Original Research Article

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Comparison of Midazolam and Propofol for Entropy - Guided Sedation During Regional Anesthesia

Nutan NM[1], Mubina Begum Bujapur[2], Nazeer Ahmed K[3], Sanjeev Birajdar[4]

[1]Consultant, Dept of Anesthesia, SSNMC Super Specialty Hospital, Bengaluru, Karnataka 560098, India, [2]Assistant Professor [3]Professor [4]Associate Professor Dept of Anesthesia, Al-Ameen Medical College, Vijayapura, Karnataka 586108, India.

Abstract

Background and Aims: This study aimed to compare the sedation using Entropy of Midazolam and Propofol in regional anesthesia in terms of Onset, Recovery and Side Effects. *Introduction:* Regional anesthesia is a safe and popular anesthetic technique. Effective sedation is essential for regional anesthetic technique too, to allay anxiety in the patients and improve their comfort, co-operation. Use of entropy will reduce over sedation of the patient and better monitoring of the hypnotic state of the patient. *Methods:* 100 ASA I/II adult patients undergoing elective surgery under regional anesthesia for lower abdominal and lower limb surgeries were enrolled in the study and randomly allocated into two groups. Group M: Midazolam 0.1% IV infusion started with 0.5 mg/kg/hr, Group P: Propofol 1% IV infusion started with 6 mg/kg/hr till entropy value reaches 60 then titrated to maintain entropy of 50 to 60 through syringe pump and was continued till the last suture was completed. *Results:* Dose required to reach the level of sedation was 0.5 mg/kg/hr vs 6mg/kg/hr and to maintain sedation was 0.17±0.04 mg/kg/hr vs 1.23±0.25 mg/kg/hr and onset of sedation was 4.17±0.42 vs 2.81±0.44 minutes where as time for recovery from sedation was 9.57±2.67 vs 6.76±0.83 minutes in GroupM vs Group P respectively. Hemodynamic changes were significantly higher in Group P than Group M. *Conclusion*: Both Midazolam and Propofol can be used for sedation under regional anesthesia. Onset of action and recovery is faster with Propofol and Midazolam is more cardio stable.

Keywords: Midazolam; Propofol; IV Sedation; BIS (Bispectral Index).

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Introduction

The meaning of sedation is to reduce anxiety that is anxiolysis. Patients undergoing surgery tend to be anxious. What seems like a minor procedure to the anesthesiologist and surgeon may represent a major deal to the patient. Although anxiety usually exists long before the patient is brought to the preoperative room, in some instances, it does not peak until after surgery. So the reduction of anxiety to tolerable levels is a human goal and should be attempted for every patient [4].

Sedation during regional anesthesia is desirable to minimize anxiety in the operating room environment. In addition many patients are concerned about the recall of intra operative events regardless of route of administration, patients satisfaction was reported to be higher

Corresponding Author: Mubina Begum Bijapur, Assistant Professor, Dept of Anesthesia, Al-Ameen Medical College, Vijayapura, Karnataka 586108, India.

E-mail: mubeen1983@hotmail.com

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in the presence of more profound sedation. The long hours of surgery under regional anesthesia in supine or lateral positions can make the patient very uncomfortable. Also during orthopedic procedures, the constant awareness of the noise of instrumentation during surgical procedures creates anxiety in the patients. After sometime because of anxiety, there is persistent tachycardia, rise in blood pressure, which results in increase in blood loss during surgery [4,11].

Anxiety is also associated with significant adverse physiological responses in form of Hypertension, tachycardia, increased myocardial oxygen consumption, Gastric erosion, Intracranial hypertension and Persistent catabolism [11] which may affect the recovery. Therefore anxiolysis is a must.

Primary objectives of conscious sedation include adequate sedation with minimal risk [2,3].

Regional anesthetic techniques can be used for a variety of surgical procedures and may offer certain advantages over general anesthesia. In order to improve patients' acceptability and comfort and to reduce stress it is necessary to provide some form of sedation during the operation.

There are various methods to provide sedation during regional anesthesia, intravenous technique is widely used and suitable agents include the benzodiazepine, opiods and other IV induction agents. Currently midazolam and Propofol are considered to be the most suitable drugs [12-14,19, 22,and 23].

