to increase patient tolerance and cooperation1,2. ERCP is performed in endoscopy suite and sedation is challenging due to patient positioning, sharing of the airway, and deep sedation requirements for sphincterotomy. Many sedatives like benzodiazepines, propofol, and fentanyl have

been used previously. Propofol, alone or combined with opioids was frequently used for ERCP3 with good tolerance but produced complications like cardiorespiratory compromise4. Ketamine provides better sedation and analgesia, but its use was limited because of emergent reactions5, sympathetic drive, and vivid dreams. A ketamine and propofol combination provide stable hemodynamics and an adequate depth of anesthesia with minimal respiratory complications6. This study aims tocompare the sedative effects of propofol-ketamine and propofol-fentanyl for the patients undergoing ERCP.

1.1 Aims and Objectives

The study aims to compare the sedative and analgesic effects of the ketamine-propofol combination compared to the fentanyl-propofol combination for patients undergoing Endoscopic Retrograde Cholangiopancreatography. The objectives of the study were to compare the two combinations concerning hemodynamic indices (HR, BP, MAP, and SPO2), propofol consumption, patient satisfaction, sedation related adverse effects, and recovery time from anaesthesia.

2. Materials and Methods

This prospective comparative double-blind study was conducted on 60 ASA I and II patients between the ages of 18 and 70 of both sexes, undergoing ERCP from August 2017 to July 2018. The patients were divided into 2 groups of 30 each with Group A receiving propofol and ketamine while Group B received propofol and fentanyl. The exclusion criteria for the study were as follows: age <18 or >70, ASA III or IV, allergy to the drugs, pregnant or lactating patients, and those refusing to take part in the study.

After getting ethical clearance and written informed consent, the patients underwent preoperative assessment and basic laboratory investigations. The patients were randomly allocated into 2 different groups on the day of the procedure by a computerized method. After a pre-anaesthetic evaluation, the patients were shifted to the endoscopy suite and premedicated with 40 mg pantoprazole (IV), 4 mg ondansetron (IV), and 0.2 mg glycopyrrolate (IM) 30 minutes before the procedure. The pulse oximetry probe, ECG leads, and blood pressure cuff was connected to the patient, and oxygen was administered by the nasal oxygen cannula at 4 litres per minute. The drug infusions were prepared by the staff nurse as per the written orders. The anaesthesiologist was blinded to the randomization process and the study drug. When the gastroenterologist was ready with an endoscope a bolus of 3ml drug from the infusion was administered and infusion started according to BMI and depth of sedation.

Infusion preparation: In a 50ml syringe, a mixture of propofol-fentanyl or propofol-ketamine was prepared using an aseptic technique for delivery via an infusion pump. The combination of propofol-fentanyl was prepared using 40ml of propofol (1%) mixed with 10 ml of normal saline. This yielded 8 mg of propofol per millilitre. For the combination of propofol-ketamine 40ml of propofol (1%) mixed with 2ml of ketamine (50mg/ml), and 8ml of normal saline, yielding a propofol - ketamine mixture with 8 mg of propofol and 2 mg of ketamine per millilitre.

For Group A patients, the propofol and ketamine infusion started at 50 mcg/kg /min and titrated according to the level of sedation. For Group B Patients abolusdose of fentanyl 1.5mcg/kg was given before the procedure. Propofol infusion started at 50 mcg/kg/min and then tailored according to the depth of sedation.

The heart rate, mean arterial pressure, and oxygen saturation were monitored continuously. A Spo2 of less than 94 was considered as desaturation for which airway interventions like jaw thrust and chin lift were done to improve oxygenation along with halting or reducing the infusion according to the depth of sedation. A MAP below 20% of the baseline was considered as hypotension while a heart rate below 50 beats per minute was considered as bradycardia and treated accordingly. Sedation was assessed by the Ramsay sedation scale with a score of 5 indicating an adequate depth of sedation. The patient was monitored in the recovery room after the procedure where the time taken to achieve an Aldrete score of 9 after stopping the infusion was considered as the recovery time.

The safety of the sedation regimen during the procedure was assessed with episodes of desaturation <94%, the requirement for airway intervention, and events of post-operative nausea and vomiting. The efficacy of the sedation regimen was assessed in terms of the total propofol consumed, the number of propofol boluses required, the time taken to respond to verbal command post-procedure, the

time taken to recovery post-procedure and the overall satisfaction of endoscopists and the patient. While the 5-point and 0-point Likert scale was used to measure patient and endoscopists' satisfaction respectively, the post-procedure pain was assessed by a 10-point visual analogue scale.

