



Original Work

Circulatory responses to propofol-ketamine combination compared to propofol alone for sedation during spinal anesthesia

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ABSTRACT: The present study was undertaken to establish the efficacy of low dose propofol-ketamine infusion in maintaining hemodynamic stability when used for sedation as compared to propofol alone during spinal anesthesia. Sixty adult patients of either sex, belonging to ASA physical status I and II undergoing urological procedures were studied in a randomized manner. After administering spinal anesthesia with 0.5% bupivacaine, patients were assigned to two groups of 30 patients each. Group I (propofol-ketamine combination) received initial loading dose of propofol and ketamine followed by a continuous infusion of low dose propofol and ketamine whereas group II (propofol alone) received a bolus dose of propofol followed by a continuous infusion of propofol only. Hemodynamic parameters like heart rate, systolic blood pressure, diastolic blood pressure and sedation scores rated on a five point scale were recorded at baseline and at the predetermined intervals of 5, 10, 15, 20, 25, 30, 45, 60, 75 and 90 minutes after spinal anesthesia. It was found that heart rate, systolic and diastolic blood pressure was significantly higher in group I patients at various intervals as compared to group II patients, however sedation scores revealed no significant difference at different time intervals between the two groups. In conclusion propofol-ketamine combination was found to confer hemodynamic stability during spinal anesthesia as compared to propofol alone.

KEY WORDS: *Spinal anaesthesia; Sedation; Propofol; Ketamine; Circulatory responses*

INTRODUCTION

Regional Anaesthesia is becoming an increasingly important aspect of anaesthesia practice. It offers several benefits to the patients including cardiovascular and respiratory stability, preservation of airway reflexes and rapid postoperative recovery¹. Some of the drawbacks of regional anesthesia however include fear of needles and pain at the puncture site² and recall of the procedures³. These factors stress the importance of sedation during surgical procedures done under regional anaesthesia. Sedation has been shown to increase patient satisfaction during regional

anaesthesia and may be considered as a means to increase the patient acceptance of regional anaesthetic techniques⁴.

An ideal sedative is one that safely provides relief from pain, anxiety and unpleasant memories for a wide variety of procedures. Several sedative and analgesic drugs have been used singly or in combination⁵⁻⁸ but no one regimen meets all of the above requirements.

Propofol, a phenol derivative produces dose-dependent sedation, hypnosis, anxiolysis and amnesia as well as possessing antiemetic properties⁹, but it lacks analgesic properties and may not produce reliable amnesia at sub-anaesthetic doses¹⁰. On the other hand, ketamine a phencyclidine derivative when used in sub-anaesthetic doses produces analgesia while preserving airway patency, increases heart rate and arterial blood pressure by activation of the

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sympathetic nervous system and reduces the incidence of spinal anaesthesia induced hypotension¹¹.

Propofol and ketamine administered in combination from separate syringes has been used successfully in a variety of settings including spinal anaesthesia¹². This combination has been favored because of the opposing hemodynamic and respiratory effects of each drug⁹. The combination has also been shown to reduce the dose of propofol required to achieve sedation¹³ and is believed to result in less toxicity than either drug alone because their complementary effects enable the use of lower doses of each drug¹⁴.

With this background we decided to compare the effect of propofol-ketamine combination to propofol alone on hemodynamics when used as a sedative adjuvant to spinal anaesthesia.

METHODOLOGY

After approval from the hospital ethical committee and written informed consent from the patients, 60 ASA physical status I and II patients of either sex, aged 18 to 75 years undergoing spinal anaesthesia for urological procedures were enrolled for the study. Patients with a history of allergic reaction to propofol and ketamine, obesity, significant central nervous system, cardiac, pulmonary, hepatic and renal disease were excluded from the study. Patients were randomly allocated to two groups of 30 patients each. Group I (propofol-ketamine combination group) and Group II (propofol alone group). The patients were premedicated with tablet Alprazolam 0.25mg in the morning on the day of the surgery.

On arrival to the operating room, patients were connected to Datex cardiocap monitor for monitoring of ECG, heart rate and NIBP. O₂ saturation was monitored with Pace-Tech pulse oximeter. Baseline measurements of heart rate, systolic and diastolic blood pressures were recorded prior to administration of spinal anaesthesia and then at 5 minutes intervals for first 30 minutes of surgery and every 15 minutes thereafter till a total duration of 90 minutes. After preloading the patients with 6ml/kg of Ringer lactate, spinal anaesthesia was given with hyperbaric bupivacaine 0.5% in sitting position using 24 G spinal needle, in doses sufficient to provide a satisfactory sensory block for the procedure to be done. The sensory block was evaluated after every 3 minutes using a cold swab until the level was sufficient for the surgery to begin.

