Original Research Article

Indian Journal of Anesthesia and Analgesia
March – April 2020; 7(2): 613–620
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.7220.25

Efficacy of Propofol-ketamine Over Propofol-butorphanol in Surgical Procedures less than 60 Minutes

Md Ayathullah[1], P Sahithya[2], Pujala Umapathy[3]

[1]Associate Professor, [2]Junior Resident, [3]Assistant Professor, Department of Anesthesiology, SVS Medical College, Mahbubnagar, Telangana 509001, India.

Abstract

Context: Propofol due to its favorable pharmacokinetic profile is widely used in TIVA. Propofol, when used alone causes decrease in cardiac index and mean arterial pressure and lacks analgesic property. To overcome these disadvantages, many adjuvant drugs are added. *Aim:* To compare two drug regimens: Propofol-ketamine and propofol-butorphanol in surgical procedures less than 60 minutes. *Settings and Design:* Hospital based comparative study was carried out at Department of Anesthesiology, SVS Medical College, Mahabubnagar. *Methods:* Sixty patients aged 18–60 years of both sexes belonging to ASA I and ASA II Grades were randomly allotted to one of two groups of 30 each. Group K received ketamine 1 mg/kg and propofol 1.5 mg/kg as inducing agent and Group B received butorphanol 20 µg/kg and propofol 1.5 mg/kg. In both the groups, anesthesia was maintained with propofol 9 mg/kg/hr *via* infusion pump. Heart rate, SBP, DBP were monitored as baseline, induction and in postinduction period after 10, 20, 30, 40 minutes. Occurrence of pain on injection with propofol was noted. Postoperative sedation was assessed using Ramsay Hunt sedation score and incidence of PONV was noted in both groups. *Statistical Analysis:* The data was analyzed using *t*-test and *p* - value of < 0.05 was considered statistically significant. *Results:* In Group B, there was significant variation in heart rate, SBP and DBP at everytime interval from baseline to end of surgery whereas there was no statistically significant change in hemodynamic parameter throughout surgery in Group K. The incidence of sedation postoperatively in Group K was 36.7% whereas in group B it was 46.7%. It was found that in Group B patients 23.3% of them had pain as compared with 56.7% in Group K showing pain. There was no statistically significant difference in two groups regarding incidence of PONV. *Conclusion:* Data and their analysis suggest that combination of Propofol-ketamine, offered better hemodynamic stability over propofol-butorphanol.

Keywords: Anesthesia technique; TIVA; Hemodynamic stability; PONV; Propofol; Ketamine; Butorphanol.

How to cite this article:
Md Ayathullah, P Sahithya, Pujala Umapathy. Efficacy of Propofol-ketamine Over Propofol-butorphanol in Surgical Procedures less than 60 Minutes. Indian J Anesth Analg. 2020;7(2):613–620.

Introduction

Total Intravenous Anesthesia (TIVA) as currently practiced uses several types of drugs, each performing a specific role. There is a perceived wisdom that they should all have rapid clearance rate and little delay between change in infusion rates, plasma levels and pharmacological actions. This allows for rapid induction, good plane of surgical stage of anesthesia and at the end of surgery,

Corresponding Author: **Pujala Umapathy,** Assistant Professor, Department of Anesthesiology, SVS Medical College, Mahbubnagar, Telangana 509001, India.

E-mail: umapujala26@gmail.com

Received on 14.11.2019, **Accepted on** 03.02.2020

smooth emergence and early recovery. There is growing interest in TIVA for the induction and maintenance of anesthesia, because of increasing availability of infusion pumps with the necessary features. Total intravenous anesthesia overcomes some of the disadvantages of traditional inhalation anesthesia in the following ways:[1]

1. The components of TIVA can be regulated independently as the need for each component changes during surgery. Both somatic and autonomic responses to varying degrees of surgical stimulation can be controlled.
2. Use of precision vaporizers can be avoided.
3. Operation theatres remain unpolluted by trace concentrations of nitrous oxide or volatile anesthetic agents. Although the evidence is unclear or controversial, inhalation of these gases may cause bone marrow depression, an increase incidence of miscarriages in pregnant operating room personnel and a decrease in the alertness of the anesthesiologist's.

