

ORIGINAL ARTICLE

Which sedation method is appropriate for spinal anesthesia: propofol or ketamine-propofol combination?

Handan Güleç, Zehra Baykal Tural, Mehmet Şahap, Münire Babayiğit, Hansa İnceöz, Aysun Kurtay, Eyüp Horasanlı

Department of Anesthesiology and Reanimation, Keçioren Training and Research Hospital, Ankara, (Turkey)

Correspondence: Dr. Handan GÜLEÇ, Keçioren Training And Research Hospital, Ankara, (Turkey); E-mail: handandrhandan@yahoo.com.tr; Phone: +903123569000; Fax: +903122130034

ABSTRACT

Background and objective: Spinal anesthesia is a preferred method in daily practice as it provides muscle relaxation and maintains spontaneous respiration during surgical procedures. Opioids, midazolam, ketamine, propofol and dexmedetomidine are the generally preferred sedoanalgesic agents. Ketofol, a mixture of ketamine and propofol, is a good analgesic and also provides sedation even at low doses.

Methodology: 54 inguinal hernia surgery patients were included and divided into two groups: propofol group (Group P, n: 27) and ketofol group (Group KP, n: 27). The ketofol mixture was obtained by mixing 2 ml of ketamine (50 mg/ml) with 8 ml saline and then adding 10 ml of propofol (%1, 10 mg/ml) to acquire a solution of 5mg/ml ketamine and 5 mg/ml propofol. The Ramsay sedation scale (RSS) and bispectral index (BIS) were used to determine the response to sedation and analgesia. Intraoperative hemodynamic parameters and medication dosages were recorded. At postoperative 12th hour visual analog scale (VAS) was performed to measure patient satisfaction and pain.

Results: Although the duration of surgery was similar in both groups, the duration in intensive care unit was significantly longer in Group P (p:0.002, Table 1). The time taken to reach Ramsay 3 value was significantly shorter in Group KP than in Group P (6.8 ± 5.1 vs 9.6 ± 7.2 minutes, p:0.042). Group KP patients were also highly satisfied and experienced less pain in postoperative period according to VAS evaluation (p: 0.04).

Conclusions: Ketofol is a good alternative for propofol in spinal anesthesia for regional surgeries with higher postoperative patient satisfaction, lower pain rates and shorter intensive care requirements.

Key words: Ketamin; Propofol; Regional anesthesia

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INTRODUCTION

Spinal anesthesia is generally preferred in daily practice as it provides adequate muscle relaxation and maintains spontaneous respiration.¹ Patients are also protected from intubation and associated aspiration pneumonia risks. Adequate sedation with spinal anesthesia reduces the stress and anxiety of patients and increases their postoperative satisfaction.² However, when administering sedation, some complications such as respiratory depression, bradycardia and hemodynamic instability might still be encountered. Also it might delay discharge of patient and sometimes might not

be preferred by surgical team in outpatient surgical procedures.

Opioids, midazolam, ketamine, propofol and dexmedetomidine are the generally preferred sedoanalgesic agents.³ Propofol, as an intravenous anesthetic, is usually applied as a slow infusion for sedation in spinal anesthesia but intermittent bolus is also a possible route of administration.⁴ As spinal anesthesia is preferred method in surgical procedures which last not longer than 3 hours and propofol's half life not lengthen in the first few hours of infusion waking might not delay in spinal anesthesia procedures that was performed by

propofol infusion.⁵ The use of propofol might also cause some cardiovascular and respiratory system complications.⁶

Ketamine performs its' effects by direct sympathetic stimulation and by reuptake inhibition of norepinephrine from the postganglionic sympathetic system.⁷ It also induces functional dissociation between the limbic and cortical system that is often referred to as 'dissociative anesthesia'. Protective airway reflexes are maintained during sedation and the high therapeutic index of ketamine makes this drug suitable for regional anesthesia.⁸ On the other hand use of this medication might also induce some complications like excessive secretory activity, nystagmus, hypertension, increased intracranial pressure and hallucinations.

Ketofol, which is created by mixing ketamine and propofol, is a good analgesic and provides sedation. Even at low doses, it provides the opportunity for adequate sedation. By protecting the muscle tone, airway reflexes and spontaneous respiration are protected.⁹

The bispectral index (BIS) is non-invasive electroencephalography which shows the level of hypnosis during sedation and anesthesia.^{10, 11} The BIS and Ramsay sedation (RSS) scale are useful methods for checking the depth of sedation.

As both positive and negative aspects have been determined for ketamine and propofol, in this we study aimed to evaluate if using propofol or a mixture of ketamine + propofol was one more effective for sedation in a group of inguinal hernia surgery patients.

METHODOLOGY

After approval from the Local Ethics Committee and obtaining informed written consent from each patient, 54 American Society of Anesthesiologists (ASA) physical status I-II adult patients who were scheduled for elective inguinal hernia surgery under spinal anesthesia were included in this study. Those who were unable to cooperate or communicate, those with a history of drug abuse such as opioids, analgesics or sedatives, and those with a history of allergy to the drugs used in this study were excluded.