3. Statistical Analysis

The sample size was calculated by using formulae n = [2σ2*(Zα/2+Zβ)2]/d2. Where Zα/2 is the critical value of the normal distribution at α/2 (e.g. for a confidence level 95%,α is 0.05 and the critical value is 1.96), Zβ is the critical value of the normal distribution at β (e.g. for a power of 80%, β is 0.2 and the critical value is 0.84) σ2 is the population variance, and d is the difference you would like to detect. The data collected was entered in Microsoft Excel and Statistical analyses were performed using the Statistical Package for Social Science (SPSS ver 18.5) software. The results were presented in tables and figures. In our study the proportions were compared using the Chi-square test of significance. The student't' test was used to determine whether there was a statistical A P-value of less than 0.05 was taken to be statistically significant. The two groups were compared in terms of mean age, gender, weight, BMI, ASA Grade, and mean blood pressure.

4. Results

A total of 60 patients were included in the study and divided randomly into 2 groups with 30 each in the propofol-ketamine and propofol-fentanyl arms. There was no statistical difference between the groups in terms of mean age, gender, weight, BMI, ASA Grade, and mean blood pressure. The characteristics of the study population was given in Table1.

Table 1: *Characteristics of the study population*

	AGE in years	**GENDER**		**ASA**		**BMI**
		MALE	FEMALE	1	2	
GROUP A	48.8 ± 7.804	17	13	16	14	22.5±1.1994
GROUPB	50.2 ± 7.718	20	10	14	16	22.4±1.8118.
P VALUE	0.488	0.426		0.606		0.854
ASA – American society of anesthesiology, BMI- body mass index, p value < 0.05 is significant						

The mean heart rate was significantly higher in group a compared to group B at intervals of 5, 10, 15, 20, and 25 minutes, as shown in figure 1 because of the sympathomimetic effect of ketamine. Since the increase in the heart rate is not more than 20% of baseline value it does not require pharmacological treatment.

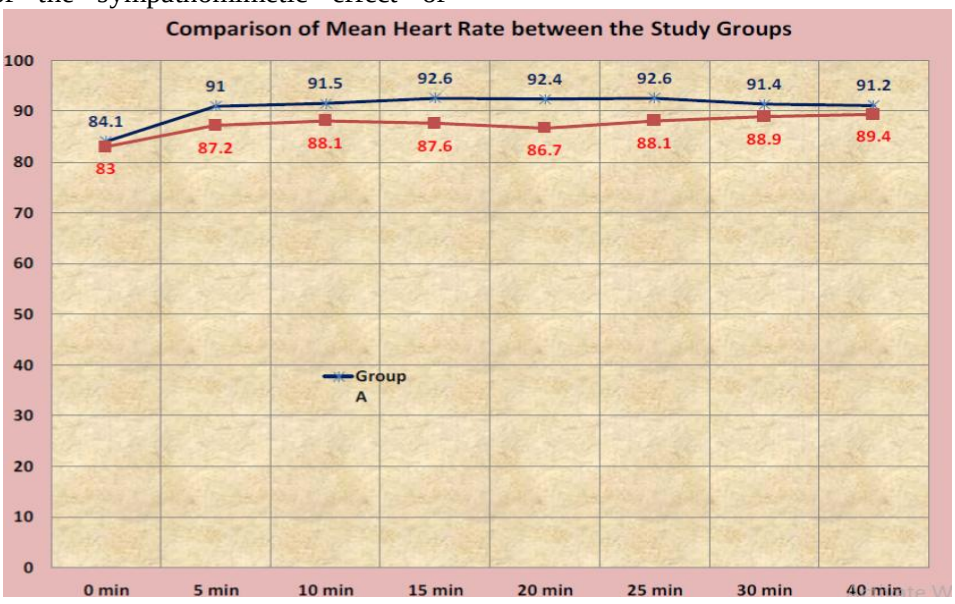

Figure1: *Line Diagram Showing Comparison of Heart Rate between Two Groups At Various Time Intervals*

In this study the mean SpO2 is significantly lower in group B as compared to group A at intervals of 5, 10, 15, 20, 25, and 30 minutes as shown in figure 2 which correlates with increased amounts of propofol consumption and causes deep sedation and apnoea. However, in group A, ketamine maintains spontaneous breathing and has lesser chances of apnoea. Airway intervention like jaw lift and chin thrust manoeuvres were more frequently required in propofol, fentanyl group.