Virtually all intravenous anesthetic agents like Thiopentone, Methohexitone, Etomidate, Buprenorphine, Morphine etc., have been tried for TIVA but they have been abandoned because of their own drawbacks.[2]

Propofol is a newer intravenous anesthetic agent, having favorable pharmacokinetic profile. It has already achieved considerable popularity for induction and maintenance of anesthesia for short-duration surgeries. Propofol is pleasant for most patients. It has a high clearance rate and rapid decline in blood concentration, making it eminently suitable for infusion. When Propofol infusion is discontinued there is rapid recovery from anaesthetic state. Ketamine which is water soluble intravenous anesthetic belongs to phencyclidine group of drugs. It is the only intravenous anesthetic which has hypnotic, analgesic and amnesic properties, and cheaper than Fentanyl and Butorphanol.[3]

Neither Propofol nor Ketamine are suitable as sole anesthetic agents. The most common adjuvant is an opioid analgesic and this is sufficient to provide complete anesthesia. Propofol produces a reduction in both cardiac index and mean arterial pressure, in contrast, Ketamine increases the same.[4]

Butorphanol, a synthetic opioid is used along with Propofol to provide analgesia. Butorphanol provides good analgesia but is associated with adverse effects like cardio depressant action, dizziness and sedation.[5]

Hence, in this study we compared two drug regimens, i.e. Propofol-Ketamine and Propofol-Butorphanol for TIVA technique in patients undergoing short surgical procedures of less than 60 minutes.

Materials and Methods

Source of Data

Sixty patients of SVS Medical College, Mahbubnagar, scheduled to undergo Elective short surgical procedures [less than 1 hour], with physical status ASAI and ASAII, in the age group 18–60 years, of both sexes were randomly selected.

The study was carried out with the approval of hospital research and ethics committee, after obtaining informed consent from patient. Those patients who required muscle relaxation and patients with anticipated difficult mask ventilation, patient with psychiatric disorders, on thyroid medication, hypertensive and with cardiac disease were not included in the study.

Study Design

Randomized, prospective, controlled study.

Inclusion criteria

1. 18–0 years of age;
2. ASA Class I and II ;
3. Patients coming for elective surgeries.

Exclusion criteria

1. Age < 18 years and > 60 years;
2. Patients with psychiatric disorders, thyroid disorders, cardiac disease, hypertension;
3. Anticipated difficult airway;
4. ASA class III and IV.

Design

The study included 60 patients randomly allocated into two groups:

Group K: 30 patients received Propofol-Ketamine combination;

Group B: 30 patients received Propofol-Butorphanol combination.

Preanesthetic evaluation included detailed history and physical examination to rule out cardiorespiratory disease and to know contraindications to drugs and techniques used.

Hemoglobin percentage, bleeding and clotting

time, HIV, HbSAg, RFT, serum electrolytes, chest *X*-ray, random blood sugars were done for each case. No special investigations were done for the study purpose.

All the patients were premedicated with injection Midazolam IV (0.01 mg/kg) 30 minutes before surgery. On arrival to the operation room an infusion line with 18-gauge cannula was started. Each patient was connected to NIBP, Pulse oximeter and ECG monitor.

Methods of collection of data

Anesthesia was induced with Propofol-Ketamine in Group K and with Propofol-Butorphanol in Group B with appropriate dosage according to body weight. Reading was collected from ECG, NIBP and pulse oximeter at regular intervals. Pain on injection with Propofol was noted while injecting Propofol, patients were continuously observed for vocal response, facial grimace, arm withdrawal or tears suggesting pain. Sedation was assessed in postoperative period using standard sedation score; Ramsay hunt sedation scoring was used. Incidence of PONV was noted.

Statistical analysis

The data was analyzed using *t*-test and *p* - value of < 0.05 was considered statistically significant.

Results

The present study was conducted on 60 patients undergoing elective short surgical procedure under TIVA belonging to American Society of Anesthesiology Grade I, Grade II physical statutes.

In this study, patients between age group of 18–60 year of both sexes were included.

Table 1 shows, age distribution in study groups. The mean age of the patients in two groups was similar at 39.833 years and 39.333 years and the difference was statistically not found to be significant.

Table 1: Age distribution in study groups

Group	Number	Mean	Standard deviation	*p* - value
Group K	30	39.833	10.75	0.1257
Group B	30	39.333	10.67	

Table 2 shows, sex Distribution in study groups. In Ketamine Group, out of 30 patients, 14 (46.7%) were females and 16 (53.3%) were male patients. In Butorphanol Group, out of 30 patients 15 (50%) were female and 15 (50%) were male patients. There was no statistically significant difference between the 2 groups.

