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Hemodynamic Stability during Induction of Anesthesia in Elderly Patients: Propofol plus Ketamine versus Propofol plus Etomidate

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Abstract:

Introduction

Hemodynamic instability of patients during induction of general anesthesia is a very important clinical concern and it is a common event associated with negative results in clinical practice. During induction of anesthesia patients are exposed to pain full procedure such as laryngoscopy and endotracheal intubation. This procedure is often associated with tachycardia, hypertension, arrhythmia and other undesirable hemodynamic changes. Hypotension and hypertension all through general anesthesia are independently associated with adverse results in patients having both abdominal and non-abdominal surgery. Majority of studies on ketamine/propofol admixture have evaluated critically ill patients in the emergency department with the evidence demonstrating a potential sparing effect on hemodynamics along with improved pain relief and sedation quality.

Materials and Methods: This is a prospective randomized double-blind study was conducted in department of Anesthesia over a period of 1 year. Patients in the age group of 18 – 65 years with American Society of Anesthesiologists (ASA) physical status II and III who were to undergo elective general, urologic, orthopedic, plastic or gynecologic surgery were included in the study. Patients on chronic opiate therapy, psychotropic or sedative medications, patients with personality disorders, severe left ventricular systolic dysfunction (ejection fraction < 30%) and pregnant/lactating mothers were excluded from the study. Thus, a sample size of 40 patients per group was considered for our study.

Results: In our study SBP, DBP, MAP which were recorded, before induction considered as the baseline, and after induction, were comparable between the two groups. SBP, DBP and MAP compared at 1, 3 and 5 mins after intubation showed statistically significant difference between the two groups with propofol-ketamine group showing better hemodynamic stability. The HR between both the groups at various time intervals were comparable and not considered statistically significant.

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Conclusion: Propofol plus ketamine can be recommended as a safe and effective combination for induction to attenuate haemodynamic responses to laryngoscopy and intubation, with superior haemodynamic stability compared to induction with etomidate alone.

Keywords: Propofol, Ketamine, Etomidate, Intubation, Hemodynamic.

Introduction

Hemodynamic instability of patients during induction of general anesthesia is a very important clinical concern and it is a common event associated with negative results in clinical practice. [1] During induction of anesthesia patients are exposed to pain full procedure such as laryngoscopy and endotracheal intubation. This procedure is often associated with tachycardia, hypertension, arrhythmia and other undesirable hemodynamic changes. [2] Hypotension and hypertension all through general anesthesia are independently associated with adverse results in patients having both abdominal and non-abdominal surgery. [3]

In particular, general anaesthesia is highly associated with morbidity and mortality. [4] This is often accompanied by a period of hemodynamic instability, especially hypotension, which could be a significant problem in patients with compromised cardiac output. [5] Hemodynamic disturbance is highly prevalent in abdominal surgery and associated with unfavorable patient outcome. An arterial blood pressure (ABP) decline below the lower limit of the vascular auto regulation curve might lead to ischemia of vital organs. [6]

Perioperative hypertension is an independent predictive factor of cardiac adverse events in abdominal and other non-cardiac surgery. Hypotension is frequent between the induction of anesthesia and the beginning of surgery. Maintaining hemodynamic stability during induction and maintenance of anaesthesia is an important task for the anesthesia providers. [7] Thus, a general anaesthetic agent with minimal effect on heart rate (HR), blood pressure (BP) cardiovascular instability, and better control of airway would be the agent of choice for general anaesthesia, commonly for gastrointestinal tract surgery. [8]

Majority of studies on ketamine/propofol admixture have evaluated critically ill patients in the emergency department with the evidence demonstrating a potential sparing effect on hemodynamics along with improved pain relief and sedation quality. studies have evaluated ketamine/propofol admixture from the standpoint of a continuous infusion for procedural sedation and analgesia. [9]

Have been a couple of systematic reviews on ketamine/propofol admixture sedation, demonstrating that ketamine/propofol admixture appears safe and efficacious for procedural sedation and analgesia and is possibly better than propofol only at reducing cardiorespiratory problems. Wealth of the evidence above has mainly focused on ketamine/propofol admixture use in terms of infusions for procedural sedation and analgesia. are limited studies addressing the potential hemodynamic preservation effects of the admixture when administered as an induction agent for endotracheal intubation. [10] Given the above associations between peri-

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intubation hypotension and increased patient morbidity and mortality, and the mounting evidence with ketamine/propofol admixture as an agent that allows potential maintenance of hemodynamics when administered for endotracheal intubation. [11]

Materials and Methods

This is a prospective randomized double-blind study was conducted in department of Anesthesia over a period of 1 year.

Inclusion criteria:

Patients in the age group of 18 – 65 years with American Society of Anesthesiologists (ASA) physical status II and III who were to undergo elective general, urologic, orthopedic, plastic or gynecologic surgery were included in the study.

Exclusion criteria:

Patients on chronic opiate therapy, psychotropic or sedative medications, patients with personality disorders, severe left ventricular systolic dysfunction (ejection fraction < 30%) and pregnant/lactating mothers were excluded from the study.

