Quest Journals
Journal of Medical and Dental Science Research
Volume 2~ Issue 1 (2015) pp: 19-24
ISSN(Online) : 2394-076X ISSN (Print):2394-0751
www.questjournals.org

Research Paper

Comparison Of Propofol And Midazolam Infusion For Conscious Sedation During Spinal Anaesthesia

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Received 20 January, 2015; **A**ccepted 07 February, 2015 © The author(s) 2014. Published with open access at **www.questjournals.org**

ABSTRACT:
Background: This study was designed to compare Propofol and Midazolam with regard to their suitability as sedative agents during spinal anaesthesia.

Methods: The study was carried out in 60 adult patients scheduled to receive spinal anaesthesia with bupivacaine (Heavy) 0.5%. The patients were divided into two groups, 30 patients in each group.
Group M : midazolam bolus and continuous infusion.
Group P :Propofol bolus and continuous infusion. Once it was confirmed that spinal block is adequate regarding sensory and motor levels with stable cardiovascular system, sedative infusion of propofol or midazolam was started to patients randomly.

Propofol was administered at bolus of 0.5 mg/kg. and subsequent infusion was titrated to a sedation score of 4 on observer's Assessment of alertness / sedation scale (OAA/S scale). Midazolam was administered at bolus dose of 0.02 mg/kg and subsequent infusion was titrated to achieve a sedation score of 4 on OAA/S scale. Intraoperative and postoperative amnesia was assessed using visual task of recall of pictures.

Results: Mean time to achieve sedation score was 10.30 ± 3.16 minutes in midazolam group as compared to 9.80± 2.78 minutes in the propofol group, showing faster onset with propofol. Meantime to recover from sedation in midazolam group was 18.17 ± 2.61 minutes & 10.40 ± 2.16 minutes in the propofol group showing faster recovery with propofol.

The dose needed to produce steady state sedation was 2.41 ± 0.265 and 0.06 ± 0.014 mg/kg/hr for propofol and midazolam respectively.

Conclusion: Propofol was more suitable than midazolam for conscious sedation during spinal anaesthesia because of its rapid onset, favourable recovery profile and low side effects. Midazolam provided better intraoperative amnesia.

Keywords:- Conscious sedation, propofol, midazolam, spinal anaesthesia, amnesia.

I. INTRODUCTION

The operating room is an anxiety provoking environment. Supplemental sedation with an intravenous agent is often required to allay fear and anxiety in patients subjected to spinal anaesthesia. Sedation is a valuable tool to make surgery under regional anesthesia convenient for the patient, the anesthetist and the surgeon[1]

Conscious sedation is a minimally depressed level of consciousness that retains the patient's ability to maintain his or her airway independently and continuously and to respond appropriately to physical stimulation and verbal commands, produced by pharmacologic or non-pharmacologic methods alone or in combination.[2] With conscious sedation only some of the centers in the medullary reticular formation and thalamus are depressed in a dose dependent manner.[3] Thus this level of sedation additionally provides the benefit of preservation of protective airway reflexes, especially in monitored anaesthesia care.

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Numerous agents have been used as sedative adjuvants to spinal anaesthesia with their own advantages and disadvantages over one another. Midazolam, a short acting water soluble benzodiazepine has a fast onset and short recovery time.[4] Because of which it is one of the most widely used sedative agent in spinal anaesthesia.

The pharmacokinetic properties of propofol particularly its rapid onset, redistribution metabolism, high clearance, favourable recovery profile and low incidence of side-effects[5] makes it suitable agent for achieving conscious sedation.

Intravenous bolus dose technique has been shown to be associated with peaks and troughts in plasma concentrations producing significant side effects and delayed recovery. Continuous infusions have been proved to produce lesser side effects, faster recovery, easy control over desired depth of sedation and should the regional block prove to be ineffective, easy conversion to general anaesthesia[6]

The objective of the study was to compare sedative, amnesic, hemodynamic and recovery characteristics of propofol and midazolam given in continuous infusion for conscious sedation in patients undergoing surgery under spinal anaesthesia.

I. METHODS

This prospective randomized study was carried out following approval from the institutional ethic committee. Patients included in this study were informed about the procedure in their own language and a written informed consent was taken from all of them.