Table 2: Sex Distribution in study groups

Sex	Group K	Group B	Total	Chi-square	*p* - value
Female	14 (46.7%)	15 (50%)	29 (48.3%)		
Male	16 (53.3%)	15 (50%)	31 (51.7%)		

Table 3 shows, intergroup comparison of changes in Systolic Blood Pressure (SBP) Period. The basal SBP in Ketamine group was 132.814.29 mm of Hg and in Butorphanol group was 135.67 13.30 mm of Hg. Both the groups were comparable statistically. On arrival, SBP in Ketamine group was 134.2014.41 mm of Hg and in Butorphanol group was 140.4711.78 mm of Hg. Both the groups were comparable statistically. SBP at induction in Ketamine group was 135.9313.58 and in Butorphanol group was 119.8713.85 mm of Hg. The difference in SBP in 2 groups was statistically highly significant with *p* - value of 0.0001. SBP at 10 minutes in Ketamine group was 133.6311.96 mm of Hg and in Butorphanol group it was 115.9023.58 mm of Hg. The difference in SBP in 2 groups was statistically highly significant. SBP at 20 minutes in Ketamine group was 135.0712.41 mm of Hg and in Butorphanol group was 122.9011.28 of mm of Hg. The difference in SBP in 2 groups was statistically highly significant. SBP at 30 minutes in Ketamine group was 133.4511.98 and in Butorphanol group was127.7617.17. The difference in SBP in 2 groups was statistically highly significant (*p* - 0.0005). SBP at 40 min in Ketamine group was 133.0011.14 mmof Hg and in Butorphanol group was 126.6014.35 mm of Hg. The difference in SBP in 2 groups was statistically highly significant.

Table 3: Intergroup comparison of changes in Systolic Blood Pressure (SBP) Period

Period	Group	N	Minimum	Maximum	Mean	SD	T value	*p* - value
Baseline	K	30	110	160	132.8	14.29	0.804	0.425
	B	30	110	158	135.7	13.31		
Arrival	K	30	110	160	134.2	14.41	1.843	0.07
	B	30	110	160	140.47	11.78		
Induction	K	30	100	168	135.9	13.58	4.536	0.0001
	B	30	100	142	119.87	13.85		
10 min	K	30	110	156	133.63	11.96	3.673	0.0001
	B	30	11	140	115.9	23.58		
20 min	K	30	110	154	135.07	12.41	3.943	0.0001
	B	29	106	140	122.9	11.28		
30 min	K	29	110	156	133.45	11.98	2.855	0.005
	B	25	70	156	127.76	17.17		
40 min	K	22	116	150	133.00	11.14	1.603	0.113
	B	20	106	150	126.6	14.35		

Table 4 shows, intergroup comparison of changes in Diastolic Blood Pressure (DBP). The baseline DBP in Ketamine group was 82.27.09 and in Butorphanol group was 80.575.894. Both the groups were comparable statistically. DBP on arrival in Ketamine group was 81.476.66 mm of Hg and in Butorphanol group was 82.536.146 mm of Hg. Both the groups were comparable statistically. On induction DBP in Ketamine group was 80.676.97 mm of Hg and in Butorphanol group was 68.937.31 mm of Hg. The difference was statistically significant. DBP at 10 minutes in Ketamine group was 78.935.21 and in Butorphanol group was 69.305.82 mm of Hg. The difference in DBP was statistically highly significant. DBP at 20 min in Ketamine group was 80.136.84 and in Butorphanol group was 71.525.44 mm of Hg. The difference in 2 groups was significant statistically. DBP at 30 min in Ketamine group was 78.146.04 mm of Hg and in Butorphanol was 74.2412.52 mm of Hg. The difference was not significant statistically. DBP at 40 min interval in Ketamine group was 77.645.33 and in Butorphanol group was 73.96.09 and it was statistically significant.