Entropy is an innovative monitoring modality which is designed to provide information on the state of central nervous system during general anesthesia [1,5,7-9]. Entropy monitoring is based on acquisition and processing of EEG and FEMG signals by using Entropy algorithm.

There are two parameters in Entropy

Fast reacting response entropy

More study and robust state entropy

State entropy consists of EEG signals calculated up to 32 Hz

Response entropy includes additional high frequencies up to 47 Hz

Parameters	Measurement Frequency Range	Display Range
Response entropy	0<f<47Hz	0 to 100
State entropy	0<f<32 Hz	0 to 91

Response Entropy

Response entropy is sensitive to the activation of facial muscles i.e. FEMG its response time is very fast and less than two seconds. Activation of response entropy to the painful stimuli may be interpreted as a sign of inadequate analgesia. Facial muscles may also give an early indicator of recovery.

State Entropy

State entropy is always less than or equal to response entropy. Estimation of hypnotic effects of anesthetic drugs in brain during general anesthesia is based on state entropy. State entropy is based on EEG signals. EEG can be considered as a measure for depth of anesthesia due to the following:

Entropy Range Guidelines

100	**Fully awake and responsive.**
60	Clinically meaningful anesthesia with low
40	probability of consciousness.
0	Suppression of cortical electric activity.

Methods

A prospective, randomized, single-blind study carried out to evaluate and compare the properties of Propofol and Midazolam in terms of hemodynamic, side effects and dosage requirement as adjuncts to spinal anesthesia. After obtaining approval from institute's Ethical Committee and patients consent, Patients ASA Grade 1 & 2, aged 19-55 years, posted for elective surgeries under regional anesthesia including lower abdominal, perineal and lower limb surgeries were enrolled in study and patients with uncontrolled Hypertension, IHD, stenotic valvular disease, pre-existing neurological deficit, sensitive to used drugs, Obesity (BMI >30) were excluded from the study.

Technique: Under standard monitoring (Pulse oximeter, NIBP and ECG). Entropy sensor was applied to the patient's forehead for Entropy monitoring. The Patients were randomly allocated into 2 groups.

The Midazolam group (Group M): Midazolam 0.1% IV infusion (dilution was done in 5% dextrose in a 50 ml syringe) started with 0.5 mg/kg/hr till entropy value reaches 60 then reduced and titrated to maintain entropy of 50 to 60 through syringe pump.

The Propofol group (Group P): Propofol 1% IV infusion (dilution was done in 5% dextrose in a 50 ml syringe) started with 6 mg/kg/hr till entropy value reaches 60 then reduced and titrated to

maintain entropy of 50 to 60 through syringe pump. Drug infusion was continued till the last suture was completed. Data was collected, Time to reach required level of sedation, Duration of surgery, Duration of infusion, HR, MAP, SpO_2 is recorded every 3 minutes till the required sedation is achieved and then every 10 minutes till the end of surgery, Time of recovery, Side effects: Nausea and vomiting: (1) No vomiting or retching. (2) Retching. (3) Occasional vomiting (1-3 times). (4) Recurrent vomiting (> 3 times). Dose to reach required level of sedation, Dose to maintain required level of sedation. Data was analyze using, Chi-square/ Fisher Exact test, Student t test. Inferential and Descriptive statistical analysis has been carried out in the present study.

Results

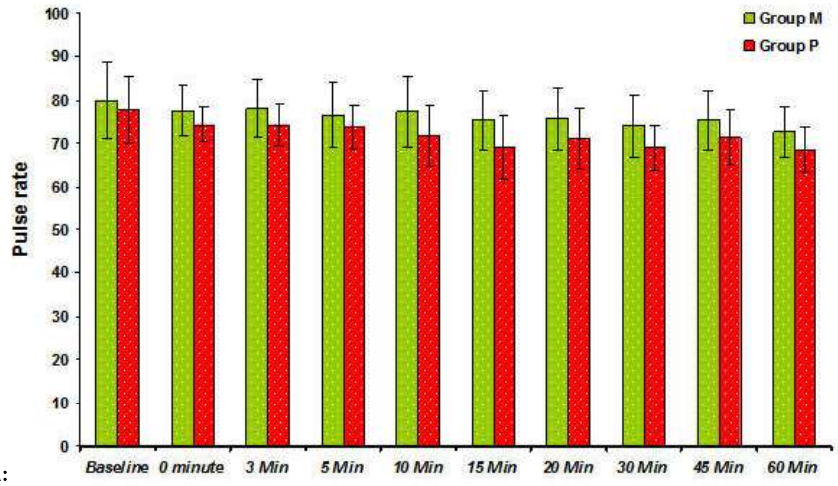
Results on continuous measurements are presented on Mean±SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance.

