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COMPARISON OF HEMODYNAMIC STABILITY OF PROPOFOL KETAMINE VERSUS ETOMIDATE KETAMINE DURING INDUCTION IN PERITONITIS CASES POSTED FOR EMERGENCY SURGERY

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Abstract

The aim: The aim of the present study is to evaluate the hemodynamic stability of propofol ketamine versus etomidate ketamine during induction of anaesthesia in peritonitis cases posted for emergency surgery.

Methods: Sixty patients with peritonitis, posted for emergency surgery under general anaesthesia, were randomly allocated to two groups. Group propofol ketamine (P + K) comprised of 30 patients ($n = 30$) were induced with propofol 1 mg/kg and ketamine 0.75 mg/kg IV. Group etomidate ketamine (E + K) comprised 30 patients induced with etomidate 0.3 mg/kg and ketamine 0.75 mg/kg. The hemodynamic effects of the combination of the drugs in both groups were compared before and after induction.

Results: The change in saturation (SPO_2) and Heartrate between the groups P + K & group E + K before induction and after intubation was similar in both groups. There was a statistically insignificant fall in systolic blood pressure (SBP) and diastolic blood pressure (DBP), and mean arterial pressure (MAP) in group P + K before and after induction when compared to group E + K.

Conclusions: The propofol ketamine and etomidate ketamine combinations have a similar haemodynamic profile and are equally effective in maintaining haemodynamic stability during induction and intubation.

Keywords: etomidate, haemodynamics, induction, ketamine, peritonitis, propofol, induction, intubation, general anaesthesia, suxamethonium.

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1. Introduction

Peritonitis is a manifestation of intra-abdominal sepsis and is a surgical emergency. The inflammation mediated by cytokines like tumour necrosis factor (TNF), interleukin-1 and interferon

can lead to local peritoneal inflammation, fluid sequestration in the gut lumen, and third space loss. The resulting hypovolemia causes a fall in cardiac output, metabolic acidosis, decreased renal perfusion and renal insufficiency. The local peritoneal inflammation causes ileus, abdominal distention, and restriction of diaphragmatic movements [1, 2]. Pain restricts the intercostal muscle movements decreasing the tidal volume and predisposing to atelectasis and ventilation-perfusion mismatch. Increased adrenal stimulation causes severe vasoconstriction and tachycardia increasing the oxygen demand. The increased demand and the decreased supply of oxygen can further aggravate sepsis and multi-organ dysfunction syndrome (MODS). The mortality increases in the patients with peritonitis presenting for emergency surgery [3]. Advanced age, comorbid illnesses, delayed presentation, and the presence of features of sepsis or organ dysfunction are some of the predictors of increased morbidity and prolonged post-operative stay in the ICU [4].

Propofol, ketamine and etomidate are the common induction agents used in general anaesthesia. Propofol decreases systemic vascular resistance and can cause profound hypotension. This hypotension can be exaggerated in patients over 50, those with hemodynamic instability, comorbidities and sepsis. Ketamine has sympathomimetic properties and increases blood pressure and heart rate, and can be used in those with hemodynamic compromise. But then, ketamine-induced tachycardia can increase the oxygen demand in an already compromised cardiovascular state. Etomidate has the advantage of cardiovascular stability, making it the drug of choice for hypotensive patients requiring general anaesthesia [4]. A judicious combination of induction agents will reduce the dose of individual agents, decrease the complications of individual drugs and increase patient safety. Propofol ketamine combination can decrease the hypotension due to propofol and decrease the sympathetic stimulation by ketamine. Etomidate and ketamine can complement each other in maintaining haemodynamic stability. In the present study, the haemodynamic stability of the propofol ketamine combination was compared with the combination of etomidate ketamine as an induction agent.

The aim of the research was to evaluate the hemodynamic stability of propofol ketamine versus etomidate ketamine during induction of anaesthesia in peritonitis cases posted for emergency surgery.