Table 4: Intergroup comparison of changes in Diastolic Blood Pressure (DBP)

Period	Group	N	Minimum	Maximum	Mean	SD	*t*-value	*p* - value
Baseline	K	30	70	94	82.2	7.09	0.97	0.33
	B	30	70	96	80.57	5.89		
Arrival	K	30	70	94	81.47	6.66	0.645	0.522
	B	30	70	96	82.53	6.14		
Induction	K	30	68	96	80.67	6.97	6.361	0.0001
	B	30	60	86	68.93	7.31		
10 min	K	30	70	90	78.93	5.21	6.78	0.0001
	B	30	60	80	69.3	5.82		
20 min	K	30	68	102	80.13	6.84	5.36	0.0001
	B	29	64	80	71.52	5.44		
30 min	K	29	68	90	78.14	6.04	1.42	0.143
	B	25	64	130	74.24	12.52		
40 min	K	22	70	90	77.64	5.33	2.215	0.031
	B	20	66	92	73.60	6.09		

Table 5 shows, intergroup comparison of HR at various time intervals. Base line heart rate in Ketamine group was 76.73 4.94 and in Butorphanol group was 74.204.96, both the groups were comparable statistically. On arrival in Ketamine group the mean heart rate was 77.804.85 and in Butorphanol group it was 79.007.62. Both the groups were comparable statistically. Mean heart rate at

induction in Ketamine group was 78.134.72 and in Butorphanol group, it was 73.008.12, the differences were significant statistically. At 10 min the mean heart rate was 77.474.81 in Ketamine group and it was 70.836.59 in Butorphanol group. Difference in both the groups was statistically significant. The mean heart rate at 20 minutes in Ketamine group was 78.807.25 and in Butorphanol group was 71.074.64; there was a significant difference when compared. At 30 minutes, the mean heart rate in Ketamine group was 78.835.91 and in Butorphanol group was 69.683.94. The difference was statistically significant. At 40 minutes, the mean heart rate in Ketamine group was 81.138.13 and in Butorphanol group was 70.405.21 this difference was highly significant.

Table 5: Intergroup comparison of HR at various time intervals

Period	Group	N	Minimum	Maximum	Mean	SD	*t*-value	*p* - value
Baseline	K	30	70	86	76.73	4.94	1.72	0.62
	B	30	64	86	74.2	4.96		
Arrival	K	30	70	88	77.8	4.82	0.727	0.47
	B	30	66	94	79.0	7.62		
Induction	K	30	70	88	78.13	4.72	2.991	0.004
	B	30	60	92	73.0	8.12		
10 min	K	30	70	86	77.47	4.81	4.452	0.0001
	B	30	60	84	70.83	6.59		
20 min	K	30	70	100	78.8	7.25	4.858	0.0001
	B	29	60	78	71.07	4.64		
30 min	K	29	68	90	78.83	5.91	4.452	0.0001
	B	64	62	78	69.68	3.94		
40 min	K	22	68	96	81.13	8.13	5.061	0.0001
	B	20	60	84	70.4	5.215		

Table 6 shows, comparison of Pain on injection with Propofol. In Group K, out of 30 subjects studied, 17 patients experienced pain on injection with Propofol (56.7%). In Group B, out of 30 subjects studied, 7 patients experienced pain on injection with Propofol (23.3%). There was a statistically significant difference between the two groups.

Table 6: Comparison of Pain on injection with Propofol

Pain on injection	Group K		Group B		Total	
	Number	%	Number	%	Number	%
Absent	13	43.3	23	76.7	36	60
Present	17	56.7	7	23.3	24	40
Total	30	100.0	30	100.0	60	100

$p = 0.008$, HS

Table 7 shows, comparison of Postoperative sedation. In Group K, out of 30 patients studied, 11 (36.7%) had postoperative sedation, whereas in Group B 17 (56.7%) had postoperative sedation. Though there was no statistically significant difference on comparison among 2 groups, it can be clearly inferred that prevalence of sedation was high in Group B.

Table 7: Comparison of Postoperative sedation

Postoperative sedation	Group K		Group B		Total	
	Number	%	Number	%	Number	%
Absent	19	63.3	13	43.3	32	53.3
Present	11	36.7	17	56.7	28	46.7
Total	30	100.0	30	100.0	60	100.0

$p = 0.121$, NS

Table 8 shows, incidence of postoperative nausea and vomiting. In Group K, out of 30 subjects studied, 6 subjects complained of PONV in postoperative period (20%). In Group B, 8 subjects complained of PONV (26.7%). The two groups (23.3%) when compared, the incidence of PONV was not significant statistically.

