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Comparison of hemodynamic changes in ketamine versus fentanyl as co-induction agent with propofol in elective surgical procedures

Yasmeen Azeem[1], Fatima Kanwal[2], Mehwish Kaneez[3], Suresh Kumar[4], Syed Muhammad Jawad Zaidi[5], Fariha Sardar[6]

[1]Fellow anesthetist, Pakistan Institute of Medical Sciences, Islamabad
[2]House Officer, Shalamar Hospital Lahore, [3]Final Year MBBS, Rawalpindi Medical University, Rawalpindi
[4]Associate Professor, Department of anesthesiology, Pakistan Institute of Medical Sciences, Islamabad
[5]Final Year MBBS, Rawalpindi Medical University, Rawalpindi,[6]Senior Demonstrator, Department of Pathology, Rawalpindi Medical University, Rawalpindi

Author`s Contribution

[1]Conception, data acquisition, revision, and approval of the final draft
[2]Designing and drafting of work
[3]Drafting and revision of work
[4]Conception and data acquisition
[5]Data analysis and interpretation
[6]Critical revision of intellectual content

Funding Source: None
Conflict of Interest: None

Received: Oct 10, 2020
Accepted: Dec 21, 2020

Address of Correspondent
Dr. Yasmeen Azeem
Fellow anesthetist, Pakistan Institute of Medical Sciences, Islamabad
dr.yasmeenazeem01@gmail.com

ABSTRACT

Objectives: To assess the hemodynamic changes caused by the co-induction of ketamine or fentanyl with propofol.

Methodology: This prospective randomized trial included 220 patients that underwent elective surgical procedures under general anesthesia with endotracheal intubation. Random allocation of patients was done into two equal groups and drugs were administered using the double-blinded technique. Group A received propofol and fentanyl while group B received propofol and ketamine given as intravenous bolus doses. Measurement of systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR) was done before induction and 10 minutes after induction before the surgical stimulus. Independent samples t-test and paired t-test were employed for analysis of the collected data.

Results: Both groups had normal hemodynamic parameters before induction; however, there was a significant difference in hemodynamic indices of both groups after 10 minutes of induction ($p<0.001$). Group A showed a significant decrease in SBP, DBP, and MAP after 10 minutes of induction ($p<0.001$). The patients in group B showed a significant increase in mean HR from baseline to 10 minutes ($p<0.001$). Group B demonstrated no change in the systolic, diastolic, and mean arterial pressures; however, group A elucidated a significant decrease in these hemodynamic parameters.

Conclusion: The combination of ketamine and propofol provides better hemodynamic stability than fentanyl and propofol. More studies are required to evaluate these changes in patients with cardiovascular comorbidities.

Keywords: Fentanyl, hemodynamic stability, Ketamine, Propofol.

Cite this article as: *Azeem Y, Kanwal F, Kaneez M, Kumar S, Jawad Zaidi SM, Sardar F. Comparison of hemodynamic changes in ketamine versus fentanyl as co-induction agent with propofol in elective surgical procedures. Ann Pak Inst Med Sci.2020; 16(4):161-165.*

Introduction

Procedural sedation is performed during a plethora of elective procedures for effective sedation and analgesia. An ideal anesthetic agent should provide rapid induction with anodyne, catalepsy, and oblivion along with safe recovery without compromising respiratory or hemodynamic status.[1] Woefully, no single medication, having all the attributes mentioned above exists so anesthesiologists use a concoction of different drugs in titrated doses to get maximal benefits.[2]

Propofol has gained a lot of popularity and is very commonly used in elective surgeries.[1,2] The profound lipid solubility, rapid induction, quick recovery time along with its amnestic and antiepileptic properties make it an efficacious anesthetic agent.[3] Nevertheless, a narrow therapeutic index, cardiorespiratory depressant effect, and poor analgesic property hinder its advantage as an effective anesthetic agent.[4] To ameliorate these constraints, various other anesthetic agents with good analgesic properties such as ketamine, fentanyl, or sevoflurane are co-administered with propofol.[5] Nonetheless, the search for an ideal co-induction agent with propofol is an area of constant and active medical research.

In the context of general anesthesia, ketamine (NMDA receptor antagonist) and fentanyl (a potent lipid-soluble opioid) have emerged as effective co-induction agents used with propofol.[6] Fentanyl or ketamine are combined with propofol to achieve balanced anesthesia with reduced side-effects. It is assumed that combining propofol with ketamine (ketofol) at low doses results in the rapid achievement of targeted sedation.[4,7] Similarly, fentanyl is also frequently co-administered with propofol due to its remarkable analgesic potential and short duration of action.[8] Even though these co-induction agents are considerably effective, their systemic adverse effects make their use quite challenging in certain patients.[9] The concurrent induction of fentanyl or ketamine with propofol leads to alterations in the blood pressure indices[7,8]. Many studies have been conducted to understand the alterations in hemodynamic homeostasis caused by these anesthetic agents; however, these studies delineated the hemodynamic changes of individual agents rather than their combination with propofol.[9,10]

The induction and maintenance of anesthesia are critical as anesthetic agents commonly interfere with cardiovascular physiology. They may cause alteration in heart rate, systolic, and diastolic blood pressure which can be worrisome for the patients.[11] There is a considerable gap in the literature when it comes to comparing the hemodynamic changes of ketamine and propofol versus fentanyl and propofol. This demands a need for a comprehensive randomized trial that compares the hemodynamic changes occurring from these two combinations after the induction of anesthesia. Thus, our study aims to compare the hemodynamic changes of ketamine versus fentanyl when co-induced with propofol.

