Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 2, April - June 2017 (Part–1)
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4217.7

Comparison of Dexmedetomidine and Midazolam with Respect to Dreaming during Sedation under Regional Anesthesia in Patients at Bhuj, Kutch: A Prospective Study

Naitik Patel*, Mandakinee Thacker*

Abstract

Background and Aim: Regional anesthesia offers several benefits over general anesthesia. But to the patient it may be stressful as they stay awake. Sedation during regional anesthesia plays an important role in reducing the stress and patient satisfaction. Present study was designed with an aim to compare 2 different IV sedation protocols midazolam and Dexmedetomidine with respect to dreaming during sedation under regional anesthesia. *Methodology:* The study was conducted at Department of Anesthesia Gujarat Adani Institute of Medical Science, Bhuj, Kutch, Gujarat. One hundred and twenty adult patients were randomly assigned to 2 groups; Group M received IV inj midazolam and Group D received inj dexmedetomidine for sedation during spinal anesthesia. Sedation was assessed on Ramsay Sedation Score. Patients were interviewed on emergence and 30 minutes later to determine the incidence of dreams. Postoperatively, patient satisfaction with the sedation was also evaluated. The patients satisfaction was assessed using a scale from 1–100. Any untoward side effects were noted. *Results:* 60 patients in each group were included in the final analysis. The incidence of dreaming was 16% in the midazolam group and 3% in the dexmedetomidine group. High level of satisfaction with the sedation was observed in dexmedetomedine group. In this group 66% patients expressed sedation as excellent, 11%- good and 15% termed it as satisfactory. Midazolam was associated with decreased patient satisfaction; 26% patients termed it as excellent, 58% good and 15% satisfactory. *Conclusion:* During spinal anesthesia with sedation, patients receiving midazolam had 5 times more dreaming than those receiving dexmedetomidine. However, dexmedetomidine provides better quality of sedation during regional anesthesia resulting in superior patient satisfaction than midazolam.

Keywords: Dexmedetomidine; Midazolam; Sedation; Spinal Anesthesia.

Introduction

In modern health care system, patient satisfaction is one of the most significant criteria. Sedation during regional anesthesia plays an important role as it gives anxiolysis and amnesia. Sedation increases patient acceptance and satisfaction of regional anesthesia techniques. It improves surgical condition as patient sleeps, and prevents any recall of events during surgery in the postoperative period. Dreaming during anesthesia and sedation remains a poorly understood phenomenon. Dreaming is purely subjective. Dreams usually make their entrance during lighter plane of unconsciousness. The dream theory was first published by Freud in 1899 [1]. 50 years later sleep neurobiology was born with the identification of rapid eye movement (REM) sleep by Aserinsky and Kleitman in 1953 [2]. But dreams can come without REM sleep. There are some studies in anesthesiology that suggest that dreaming can occur during general anesthesia [3]. Up to 22% of subjects undergoing general anesthesia have reported dreams. Eer et al [4] and Stait et al [5] found that approximately 20 to 25% of patients undergoing sedation for colonoscopy had dreams, which is comparable to that found during general anesthesia. Cheong et al [6] studied adjunct sedation during spinal anesthesia

Author's Affiliation:
*Associate Professor, Department of anesthesia , Gujarat Adani Institute of Medical Science, Bhuj, Gujarat.

Corresponding Author:
Naitik Patel, Associate Professor, Department of Anesthesia, Gujarat Adani Institute of Medical Science, Bhuj, Gujarat 370001.
E-mail: patelnaitik27@yahoo.com, researchguide86@gmail.com

Received on 09.02.2017
Accepted on 15.02.2017

with ketamine and it was associated with a high incidence of dreaming.

Dexmedetomidine sedation is being increasingly used during regional anesthesia and some day care surgical procedures. There were no studies of dreaming incidence with dexmedetomidine sedation. So we conducted this prospective study in comparison with midazolam sedation during spinal anesthesia.

