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ORIGINAL RESEARCH ARTICLE

ANESTHETIC PROPERTIES OF PROPOFOL AND KETOFOL (KETAMINE WITH PROPOFOL): A COMPARATIVE STUDY

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ABSTRACT

Background: Surgical procedures require a safe anesthesia and safe anesthetic agents for this purpose use of small dose of sedative agent or any other anesthetic agent in order to reduce the dose requirement as well as adverse effects of the main inducing agent. Therefore, this study was carried out using ketamine with propofol (KETOFOL) to compare the hemodynamic stability (Heart rate and Mean arterial pressure) and induction doses.

Methods: Fifty patients of age 18 to 60 years of ASA II and I scheduled for elective surgery to be performed under general anaesthesia were randomly selected and divided into two groups. Patient in Group-P received 50 mg propofol and Group-K received 50 mg (25mg ketamine with 25 mg propofol) intravenously bolus slowly and then 10 mg in every 10 seconds until the loss of eyelash reflex and verbal response. The hemodynamic response was noted at different given time. Chi square test and student's t test were used for analysis.

Results: The study showed that the hemodynamic (heart rate and mean arterial pressure) was maintained and decrease in dose requirement for propofol for induction in (ketamine with propofol Ketofol group whereas there was significant decrease in hemodynamic (heart rate and mean arterial pressure) in Propofol group.

Conclusions: Our study concluded that fluctuations in heart rate and mean arterial pressure from baseline were more in propofol group compared to ketofol (ketamine with propofol) group. Therefore, Ketofol achieved better hemodynamic stability over propofol alone and also induction dose of propofol was reduced.

INTRODUCTION

Combination therapy has been now accepted as it can offer advantages over monotherapy.[1] A small dose of sedative or other anaesthetic agents in order to reduce the dose of induction agent as well as unwanted effects therefore, the benefits of combination therapy should include desired effect at low dose, minimum adverse effects and cost effectiveness .[2] Propofol is a short acting anesthetic agent, which is used widely for sedative-hypnotics, and for induction of anesthesia. The most important advantage of propofol is the rapid return of consciousness with the minimal residual central nervous effects. Injecting propofol has been known to cause pain on injection. Injecting 1% lidocaine can help to minimize this side effect. Also low dose ketamine reduces the pain associated with propofol injection. It has an induction dose of 1.5 to 2.5mg/kg intravenous with blood level 2 to 6 mcg/ml.[3] It's adverse effects are dose related, can decreases the systemic blood pressure either with bradycardia or no change in heart rate.[4]

Ketamine, NMDA receptor antagonist, is a phencyclidine derivative that produces dissociative anaesthesia, profound analgesia and amnesia with an induction dose of 1 to 2mg/kg. The hemodynamic changes include increased in systemic and pulmonary arterial blood pressure, heart rate, cardiac output, cardiac work and myocardial oxygen requirement after intravenous administration.[5] The incidence of emergence hallucinations effect can be reduced by co-administration of propofol, benzodiazepine and barbiturates.[6]

The objective of this study was to compare the average requirement of amount of anesthetic solution for induction as well as the hemodynamic effects between groups.

METHODS

This is a Hospital based prospective, comparative study conducted in College of Medical Sciences-Teaching Hospital, Bharatpur for a period of six months from March 2021 to August 2021. Total 50 Patients scheduled to undergo elective general, orthopedic or gynecological surgery under general anaesthesia were enrolled in the study. Following Institutional Review committee approval (Ref. No: CMSTH-IRC/2021-139) a written informed consent was obtained from all the 50

patients meeting the inclusion criteria and not having any of the exclusion criteria before enrollment in the study.
Patients enrolled into the study were randomly divided into one of the two groups by random closed enveloped method. Group-P (PROPOFOL) received propofol 50 mg bolus followed by 1ml in every 10 seconds where as Group-K (KETOFOL): received ketofol 50mg (ketamine 25mg with propofol 25mg) followed by 1ml in every 10 seconds until the loss of eyelash reflex.

Patients scheduled to undergo elective surgery under general anaesthesia with ASA grade I and II and between age group of 18–60yrs were included in the study.

Patients with comorbid condition like; significant cardiovascular, renal, hepatic or respiratory disorders, Psychiatric illness, under medications: benzodiazepines, clonidine, beta-blockers or thyroxin, Patients having allergy to study solution and Pregnant women were excluded from study.

Group-K (KETOFOL) was prepared with 50mg (1ML) of ketamine and (4ML) of Normal Saline (NS) i.e. total 5 ml mixed with 50mg (5ML) of propofol in a 10ML Syringe. The ratio of 1:1 was designed for KETOFOL group.