2. Materials and methods

The double-blinded, randomized prospective clinical trial was conducted as a single-centre study at a tertiary care institute. The institutional ethical committee approval of Gandhi Medical College (registration NO: 16102002021D dated 28/6/2017) was obtained.

60 patients aged 45 to 60 years, presenting with peritonitis and posted for emergency surgery under general anaesthesia between January 2017 to January 2018, were enrolled in the study. Patients with a history of hypersensitivity to propofol, etomidate and ketamine, primary or secondary adrenal insufficiency, renal or hepatic impairment, hypertension, difficult airway, BMI > 33 and pregnant women were excluded from the study. The patients were randomly allocated into two groups by computer randomization. Both the patient and the primary investigator were blinded to the drugs used. Group – P + K: comprised 30 patients ($n = 30$) induced with propofol 1 mg/kg and ketamine 0.75 mg/kg. Group – E + K: comprised of 30 patients ($n = 30$) induced with etomidate 0.3 mg/kg and ketamine 0.75 mg/kg.

All patients were monitored in the operating room with a pulse oximeter, non-invasive blood pressure (NIBP) monitors and ECG. The pre-induction vitals were noted. Two 16G intravenous cannulas were inserted, and the patients were hydrated with a lactated ringer to optimize the preoperative blood pressure. All the patients were pre-oxygenated with 100 % O_2 for 3 minutes. Pre-medicated was uniform with glycopyrrolate 0.2 mg and fentanyl 2 μg/kg intravenously. The patients were induced with either of the drug combinations depending upon the group. The heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), saturation (SPO_2) and ECG were noted at one minute after induction. Rapid sequence intubation (RSI) was done with suxamethonium 2 mg/kg, with an appropriate size cuffed endotracheal tube. The heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), saturation (SPO_2) and ECG were noted at one and three minutes after intubation. Anesthesia was maintained with oxygen,

nitrous oxide and sevoflurane with intermittent non-depolarizing muscular relaxant vecuronium 0.05 mg/kg. At the end of the surgery, the neuromuscular blockade was reversed with neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg. Patients were extubated after regaining reflexes and shifted to ICU.

Statistical analyses. The sample size (60 people) was calculated using the formula $\alpha = 0.05$ and $d = 0.12$. Randomization was achieved using computer randomization. Continuous variables were presented on Mean ± SD, and results on categorical measurements were presented as percentages (%). Student t-test (two-tailed, independent) was used at a common level of significance $\alpha = 0.05$. Leven's test for homogeneity of variance was performed to assess the homogeneity of variance. Chi-square/ Fisher Exact test was used to find the significance of study parameters on a categorical scale between two groups. The statistical software Open Epi, Version 2.3, was used to analyse the data, and Microsoft Excel was used to generate graphs and tables.

3. Results

A total of 60, comprising 27 males and 3 females in each group, were enrolled in the study. The age of the participants ranged from 45 to 60 years, with a mean age of 53.33 in group P + K group and 51.1 in the E + K group. The demographic data were comparable in both groups (**Table 1**). The haemodynamics were compared as heart rate, systolic, diastolic and mean blood pressures measured before induction, one minute after induction, one minute and 3 minutes after intubation. Among the haemodynamics, the HR and saturations were comparable in both groups as measured one minute after induction, one- and three minutes post-intubation ($p > 0.05$) (**Table 2**). There was a statistically significant fall in the blood pressure, both systolic and diastolic, 1 minute after induction in group P + K as compared to group E + K ($p < 0.05$). However, there were no statistically significant differences in the systolic and diastolic blood pressures in both groups as measured 1 and 3 minutes after intubation (**Tables 3, 4**).

Hence among the haemodynamic parameters, statistically significant differences between the groups were seen only in the SBP and DBP measured one (1) minute after induction. All other parameters of HR, SPO_2, SBP & DBP at 1 & 3 minutes after intubation were comparable in both groups, $p > 0.05$.