Methodology

The study was conducted at Department of Anesthesia Gujarat Adani Institute of Medical Science, Bhuj, Kutch, Gujarat. Ethical approval was taken from institutional review board and ethical committee of the college and written informed consent was obtained from all participants. 120 ASA I and II patients, aged 30- 60 years, undergoing elective surgeries under spinal anesthesia were randomly allocated into 2 groups of 60 each. Group D to receive dexmedetomidine 1 μ g/kg in 10 ml normal saline, and Group M to receive midazolam 0.05 mg/kg in 10 ml normal saline which was given slowly over 10 minutes. Patients with obstructive sleep apnea, psychotic or major affective disorders, those taking hypnotics, patients with raised renal parameters, coagulation disorders, spinal deformities and were excluded from the study. Pre-anesthetic check-up was carried out preoperatively with a detailed history, general examination and systemic examination, airway assessment, and spinal column examination.

Patients received tab ranitidine 150 mg and tab alprazolam 0.5 mg previous day night and they were nil orally on the day of surgery. Inside the OR, IV line was secured with 18G cannula. After preloading with 500 ml of lactated Ringer's solution, the drug for the study was given depending on the group on random allocation according to computer based numbers. Spinal anesthesia was administered using a 25-G Quincke spinal needle at the L3- 4 intervertebral space with 3 to 3.2 ml of 0.5% hyperbaric bupivacaine. Oxygen was administered at 4 L/min through a simple mask during the procedure. Intraoperative monitoring included electrocardiography, pulse oximetry and noninvasive sphygmomanometry. The level of sedation was evaluated using six point Ramsay Sedation Scale (RSS)

1- Patient fully awake and oriented;

2- Patient cooperative, drowsy and tranquil;

3- Patient asleep but responds to oral commands;

4- Asleep, but responds to light glabellar tap;

5- Asleep, sluggish response to light glabellar tap;

6- Asleep, no response.

Any patient having an RSS score < 3 received repeated doses of midazolam 0.02 mg/kg in Group

M and dexmedetomidine 0.2 μ g/kg in Group D to maintain the sedation level of RSS score ≥ 3.

Patients were interviewed at the end of the surgery and 30 minutes later in recovery room to determine the incidence of dreams. Dreaming during sedation was defined as any experience that was described by the patient as dreaming and was thought by the patient to have occurred between the induction of sedation and the first moment of awakening after surgery. Postoperatively patient satisfaction with the sedation was evaluated.

Patient satisfaction was rated on a 100-point numerical rating scale (1=no satisfaction, 100 =maximum satisfaction). 81-100 was considered as excellent; 61-80 as good; 41-60 as satisfactory, and < 41 as poor. Sensory block was assessed by pin prick with 23G hypodermic needle every 2 min for initial 10 min. Motor block were recorded at the same intervals. Blood pressure, heart rate was recorded at baseline and every five minutes. Operation was performed once the sensory level of T10 was achieved.

Considering the time of intrathecal injection as time zero, the time to onset of sensory block was taken as the time taken to reach the level of T6. The time of requisition for analgesics is taken as the duration of the sensory block and was recorded. The level of motor block was assessed with modified Bromage scale (0 = no paralysis, able to flex hips/knees/ankles; 1 = able to move knees, unable to raise extended legs; 2 = able to flex ankles, unable to flex knees; 3 = unable to move any part of the lower limb) and were recorded.

Statistical Analysis

The data was coded and entered into Microsoft Excel spreadsheet. Analysis was done using SPSS version 15 (SPSS Inc. Chicago, IL, USA) Windows software program. The variables were assessed for normality using the Kolmogorov-Smirnov test. Descriptive statistics were calculated. Means of both groups were compared by independent student t-test. Data for heart rate and mean arterial pressure were analyzed using a Friedman test. Chi-square analysis was used for comparison of categorical variables. Level of significance was set at p=0.05.

Results

There was no statistically significant difference between the two groups in terms of demographic characteristics. All patients were females and posted for gynecological procedures (Table 1).

Ramsay sedation score was taken after completing the IV administration of the drug and that time is taken as 0 min and assessed every 15 min for the total of 150 minutes (Table 2). 32 patients in Group D received additional dose of 0.2 μg/kg of dexmedetomidine, 38 in Group M received first additional dose of 0.02 mg/kg of midazolam and 4 patients required second additional dose of 0.02 mg /kg of midazolam out of 60 patients in each group. All patients were maintained at 4 or 3 levels in Ramsay sedation scores.