60 ASA grade 1 and 2 patients, between 18 to 60 years of age, weighting 40 to 70 kg, of both genders, scheduled for elective lower limb or lower abdominal surgical procedures which were anticipated to complete within 2 hours, were included

Patient with history of allergic reaction to the study drugs, obese patient those with significant cardiac, pulmonary hepatic or renal dysfunction were excluded from the study.

This study was carried out in 60 adult patients scheduled for receive spinal anaesthesia with bupivacaine (Heavy) 0.5%. These patients were divided into two groups, 30 patients in each group.

Group M: Midazolam bolus and continuous infusion.
Group P: Propofol bolus and continuous infusion.

Sedative premedication was not given to any patient to avoid interference with results. One intravenous cannula (20G) was inserted into patient's dorsum of hand and ringer lactate infusion was started for preloading. Another wide bore intravenous access (20G) was obtained on forearm/hand of other limb, for administration of study drug infusion.

Subarachnoid block was given in sitting position with 25G, Quincke needle by injecting sufficient dose of hyperbaric bupivacaine 0.5% in order to achieve an adequate sensory block and it was assessed 10 minutes after injection of spinal drug and noted. All patients were given supplemental oxygen via venture mask at 4 litres/minute.

Once it was confirmed that spinal block is adequate regarding the sensory and motor levels with stable cardiovascular system, sedative infusion of propofol or midazolam started to patients who were randomly allocated to receive propofol or midazolam infusion.

Propofol was administered at bolus dose of 0.5 mg/kg and subsequent infusion was titrated to achieve a sedation score of 4 on the observer's Assessment of Alertness/Sedation scale (OAA/S Scale). Midazolam was administered at bolus dose of 0.02 mg/kg and subsequent infusion was titrated to achieve a sedation score of 4 OAA/S scale.

Heart rate, blood pressure, SPO_2 and respiratory rate were recorded initially at 5 min interval for 30 minutes and later at 10 minute interval till the end of procedure.

Observer's Assessment of Alertness 1 Sedation scale (OAA/S Scale)

Responsiveness	Speech	Facial Expression	Eyes	Score
Responds readily to name spoken in normal tone	Normal	Normal	Clear, no ptosis	5
Lethargic, response to name spoken in normal tone	Mild slowing	Mild relaxation	Glazed or mild ptosis (< half the eye)	4
Responds only after name is called out loudly & repeatedly	Slurring or prominent slowing	Marked relaxation	Glazed or marked ptosis	3
Responds only after mild prodding or shaking	Few recognizable words	Marked relaxation	Glazed or marked Ptosis	2
Dose not respond to mild prodding or shaking	Few recognizable words	Marked relaxation	Glazed or marked Ptosis	1

Visual task or recall of pictures:

Immediately prior to sedative infusion, each patient was shown a picture of commonly occurring object (e.g. Kite, dog, tree) to assess their baseline recall (picture 1). 30 minutes after starting the sedative infusion, another picture (picture 2), different from the first picture was shown to the patient for assessing intraoperative recall. Similarly at the end of sedative infusion, a third picture (picture 3) was shown to the patient . Each picture was shown to the patient for 30 seconds, during which patient was prompted to describe all details he or she has seen in the picture.

After 2 hours postoperatively, the patient was asked to recall all the pictures shown to him. Those correctly recalled were analyzed. If the recall of picture was unsuccessful, the patient were asked to recognize any previously presented pictures among other pictures that they have not seen, by showing a mixed collection of seen and unseen pictures.

During the intra-operative period, evidence of pain on commencement of injection, bradycardia, hypotension, apnea, involuntary movements, fall in oxygen saturation and confusion etc. were noted. The sedative infusion was stopped at the end of surgery.

Duration of sedation was taken as time from the commencement of infusion to the stoppage of infusion and total drug was measured in miligrams.

In the immediate postoperative period, time taken by the patient to achieve sedation score of 5 and correctly give full name and address (recorded preoperatively) noted as recovery time.

Postoperative side effects if any such as nausea, vomitting, apnea, confusion was noted and treated.

II. STATISTICAL ANALYSIS

The results were analyzed using student's paired and unpaired 't' test and chi-square test. A 'p' value of <0.05 was considered as statistically significant, whereas 'p' value of <0.001 was taken as highly significant.