After computerized random number generation, 54 consecutive patients were divided into two groups: sedation with propofol group (Group P, 27 patients) and sedation with ketofol group (Group KP, 27 patients). All patients received premedication with 0.03 mg/kg midazolam intravenously before

anesthesia and were undergone non-invasive blood pressure, pulse oxymetry, electrocardiographic analysis and BIS (Aspect® Medical Systems, BIS A-2000, Norwood, MA, USA) were also monitored. The patients were preloaded with 6 ml/kg of isotonic saline solution prior to the initiation of spinal anesthesia. Spinal anesthesia was performed by using the midline approach with a 26-gauge Quincke needle at the L2-3 or L3-4 intervertebral space while the patient was in the sitting position.

After ensuring free cerebrospinal flow, 10mg (2ml) of 0.5% hyperbaric bupivacaine was injected. A sensory dermatomeal level of at least T10 was judged as an appropriate sensory block level.

The ketofol mixture was obtained by diluting 2 ml of ketamine (50 mg/ml) in 8 ml saline then adding 10 ml of propofol (%1, 10 mg/ml) to acquire a solution of 5mg/ml ketamine and 5 mg/ml propofol.

In Group P, propofol was given at a dose of 1.0 mg/kg and then an additional dose of 0.5 mg/kg was given to increase the RSS upto 3. In Group KP, ketofol was given at a dose of 1mg/kg ketofol and then an additional dose of 0.5 mg/kg was given to increase the RSS upto 3. In follow up period we aimed to keep RSS at 3-4 level.

All subjects received 5 L/min of oxygen through simple face masks. All monitoring measurements were recorded every 5 minutes during surgery. When the mean blood pressure decreased by more than 20% of the baseline, 5 mg of ephedrine was injected. In addition, the BIS and RSS were checked continuously in order to monitor the sedation level by same anesthesiologist for every subject. BIS monitoring was used to maintain the same depth of intraoperative sedation for all patients. The RSS was used to determine the response to sedation and analgesia. It was graded between 1-5 (deep sedation: 1, patient awake: 5). The Modified Aldrete Scale criteria were used for postoperative discharge from PACU with recovery discharge criteria on a scale of 0-10.

Patient satisfaction and postoperative pain was evaluated by classical visual analog scale (VAS) which ranges between 0 (highly satisfied / no pain) and 10 (not satisfied / severe pain). VAS was evaluated at postoperative 12th hour for each subject.

Statistical analysis was performed by using Statistical Package for the Social Sciences 15.0 (SPSS 15.0, SPSS Inc, Chicago, IL) software. All quantitative data were analysed with the Kolmogorov-Smirnov test for distribution analysis. Data with normal distribution were expressed as mean \pm standard

deviation and data with skew distribution were expressed as median (inter quartile range). According to the distribution status of quantitative data, the independent sampling t-test or Mann Whitney U-test was used. The Chi-square test was used to compare categorical variables. Confidence interval was accepted as 95% and a p value <0.05 was accepted as statistically significant.

RESULTS

The two groups were similar in terms of age, gender, body weight and preoperative ASA evaluation. Yet there was a slight male dominance in group KP without statistical significance (p:0.06, Table-1).

Table 1: Comparison of demographic data

Parameter	Ketofol group (n:27)	Propofol group (n: 27)	P value
Age (year)	42.1 ± 10.1	45.3 ± 12.7	0.313
Gender (F/M)	9/18	16/11	0.06
Body weight (kg)	77.3 ± 9.1	78.7 ± 15.6	0.695
Operation duration (min)	45 (12)	45 (10)	0.820
PACU duration (min)	15 (0)	20 (5)	0.0002
ASA 1/ ASA 2	12/15	12/15	1

Although the duration of surgery was similar in both groups (with a median of 45 minutes), the duration

Table 2: Comparison of study groups

Parameter	Ketofol group (n:27)	Propofol group (n: 27)	P value
Duration to reach RSS 3	6.8 ± 5.1	9.6 ± 7.2	0.042
Total medication dose (mg/kg)	2.3 ± 0.4	2.5 ± 0.4	0.897
BIS 5 min	72.1 ± 16.1	77.5 ± 12.3	0.137
BIS 20 min	72.3 ± 10.8	74.5 ± 8.8	0.173
BIS 40 min	81.5 ± 9.8	82.1 ± 6.5	0.251
SpO ₂ 5 min	98 (4)	99 (2)	0.346
SpO ₂ 20 min	98 (1)	99 (1)	0.605
SpO ₂ 40 min	99 (1)	99 (1)	0.694
Aldrete G	8.96 ± 0.7	8.63 ± 0.49	0.073
Aldrete S	9.59 ± 0.5	9.19 ± 0.39	0.002
Postoperative nausea/vomiting	0/27	2/27	0.15
Postoperative 12 th hour VAS for satisfaction	8.3 ± 2.4	7.1 ± 1.9	0.04
Postoperative 12 th hour VAS for pain	1.1 ± 0.7	4.1 ± 1.2	0.02