Table 1: Demographic Data

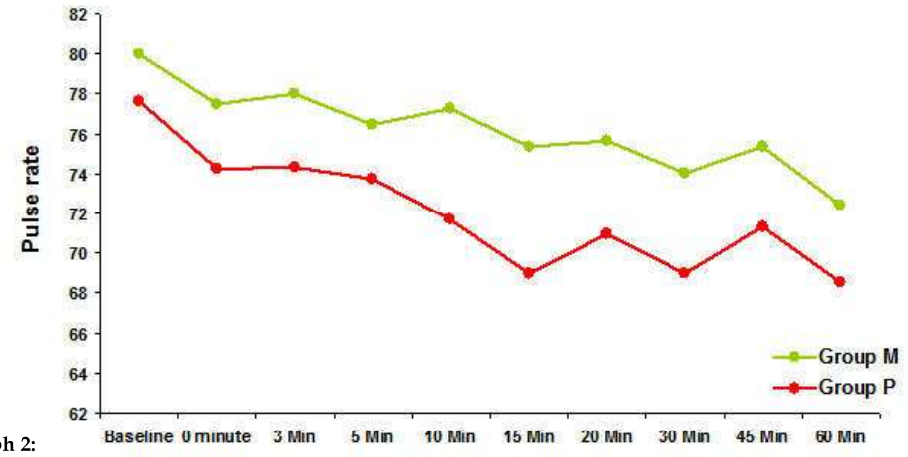
Demographic data	Group M	Group P	p value
Age, years	32.86± 5.44	34.02± 6.58	0.339
ASA Physical Status I/ II	49/1	37/13	0.001
Weight, kg	61.88±6.19	61.04±5.76	0.484

Table 2: Comparison of pulse rate in two groups of patients studied

Pulse rate	Group M	Group P	p value
Baseline	79.98±8.97	77.68±7.65	0.171
0 minute	77.52±5.87	74.30±3.91	0.002**
3 minutes	78.04±6.69	74.34±4.77	0.002**
5 minutes	76.52±7.47	73.74±4.9	0.030*
10 minutes	77.30±8.20	71.70±7.06	<0.001**
15 minutes	75.38±6.94	68.98±7.34	<0.001**
20 minutes	75.66±7.12	71.00±7.10	0.001**
30 minutes	74.06±7.05	69.02±5.32	<0.001**
45 minutes	75.36±6.80	71.36±6.50	0.003**
60 minutes	72.46±5.74	68.56±5.28	0.001**



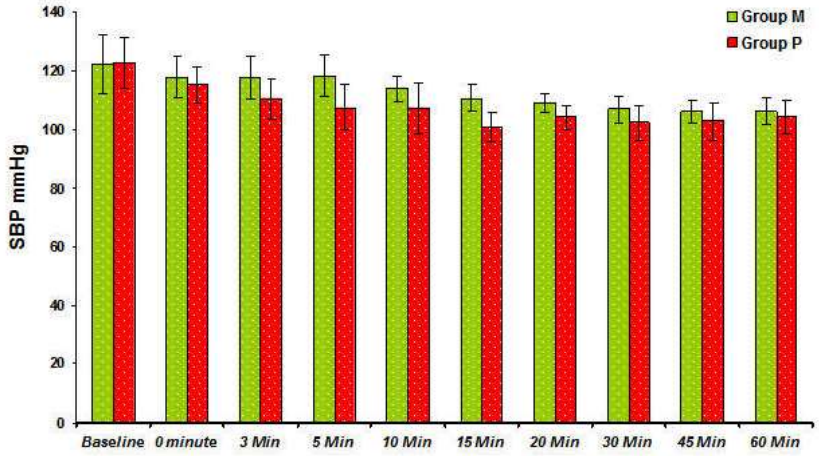
Graph 1:



Graph 2:

Table 6: Comparison of SBP mmHg in two groups of patients studied

SBP mmHg	Group M	Group P	P value
Baseline	122.04±9.82	122.56±8.63	0.779
0 minute	117.88±7.00	115.4±6.06	0.061+
3 minutes	117.72±7.02	110.40±6.80	<0.001**
5 minutes	118.36±6.87	107.62±7.87	<0.001**
10 minutes	113.92±4.26	107.32±8.66	<0.001**
15 minutes	110.70±4.79	100.72±4.97	<0.001**
20 minutes	109.06±3.37	104.18±4.23	<0.001**
30 minutes	106.90±4.74	102.34±6.09	<0.001**
45 minutes	106.10±4.19	102.92±6.44	0.004**
60 minutes	106.18±4.71	104.54±5.81	0.124



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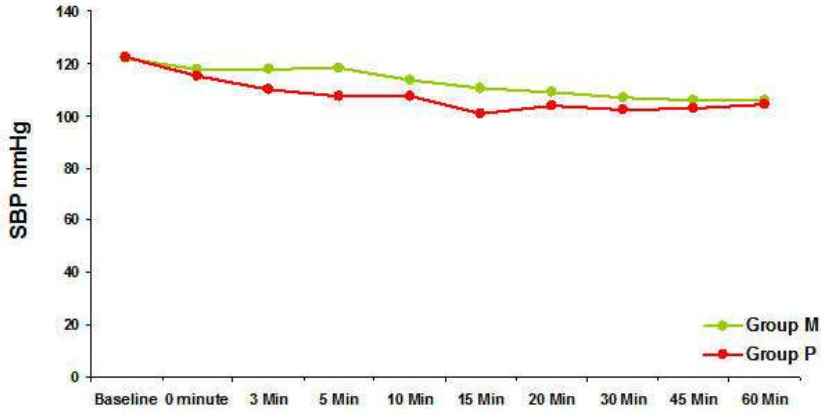
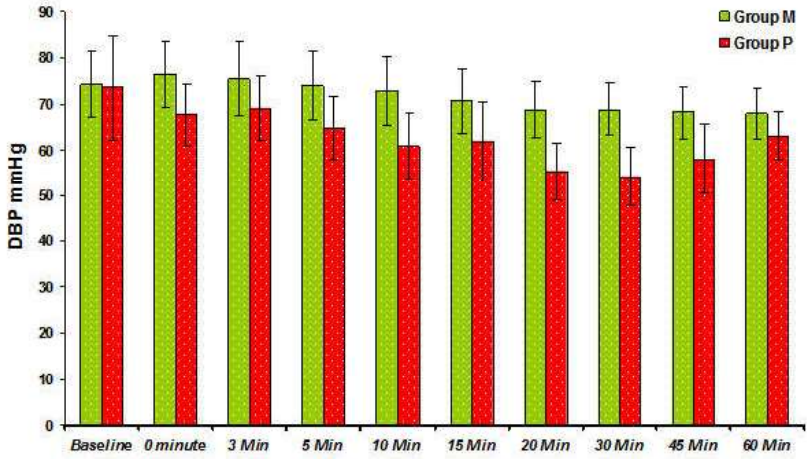


Graph 5:

Table 7: Comparison of DBP mmHg in two groups of patients studied

DBP mmHg	Group M	Group P	P value
Baseline	74.28±7.18	73.6±11.38	0.722
0 minute	76.54±7.17	67.52±6.73	<0.001**
3 minutes	75.34±8.02	68.96±6.90	<0.001**
5 minutes	74.00±7.37	64.66±6.86	<0.001**
10 minutes	72.86±7.40	60.76±7.14	<0.001**
15 minutes	70.68±6.99	61.84±8.79	<0.001**
20 minutes	68.88±6.01	55.38±6.29	<0.001**
30 minutes	68.90±5.67	54.16±6.30	<0.001**
45 minutes	68.08±5.62	57.96±7.60	<0.001**
60 minutes	67.98±5.53	63.00±5.23	<0.001**