All the patients were pre oxygenated and induction was started with slow bolus dose of 10 ml of respective group drug and then tested for abolition of eyelashes reflex if not 1 ml solution was keep on adding for every 10 seconds till abolition of eyelash reflex. The total dose was considered as the induction dose. Then followed by rocuronium 50 mg and 100 mcg fentanyl and intubated the patients at 3 min from the time of induction started. While doing this data of HR, MAP was recorded every minutes and the last data was collected after 5 minutes after intubation time.

The data retrieved were entered in Excel spread sheet and analyzed using statistical program for social sciences (SPSS). The gender and ASA of patients were compared using Chi square test. Rest others were compared using Student's t test. All data were reported as mean values ± 1 SD. Overall significance level was maintained at $p < 0.05$.

RESULTS

The present study was conducted in 50 ASA I and II patients of either sex and age between 18 to 60 years scheduled for elective surgeries. Demographic data were comparable for age, weight, ASA and sex in both the groups. Our study showed (Table: 1&2) that the baseline heart rate in Propofol and Ketofol group were [79.28±9.57] and [80.96±8.26] respectively. Propofol group showed significant decrease in heart rate ($p<0.001$) at all observations i.e. 1,2,3,immediately after intubation and 5 minutes after intubation, whereas in ketofol group, heart rate remained significantly above baseline ($p<0.05$) at 1,2 3 minutes with non-significant changes at immediately after intubation and 5 minutes after intubation. The differences between the changes in two groups were statistically significant ($p<0.05$).

Table 1: Heart rate

Group (Mean ±SD)	Propofol	Ketofol	p value
Baseline	79.28 ± 9.57	80.96 ± 8.26	0.510
1 minute after induction (HR_1)	74.68 ± 8.29	83.28 ± 9.46	0.001*
2 minute after induction (HR_2)	72.08±7.66	82.20±9.35	<0.001*
3 minute after induction, just before intubation (HR_3)	72.48±7.46	82.28±8.70	<0.001*
Immediately after intubation (HR_4)	73.68±7.66	81.00±8.90	0.003*
5 minute after intubation (HR_5)	74.24±8.46	79.92±7.56	0.016*

Table 2: Comparison of mean HR with mean baseline

Group	Propofol	P value	Ketofol	P value
1 minute after induction (HR_1)	-4.6 (-5.8%)	<0.001*	2.32(2.87%)	<0.001*
2 minute after induction (HR_2)	-7.2 (-9.08%)	<0.001*	1.24(1.53%)	0.036*
3 minute after induction and just before intubation (HR_3)	-6.8 (-8.5%)	<0.001*	1.32(1.63%)	0.012*
Immediately after intubation (HR_4)	-5.6 (-7.06%)	<0.001*	0.04(0.05%)	0.948
5 minute after intubation (HR_5)	-5.4 (-6.8%)	<0.001*	-1.04(-1.28%)	0.095

Baseline average MAP (Table: 3&4) in propofol and ketamine with propofol group were 94.24±6.80 and 91.52±7.16 respectively. The result showed significant fall in MAP from baseline at all observations in propofol group ($p<0.001$), however, ketofol group showed non-significant increase in MAP at 1 minute after induction ($p=0.094$) followed by significant decrease in MAP from baseline at all other observations ($p<0.05$). The difference of MAP between the two groups were significant at 2,3,immediately after intubation and 5 minutes after intubation of observations (p value<0.05) while it was not significant at 1 minute of induction (p value=0.346).

In our study, the average weight of patient was around 60 kg Considering the average induction dose of propofol as 2 mg/kg on the basis of different studies, [10] the required dose of propofol would be around 120 mg However, the result of our study showed (Table: 5) the mean induction dose of Propofol was 100.80 ± 14.12 mg and 88.40 ± 10.68mg in Propofol group and Ketofol (ketamine with propofol) group respectively. The difference in the induction dose of drugs between the two groups (p value=0.001) was statistically significant.

