

A comparative study of ketofol (ketamine and propofol) with propofol alone to see effect on blood pressure during induction and maintenance phase of anaesthesia in patients undergoing laparoscopic cholecystectomy

¹Dr. Priyanka Thakur, MD, Department of Anaesthesia, Indira Gandhi Medical College, Shimla HP India

²Dr. Prteet Negi, MS, Department of General Surgery, Dr. Rajender Prasad Medical College Kangra, Tanda H.P India

³Prof. Dr Ajay Sood, MD, Department of Anaesthesia, Indira Gandhi Medical College, Shimla HP India

⁴Dr. Aparna Sharma, MD, Department of Anaesthesia, Indira Gandhi Medical College, Shimla HP India

Corresponding Author: Dr. Prteet Negi, MS, Department of General Surgery, Dr. Rajender Prasad Medical College Kangra, Tanda H.P India

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Abstract

Background: In this study, we aimed to evaluate the intra and post-operative hemodynamic effects of ketamine-propofol mixture (Ketofol) infusion in comparison with propofol infusion.

Methods: Prospective, randomized, double blinded controlled trial. After approval by the research ethics committee and written informed valid consent of the patients, the proposed study was carried out for a period of one year in 60 patients, in ASA-I and ASA-II patients, aged between 19 to 60 years of either sex, who were posted for laparoscopic cholecystectomy surgery at Indira Gandhi Medical College, Shimla.

Results: MAP for group P was significantly decreased in first 3 minute(78.80 ± 11.62) ,5min(78.50 ± 10.10) ,10 minutes(77.30 ± 9.12),then every 5 minutes before extubation ($78.40 \pm 9.50, 77.43 \pm 9.63, 77.47 \pm 8.16$),on extubation(78.07 ± 9.38),30 minutes of postoperative period(79.10 ± 9.16), 1 hr of postoperative

period(77.10 ± 8.77) , 1hr30 min of postoperative period(76.47 ± 8.13) and 2 hr of postoperative period (76.10 ± 8.08) as compared to basekine MAP(88.30 ± 16.42).

Conclusion: Infusion of hypnotic doses of ketofol leads to increase in diastolic and systolic blood pressure and improves blood pressure stability in addition to inducing more as compared with propofol infusion

Keywords: SBP, MAP, DBP, Propofol, Ketamine

Introduction

Propofol is one of the most commonly used drugs for the induction and maintenance of anesthesia. Quick wakening up and short context-sensitive half-life after prolonged intravenous infusion are among the advantages of this drug, which in turn increase the tendency for using this drug for the maintenance of anesthesia in outpatient operations, emergencies and intensive care units. ¹⁻² However, cardiovascular complications caused by the administration of this drug

including reduced cardiac contractility, decreased heart rate, reduced peripheral vascular resistance, suppression of baroreceptor reflex and sudden decrease in blood pressure, especially in elderly patients and those with an underlying cardiac disease, and shocks have limited the use of this drug.³⁻⁵

The existing evidence suggests that the use of low doses and titers of ketamine can be effective in reducing the cardiovascular effects of propofol; nevertheless, this administration method can increase the chance of waking up during anesthesia. Some studies have reported the effect of anesthesia induction using a single propofol dose and low ketamine doses on the hemodynamic stability of patients in short-term outpatient operations in emergency departments. On the other hand, no report has been published so far regarding hemodynamic changes due to propofol infusion in more prolonged operations.

Material and methods

Study Design: Prospective, randomized, double blinded controlled trial. After approval by the research ethics committee and written informed valid consent of the patients, the proposed study was carried out for a period of one year in 60 patients, in ASA-I and ASA-II patients, aged between 19 to 60 years of either sex, who were posted for laproscopic cholecystectomy surgery at Indira Gandhi Medical College, Shimla.

Exclusion Criteria: patient's refusal, uncontrolled hypertension, laproscopic cholecystectomies converted to open cholecystectomies, drug allergy.

The patients were randomized into two groups:

Group P: Patients received Propofol for induction and maintenance of anaesthesia

Group KP: Patients received combination of Ketamine and Propofol for induction and maintenance of anaesthesia.

The study drug infusion was prepared by an anaesthesiologist who did not participate in collection of data in that study. Anaesthesiologist who collected data, the operating surgeon and the patient were blinded to drug infusion.

Patient recruitment into the study

All patients underwent a routine pre-anaesthetic check up. During this, thorough history and general physical examination of the patient was carried out. Routine investigations such as haemoglobin, fasting or random blood sugar, blood urea, serum creatinine, serum electrolytes, ECG and chest X-ray were documented.

Study protocol was explained to all the patients during pre-anaesthetic evaluation and informed consent was taken and signed.

The patients were made familiar with visual analogue score, VAS (0 for no pain and 10 for the worst imaginable pain). The patient was instructed for a fasting period of 6 hrs. Tablet Alprazolam was advised to patient as per department protocol.

Study Drug

For induction of anaesthesia: Study drug was given slowly till loss of verbal response

For maintenance of anaesthesia: Study drug was infused at a rate of 50 mcg/kg/min for 10 min and then 25 mcg/kg/min.