Immediately after spinal anaesthesia, patients assigned to group I received an initial loading dose of propofol 0.4mg per kg and ketamine 0.1mg/kg followed by a continuous infusion of 1.2mg/kg/hr propofol and 0.3mg/kg/hr of ketamine. Group II patients received a bolus of 0.5mg/kg of propofol

only followed by a continuous infusion of 1.5mg/kg/hr. The study drugs (Propofol or admixture of propofol-ketamine) were prepared by an anesthesiologist not involved in the study and the anesthesiologist assessing the level of sedation was blinded to the sedative infusion being administered. The level of sedation was recorded every 5 minutes and subsequent infusion rates titrated to maintain the sedation score at or around level 3 on a five point sedation score as shown in **table I**. The sedative infusion was stopped during the surgical procedure if the respiratory rate fell to less than eight breaths per minute, the infusion otherwise was discontinued at the end of surgical procedure. Total sedative and vasopressor requirements were noted. Oxygen was administered through a face mask to those patients who exhibited a SpO₂ of 95% or less. Observations were continued in the recovery room till a total duration of 90 minutes from the start of surgery. Patients remained in the recovery room until sensory functions returned to normal.

Table 1: Sedation Score

Score	Degree of Sedation
1	Fully awake and oriented
2	Drowsy
3	Eyes closed but arousable to command
4	Eyes closed but arousable to mild physical stimulation
5	Eyes closed but unarousable to mild physical stimulation

The data was collected, tabulated and statistically analyzed using the student's t-test. Values were expressed as mean ± SD and a p value of <0.05 was taken as significant and p <0.001 as highly significant.

RESULTS

The patient data was comparable between the two groups on the basis of age, weight and sex distribution (**Table 2**). Duration of surgery was shorter in group II as compared to group I. The total dose of propofol administered was similar in both the groups (95 ± 35mg and 100 ± 40mg in groups I and II respectively), while as in group I, patients received additional 22 ± 11mg ketamine combined with propofol. The sedation scores showed no significant difference between the two groups with constant degree of sedation being

maintained throughout the procedure. Four patients in group II experienced a hypotensive episode and needed ephedrine supplementation for treatment of hypotension.

Table 2: Demographic variables of the patients in the two groups

	Group I	Group II
Number	30	30
Age (yrs)	57.63±7.98	57.87±6.69
Weight (Kg)	56.86±6.64	57.53±5.86
Sex (M/F)	27/3	27/3
Surgical time (min)	59±13	42±27
Total Propofol (mg)	95±35	100±40
Total Ketamine (mg)	22±11	---
Sedation score	2.93±0.82	2.82±0.72
Ephedrine required	None	4

Values are expressed as mean±SD

Changes in heart rate and arterial blood pressure after the spinal anesthesia and sedative administration are shown in **figure 1**. It has been observed that the changes in the heart rate in the two groups did not differ significantly at predetermined intervals during the procedure. On the other hand both systolic and diastolic blood pressures remained significantly higher in group I patients, when compared to group II patients at similar time intervals. There were no significant differences in respiratory rate, SpO₂ and the need for oxygen supplementation between the two groups.

DISCUSSION

Spinal anesthesia is one of the commonest techniques of regional anesthesia. The impediments to the effective use of spinal anesthesia are the predictable decreases in arterial blood pressure and heart rate through the accompanying sympathectomy with its attendant vasodilatation

and blockade of cardio accelerator fibres. Another clinically important impediment to successful block is inadequate sedation.

The goals of sedation during spinal anesthesia are to provide an adequate level of sedation while minimizing pain and anxiety, maximizing amnesia, minimizing the potential for adverse drug-related events, controlling behavior, and maintaining a stable cardiovascular and respiratory status.

Propofol infusion provides excellent sedation during spinal block. The advantages to its use are that the technique is safe, simple, depth of sedation can be easily altered and recovery is within 5 minutes after stopping the infusion¹⁴. However it has some properties that limit its usefulness. It causes reduction in myocardial contractility and in peripheral vascular resistance, leading to reduction of mean arterial pressure. However, ketamine has a stimulant effect on intact sympathetic nervous system which may offset the depressant effect of propofol.

A number of studies have demonstrated that the combination of ketamine and Propofol for sedation is safe and effective. The combination of the two agents appears to reduce side effects of each medication used alone, and allows for a rapid recovery time¹⁵. Hence we decided to evaluate the effectiveness of the propofol-ketamine combination for sedation and maintenance of stable hemodynamics. We observed that propofol-ketamine combination as an infusion provided a comparable sedation to propofol only and the hemodynamics remained stable during spinal anaesthesia with propofol-ketamine infusion as compared to patients receiving propofol only.