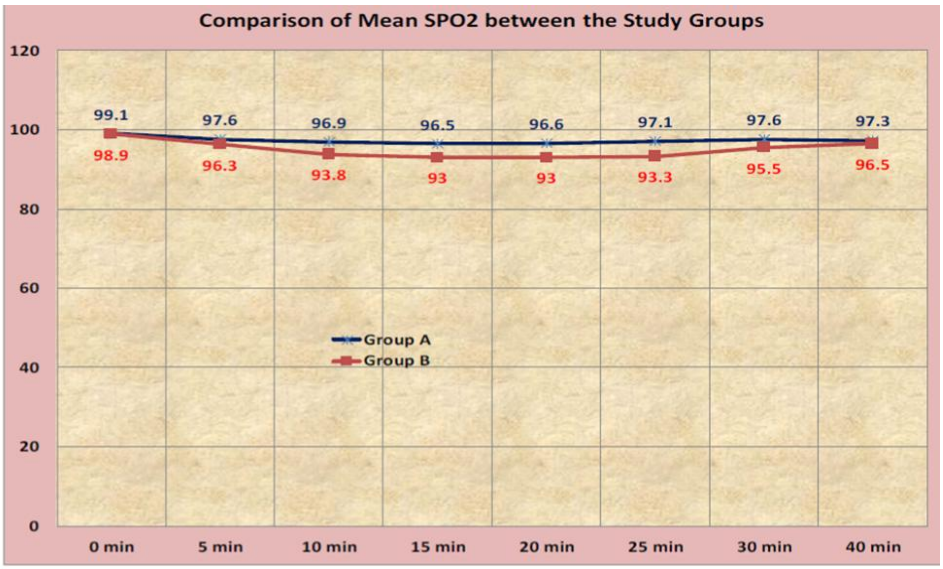

Figure2: *line Diagram Showing Comparison of Spo2 Between Two Groups At Various Time Intervals*

The mean dose of propofol used in group A was 183.7 ± 25.118 which is lower than that used in group B which was 209.7 ± 20.254. This difference is statistically significant. (Table 2)

Table 2: *Propofol Consumption In The 2 Groups*

Group	N	Mean	SD	't' value	'p' value
Group A	30	183.7	25.118		
Group B	30	209.7	20.254	19.478	*<0.001*
SD- standard deviation, p value < 0.05 is significant.					

In group A the recovery time was 4 ± 1.066 as compared to 5.3 ± 1.061 in group B which is statistically significant. (Table3) lower than that in group B which was 9.8 ± 1.223. This correlates with the lower amounts of propofol consumption in group A. (Table 3)

The time taken to achieve an Aldrete score >9 in group A was 7.3 ± 1.493 which is significantly

Table 3: *Time taken for recovery and to achieve an Aldrete score in the two groups*

	Time taken for recovery			Time taken to achieve Aldrete score		
	Mean ±SD	T value	P-value	Mean ±SD	T value	P-value
Group A	4±1.066			7.3 ± 1.493		
Group B	5.3±1.061	24.578	<0.001	9.8 ± 1.223	47.683	<0.001

In this study, the patient satisfaction score was significantly higher in group A at 4.1 ± 0.740 compared to that in group B at 3.2 ± 0.791. (Table 4) The mean endoscopist satisfaction score in group A was 8.5 ± 0.900 which is significantly higher than 6.9 ± 0.828 in group B. (Table 4)

Table4: *patient and endoscopist satisfaction score*

Patient satisfaction score					Endoscopist score		
Group	N	*Mean±SD*	*'t' value*	*'p' value*	*Mean± SD*	*'t' value*	*'p' value*
Group A	30	4.1 ± 0.740			8.5 ± 0.900		
Group B	30	3.2 ± 0.791.	20.706	<0.001	6.9 ± 0.828	51.397	<0.001

In group, A 21 patients (70%) did not require any airway intervention while in group B, 7 patients (23.3%) did not require airway intervention. Airway intervention was only limited to chin lift and jaw thrust, as none of the patients required intubation.(Table 5)

Table5: *Requirement of airway intervention between two groups*

	Adverse effect					χ^2 ***value***	***P-value***
Group	A,1	A,1,2	A,1,2,3	Nil	Total		
Group A	3	4	2	21	30		
	10.0%	13.3%	6.7%	70.0%	100.0%		
Group B	7	8	8	7	30	13.553	*0.004*
	23.3%	26.7%	26.7%	23.3%	100.0%		

A 1-Chin lift, a 2-Neck extension, A3-Jaw thrust, A4-Bag and mask ventilation, A 5-Intubation.

