International Surgery Journal
Jain S et al. Int Surg J. 2018 Sep;5(9):3134-3138
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: http://dx.doi.org/10.18203/2349-2902.isj20183736

Original Research Article

Assessment of effect of various concentration of ketamine-propofol (ketofol) on haemodynamic parameters and LMA insertion conditions

Sunita Jain[1]*, Raju Singh Rathore[1], Ashfaq Modiwala[2]

[1]Department of Anesthesiology, [2]Department of Preventive and Social Medicine, Amaltas Institute of Medical Sciences, District Dewas, Madhya Pradesh, India

Received: 20 June 2018
Accepted: 23 July 2018

***Correspondence:**
Dr. Sunita Jain,
E-mail: jainsunita25@gmail.com

ABSTRACT

Background: The purpose of this study is to compare the effect of various concentration of ketamine-propofol (ketofol) on LMA insertion condition and hemodynamic parameters.
Methods: Hundred patients of ASA I, II, aged between 18-65 years, were randomized in group A, B, C and D, each consist of 26, 25, 25, 24 patients respectively. They were premedicated with injection GPL, injection midazolam, injection fentanyl and induced with ketofol in 1:1, 1:2, 1:3 and 1:4 ratio in Group A, B, C, D respectively. 60 seconds after induction LMA insertion condition including mouth opening, swallowing, coughing, head and body movements, laryngospasm, ease of LMA insertion, apnea time, and time of LMA insertion were recorded. They were scored 1 to 3. Hemodynamic parameters- heart rate, noninvasive blood pressure and SPO2 were recorded before induction (T1), immediately following induction (T2), immediately after LMA insertion (T3), 5mins after LMA insertion (T4) and 10 mins after LMA insertion (T5).
Results: Total 100 patients were included in this prospective randomized double-blind study between April 2017 to March 2018. Pulse rate at (T3) was significantly lower (P-0.06) in group C and D. Diastolic BP was found lower at (T2) time (P-0.04) in group C and D. Apnea time was longest in group A (P-0.002) LMA insertion time was minimum in group B (P-0.008).
Conclusions: Addition of low dose of ketamine in propofol favour LMA insertion, due to opposite effect on muscle tone, better relaxation but heart rate, blood pressure remains stable with 1:1, 1:2 ratio of ketofol.

Keywords: Ketamine, Ketofol, LMA insertion, Propofol

INTRODUCTION

Anesthesiologists are often expected to provide safe, smooth and effective anesthesia. The ideal agent for this should have greater margin of safety in all age groups, also have quick onset and offset with the target outcome being an adequate level of anesthesia, analgesia, sedation, minimal anxiety, maximal amnesia, minimal drug related adverse effect while maintaining cardiovascular respiratory stability.[1,2] Currently no Indi dual agent is available which encompasses this aim, with the use of propofol and ketamine mixture the undesired effect of both decreases.[3] Propofol is sedative hypnotic agent with a short onset duration and recovery time.[4] This property makes propofol an ideal agent for anesthesia but can cause cardio respiratory instability and depression at the doses needed for laryngeal mask insertion.[5,6,7] The ketamine stimulate sympathetic nervous system and increases blood pressure along with increasing the heart rate. It has been reported that intra operative hemodynamic is more stable in studies where propofol and ketamine were combined.[8,9] The hypothesis of the

study is to compare the combination of two drugs namely propofol and ketamine (ketofol) in various concentration to achieve desired end point, their effect on hemodynamic and laryngeal mask insertion condition.

METHODS

A 100 patients of ASA class I, II scheduled for elective surgery that was last up to for two hours, between 18-65 years of either sex were included in the study during July 2017-June 2018. After approval from local research ethical committee written informed consent was obtained from patients. Patients with increased aspiration risk, body mass index >30, allergy to any agent used in study, predicted difficult airway, mallampati <2, patients with clinically significant cardio respiratory, psychiatric illness were excluded from study. Patients were randomly divided into four groups, randomization was computer based, each has 26,25,25,24 patients. Group A received ketofol in 1:1, Group B in 1:2, Group C in 1:3 and Group D in 1:4 ratio i.e. Ketamine: Propofol: 50:50 mg, 50:100mg, 50:150 mg, 50:200 mg respectively. To prepare the mixture Ketamine 1ml=50 mg, Propofol 1% was used. Mixture was made by adding appropriate amount of ketamine in decided amount of propofol. In preparation room. Patients were placed I.V. catheter and RL started, on OT table, standard monitor for NIBP, ECG, Spo2 has been placed.