There was no difference between the groups regarding time of onset 7.5 ± 2.5 min in Group D and 7.8 ± 2.4 min in Group M. The time required for two segment regression from the highest segment of the block was 128.5 ± 9.55 min in Group D and 98.6 ± 9.60 min in Group M. Duration of sensory blockade was longer in Group D (265.32 ± 15 min) compared to Group M (185.2 ± 15 min) and was statistically significant.

The average heart rate was significantly lower in Group D compared to Group M ($p < 0.001$). Significantly more number of patients in Group D had intra operative heart rate < 50/min compared to Group M ($p < 0.001$). Transient hypotension was more common in Group D patients compared to patients in Group M ($p < 0.001$). Postoperative nausea was found in 10 patients in Group D and only 3 patients in Group M which was statistically significant. Incidence of vomiting and nausea was also more in these patients may be because of hypotension (Table 3). 10 patients out of 60 patients in midazolam group had dreams compared to only 2 patients in dexmedetomidine group, with p value < 0.001. Majority of patients in both group had no dreams. Patients receiving dexmedetomidine were significantly more satisfied with the sedation.

Table 1: Demographic characteristics of the participants involved in the study

Variables	Group D (Mean ± SD)	Group M (Mean ± SD)	P value
Age (years)	41.7±9.50	40.79±8.64	0.3
Weight (KG)	53.51±6.21	52.6±5.60	0.5
Height (CM)	150.21±5.21	153.12±5.15	1.0
Duration of Surgery	112.12±22.01	115.3±22.43	0.45

Statically significant difference at p=0.05
SD: Standard Deviation

Table 2: Ramsay sedation score of the participants involved in the study

Time	Group D (Mean ± SD)	Group M (Mean ± SD)
0 Min	2	2
15Min	3.88±0.5	3.84±0.1
30 Min	4.23±0.21	3.83±0.4
45 Min	4.59±0.3	4.24±0.32
60 Min	4.62±0.5	4.45±0.12
75 Min	4.57±0.12	4.44±0.65
90 Min	4.56±0.12	4.41±0.21
120 Min	4.11±0.32	4.03±0.42
150 Min	3.28±0.23	3.23±0.89

SD: Standard Deviation

Table 3: Side effects occur to the participants involved in the study

Side effects	Group D	Group M	P value
Hypotension	15	5	0.01
Bradycardia	12	3	0.001
Shivering	0	10	0.0002
Nausea	10	3	0.003
Vomiting	1	0	0.12

Statically significant difference at p=0.05

Discussion

Sedation is the depression of a patient's awareness to the environment and reduction of patients' responsiveness to external stimulation. There are different indications for sedation during regional anesthesia. Either an initial bolus or continuous infusion of sedative drugs can be used to provide anxiolysis. Most of our patients are anxious when they come to Operation Theater and more so before regional block. Also, sedation reduces the postoperative recall of intraoperative events. Patient's acceptance of a regional block has shown to be increased with sedation. Present study evaluated the patients for incidence of dreams and satisfaction with sedation under two different drugs i.e dexmedetomidine and midazolam boluses during spinal anesthesia. Sedation was maintained in both the groups between Ramsay sedation score [3].

All are female patients between 30- 50 years. 16% of patients in midazolam group compared to only 3% of patients in dexmedetomidine group told that they had dreams during sedation. Patients receiving dexmedetomidine were significantly more satisfied with the sedation than patients who received midazolam for sedation. Intravenous dexmedetomidine which was used for sedation had increased the duration of analgesia of spinal anesthesia compared to midazolam.