III. RESULTS

The groups P and M were found to be comparable in respect of age, weight, sex distribution (Table 1 : Patient characteristics)

Table 1: Patient Characteristics

Group	Propofol	Midazolam
No of cases	30	30
Mean age (years)	35.17 ± 11.91	36.40 ± 12.82
Male : Female	16 : 14	15 : 15
Mean weight (kg)	59.27 ± 6.98	58.23 ± 9.68

Mean duration of surgery, which was taken as time from surgical incision to surgical closure, was comparable in both the groups (88.66 ± 27.20 Vs. 90 ± 25.56) and so was mean duration of sedative infusion.(table 2)

Table 2 : Procedure characteristics

Group	Propofol	Midazolam
Mean duration of surgery (min)	88.66 ± 27.20	90 ± 25.56
Mean duration of infusion (min)	98.67 ± 28.65	101 ± 32.63
Mean infusion rates (mg/kg/hr) required (mg)	2.41 ± 0.265	0.06 ± 0.014
Mean of maximum level of sensory blockade	T8	T8

Mean of maximum level of sensory blockade achieved after spinal anaesthesia was comparable as well. Mean infusion rates were 2.41 ± 0.265 mg/kg/hr for propofol and 0.06 ± 0.014 mg/kg/hr for midazolam which were required to maintain the same level of sedation.

Table 3 : Sedative Properties

Group	Propofol	Midazolam
Mean time to achieve sedation score 4 (min)	9.80 ± 2.78	19.30 ± 3.16
Mean time take to recover from sedation	10.40 ± 2.16	18.37 ± 2.61

The time taken to reach OAA/S score of 4 was 9.80 ± 2.78 minutes in propofol group while it was 19.30 ± 3.16 minutes in the midazolam group, the difference being statistically highly significant ($p < 0.001$).

Mean time to recover from sedation was noted to be 10.40 ± 2.61 minutes in the propofol group and 18.17 ± 2.61 minutes in the midazolam group, this difference being statistically highly significant ($p < 0.001$).

Mean heart rate, mean values of SPO_2 and mean respiratory rates remained stable throughout the procedure. Similarly mean arterial pressure values were not significantly altered from their respective baseline values in both the groups, throughout the procedure, barring a few statistically insignificant changes. ($p > 0.005$).

Table 4: Comparison of recall of pictures

		Group M	Group P	P Value
Recall of picture 1	Present	30 (100%)	30 (100%)	
	Absent	0 (0%)	0 (0%)	
Recall of picture 2	Present	0 (0%)	5 (16%)	0.052
	Absent	30 (100%)	25 (83%)	
Recall of picture 3	Present	2 (7%)	19 (63%)	<0.001
	Absent	28 (93%)	11 (37%)	

Baseline recall was comparable in both groups as evidenced by recall of picture 1. Intraoperative amnesia was deep in both the groups as evidenced by 16% of the patients in the propofol group being able to recall picture 2 and non of patients being able to recall the same in the midazolam group.

Recall of picture 3 was present in 63% of patients in propofol group and 7% of patients in midazolam group, showing significantly lesser postoperative impairment of recall with propofol as compared to midazolam in which amnesia extended into the postoperative period as well. This difference was found to be statistically highly significant.

There were negligible postoperative side effects in either of the groups. (Table 5)

Table 5: Postoperative side effects

Group	Propofol	Midazolam
Bradycardia	0%	0%
Hypotension	3%	0%

Airway problems	0%	0%
Giddiness	0%	10%
Nausea/Vomiting	0%	7%

3% of patient in propofol group developed hypotension which subsided on IV fluid administration. 10% of patient in midazolam complained of giddiness and 7% of patient in the same group complained of mild nausea which subsided without any treatment.

IV. DISCUSSION

Sedation has show to increase patient satisfaction during regional anaesthesia and may be considered as a means to increase the patients acceptance of regional anaesthetic techniques.

Loud noises, untoward remarks etc. perceived in intraoperative period by patients, can have long term undesirable effects on their psyche.[7] The provision of good sedation, thus becomes increasingly important.

Conscious sedation is a very light form of anaesthesia where sedative drugs are used in very low doses so that the patient is rendered free of anxiety and discomfort.[2]

An ideal supplemental sedation should provide effective anxiolysis, an easily controllable level of sedation, predictable depth of amnesia rapid and clear headed recovery, amnesia and minimal intraoperative and post operative side effects.