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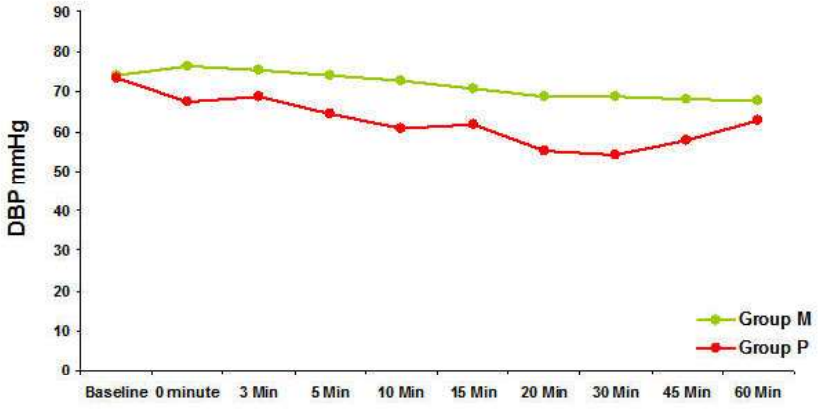
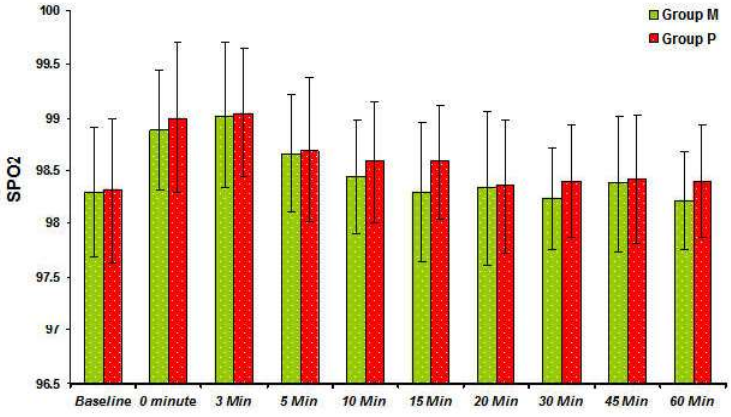


Graph 7:

Table 8: Comparison of SPO2 in two groups of patients studied

SPO2	Group M	Group P	P value
Baseline	98.3±0.61	98.32±0.68	0.878
0 minute	98.88±0.56	99.00±0.70	0.346
3 minutes	99.02±0.68	99.04±0.60	0.877
5 minutes	98.66±0.56	98.7±0.68	0.748
10 minutes	98.44±0.54	98.58±0.57	0.213
15 minutes	98.3±0.65	98.58±0.54	0.021*
20 minutes	98.34±0.72	98.36±0.63	0.883
30 minutes	98.24±0.48	98.4±0.53	0.117
45 minutes	98.38±0.64	98.42±0.61	0.749
60 minutes	98.22±0.46	98.4±0.53	0.075+



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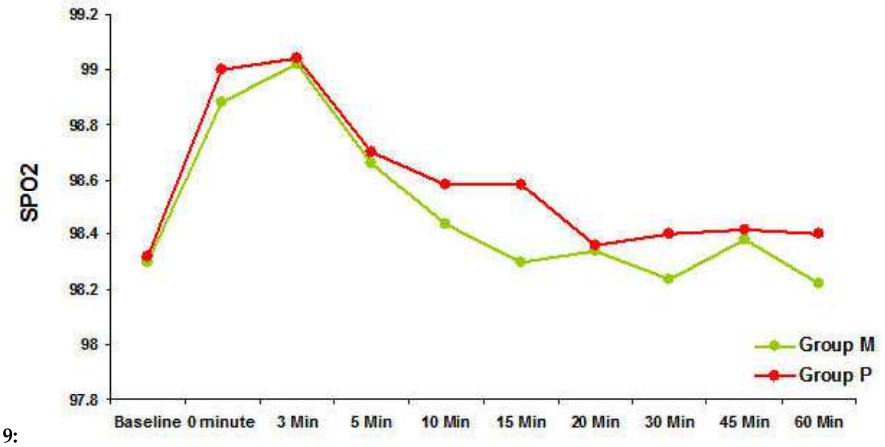
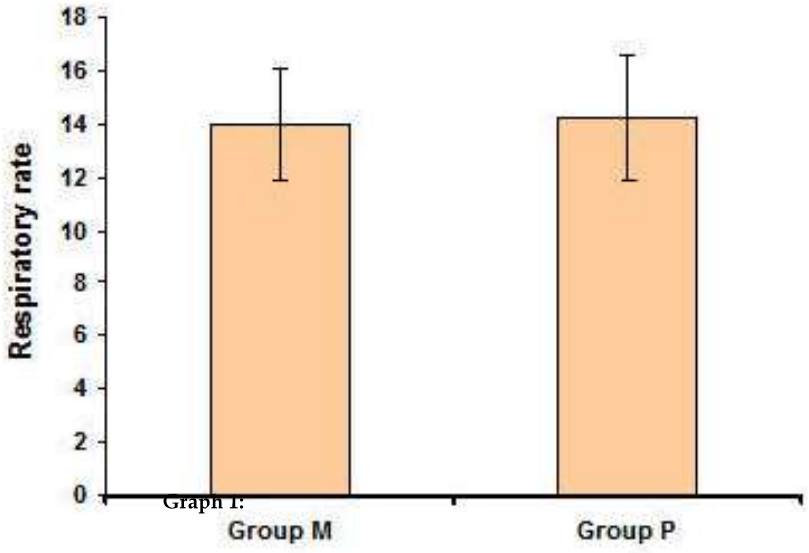