Patients premedicated with Iv Glycopyrrolate 0.004 mg/kg, Iv Midazolam 0.02mg /kg, Iv Fentanyl 1-2 µg/kg followed by Iv ketofol mixture 0f 1:1,1:2,1:3,1:4 ratio as decided for various group, at 10 ml/60 sec till loss of consciousness was achieved. The anesthesiologist who prepared the ketofol mixture of different concentration was no more part of study further.

Laryngeal mask airway with deflated cuff was inserted by an experienced anesthetist using a water-soluble lubricant as per guideline of manufacturer 60 second after induction. If patient remains apneic for more than 30 seconds patient ventilation was assisted manually with bag and mass. LMA size 3 for patients ≤155 cm, size 4 for 155-180 cm and size 5 for ≥180 cm was used.

A cuff was inflated with proposed amount of air using injector. Effective ventilation was confirmed by capnography and chest expansion. A maximum 3 attempts were allowed for insertion of LMA, scoring was done for 1st attempt only.

If LMA could not be inserted in 3 attempts than alternative airway device was used. After successful placement of LMA anesthesia was maintained with isoflurane 1.5-2 % dial concentration, 50 % of N_2O and 50 % O_2 was used following LMA insertion patients were manually ventilated until spontaneous respiration was returned, and this period was recorded as apnea time.

Later on, patients were paralyzed and ventilated with synchronized intermittent mandatory ventilation mode until end of operation followed by reversal in usual manner. Condition of insertion of LMA were assessed using 6 variable mouth opening (1-full, 2-partial and 3-none), swallowing (1-nil, 2-mild and 3- severe), laryngospasm (1-nil, 2-mild, and 3-severe) and ease of LMA insertion (1- easy, 2- difficult and 3- impossible). Cessation of respiration for 30 sec was accepted as apnea and apnea time was recorded. Number of attempts for successful LMA insertion time was also noted.

RESULTS

Hundred patients were studied in this prospective randomized trial. They were divided into 4 groups, they are Group A (26 patients), Group B (25 patients), Group C (25 patients) and Group D (24 patients). Out of 100 52 were male and 48 were female patients.

Demographic data including age, weight, height and BMI were depicted in Table1, have no significant difference among them. The mean age was 37.5±15.5 in Group A, 38.2±8.7 in Group B, 39.3±13.9 in Group C and 44.4±15.9in Group D, was comparable (Table1). The BMI in Group A was 22.28±3.5, in Group B 22.5±2.6, in Group C 22.4±2.3 and in Group D 23.4±3.4. BMI was comparable among all groups and do not show any difference (Table1).

Table 1: Demographic data.

Parameters	Group A (26)	Group B (25)	Group C (25)	Group D (24)
Age	37.5±15.5	38.2±8.7	39.3±13.9	44.4±15.9
Weight	56.5±9.6	57.7±10.9	58.9±8.5	61.8±10.5
Height	159.2±7.1	159.6±8.4	161.9±8.8	162.5±8.9
BMI	22.28±3.5	22.5±2.6	22.4±2.3	23.4±3.4

Values are presented as mean ± SD or numbers of patient

Hemodynamic parameter included pulse rate, systolic blood pressure, diastolic blood pressure and mean blood pressure have shown in Table 3. Pulse rate was low at T1 time (before induction) in Group D, when compared to

group A, B and C, was statistically significant (P-0.03), (Table 1). At T2 time pulse rate was comparable in all groups. At T2 time the pulse rate was 77.33±2.69 in Group D, it was lowest among all 4 Groups as depicted in Table 3.

Table 2: LMA insertion parameters.

Parameters	Group A	Group B	Group C	Group D
Mouth opening 1/2/3	24/2/0	24/1/0	25/0/0	24/0/0
Coughing 1/2/3	26/0/0	25/0/0	25/0/0	24/0/0
Swallowing 1/2/3	25/1/0	24/1/0	25/0/0	24/0/0
Neck and body movement 1/2/3	22/4/0	25/0/0	20/5/0	20/4/0
Laryngospasm 1/2/3	26/0/0	25/0/0	25/0/0	24/0/0
Attempt of LMA insertion 1/2/3	21/5/0	23/2/0	24/1/0	24/0/0
Ease of insertion Easy/difficult/impossible	23/3/0	23/0/2	23/2/0	24/0/0

Values are presented as number of patients

Systolic blood pressure failed to show any difference and was comparable among all 4 groups at any time. Diastolic blood pressure at T1, T3, T4 and T5 time was comparable in all 4 groups but at T2 time it was 71.80±2.56 in Group A, 65.44±2.16 in Group B, 66.48±1.71 in Group C, 63.50±1.82 in Group D, the value was significantly less (P-0.04) in Group D as depicted in Table 3.

Table 3: Haemodynamic parameters.