Thus, a sample size of 40 patients per group was considered for our study.

Weight of the patient was recorded. Patients were randomly divided using sealed envelope method into two groups. Group - KP received Inj. ketofol i.e., combination of Inj. Propofol 1mg/kg and Inj. Ketamine 0.75mg/kg diluted up to 10ml using Normal Saline 0.9% in a single syringe Group – E received Inj. Etomidate 0.3mg/kg diluted up to 10ml with Normal Saline 0.9% in a syringe. One anesthesiologist prepared and injected the drugs while the second anesthesiologist observed the parameters making the study double blind.

On arrival in the operation theatre, an intravenous cannula of 20G was inserted into the arm. Patient was pre-loaded with 5 ml/kg of Ringer lactate (RL). All patients were monitored non-invasively for arterial blood pressure (BP), heart rate (HR), oxygen saturation (SpO_2) and ECG changes. The pre-operative parameters BP (Systolic, diastolic and mean), HR and SpO2 were recorded. Pre-medication in the form of Inj. Fentanyl 2μg/kg IV and Inj. Midazolam 0.03mg/kg IV was given. After a period of two min., vitals parameters (BP, HR, SpO_2) were noted and these values were considered as baseline parameters. The patients were induced with either Ketofol (Group-KP) or Etomidate (Group-E) given intravenously over a period of 30-45 seconds.

Side-effects such as pain on injection and myoclonus were noted. Loss of eye lash reflex was the parameter used to confirm induction. Hemodynamic parameters were noted after induction. After giving Inj. Vecuronium in a dose of 0.1mg/kg, patients were ventilated with bag and mask using 100% O_2 for 3 minutes and trachea was intubated with appropriately sized cuffed endotracheal tube. Anesthesia was maintained with Isoflurane 1% in nitrous oxide and oxygen (50:50). The vital parameters (SBP, DBP, MAP, HR and SpO_2) of the

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patient were noted immediately after intubation (0 minute), from there onwards every 2 minutes for a period of 10 minutes and then at 15 minutes. During this period, hypertensive episodes (increase in MAP by 20% from baseline) were treated by adjusting the dial concentration of inhalational agents. Hypotensive episodes (decrease in MAP by 20% from baseline) were corrected using Inj. Mephentermine 5mg IV. To treat tachycardia (HR >110 bpm) Inj. Esmolol 0.5mg/kg IV was given and for bradycardia (HR < 50 bpm) Inj. Atropine 0.06mg/kg IV was given.

Statistical analysis

All data was presented as Mean ± Standard Deviation (SD). Demographic data was analyzed using Chi-square test and statistical significance in mean difference was done using student's t test. All statistical analysis was made using Minitab 15. *P* value of < 0.05 was regarded as statistically significant and $p < 0.001$ was taken as highly significant.

Results

A total of 80 patients were randomly allocated into two groups. All of these patients completed the study and their data was analyzed. The demographic and clinical characteristics of the patients in both the groups are presented in Table 1, there was no statistically significant difference between both the groups.

Table 1: Distribution of Mean Age of two groups.

Parameters	**Propofol-Ketamine (Mean ± SD)**	**Propofol-Etomidate (Mean ± SD)**	p-value
Age	41.41 ± 8.26	40.18 ± 9.38	0.375

Table 2: Distribution of gender between two groups.

Gender	**Propofol-Ketamine (N = 40) (%)**	**Propofol-Etomidate (N = 40) (%)**	p-value
Male	25 (62.5)	26 (65)	0.493
Female	15 (37.5)	14 (35)	

Table 3: Distribution of weight between two groups.

Weight (kg)	**Propofol-Ketamine (N = 40) (%)**	**Propofol-Etomidate (N = 40) (%)**	p-value
40-50	17 (42.5)	12 (30)	0.184
51-60	9 (22.5)	13 (32.5)	
61-70	14 (35)	15 (37.5)	

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Table 4. Systolic Blood pressure of both the Groups

Duration	Propofol-Ketamine (Mean ± SD)	Propofol-Etomidate (Mean ± SD)	P-Value
Baseline	116.31 ± 7.23	117.74 ±8.28	0.482
1 min after intubation	136.21± 9.31	139.27 ± 15.52	0.007
3 mins after intubation	116.66 ± 6.78	118.87 ± 12.49	0.026
5 mins after intubation	111.36± 8.28	112.37 ± 11.59	0.019

Table 5. Diastolic Blood pressure of both the Groups

Duration	Propofol-Ketamine (Mean ± SD)	Propofol-Etomidate (Mean ± SD)	P-Value
Baseline	77.13± 7.20	77.35 ± 7.27	0.675
1 min after intubation	89.74± 7.65	91.85 ± 10.67	0.017
3 mins after intubation	77.25± 7.67	72.10 ±7.76	0.040
5 mins after intubation	70.21± 7.41	69.37 ± 6.64	0.90