Graph 9:

Table 9: Comparison of Respiratory rate in two groups of patients studied

Respiratory rate	Group M	Group P	P value
RR	14.00±2.08	14.22±2.34	0.621

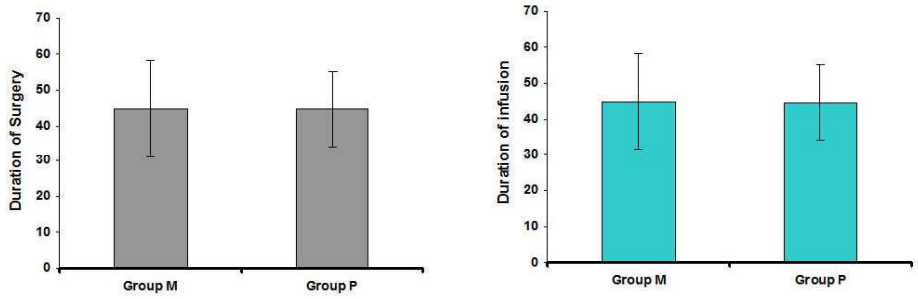


Graph 1:

Graph 10:

Table 10: Comparison of variables in two groups of patients studied

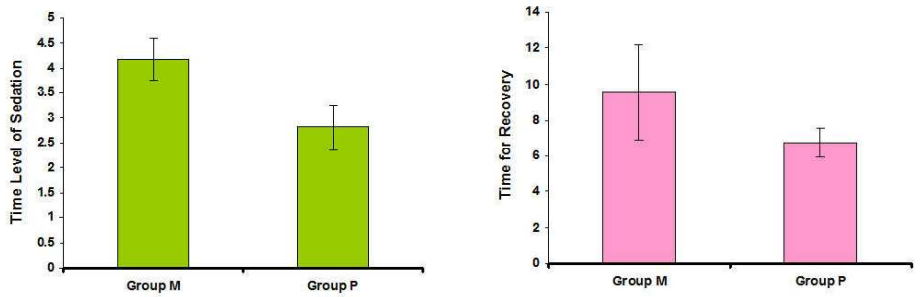
Variables	Group M	Group P	P value
Duration of Surgery	44.70±13.56	44.60±10.49	0.967
Duration of infusion	44.70±13.56	44.60±10.49	0.967



Graph 11:

Table 11: Comparison of variables in two groups of patients studied

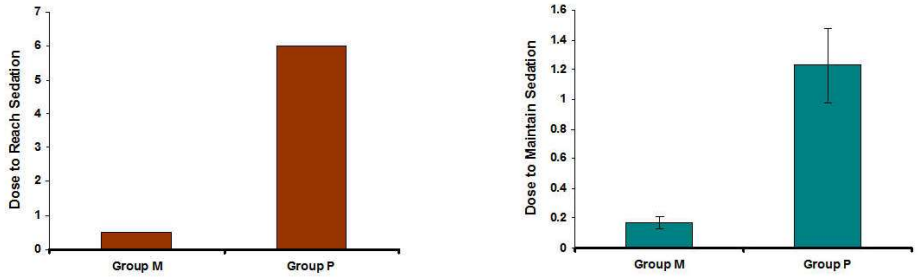
Variables	Group M	Group P	P value
Time Level of Sedation	4.17±0.42	2.81±0.44	<0.001**
Time for Recovery	9.57±2.67	6.76±0.83	<0.001**