Methodology

This prospective double-blinded randomized trial was conducted in the department of anesthesiology PIMS, Pakistan from June 2016 till December 2017. The institutional research ethics forum granted ethical permission for the execution of the study. Each participant signed a written consent form before their involvement in the study. Patients that refused to be a part of the study were excluded.

Our study included patients undergoing short elective surgical procedures with the American Society of Anesthesiologists (ASA) score I and II. Patients with drug allergies (especially to ketamine, fentanyl, and propofol), pregnancy, convulsions, monoamine oxidase inhibitor use, and jaundice were excluded. Furthermore, patients with cardiovascular comorbidities (severe hypertension, heart failure, and cardiomyopathy), duration of surgery lasting more than 80 minutes, and patients having difficult intubation (Mallampati score above II) were also excluded from the study. After application of this rigorous exclusion criteria, a total of 220 participants were ultimately represented in the study cohort. The sample size was calculated with 95% Confidence level, 80% power of the study, and taking the magnitude of mean SBP i.e., 129.76±9.47mmHg[12] with ketamine and 126.20±9.20mmHg[12] with fentanyl in patients undergoing short elective surgical procedures.

In all patients, induction of general anesthesia was done followed by endotracheal intubation. The blood pressure of all patients was measured at baseline (before the induction of anesthesia) and 10 minutes after the induction of anesthesia before the surgical stimulus. Pertinently, patients were randomly assigned into two groups of 110 patients each, and drugs were administered using double-blinded technique. In group A, induction of anesthesia was done with 1.0 mg/kg body weight of propofol and 1.0 mcg/kg body weight of fentanyl. In group B, induction was done with propofol 1.0 mg/kg body weight and ketamine 1.0 mg/kg body weight. In both groups, the anesthetic agents were given as intravenous bolus doses. The systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR) were monitored at baseline in the supine position. After the complete induction of anesthesia, the same parameters were measured after 10 minutes before the surgical stimulus.

All drugs were administered using a double-blinded technique. To ensure a double-blind study, drugs were made by a separate person, administered by a different person, and the hemodynamic changes were observed by a different observer. This technique helped us to ensure a double-blinded study design.

The demographics of the study participants across gender, ASA score, and type of surgery were tabulated. Categorical variables like gender, ASA score, and type of elective surgery were presented as frequencies and percentages. Quantitative variables like age, SBP, DBP, MAP, and HR were presented with means and standard deviations. A paired t-test was used to assess the significant difference in means of SBP, DBP, MAP, and HR at baseline and 10 minutes within each group. An independent samples t-test was employed to assess the significant difference between both groups. A p-value of less than 0.05 was considered statistically significant. Data were eventually analyzed on SPSS version 23.

Results

In our study participants, the mean age was found to be 46.19±13.19 years. The demographics of the study participants across gender, ASA score, and type of surgery performed across both groups are delineated in Table I.

Table II elucidates the comparison of hemodynamic changes among the study groups. A paired t-test was used to compare the mean values at baseline and after 10 minutes within each group. An independent sample t-test was applied to compare means between the two groups.

Discussion

Propofol due to its favourable pharmacokinetic properties is profoundly used as a procedural sedation agent.[3] Our study demonstrates that propofol when combined with ketamine or fentanyl causes considerable alterations in hemodynamic parameters. In group A, it has been demonstrated that co-inducted of propofol and fentanyl causes a significant decrease in SBP, DBP, and MAP at 10 minutes. Similar alterations in SBP, DBP, and MAP were observed in other randomized trials that evaluated hemodynamic changes caused by the co-induction of fentanyl and propofol.[2,7,8] The significant decrease in these blood pressure indices is attributed to a central sympathetic inhibition of fentanyl and cardio-depressant properties of propofol.[8,13] However, another study conducted at Ahvaz, Iran reported no significant difference in hemodynamic parameters i.e. SBP, DBP, and MAP after co-induced with propofol and fentanyl.[14]

The results of our study showed no significant change in SBP, DBP, and MAP from baseline to 10 minutes in group