Table 3: MAP in mmHg

Group (Mean ±SD)	Propofol	Ketofol	P value
Baseline	94.24±6.80	91.52±7.16	0.175
1 minute after induction (MAP_1)	90.61±6.34	92.37±6.72	0.346
2 minute after induction (MAP_2)	85.71±5.89	89.13±5.60	0.040*
3 minute after induction and just before intubation (MAP_3)	85.09±4.95	88.20±5.06	0.033*
Immediately after intubation (MAP_4)	85.73±4.82	88.56±4.74	0.042*
5 minute after intubation (MAP_5)	85.77±4.15	89.28±4.90	0.009*

Table 4: Comparison of MAP with baseline

Group	Propofol	P value	Ketofol	P value
1 minute after induction (MAP_1)	-3.6 (-3.82%)	<0.001*	0.9 (0.98%)	0.094
2 minute after induction (MAP_2)	-8.5 (-9.01%)	<0.001*	-2.4 (-2.62%)	0.001*
3 minute after induction and just before intubation (MAP_3)	-9.1 (-9.6%)	<0.001*	-3.3 (-3.61%)	<0.001*
Immediately after intubation (MAP_4)	-8.5 (-9.01%)	<0.001*	-2.9 (-3.17%)	0.001*
5 minute after intubation (MAP_5)	-8.4 (-8.9%)	<0.001*	-2.24 (2.45%)	0.006*

Table 5: Total induction dose

Group	Propofol	Ketofol	P value
Total induction dose of Propofol (Mean ±SD)	100.80±14.12	88.40±10.68	0.001*

DISCUSSION

Patient safety has always been the utmost priority for the physicians of both ancient and modern eras. Propofol, a widely used hypnotic agent, has peculiar advantages yet some disadvantages.[7]Induction of propofol with 2-2.5mg/kg results in 25-40% reduction in systolic blood pressure with similar changes in mean arterial pressure leading to hemodynamic instability hence drugs like ketamine and midazolam have been widely studied as co-induction agents to propofol to minimize its induction dose and hence side effects.

Ketamine is known to increase blood pressure due to its sympathomimetic properties and in addition preserves the respiratory drive.[7] The baseline anxiety is known to increase the anesthetic requirement.[8] Therefore, the aim of our study was to compare the effects of propofol with or without ketamine on changes in hemodynamic and induction dose.

We found in ketofol group, heart rate remained significantly above baseline ($p<0.05$) at 1,2 3 minutes ($p<0.05$) with non-significant changes at immediately after intubation and 5 minutes after intubation. Other studies also shown similar finding like, Yadav et al. did a prospective, randomized, double-blind study to compare between ketamine and midazolam as co-induction agent to propofol during induction in fifty ASA I and II patients undergoing elective surgery under general anaesthesia. The study showed statistically significant difference between the two groups.[9] Ketamine group had least change in heart rate from baseline compared to midazolam group similarly, Srivastava et al.[10] compared hemodynamic changes during induction using ketamine and midazolam as a co-induction agent to propofol among sixty-eight patients of ASA I and II undergoing elective surgery. They concluded that ketamine group had least change in heart rate from baseline which further supports our study. Likewise, Kalita A and Ahmed ALM did a prospective, randomized, clinical study on 150 patients of ASA I and II undergoing elective surgeries under general anaesthesia. They observed that fall in heart rate was significantly lesser in the ketamine group compared with midazolam group at 1 minute after induction.[11]

Since MAP is true driving pressure from peripheral blood flow and it does not change as a pressure wave form moves distally and also it is not altered by distortions generated by recording system, therefore, we have compared BP in terms of MAP in our study which shown MAP value remains more stable in Ketofol group when compared with Propofol alone. Similar findings like our study was seen in Yadav et al, Srivastava et al and Kalita A and Ahmed ALM.[9-11] They concluded that ketamine provides better hemodynamic stability as a co-induction agent.

Our study showed the mean induction dose of Propofol in Ketofol group was less than Propofol alone and the difference in the induction dose of drugs between the two groups (p value=0.001) was statistically significant. Similar to that observed by Kalita A and Ahmed ALM in which the mean induction dose of propofol in the midazolam group was 1.65 mg/kg and in the ketamine group was 1.43 mg/kg.[11] The difference between the groups was significant. Likewise, similar findings in studies by Srivastava et al, Rajkumar et al, Sukhminder Jit Singh Bajwa et al. and Ramdev et al.[10,12,13,15]

Ketamine with Propofol is an NMDA receptor antagonist and Propofol acts on GABA receptor. Although both the agents act in different receptors, reduction in the Propofol dose along with ketamine is due to the additive sedation effect of both the drugs.[14,16] Thus, our study showed Ketofol reduces the

induction dose as well as better in terms of hemodynamic stability compared to propofol alone.

CONCLUSION

With the Present study we concluded Combination therapy KETOFOL (ketamine with propofol) was associated with hemodynamic stability as well as appears to be cost-effective by significantly reducing the total induction dose of drug.

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CONFLICT OF INTEREST: None

FINANCIAL DISCLOSURE: None

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