Table 6. Mean Arterial pressure of both the Groups

Duration	Propofol-Ketamine (Mean ± SD)	Propofol-Etomidate (Mean ± SD)	P-Value
Baseline	85.23 ± 7.2	87.29 ± 8.16	0.061
1 min after intubation	103.36 ± 8.28	106.38 ± 13.68	0.002
3 mins after intubation	88.54± 6.28	88.34 ±9.37	0.059
5 mins after intubation	81.51 ± 8.39	83.25 ± 9.45	0.021

Table 6. Mean Heart rate of both the Groups

Duration	Propofol-Ketamine (Mean ± SD)	Propofol-Etomidate (Mean ± SD)	P-Value
Baseline	80.47 ± 8.60	83.27 ± 8.36	0.210
1 min after intubation	93.25 ± 9.69	99.86 ±9.57	0.738
3 mins after intubation	88.36 ± 8.29	87.16 ± 8.87	0.549
5 mins after intubation	84.32 ± 8.36	85.61 ± 8.33	0.598

Analyzing the results of our study the hemodynamic parameters (SBP, DBP, MAP, HR) which was recorded before induction considered the baseline value and also after induction were comparable between the study group and are statistically insignificant with a P-value of > 0.05. The systolic blood pressure measured at 1, 3 ,5 mins after intubation showed statistically significant difference between the study groups with group PK showing better hemodynamic stability. DBP measured at 1, 3 minutes after intubation showed significant difference between the study groups in which group PK is found superior at 1

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minute and group E showing better hemodynamic stability at 3 mins. DBP at 5 mins were comparable between the groups. MAP at 1, 3, 5 minutes after intubation between the study groups showed significant difference, with group PK showing better hemodynamic stability. HR between the study groups at various time intervals were comparable and are statistically insignificant.

Table 2 shows mean and 95 % CI of hemodynamic variables in both the groups at baseline, after induction and three-time intervals after intubation.

Discussion

Different ages of patients do require different anesthesia concerns in every day practice for anesthesiologists. [9] Hemodynamic changes due to anesthesia in various surgeries have become a great concern in physicians of operation room and evidence show that changes in blood pressure, either increase or decrease, independently are associated with side effects and complications in patients undergoing surgery. All methods used in anesthesia induction are designed so that the hemodynamic stability is maintained especially in older patients that the need for surgery is increasing and complications of anesthesia are higher. [10]

Ketamine and etomidate both are drugs with least undesirable effects on hemodynamic changes and could be used with propofol to reduce its undesirable effects. In this clinical trial, we studied effects of ketamine + propofol and etomidate + propofol use for induction of anesthesia on hemodynamic variables. Consequently, there was significant decrease in SAP, DAP and MAP after induction and 3-6 minutes after intubation in ketofol group. Kamalipour and coworkers also reported significant decrease after induction of anesthesia in patients inducted with ketamine and propofol. [11] This finding indicates that the dose of Ketamine administered during the induction of anesthesia may not be high enough to neutralize the cardio-depressant effect of propofol. Unlike our findings, Bawja and coworkers reported minimal increase in SAP and DAP after induction which slowly reduced to normal values, these minimal changes were proposed to be due to antagonistic properties of propofol (decrease in blood pressure) and ketamine (increase in blood pressure). [12]

We also observed a significant decrease in HR after induction and 6 minutes after intubation and an increase 1 minute after intubation in ketofol group. Similar to our findings, Mi and coworkers reported a decreasing trend of HR in patients induced using ketamine and propofol. [13] However, other reports indicated an increase in HR after induction with ketamine and propofol. [14] Also in the available only study evaluating effects of ketamine and propofol in old patients, significant increase in HR after induction was reported. [15] Increase in heart rate with propofol and ketamine is explained on the basis of cardio stimulant effect of ketamine and stress response during intubation. [16] However, the decrease in HR in our study may be due to the difference in the dose of ketamine used in different studies and gentle intubation that would prevent stress response. However, we did not study HR after induction and after intubation separately.

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In our study there were no changes in SaO_2 after induction with values of 95% in ketofol group which is in line with the other studies reporting similar findings. [17] In this study, also there was significant decrease in SAP, DAP and MAP after induction and 6 minutes after intubation and significant increase in SaO_2 after induction and intubation. We found only one study evaluating effect of etomidate and propofol on hemodynamic changes after induction and intubation. [18] Saricaoglu and coworkers [19] observed no reduction in MAP and SAP in comparison to basic values. These results are indicative of hemodynamic stability after induction with etofol.

In our study we found no difference in SAP, DAP, MAP, HR and SaO_2 after induction and intubation between groups. Due to these results, we can consider similar results for ketamine + propofol and etomidate + propofol in establishing hemodynamic stability in old patients. [20]

Conclusion:

In our study indicated that induction with both ketamine + propofol and etomidate + propofol are both effective in maintaining hemodynamic stability and preventing hemodynamic changes due to propofol administration. Propofol plus ketamine can be recommended as a safe and effective combination for induction to attenuate haemodynamic responses to laryngoscopy and intubation, with superior haemodynamic stability compared to induction with etomidate alone. Further randomised clinical trials are required to check the efficacy and safety in patients with cardiovascular disease and critically ill patients.

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