Parameters	Time	Group A	Group B	Group C	Group D	p-value
Pulse	T1	2.21±3.07	2.18±3.12	1.82±3.44	1.89±2.48	0.39
	T2	2.17±3.08	2.13±3.61	2.21±3.05	1.84±2.42	0.075
	T3	2.25±2.62	2.13±3.38	2.18±3.05	1.85±2.69	0.067
	T4	2.16±3.06	2.12±3.64	2.15±2.88	1.91±2.79	0.54
	T5	2.13±2.95	2.13±3.91	2.13±3.06	1.89±2.93	0.42
SBP	T1	3.37±3.30	3.12±3.66	3.02±3.02	3.03±2.65	0.28
	T2	3.10±3.63	2.75±2.73	2.75±2.77	2.74±2.76	0.093
	T3	2.98±3.67	2.69±2.24	2.66±2.17	2.72±3.46	0.143
	T4	2.81±3.10	2.73±2.81	2.68±3.18	2.78±3.84	0.24
	T5	2.65±2.77	2.71±3.12	2.64±3.02	2.70±4.14	0.14
DBP	T1	1.98±2.75	1.84±2.30	1.78±1.88	1.73±1.93	0.416
	T2	1.86±2.56	1.63±2.16	1.66±1.71	1.52±1.82	0.04
	T3	1.75±2.20	1.60±1.84	1.60±1.78	1.54±2.17	0.55
	T4	1.70±2.28	1.59±1.90	1.61±2.28	1.61±2.13	0.76
	T5	1.58±1.92	1.59±2.01	1.65±2.30	1.56±2.57	0.31
MBP	T1	2.45±2.95	2.53±2.97	2.27±2.62	2.25±1.67	0.76
	T2	2.30±2.62	2.04±2.29	2.06±2.08	2.00±2.18	0.14
	T3	2.18±2.63	1.99±2.12	2.02±1.92	1.96±2.86	0.641
	T4	2.09±2.51	1.99±2.25	2.02±2.57	2.04±2.75	0.47
	T5	1.98±2.46	1.98±2.47	2.05±2.50	1.97±3.00	0.43

Inova and turkey HSD test was used; values are presented as mean±SD; p-value less than 0.05 is significant.

Mean BP was comparable in all 4 groups. Among insertion criteria 2 patients in Group1 and 1 patient in Group2 presented with grade II mouth opening, rest all the patients have shown grade I mouth opening as shown in Table 2. None of the patients among 100 had coughed after induction. 4 Patients in Group A and in Group D showed neck and body movements. LMA insertion could not be done in 2 patients of Group B while it was difficult in 3 patients of group A and 2 patients of Group C. All the patients of Group D had easy insertion of LMA as

depicted in Table 2. None of the patients had undergone laryngospasm after induction (Table 2). Apnea time, and LMA insertion time is depicted in Table 4, it shows that apnea time was longest in Group A and was statistically significant (P-0.002). The patients of Group C and Group D took less time in LMA insertion comparing to Group A and B. It was statistically significant as shown in Table 4.

Table 4: Apnea time and LMA insertion time.

Parameters	Group A	Group B	Group C	Group D	p-value
Apnea time	14.83±54.9	9.80±64.5	6.75±42.5	6.20±50.01	0.0002
LMA insertion time	405.0±1.28	2.73±1.34	385.0±0.95	370.0±0.79	0.0089

Values are presented as mean±SD or number of patients.; p-value less than 0.05 is significant.

DISCUSSION

There is no real standard dosing regimen establish to prepare ketofol, most studies had conducted with 1:1 ratio comparing with either of propofol, katamine.[10] This study has planned to compare effect of various combinations of ketamine-propofol (ketofol) on hemodynamic and LMA insertion condition. While comparing hemodynamic parameter including heart rate systolic, diastolic and mean BP among inter and intra group, heart rate at T3 time (Table 3) found lowest in group D it suggests that propofol causes dose dependent cardiac depression.[11,5] Propofol concentration in ketofol mixture is continuously increasing from A to D group.

Diastolic BP shows statistically significant difference at T2 times (p-0.04), is high in group A (Table 3) suggesting cardio protective action of ketamine and group D showed lowest diastolic BP as containing highest propofol fraction (1:4) in mixture (p-0.04). Group A that contained high fraction of ketamine showed high DBP. Gupta et al who compared ketamine, fentanyl and butorphanol before propofol induction in LMA insertion found higher systolic and diastolic BP in ketamine group.[12] These findings are also supported by Goh et al who compared ketamine, fentanyl or saline during LMA insertion prior to propofol induction.[13] In the present study it has been observed that apnea duration was highest in group A.