Table 1
Demographic distribution in the study

Gender	Group P + K	Group E + K
Male	27 (90 %)	27 (90 %)
Females	3 (10 %)	3 (10 %)
Age in Mean ± SD	53.33 ± 9.93	51.1 ± 8.08

Table 2
Comparison of heart rate and saturation

Parameter		Group P + K Mean ± SD	Group E + K Mean ± SD	P Values
Heart Rate	Before induction	110.87 ± 12.58	111.7 ± 13.6915529	0.807
	1 minute after induction	117.20 ± 12.41	118.4 ± 12.55772876	0.7111
	1 minute after intubation	117.90 ± 11.65	118.2 ± 11.43617973	0.9202
	3 minutes after intubation	109.87 ± 10.05	109.23 ± 9.736	0.8031
SPO_2	Before induction	96.47 ± 4.52	96.2 ± 3.58	0.7985
	1 minute after induction	99.13 ± 1.22	99.4 ± 1.037	0.3595
	1 minute after intubation	99.23 ± 1.01	99.67 ± 0.66	0.0505
	3 minutes after intubation	99.33 ± 0.96	99.67 ± 0.95	0.1732

Table 3
Comparison of systolic blood pressure in both groups

SBP	Group E + K Mean ± SD	Group P + K Mean ± SD	P Values
Before Induction	109.3 ± 12.28	106.17 ± 10.17	0.29
1 minute after induction	102.77 ± 10.84	101.67 ± 8.31	0.71
1 minute after intubation	106.5 ± 10.01	103.70 ± 6.50	0.27
3 minutes after intubation	107.1 ± 7.80	104.43 ± 7.65	0.46

Systolic BP is statistically insignificant at 1 minute after induction, 1 and 3 minutes after intubation.

Table 4
Comparison of diastolic blood pressure in both groups

DBP	Group E + K Mean ± SD	Group P + K Mean ± SD	P Values
Before Induction	69.5 ± 9.02	67.37 ± 7.70	0.3293
1 minute After Induction	63.9 ± 8.93	65.40 ± 6.33	0.46
Postintubation 1 minute	65.5 ± 7.44	61.77 ± 6.69	0.14
Postintubation 3 minutes	67.63 ± 5.93	62.90 ± 6.13	0.07

Diastolic BP is statistically insignificant at 1 minute after induction, 1 and 3 minutes after intubation.

4. Discussion

Peritonitis presenting as an acute abdomen is a surgical emergency. Proper preoperative optimization of the patient is needed to correct the shock, dehydration, and oliguria. The patients require an emergency laparotomy to identify and treat the cause of peritonitis. The laparotomy can help to remove the focus of sepsis if present. The technique of choice is general anesthesia with rapid sequence endotracheal intubation with controlled ventilation. However, the surgery's emergency nature can compromise the patients' adequate preoperative optimisation. The induction agents cause a fall in systemic vascular resistance, which will be exaggerated in the presence of sepsis. In addition, the premedication given before the induction of anaesthesia can inhibit compensatory tachycardia. These factors place patients with peritonitis at risk of developing acute hypotension immediately after induction of anaesthesia. The choice of induction agents is important to prevent the sudden and undesirable falls in blood pressure [5]. The frequently used induction agents are propofol, ketamine and etomidate. Etomidate has cardiovascular stability, but its use is limited due to cost factors, non-availability, and side effects. Ketamine increases sympathetic stimulation and has been used in combination with propofol. The present study compares the haemodynamic effects of the propofol ketamine combination with the etomidate ketamine combination.

The two groups, P + K and E + K, were comparable in the demographic data. The statistically similar age distribution achieved by randomization helped us to alleviate the confounding factors of pharmacokinetics, like distribution metabolism and excretion. The drug combination and the dosage of the present study were done in accordance with the study conducted by Hosseinzadeh H et al. [5]. Pre-induction vitals like heart rate, SPO_2, and systolic and diastolic blood pressures were comparable in both groups. Group – P + K received an injection of propofol 1 mg/kg IV + injection of ketamine 0.75 mg/kg IV, and Group – E + K received an injection of Etomidate 0.3 mg/kg IV + injection of ketamine 0.75 mg/kg.