Study Drug Preparation

In a 50ml syringe- 50 ml study drug was loaded

- **Group P:** 50 ml of Propofol 1% (10mg/ml). [1ml of study drug was containing Propofol 10mg]
- **Group KP:** 40 ml of Propofol 1% (10mg/ml) + 10 ml of Ketamine (10mg/ml).

Results

The socio-demographic variable in both groups were comparable.

Table 1: Comparison of MAP of group K at different time intervals

Duration	Group – K (n=30)		t _{cal}	p-value	Results
	Mean ± S.D				
Baseline	92.86 ± 10.24				
Induction		97.43 ± 9.73	1.772	0.0816	Not Significant
Intubation		96.20 ± 12.38	1.139	0.2595	Not Significant
IO1		96.03 ± 8.33	1.315	0.1936	Not Significant
IO2		95.67 ± 8.40	1.162	0.2500	Not Significant
IO3		94.43 ± 8.15	0.657	0.5137	Not Significant
IO5		95.17 ± 8.73	0.940	0.3510	Not Significant
IO10		94.93 ± 7.19	0.906	0.3686	Not Significant
IO5		95.50 ± 6.55	1.190	0.2391	Not Significant
IO5		96.43 ± 6.16	1.636	0.1072	Not Significant
IO5		98.40 ± 6.25	2.529	0.0142	Significant
Extubate		101.5 ± 8.39	3.575	0.0007	Significant
PO30min		98.23 ± 8.13	2.250	0.0283	Significant
PO1hr		94.40 ± 7.66	0.660	0.5121	Not Significant
PO1hr30min		91.43 ± 8.13	0.599	0.5515	Not Significant
PO 2hr		89.27 ± 7.82	1.536	0.1324	Not Significant

Hence MAP for group K was significantly increased during last 5 minute of intraoperative period (98.40 ± 6.25), during extubation (101.5 ± 8.39) and first 30 minutes of postoperative period (98.23 ± 8.13) as compared to its baseline (92.86 ± 10.24).

Table 2: Comparison of MAP of group P at different time intervals

Duration	Group – P (n=30)		t _{cal}	p-value	Results
	Mean ± S.D				
Baseline	88.30 ± 16.42				
Induction		89.27 ± 17.92	0.219	0.8277	Not Significant
Intubation		88.70 ± 16.44	0.0943	0.9252	Not Significant
IO1		87.73 ± 15.99	0.136	0.8921	Not Significant
IO2		88.37 ± 16.95	0.016	0.9871	Not Significant
IO3		78.80 ± 11.62	2.587	0.0122	Significant
IO5		78.50 ± 10.10	2.784	0.0072	Significant
IO10		77.30 ± 9.12	3.208	0.0022	Significant

IO5		78.40 ± 9.50	2.855	0.0059	Significant
IO5		77.43 ± 9.63	3.128	0.0028	Significant
IO5		77.47 ± 8.16	3.235	0.0020	Significant
Extubate		78.07 ± 9.38	2.963	0.0044	Significant
PO30min		79.10 ± 9.16	2.680	0.0096	Significant
PO1hr		77.10 ± 8.77	3.295	0.0017	Significant
PO1hr30min		76.47 ± 8.13	3.536	0.0008	Significant
PO 2hr		76.10 ± 8.08	3.651	0.0006	Significant

Hence MAP for group P was significantly decreased in first 3 minute(78.80 ± 11.62) ,5min(78.50 ± 10.10) ,10 minutes(77.30 ± 9.12),then every 5 minutes before extubation (78.40 ± 9.50,77.43 ± 9.63,77.47 ± 8.16),on extubation(78.07 ± 9.38),30 minutes of postoperative period(79.10 ± 9.16), 1 hr of postoperative period(77.10 ± 8.77) , 1hr30 min of postoperative period(76.47 ± 8.13) and 2 hr of postoperative period (76.10 ± 8.08) as compared to basekine MAP(88.30 ± 16.42).

Discussion

Tang et al. ⁶ compared the effects of addition of low dose ketamine to propofol-fentanyl and propofol-fentanyl alone for sedation in 80 patients who were candidates for gynecologic diagnostic laparoscopy. They observed that mean blood pressure was consistently higher in the Ketamine group, as sympathomimetic effects of ketamine might have overcome the cardiovascular effects of propofol, thereby maintaining hemodynamic stability in these patients compared to the propofol-treated patients. In contrast with our findings, a study performed by Singh et al. ^{7,8} comparing the cardiovascular effects of propofol alone and in combination with ketamine or fentanyl for sedation in patients undergoing endoscopic ultrasonography showed no significant differences in the mean blood pressure or heart rate at any time point among the groups. These conflicting results are

probably related to the type of the procedures, as tubal ligation is a surgical operation, while endoscopy is a minimal invasive procedure ⁶

Conclusion

Infusion of hypnotic doses of ketofol leads to increase in diastolic and systolic blood pressure and improves blood pressure stability in addition to inducing more as compared with propofol infusion

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