It was statistically significant (p - 0.002). It has been shown in various animals and human studies that bolus dose of ketamine depresses the respiratory response to CO_2, similar to opioid. Similarly, there are studies stating that hypoxemia and apnea have been observed following I.V. administration of katamine.[14,15]

In this study group A having highest fraction of ketamine in ketofol so the blood level of ketamine rises rapidly. LMA insertion time was significantly (p-0.0089) less in groups C and D comparing group A and B. Ketamine produces increase in muscle tone some time spasm. In groups C and D higher concentration of propofol suppresses this effect and made LMA insertion easy.

CONCLUSION

Addition of low dose of ketamine with propofol makes LMA insertion easier comparing to addition of higher dose of ketamine with propofol. Apnea duration and LMA insertion time is longer when ketamine is added in 1:1 and 1:2 ratio in ketofol mixture. Addition of small dose of ketamine to propofol favors LMA insertion. Further studies with larger study population are needed to get the more information.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Ketofol. D simmers, commentator: H Moodliar moderator: S Govender. Discipline of Anasthetics. 8 Feb 2013;No. 5. Available at: http://anaesthetics.ukzn.ac.za/libraries/documents2011/dale_simmers_-_ketofol.sflb.ashx
2. Arora S. Combining ketamine and propofol ("ketofol") for emergency department procedural sedation and analgesia: a review. Western J Emerg Med. 2008 Jan;9(1):20.
3. Rapeport DA, Martyr JW, Wang LP. The use of "ketofol" (ketamine – propofol admixture) infusion in conjunction with regional anaesthaesia. Anaesth Intensive Care. 2009;37(1):121-3.
4. Handa-Tsutsui F, Kodaka M. Propofol concentration requirement for laryngeal mask airway insertion was highest with the ProSeal, next highest with the Fastrach, and lowest with the Classic type, with target-controlled infusion. J Clinical Anesthes. 2005 Aug 1;17(5):344-7.
5. Hug JC, McLeskey CH, Nahrwold ML, Roizen MF, Stanley TH, Thisted RA, et al. Hemodynamic effects of propofol: data from over 25,000 patients. Anesthes Analges. 1993 Oct;77(4 Suppl):S21-9.
6. Larsen R, Rathgeber J, Bagdahn A, Lange H, Rieke H. Effect of propofol on cardiovascular Dynamics and coronary blood flow in geriatric patients. Anesthesia. 1998; 43(suppl) 25-31.

7. Kazama T, Ikeda K, Morita K, Kikura M, Doi M, Ikeda T, et al. Comparison of the effect-site keOs of propofol for blood pressure and EEG bispectral index in elderly and younger patients. Anesthesiol: J Am Soc Anesthesiolog. 1999 Jun 1;90(6):1517-27.
8. Gray C, Swinhoe CF, Myint Y, Mason D. Target controlled infusion of ketamine as analgesia for TIVA with propofol. Can J Anaesth. 1999;46:957-61.
9. Guit JB, Koning HM, Coster ML, Niemeijer RP, Mackie DP. Ketamine as analgesic for total intravenous anesthesia with propofol. Anesthesia. 1991;46:24-7.
10. Ozgul U, Begec Z, Karahan K, Erdogan MA, Aydogan MS, Colak C, et al. Comparison of propofol and ketamine-propofol mixture (Ketofol) on laryngeal tube-suction II conditions and hemodynamics: a randomized, prospective, double-blind trial. Current Therap Res. 2013 Dec 1;75:39-43.
11. Claeys MA, Gepts E, Camu F. Hemodynamic changes during anaesthesia induced and maintained with Propofol. Br J Anaesth. 1988;60:3-9.
12. Cheam EW, Chui PT. Randomized double blind comparison of fentanyl, mivacurium, or placebo to facilitate laryngeal mask airway insertion. J Anaesthes. 2000;55:32332-6.
13. Esa K, Azarinah I, Muhammad M. A comparison between laryngeal tube suction II airway and proseal laryngeal mask airway in laparoscopic surgery. Med J Malaysia. 2011;66:182-6.
14. Frizelle HP, Duranteau J, Samii K. A comparison of propofol with propofol – ketamine combination for sedation during spinal anaesthesia. Anaesth Analg. 1997;84:1318-22.
15. Tomatir E, Atalay H, Gurses E. Effects of low dose Ketamine before induction on propofol anaesthesia for pediatric magnetic resonance imaging. Paediatr Anaesth. 2004,14;845-50.

Cite this article as: Jain S, Rathore RS, Modiwala A. Assessment of effect of various concentration of ketamine-propofol (ketofol) on haemodynamic parameters and LMA insertion conditions. Int Surg J 2018;5:3134-8.