Our results correlate with those of Frizelle et al who demonstrated that propofol-ketamine combination, given as infusion during spinal anesthesia, provided hemodynamic stability¹². Similar results were also obtained by Guit et al, who recommended propofol-ketamine combinations for TIVA also when stable hemodynamics are required¹⁶.

Hemmingsen et al in their study observed that during spinal anesthesia patients could be kept hemodynamically stable by intravenous administration of ketamine¹¹.

CONCLUSION

We conclude that although propofol infusion in sub-anesthetic doses is an effective sedative adjuvant during spinal anesthesia, the propofol-ketamine combination has definite advantages over propofol alone for providing hemodynamic stability during spinal anesthesia.

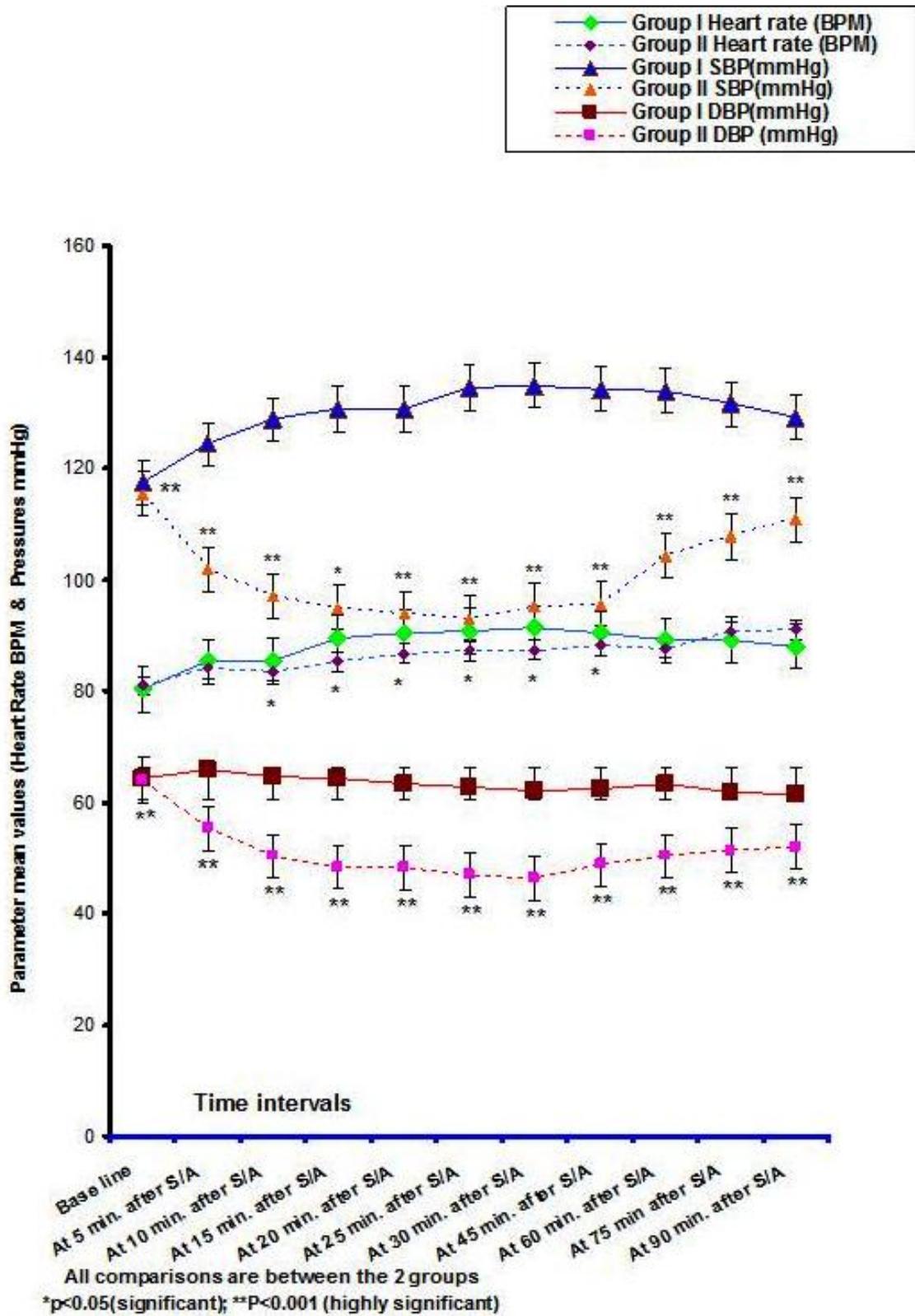


Figure 1: Circulatory variables during peri-operative period in the two groups at different time intervals

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