In the present study, there was no significant increase in the heart rate when ketamine was combined with either propofol or etomidate as measured after induction. Kamalipour H et al. [6] noted a similar increase in the heart rate when they used the propofol ketamine combination for induction of anesthesia. A similar increase in the heart rate with ketamine was noted in the studies by Singh Bajwa et al. [7]. Korgoankar et al. [8] reported insignificant increases in the heart rate when ketamine was used in combination with alfentanil. The findings were confirmed in the study by Katz et al. [9], where the author used ketamine with Alfentanil. In the study of Mayer et al. [9] and Mi et al. [10] studies there was a slight decrease but not significant in heart rate in the propofol-fentanyl group as compared to propofol-ketamine combination Studies of Mi et al. also showed that after induction, the PR did not alter significantly when propofol was used alone but decreased between 5 and 35 % in patients who were given fentanyl 4 μg/kg prior to the induction of anaesthesia [10, 11].

In the present study, the haemodynamics between the two groups were comparable; systolic and diastolic blood pressure were similar in both P + K group E + K group and were not statistically significant. Miner et al. [13] reported a different finding: they found that etomidate and propofol resulted in similar rates of sedation, subclinical respiratory depression, hypoxia, apnea, and clinical events related to respiratory depression; propofol had a higher rate of procedural success than etomidate, and none of these differences resulted in clinically significant adverse events. It was reported that both medications were similarly safe for use in procedural sedation. Similar results have been reported by Rocchio et al. [14]. There was no statistically significant fall in blood pressure in the study by Bajwa et al. [7]. The authors concluded that the antagonistic properties of propofol (decrease in blood pressure) and ketamine (increase in blood pressure) can accord hemodynamic stability. In their study, Kaushal et al. [15] concluded that etomidate provides more stable hemodynamic parameters than propofol. Others have studied the effect of propofol and etomidate with similar results [16–19].

The authors concluded that both methods of induction-ketamine + propofol and etomidate + propofol are effective in maintaining hemodynamic stability and preventing hemodynamic changes due to propofol administration. Our study also has similar results that both Propofol ketamine and etomidate ketamine groups are comparable in providing haemodynamic stability during induction of anesthesia [20, 21]. Though there was a decrease after induction in the Propofol ketamine combination, both propofol ketamine and etomidate ketamine combinations had similar hemodynamic profiles post-intubation.

Study limitations. The present study's main limitation was that the population comprised patients with peritonitis, where rapid sequence induction and intubation are mandatory due to the increased risk of aspiration. As such, succinylcholine was used for intubation, and the post-induction time was 1 minute. Hence the effect of the induction agents could be studied only for 1 minute.

Prospects for further research: Greater experience with planned emergency research will hopefully pave the way for future prospective randomized trials in the critically ill patient population. By publishing the current study protocol, we hope to provide researchers considering planned emergent use research with tools to accomplish such a trial that adheres to regulatory and institutional policies.

5. Conclusions

The present study concludes that the combination of Propofol ketamine is similar in maintaining haemodynamic stability as compared to the combination of etomidate ketamine. the propofol-ketamine combination may be recommended as an effective and safe induction agent for attenuating hemodynamic responses to laryngoscopy and intubation, with superior hemodynamic stability compared to etomidate and a combination of thiopental-ketamine in patients undergoing surgery in general anesthesia. Although, further well-designed randomized clinical trials to confirm the safety and efficacy of this combination, especially in patients with cardiovascular disease or critically ill patients undergoing surgery, are warranted. Propofol ketamine can be an alternative to the etomidate ketamine combination in emergency laparotomy cases.

Conflict of interest

The authors declare that there is no conflict of interest in relation to this paper, as well as the published research results, including the financial aspects of conducting the research, obtaining and using its results, and any non-financial personal relationships.

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Data availability

Data will be made available on reasonable request.

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