Dexmedetomidine is the pharmacologically active dextroisomer of medetomidine, has an imidazoline structure and is a potent and selective agonist of the ± -2 adrenoceptor. Dexmedetomidine shows 8 times greater selectivity for ± -2 than ±- 1 receptors compared with clonidine. A high density of ± -2 receptors exists in the locus ceruleus, a small brain stem structure that is important in modulating vigilance. The locus ceruleus is part of an endogenous sleeppromoting pathway [7]. These neurons have inhibitory control over [3]-aminobutyric acid (GABA)–containing neurons in the ventrolateral preoptic nucleus of the anterior hypothalamus and, in turn, affect the higher centers in the brain associated with loss of wakefulness. The clinical sedative response of ±-2 adrenergic agonists is similar to natural sleep and patients are easily arousable and able to follow commands after minimal stimulation. Present evidence suggests that there are 3 major receptor subtypes for dexmedetomidine: ±2A, ±2B, and ±2C. It has become evident that the ±2A and ±2C subtypes predominate in the CNS and is responsible for the sedative, analgesic, and sympatholytic components of agonist action [8]. Lee et al reported that when a loading dose of dexmedetomidine 1 μg/kg for 10 min was administered on the average, the peak concentration was reached in 17 min, and the termination half-life was 2 hr and 10 min [9]. However, the spinal anesthesia itself is reported to have sedative effects. It reduces the requirements of the sedative drugs, and a positive correlation has been exhibited between the depth of sedation and the extent of the block. This effect is explained by the hypothesis of decrease in afferent sensory input with consecutive reticulothalamo- cortical inhibition. Low loading dose of dexmedetomidine is believed to bring adequate sedation during regional anesthesia [10,12].

Bispectral index (BIS) is a widely used quantitative parameter for evaluating anesthesia and sedation levels. Dexmedetomidine is a novel sedative, providing sedation while patients remain cooperative an can be easily aroused; as a consequence, BIS used with dexmedetomidine may poorly characterize sedation. Thus, the BIS values are higher with dexmedetomidine [13]. In our study patients within 90 min from the loading dose of dexmedetomidine had satisfied sedation, but 32 patients over 90 min from the loading dose of dexmedetomidine had to receive additional dose to maintain the sedation level >3 while the remaining 28 did not receive any additional dose.

Midazolam is a benzodiazepine that exerts its pharmacologic effect by facilitating GABA, the major inhibitory neurotransmitter of the CNS. Midazolam enhances the affinity of the receptors for GABA, as a result of which, there is enhancedopening of chloride gated channels resulting in increased chloride conductance. The subsequent enhanced opening of chloride channels leads to hyperpolarization of the neuron and resistance to stimulation [14]. Midazolam also acts directly by activation of alpha-1 subunits of GABA-A receptors whereas anxiolytic effect is due to alpha-2 subunit activity. Alpha-1 containing GABA-A receptors are the most numerous accounting for 60%. Alpha-2 subtypes are less common and present in hippocampus and amygdala. GABA receptors are large macromolecules and provide separate attachment sites for GABA, benzodiazepines, barbiturates, etomidate, propofol, neurosteroids and alcohol. Kim DK et al conducted a study on two hundred twenty adult patients between IV infusion of propofol or midazolam for deep sedation during spinal anesthesia. The proportion of dreamers was 39.8% (43/108) in the propofol group and 12.1% (13/107) in the midazolam group. They concluded that during spinal anesthesia with deep sedation, dreaming was almost 5 times more common in patients receiving propofol infusion than in those receiving midazolam, although dreaming did not influence satisfaction with the sedation [15]. Similar study was conducted by Stait ML et al [16].

Normal psychological responses to anxiety and fear are not usually harmful; however, in a medically compromised patient they may present a risk to the patient's health. Epilepsy, asthma, hypertension and angina are examples of systemic diseases that may be exacerbated by stress. Anxious patients with these medical conditions can often be benefited from receiving sedation. Anxiety and pain can cause over activity of the sympathetic nervous system leading to hypertension, tachycardia, and arrhythmias. Sedation reduces psychological responses to anxiety and fear. Patients who have involuntary movements due to neuromuscular disease may wish to, but are unable to physically cooperate. It is often difficult to treat patients with management in this group of patients also.