Graph 12:

Table 12: Comparison of variables in two groups of patients studied

Variables	Group M	Group P	P value
Dose to Reach Sedation	0.50±0.00	6.00±0.00	-
Dose to Maintain Sedation	0.17±0.04	1.23±0.25	<0.001**



Graph 13:

Discussion

Regional anesthesia has become important anesthesia technique which is more popular and emerging as a safe anesthetic procedure. And most of the studies have shown that patients experience anxiety for any type of surgical procedures.

Hohener et al. report an incidence of anxiety of around 50% before receiving a regional block in their study. The study revealed Anxiety was related to higher incidence of nausea and vomiting.

Sedation is a well recognized technique to improve patients' acceptance and comfort during regional anesthesia [4]. The use of this technique is growing exponentially. Many studies have shown that use of different methods of monitoring hypnotic state of the patient is advantageous, as the incidence of side effects is lower and the amount of infused drugs is decreased [2].

Sedative-hypnotic drugs as well as narcotics are commonly used perioperatively to make regional anesthesia more tolerable for patients by reducing anxiety and providing an appropriate degree of sedation, amnesia and analgesia [3]. Dose required to reach the level of sedation in group M is 0.5 mg/kg/hr and to maintain sedation was 0.17± 0.04 mg/kg/hr and onset of sedation was 4.17±0.42 minutes where as time for recovery from sedation was 9.57±2.67 minutes which was statistically greater than Group P. In Group P, dose to reach the level of sedation was started with 6 mg/kg/ hr to reach required values of Entropy where as to maintain sedation was 1.23±0.25 mg/kg/hr. Onset of sedation in group p was 2.81±0.44 minutes where as time for recovery from sedation was 6.76±0.83 minutes. Hemodynamic changes were significantly higher in Group P than Group M more with DBP. Whereas fall in SpO_2 is more in Group M than Group P but it's not statistically significant.

E. Wilson, A. David and their group in 1990 compared the sedative effects of Midazolam and Propofol during spinal anesthesia [16]. In their study, 40 patients undergoing orthopedic surgery under spinal anesthesia received an infusion of either 1% Propofol or 0.1% Midazolam was given at a rate adjusted to maintain a similar level of sedation. The mean time to reach this required level was similar in both groups. Quality and ease of control of sedation were good in all patients.

Restoration of higher mental function was significantly faster following Propofol. Amnesia for the immediate postoperative period was significantly greater after Midazolam ($p = 0.0001$).

Hidaka S, Kawamoto M. et al., in 2005 did a comparative study on the effects of Propofol and Midazolam on cardio-vascular autonomic nervous system during spinal and epidural anesthesia [6]. Ninety eight patients were randomly divided into two groups, one group received Midazolam infusion while the other received Propofol infusion until BIS reached 75. The time to reach required sedation was 11 min in Midazolam group (Group I) while it was 6 min in Propofol group (Group II) ($p=0.0$). Fall in MABP was greater with Propofol. Recovery in with Midazolam was slower than with Propofol (18.6 ± 6.5 vs 10.10±3.65 min) ($p=0.00$). They concluded that both Midazolam and Propofol are effective sedatives, but onset and offset was quicker with Propofol, while Midazolam was more cardio stable.

In the present study it was found that both Midazolam and Propofol are effective sedatives in regional anesthesia with Propofol being faster onset and recovery from sedation where as Midazolam causes sedation which is hemodynamically more stable.

Hohener et al showed that Propofol is a substance nearest to an ideal agent for sedation during regional anesthesia because of its favorable pharmacokinetic profile with rapid onset and offset

Conclusion

Current study showed that both Midazolam and Propofol can be used for sedation in regional anesthesia. Propofol has a faster onset of action and recovery from the sedation where as Midazolam found to be more cardio stable.

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