Table 8: Incidence of Postoperative nausea and vomiting

Postoperative nausea and vomiting	Group K		Group B		Total	
	Number	%	Number	%	Number	%
Absent	24	80	22	73.3	46	76.7
Present	6	20	8	26.7	14	23.3
Total	30	100	30	100	60	100

$p = 0.542$, NS

Discussion

Total intravenous anesthesia has been a subject of interest for all anesthesiologists, as this is now well-established as an appropriate alternative to the traditional approach of volatile anesthetics alone; indeed sometimes it is the preferred alternative.

The availability of drugs with short blood-brain equilibration times enables the clinician to use intravenous anesthetics and analgesics where controllability is easy and rapid. The advent of continuous infusion system has made administering TIVA all the more popular and convenient. But, even today, we are still without any one intravenous drug that can alone provide all the requirements of anesthesia (i.e. unconsciousness, analgesia and muscle relaxation). Hence, there is need to administer several different agents to produce the desired results. This in turn leads to important and significant drug interactions.[6]

We studied two drug regimens; Propofol-Ketamine, (Group K) and Propofol-Butorphanol, (Group B) for TIVA technique. In the present study, with Group K, there was no statistically significant change in heart rate, systolic blood pressure and diastolic blood pressure during postinduction and maintenance of anesthesia throughout the procedure when compared to Group B.

A similar study was done by Dunnihoo M et al.[7] using Propofol-Ketamine on cardiovascular response and wake up time. They showed that this combination maintained better hemodynamic stability and there was no significant change in heart rate and arterial blood pressure throughout the procedure.

In another study conducted by Furuya A et al.[8] investigated for arterial pressure changes during the induction of anesthesia with Propofol by adding intravenous Ketamine in 12 patients. Authors concluded that administration of Ketamine before induction with Propofol preserved hemodynamic stability in terms of blood pressure and heart rate compared with induction with Propofol alone.

The advantages of Ketamine in terms of better hemodynamically intraoperatively, when combined with Propofol have been studied by numeros investigators. Hernandez C et al.[9] compared three techniques for intravenous anesthesia (Propofol-Ketamine and Propofol-Fentanyl). They found that Propofol-Ketamine are most stable hemodynamically.

In the present study in Group B, basal, postinduction and intraoperative hemodynamic variables like heart rate, systolic blood pressure and diastolic blood pressure were monitored. We found that there was statistically significant decrease in heart rate after induction and during maintenance phase of anesthesia. A significant decrease in systolic blood pressure and diastolic blood pressure were also observed after induction and during maintenance of anesthesia with Propofol-Butorphanol.

A study was conducted by Mayer M et al.[10] where they compared the hemodynamic and analgesic effects of Propofol-Ketamine with Propofol-Fentanyl an opioid similar to Butorphanol. They found that distinct decrease in mean arterial blood pressure and heart rate after induction and maintenance of anesthesia with Propofol-Fentanyl were seen. Saha K et al.[11] conducted a randomized double-blind study to evaluate the efficiency of combination of Propofol-Ketamine and Propofol-Fentanyl in 60 patients undergoing minor surgery. They showed that significant decrease in heart rate after induction and maintenance of anesthesia with Propofol and Fentanyl. A significant decrease in systolic blood pressure was also observed.

Propofol, a modern intravenous hypnotic, produces a reduction in both cardiac index (CI) and Mean Arterial Pressure (MAP). Ketamine, a potent analgesic in contrast causes an increase in mean arterial blood pressure and cardiac index. The aim of present study was to investigate whether the combination of Propofol-Ketamine or Propofol-Butorphanol can give better hemodynamic stability during induction and maintenance of anesthesia. The present study concluded that, the single-dose of Ketamine during induction of anesthesia was enough to neutralize the cardio-depressant effect of Propofol. During the maintenance of anesthesia, there was better hemodynamic stability in Ketamine group than in Butorphanol group. Butorphanol intensified the fall in arterial blood pressure after Propofol induction and patients in this group were more sedated.

A difference in incidence of sedation in two groups was noted. In Ketamine group, the incidence was 36.7% where as in Butorphanol group, the incidence was 56.7%.

A study, conducted by Rosendo MF et al.[12] showed the effect of Ketamine and Propofol in terms of respiration, postoperative mood, perception and cognition. They concluded that, a mixture of Propofol and Ketamine provided hemodynamic stability during anesthesia and produced a positive mood state during recovery period without side-effect. The combination also appeared to prompt early recovery of cognitive function. This may be due to the fact that Propofol inhibits NMDA receptors in Hippocampus neurons, which may have contributed to the positive effect on mood. Sedative effects of Propofol are partially antagonized by arousal effect of Ketamine.[13]

Pain on injection with Propofol is attenuated by various methods like injection of Propofol in carrier fluid, large vein, and use of antiemetics, analgesics and anesthetic drugs.