Conclusion

Sedation is an important tool for anesthesiologists to provide a better quality of care during regional anesthesia. Our study demonstrates that the high satisfaction with anesthesia was obtained when there was adequate preoperative information regarding anesthesia procedure, effective management of patient anxiety with intraoperative sedation and efficient postoperative pain care. Even though dexmedetomidine had lower incidence of dreaming, patients satisfaction was significantly higher as compared to midazolam. Midazolam provided good sedation and had higher incidence of dreaming, and provided more hemodynamic stability.

References

1. Freud S. Die Traumdeutung. 1st edition. Vienna: Franz Deuticke, 1899.
2. Aserinsky E, Kleitman N. Regularly occurring periods of eye motility, and concomitant phenomena, during sleep. Science. 1953 Sep 4; 118(3062):273-4.
3. Strickland RA, Butterworth JF 4th. Sexual dreaming during anesthesia: early case histories (1849–1888) of the phenomenon. Anesthesiology. 2007 Jun; 106(6):1232-6.
4. Eer AS, Padmanabhan U, Leslie K. Propofol dose and incidence of dreaming during sedation. Eur J Anaesthesiol. 2009 Oct; 26(10):833-6.
5. Stait ML, Leslie K, Bailey R. Dreaming and recall during sedation for colonoscopy. Anaesth Intensive Care. 2008 Sep; 36(5):685-90.
6. Cheong SH, Lee KM, Lim SH, Cho KR, Kim MH, Ko MJ, et al. The effect of suggestion on unpleasant dreams induced by ketamine administration. Anesth Analg. 2011 May; 112(5):1082-5.
7. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. Anesth Analg. 2000; 90:699–705.
8. Nelson LE, Lu J, Guo T, Saper CB, Franks NP, Maze M. The alpha 2-adrenoceptor agonist dexmedetomidine converges on an endogenous sleep-promoting pathway to exert its sedative effects. Anesthesiology. 2003 Feb; 98(2):428-36.
9. Lee S, Kim BH, Lim K, Stalker D, Wisemandle W, Shin SG, et al. Pharmacokinetics and pharmacodynamics of intravenous dexmedetomidine in healthy Korean subjects. J Clin Pharm Ther. 2012 Dec; 37(6):698-703.
10. Gentili M, Huu PC, Enel D, Hollande J, Bonnet F. Sedation depends on the level of sensory block induced by spinal anaesthesia. Br J Anaesth. 1998 Dec; 81(6):970-1.
11. Pollock JE, Neal JM, Liu SS, Burkhead D, Polissar N. Sedation during spinal anesthesia. Anesthesiology. 2000 Sep; 93(3):728-34.
12. Hwoe-Gyeong Ok, Seung-Hoon Baek, Seong-Wan Baik, Hae-Kyu Kim, Sang- Wook Shin, Kyung-Hoon Kim. Optimal dose of dexmedetomidine for sedation during spinal anesthesia. Korean J Anesthesiol. 2013 May; 64(5):426-31.
13. Kasuya Y, Govinda R, Rauch S, Mascha EJ, Sessler DI, Turan A. The correlation between bispectral index and observational sedation scale in volunteers sedated with dexmedetomidine and propofol. Anesth Analg. 2009 Dec; 109(6):1811-5.
14. Goodchild CS. GABA receptors and benzodiazepines. Br J Anaesth. 1993 Jul; 71(1):127-33.
15. 15. Kim DK, Joo Y, Sung TY, Kim SY, Shin HY. Dreaming in sedation during spinal anesthesia: a comparison of propofol and midazolam infusion. Anesth Analg. 2011 May; 112(5):1076-81.
16. Stait ML, Leslie K, Bailey R. Dreaming and recall during sedation for colonoscopy. Anaesth Intensive Care. 2008 Sep; 36(5):685-90.
17. Aho M, Erkola O, Kallio A, Scheinin H, Korttila K. Dexmedetomidine infusion for maintenance of anesthesia in patients undergoing abdominal hysterectomy. Anesth Analg. 1992; 75:940–6.
18. Kuzucuoðlu T, Bölükbaþýoðlu I, Arslan G, Yücel E, Ayaz B: Comparison of the activity and reliability of intravenous administration of midazolam and dexmedetomidine on sedation levels under epidural anesthesia. Agri. 2010 Jul; 22(3):121-30.