Continuous infusions have been proved to produce lesser side effects, fast recovery, easy control over the desired depth of sedation.[6]

We had chosen the observer's Assessment of Alertness / Sedation scale (OAA/S) for assessment of sedation over the scales as it is easier to users, comprehensive and inclusive of parameters such as facial expression, eyelid ptosis and to speech which are not in other sedation scale.[8]

Sedation: In our study, the desired level of sedation was achieved much faster by propofol infusion as compared to midazolam (9.80 ± 2.78 Vs. 19.30 ± 3.16) and the difference in the findings was seen to be highly significant ($p < 0.001$).

Similarly, recovery with propofol was much faster than with midazolam (10.40 ± 2.16 Vs. 18.17 ± 2.61) and the difference in the findings was again statistically highly significant ($p < 0.001$).

In 2008, Hassan S A1- Khayat et al [9]and in 1990 Wilson E et al[10] and in 1991 Paul F White ,Jean B Negus[11] have studied the effects of propofol and midazolam infusions as sedative supplementations to regional anaesthesia and their findings were comparable to ours.

In 2009, Priyanka Khurana, Ankit Agrawal et al[12], in their study of comparison of midazolam and propofol for BIS- guided sedation uring regional anaesthesia observed that the time to reach desired sedation was 11 minutes in midazolam group while it was 6 minutes in propofol group. Recovery with midazolam was slower than with propofol (18.6 ± 6.5 Vs. 10.10 ± 3.65 Min). Their findings were similar to our findings.

In 2011, Patki A, Shelgaonkar VC et al[13] studied equisedative infusions of propofol and midazolam for conscious sedation under spinal anaesthesia. In their study it was found that propofol has advantage of providing faster onset of sedation, rapid clear headed recovery from same as compared to midazolam. Thus their findings were comparable to ours.

Vital Parameters: Propofol and midazolam both are known to inhibit sympathetic activity and decrease systemic vascular resistance resulting in some amount of bradycardia and hypotension.[14][15] We observed that , both propofol and midazolam in sedative infusions did not significantly alter mean heart rate or mean arterial pressure throughout the procedure our findings were comparable to those of some other authors who found that subsanaesthetic sedative doses of midazolam and propofol do not alter baseline cardiovascular varibales.[16]

Similarly, both these drugs are also known to depress respiratory function when give in inducing doses.[17][18][19] In our study, neither propofol or midazolam infusion, caused any significant alteration in mean respiratory rate or mean SPO_2 throughout the procedure, this could be possibly attributed to the fact that they were administered in subanaesthetic infusions.

Amnesia:

Both propofol and midazolam possess the property of causing transient antorograde amnesia with impairment of chiefly explicit memory.[20] While intraoperative amnesia is desirable for the psychological well being of the patient, postoperative amnesia is undesirable, as the ambulatory patient is expected to remember postsurgical discharge instructions in day-care surgical procedures.

As discussed earlier, we used the visual task of recall of pictures to assess intraoperative and postoperative recall. It appeared to us that midazolam produced deeper intraoperative amnesia in comparison to propofol, the amnesia with midazolam extended into the postoperative period as well. It was found that significantly lesser postoperative impairment of recall with propofol.

Our findings were comparable to those seen by other authors who used similar tasks for assessment of amnesia.

Postoperative side effects:

There were negligible postoperative side effects in either of the groups.

It was found that in the midazolam group only 2 patients complained of nausea and 3 patients in the same group complained of giddiness which subsided without any treatment.

In the propofol group, only one patient had a episode of hypotension which was treated with intravenous fluids. There was no episode of vomiting, airway obstruction etc. in any of the patients in both the groups.

V. CONCLUSION

When given as a sedative adjunct to spinal anaesthesia, both propofol and midazolam offer good sedation and good cardiorespiratory stability.

From our study :

1. Propofol was found to be superior to midazolam with respect to onset of sedation and clear headed recovery with significantly lesser postoperative impairment of recall.
2. In the midazolam group, time required to reach desired sedation (OAA Score 4) and recovery time from sedation was more as compared to propofol. Midazolam offered better intraoperative amnesia but it extended into the postoperative period.

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