5. DISCUSSION

ERCP is a lengthy uncomfortable procedure that plays a crucial role in treating gall bladder disease. Anesthesia for it is challenging it is performed in the day-care setting. The selection of a sedative drug that improves patient cooperation and minimizes cardiac and pulmonary complications is vital. Previous studies show that a propofol-ketamine combination achieves better patient satisfaction and prevents airway obstruction. In this study we compared the propofol-ketamine and propofol-fentanyl combination and observed that propofol and ketamine in a proper proportion is a better sedative for ERCP.

In our study there was no statistically significant difference in the study groups concerning the age distribution, gender distribution, weight distribution, BMI distribution, and ASA Grade distribution comparable to the previous studies.

The mean heart rate was significantly higher in group A compared to group B at intervals of 5, 10, 15, 20, and 25 minutes, because of the sympathomimetic effect of ketamine. Hossam Ibrahim et al7 showed patients of the ketamine-propofol group had more stability in heart rate because of the antagonizing effect of propofol and ketamine. Riham Hasanein et al6 concluded that in his study tachycardia occurred in 3 patients of propofol-ketamine group due to sympathomimetic effects of ketamine and bradycardia occurred in 9 patients in the ketamine-fentanyl group likely due to sympatholytic effects of fentanyl.

There was no statistically significant difference between the groups in terms of the mean arterial pressure. Ketamine is expected to have sympathomimetic effects causing increased mean arterial pressure, but we noticed there is no rise in blood pressure during the procedure likely attributed to systemic vasodilation by propofol. The previous studies7,8 also observed that there is no statistical significance difference (p-value 0.505) in mean arterial pressure between the propofol-ketamine and propofol-fentanyl groups. Hassan HI11 noticed a fall in MAP in the propofol-dexmedetomidine group concluding that propofol-ketamine maintains stable hemodynamics, when comparing the 2 groups.

The mean SpO2 is significantly lower in group B as compared to group A at intervals of 5, 10, 15, 20, 25, and 30 minutes which correlates with increased amounts of propofol consumption and causes deep sedation and apnoea. However, in group A, ketamine maintains spontaneous breathing and has lesser chances of apnoea. Our study results concur with previous studies 6,7,14 which show that the fentanyl group has more episodes of desaturation requiring airway intervention compared to ketamine group. Ketamine is advantageous for maintaining intact airway reflexes and thus avoids respiratory compromise.

Our study shows that the propofol consumption in group A is significantly lower than that used in group B. As the fentanyl has more analgesic effects with less sedation property this makes ketamine a better choice to provide adequate depth of anesthesia with less propofol usage. Two other studies9,12 also observed that propofol consumption is less in the propofol-ketamine group compared to propofol -fentanyl or propofol-dexmedetomidine group which can be attributed to the additive sedative effect of propofol and ketamine.

ERCP is a day-care procedure so, quick post-operative recovery and early return of spontaneous respiration is vital in drug selection. In our study, we observed that in Group A (ketamine-propofol) the recovery time and time taken to achieve an Aldrete score >9 was significantly lower as compared to Group B.

This observation is in parallel to the study by Akin 15 et al who found better maintenance of the MAP without prolonging recovery in the ketamine–propofol (1:3) combination group than in the propofol monotherapy group. But in other studies 6, 14 they noticed increased recovery time in the propofol-ketamine group. A prolonged time to achieve Aldrete score was seen in two studies 7, 10 in ketamine group. The difference in our results can be due to increased ketamine dose or propofol-ketamine proportion as explained by Riham Hasanein et al6and in many other studies 16,17,18where they used combinations of ketamine and propofol in the ratio of 1:1 to 1:5 and proposed that higher ketamine concentrations lead to delayed

recovery. In our study we used ketamine to propofol in the ratio of (1:4) which is the same proportion used by Daabis et al19who concluded that this concentration is better in providing adequate sedation without other side effects.

In this study, group A had a significantly higher patient and endoscopist satisfaction score compared to group B. KhajaviM et al13 showed that ketamine-propofol combination has superior patient satisfaction versus fentanyl-propofol which is identical to our results.

6. Conclusion

From our study we concluded that ketamine-propofol group had better respiratory parameters, requires lesser airway manoeuvres, better hemodynamic stability, lesser consumption of total propofol, lesser recovery time, lesser time to achieve Aldrete score > 9, better patient satisfaction and endoscopist satisfaction than Fentanyl-propofol group.

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