Table I. Demographics of the study participants

Parameters		Group A (n=110)	Group B (n=110)	Total (n=220)
Gender	Male	46 (41.8%)	62 (56.4%)	108 (49.1%)
	Female	64 (58.2%)	48 (43.6%)	112 (50.9%)
ASA	ASA-I	62 (56.4%)	59 (53.6%)	121 (55%)
	ASA-II	48 (43.6%)	51 (46.4%)	99 (45%)
Type of surgery	Amputation	21 (19.1%)	23 (20.9%)	44 (20.0%)
	Appendectomy	12 (10.9%)	14 (12.7%)	26 (11.8%)
	Hernia/Mesh repair	12 (10.9%)	11 (10.0%)	23 (10.5%)
	Laparoscopic surgery	10 (9.1%)	16 (14.5%)	26 (11.8%)
	Tonsillectomy	10 (9.1%)	20 (18.2%)	30 (13.6%)
	Septoplasty	24 (21.8)	16 (14.5%0	40 (18.2%)
	Squint surgery	21 (19.1%)	10 (9.1%)	31 (14.1%)

Table II. Comparison of hemodynamics parameters in both groups

Parameter	Timing	Group A	Group B	p-value**
Systolic Blood Pressure (SBP)	At Baseline	130.17±5.94	129.58±5.53	0.446
	At 10 Minutes	120.26±6.07	129.92±6.04	<0.001
	p-value*	<0.001	0.672	-
Diastolic Blood pressure (DBP)	At Baseline	89.68±5.76	90.01±6.31	0.688
	At 10 Minutes	76.34±6.35	91.38±6.08	<0.001
	p-value*	<0.001	0.107	-
Mean arterial pressure (MAP)	At Baseline	103.17±4.29	103.20±4.57	0.96
	At 10 Minutes	92.97±4.58	104.22±4.62	<0.001
	p-value*	<0.001	0.097	-
Heart rate (HR)	At Baseline	79.95±6.10	79.76±6.24	0.827
	At 10 Minutes	80.53±6.88	89.83±5.86	<0.001
	p-value*	0.498	<0.001	

*Paired t-test
**Independent samples t-test

B. This indicates that ketofol acts as an efficacious anesthetic agent with minimal hemodynamic changes. In our study, an equivalent amount of propofol and ketamine was used for induction which balanced the antagonistic hemodynamic effects of the two agents leading to stabilized blood pressure indices. Kayalha H et al. reported similar findings in their trial indicating insignificant changes in mean blood pressure indices.[15] Moreover, a few studies have also reported a significant ($p<0.05$) increase in SBP, DBP, and MAP after induction of ketofol which is contrary to our findings.[14] In these studies, the dose of infused ketamine was higher that might explain the increase in hemodynamic indices as ketamine has a dose-dependent cardio-stimulatory effect.[16,17] Another study comparing two groups with the induction of ketamine and propofol in a ratio of 1:2 and 1:3 in groups I and II, respectively reported that as the proportion of propofol was increased in group II blood pressure decreased.[18] This finding augments the dose-dependent cardio-inhibitory effect of propofol indicating that propofol counters the stimulatory hemodynamic effect of ketamine when used in increased proportion.

No significant change was observed in the HR of patients in group A at 10 minutes after the co-induction of fentanyl and propofol. Another study also observed similar findings showing an insignificant change in HR after the co-induction of fentanyl and propofol.[6] On the contrary, another study elucidated the contradictory finding of a significant decrease in heart rate that can be due to centrally acting sympatholytic activity of fentanyl.[5] Moreover, our study showed an increase in the mean HR after 10 minutes of ketofol induction. Another study also showed a significant increase in heart rate after 10 minutes of ketofol induction ($p< 0.05$).[16] The cardio-stimulatory effect of ketamine on myocardial tissue might be the reason for the increase in heart rate.[15,17]

Both ketamine and fentanyl are efficacious co-induction agents for use with propofol; however, the hemodynamic changes after their co-administration must be kept in mind. There is a strong need for clinical evaluation and risk stratification of the patients according to their cardiovascular co-morbidities before choosing the right co-induction agent with propofol. Nevertheless, ketofol should be preferred when hemodynamic stability is needed. A study conducted in Lebanon also reported ketofol as a better induction agent with improved hemodynamic stability.[19] More studies are required to evaluate alterations in hemodynamic parameters of these co-induction agents in patients with cardiovascular comorbidities.[11] The study helps to increase the existing knowledge of these hemodynamic changes caused by these blends of anesthetic agents used and blaze new horizons of research in the field of anesthesiology. Hence, serious consideration should be given to our results as we recruited a relatively larger number of patients in our study. The results of the trail improve the practical implementation in the field of anesthesiology and help the anesthetists to understand the hemodynamics changes induced by these co-inductions agents with propofol.

Conclusion

The combination of ketamine and propofol provides superior hemodynamic stability than fentanyl and propofol. Fentanyl significantly reduces systolic, diastolic, and mean arterial pressure when co-induced with propofol. The concoction of ketamine and propofol significantly increases the heart rate in patients undergoing short elective surgical procedures. More studies are required to evaluate alterations of these hemodynamic parameters by these agents in patients with cardiovascular comorbidities.

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