of stay in PACU was significantly longer in Group P (20 min vs 15 min, p:0.002, Table 1). The time taken to reach Ramsay 3 value was significantly shorter in Group KP than in Group P (6.8 ± 5.1 vs 9.6 ± 7.2 min, p:0.042, Table 2). Mean RSS after reaching threshold value were similar between groups during the followup period. The intraoperative BIS values at 5, 20 and 40 minutes were determined to be similar in both groups. Hemodynamic and respiratory parameters were similar between groups during surgical procedure. VAS for pain at postoperative 12th hour was significantly higher in group P (4.1 ± 1.2 vs 1.1 ± 0.7, p:0.02) and VAS for satisfaction at postoperative 12th hour was significantly higher in group KP (8.3 ± 2.4 vs 7.1 ± 1.9, p:0.04) (Table 2).

DISCUSSION

According to ASA data (2006), high dose of sedation has been reported to lead to respiratory depression and is an important reason for anesthesia related malpractice.¹² Anesthesia is a balance between the patient's state of wakefulness and the need for anesthetic medication. If an insufficient dose is administered, the patient's wakefulness increases while a high dose causes haemodynamic instability, prolonged awakening time and some other complications.¹³

In relation to the response to sedation and analgesia, we decided to use the RSS in the current

study because it is easy to apply.¹⁴⁻¹⁶ The ideal sedative agent for regional anesthesia should have a rapid onset of action, produce a level of sedation sufficient for patient comfort, and have a short duration of action.⁷ Generally, the intermittent intravenous application in sedation does not allow for the adjustment of the plasma concentration level of the medication and extends the time to waking.¹⁷ On the other hand continuous infusion allows to maintain fairly stable concentration of the medication. In the current study, additional doses were applied intermittently rather than as a continuous infusion but to avoid excessive dosing we closely monitored Ramsay score and BIS during surgical procedures. In fact continuous infusion might allow to maintain a fairly stable blood concentration of the medication and with intermittent boluses the blood concentration might be more variable yet we preferred intermittent boluses as we and surgical support team had more experience with intermittent boluses previously. As BIS and Ramsay scores were similar between study groups we believe that an adequate but not excessive dosing was achieved.

According to the Ramsay scale, sedation was obtained more quickly in Group KP than in Group P and this was statistically significant (6.8 ± 5.1 vs 9.6 ± 7.2 minutes, $p=0.042$). This is an expected result as we used more medications in KP group (ketamine + propofol vs propofol alone). None of patients had a score of 5 according to RSS during surgical procedure.

A pharmacological disadvantage of propofol is its' relatively narrow therapeutic range. Unlike opioids and benzodiazepines, an antagonist is not available to reverse the effects. Despite its' high potential to induce respiratory depression and cardiovascular instability, propofol is a routinely administered agent by anesthesiologists.¹⁸ No respiratory depression or cardiovascular problems were encountered in either group of the current study and this was thought to be associated with the close monitorization of BIS and RSS. Although anesthetic medications affect all organs and systems, the central nervous system is the most effected one. Cognitive functions are affected to various degrees following anesthesia.

Rapid recovery of the patients' mental functions is an important in general anesthesia practice.¹⁹ In the current study, the modified Aldrete score was used postoperatively and the most rapid recovery in PACU was observed in Group KP. The slower recovery time of Group P was considered to be associated with the greater amount of medication applied to reach Ramsay score 3.

Deep anesthesia and hypnosis are monitored with the Bispectral Index (BIS). Clinical studies have shown reduced usage of anesthetic agents and early recovery with the use of BIS.²⁰ In the current study, by maintaining BIS at 70-80 we tried to administer adequate sedation and depending on that, the medication dosage was titrated. In literature there are multiple studies that target different BIS values for adequate sedation. Newson et al reported adequate sedation with value BIS between 40-60.²¹ On the other hand some authors reported higher BIS values for adequate sedation. Dobler reported that a BIS value between 75-85 was required for endoscopic procedures and Liu et al reported that BIS should be greater than 80 for procedures that are performed under regional anesthesia.^{11,22} There was no statistically significant difference between the groups as seen in Table 1, but a greater amount of medication was administered to the propofol group to obtain the desired BIS level. On the other hand we think that additional anesthetic effects of propofol and ketamine might have caused a deeper anesthesia level despite of similar BIS values in ketofol group compared to propofol alone group.

Ketofol obtained by mixing ketamine with propofol provided appropriate analgesia and sedation.

CONCLUSION

Our results indicate that intravenously administered ketofol produces faster recovery time and safe sedation compared to propofol alone. Ketofol is a good alternative for propofol in spinal anesthesia for regional surgeries with higher postoperative patient satisfaction, lower pain rates and shorter intensive care requirements

Conflict of interest: The authors have no conflict of interest to declare.

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