Of the 2 groups studied, Butorphanol group enabled to abolish the pain on injection with Propofol. Incidence of pain was 23.3% in group B, where as in Ketamine group it was 56.7%. This is consistent with study done by Agarwal A et al.[14] where they found that effective method of attenuating Propofol induced pain is with pretreatment by Butorphanol.

One major disadvantage of TIVA is PONV, which is the rate limiting factor in patient discharged from postoperative ward. In the present study, the incidence of PONV in Group K was 20.0% where as in Group B it was 23.3%. The difference between the 2 groups was statistically insignificant.

Conclusion

The present study is conducted to evaluate and compare two drug regimens; i.e. Propofol-Ketamine and Propofol-Butorphanol for TIVA technique in patients undergoing short surgical procedures. Propofol-Ketamine (Group K) combination has the advantage of offering better hemodynamic stability and postoperative recovery in terms of sedation when compared to Propofol-Butorphanol combination. Attenuation of pain on injection was the only advantage with the Propofol–Butorphanol (Group B) combination. Incidence of PONV is similar in both the groups.

Key Messages: Combination of Propofol-ketamine can be used for total intravenous anesthesia in short surgical procedures of duration of less than 60 minutes.

Support: Nil

Conflicts of interest: Nil

References

1. Robert FJ. Total intravenous anesthesia. Anesthesiology 1996;84:149–51.
2. Sandin R, Nordstrom O. Awareness during total intravenous anesthesia. Br J Anesth 1993;71:782–87.
3. Vasanth S, Radhakrishnan A, Keshavan VH. Effect site concentration of propofol at induction and recovery of anesthesia: A correlative dose-response study. Indian J Anesth 2018;62:54–60.
4. Scheepstra GL, Booij LH, Rutten CL, et al. Propofol for induction and maintenance of anesthesia: Comparison between younger and older patients. Br J Anesth 1989:62: 54–60.
5. Cheng KI, Chu KS, Fang YR, et al. Total intravenous anesthesia using Propofol and Ketamine for ambulatory gynecologic laparoscopy. Kaohsiungc J Med Sci 1999;15(9):536–41.
6. Michel Foehn ER. Adult and pediatric anesthesia/ sedation for gastrointestinal procedures outside of the operating room. Curr Opin Anesth 2015;28(4):469–77.
7. Dunnihoo M, Wuest A, Meyer M, et al. The effects of total intravenous anesthesia using propofol, ketamine, and vecuronium on cardiovascular response and wake up time. Am Assoc Nurse Anesthetists J 1994;62(3):261–63.

8. Furuya A, Matsukawa T, Ozaki M, et al. Intravenous ketamine attenuates arterial pressure changes during the induction of anesthesia with propofol. Eur J Anesthesiol 2001;18(2):88–92.
9. Hernandez C, Parramon F, Garcia-Velasco P, et al. Comparative study of 3 techniques for total intravenous anesthesia: Midazolam-ketamine, propofol-ketamine, and propofol-fentanyl. Rev Esp Anestesiol Reanim 1999;46:154–58.
10. Mayer M, Ochmann O, Doenicke A, et al. The effect of Propofol-Ketamine anesthesia on hemodynamics and analgesia in comparison with Propofol-Fentanyl]. [Article in German]. Anesthesist 1990;39(12):609–619.
11. Saha K, Saigopal M, Sundar R. Comparative evaluation of propofol ketamine and propofol fentanyl in minor surgery. Indian J Anesth 2001;45:100–103.
12. Rosendo MF, Laura CD, Merritt TM, et al. The effects of small-dose ketamine on propofol sedation: Respiration, postoperative mood, perception, cognition and pain. Anesth Analg 2001;92(6):1465–469.
13. Kaur J. Dose sparing of induction dose of Propofol by Fentanyl and Butorphanol: A comparison based on entropy analysis. Saudi J Anesth 2013;7:128–33.
14. Agarwal A, Raza M, Dhiraaj S, et al. Pain during injection of propofol: The effect of prior administration of butorphanol. Anesth Analg 2004;99(1):117–19.