# Intraoperative Sedation During Epidural Anesthesia: Dexmedetomidine Vs Midazolam

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**Citation**

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**Abstract**

Background: This study evaluated the ability of dexmedetomidine to provide sedation during epidural anesthesia compared with midazolam, examining the cardiorespiratory variables, analgesic requirements and side effects.

Patients and Methods: Sixty patients undergoing inguinal herniorraphy under regional anesthesia were randomized into two groups to receive either dexmedetomidine or midazolam for intraoperative sedation. Cardiorespiratory effects, level of sedation, quality of analgesia, time to first analgesic requirement were evaluated.

Results: There were significant declines in HR and MAP values compared to baseline in both groups but the difference between groups was not significant. There were higher sedation levels in midazolam group and 16 patients receiving midazolam needed dose adjustment. The time to first analgesic requirement was significantly longer in dexmedetomidine group.

Conclusion: Supplement of intravenous dexmedetomidine in patients receiving epidural anesthesia may provide a good sedative effect and postoperative pain management without any clinically important untoward cardiorespiratory reactions.

## INTRODUCTION

Central neuraxial anesthesia is a widely used method and may be associated with stress, anxiety and even embarrasment causing intraoperative discomfort. Although some patients tolerate being awake during surgical precedures without any medication, in some patients sedatives are required to limit discomfort. Administration of a sedative agent however, is associated with a risk of side effects, especially cardiorespiratory problems. Pharmacologic agents that create an adequate level of sedation without any clinical side effects are of increasing interest to clinicians ([1]) .

Alpha-2 adrenoceptor agonists have been recently used for their sedative, analgesic and perioperative sympatholytic and cardiovascular stabilizing effects with reduced anesthetic requirements ([2]) . Dexmedetomidine (a potent -2 adrenoceptor agonist) is more selective to the -2 adrenoceptors than clonidine. It has many pharmacodynamic properties that might be desirable in medication used to supplement general anesthesia and its effects are readily reversible with atipamezole, an -2 adrenoceptor antagonist ([3]) . Potential desirable effects include decreased requirements of anesthetics and analgesics, a diminished sympathetic response to stress and the potential for cardioprotective effects against myocardial ischemia with minimal effects on respiration ([4]) . Although a primary indication for dexmedetomidine has been the sedation of critically ill patients, it can also be used for intraoperative sedation ([5]) .

The purpose of this study was to evaluate the cardiorespiratory end-points of dexmedetomidine and midazolam in providing sedation during epidural anesthesia. Postoperative analgesia requirements and satisfactory outcomes were also investigated.

## PATIENTS AND METHODS

This prospective, randomized, double-blind study was conducted with a population of patients undergoing elective inguinal herniorraphy. After Institutional Ethics Committee approval and written informed consent of the participants, a total of 60 adult male patients (aged 30-65 yr, American Society of Anesthesiologists-ASA-physical class I-II)

enrolled in the study. All patients have normal renal, hepatic function and no history of allergy or chronic use of medical therapy. The patients with second or third degree of heart block, current history of psychiatric disorders, history of sleep apnea, or patients with a body mass index greater than 40 $kg/m^2$ were excluded.

All patients received no premedication and monitorized by non-invazive blood pressure, electrocardiogram (ECG) and pulse oxymetry on arrival to the operating room. A computer-generated randomization list was used to assign patients to one of two study groups. Before the insertion of epidural catheter, the patients in the first group (group D) received sedation with an intravenous loading dose of 1 $\mu g.kg^{-1}$ dexmedetomidine and the second group (group M) received 0.04 $\mu g.kg^{-1}$ midazolam via a syringe infusion pump over a 10-min period. After then, an epidural catheter was inserted at $L_{4-5}$ with loss-of-resistance to saline and the patient in the lateral decubitus position. A 4 ml test dose of 2% lidocaine was given followed by 75 mg 0.5% plain bupivacaine. When the analgesia level became adequate for surgery continuous infusions of 0.5 $\mu g.kg^{-1} h^{-1}$ dexmedetomidine and 0.04 $\mu g.kg^{-1} h^{-1}$ midazolam were started in study groups respectively. Drug infusions were discontinued if one of the following adverse events was observed: apnea lasting longer than 20 s, hemoglobin oxygen saturation lower than 90%, decrease of heart rate (HR) below 50 beats. $min^{-1}$ , mean arterial pressure (MAP) below 30% of the initial value. The evaluation of quality of sedation was based on a six point Ramsay Sedation Score (RSS) and according to the sedation level infusion dose was decreased to one half or increased to twice to maintain the RSS≤4. The quality of analgesia was assessed by using a 100-mm visual analog scale (VAS) in which 0 represents no pain at all and 100 represents incredible pain. If the patient reported pain exceeding 60 mm on the scale, intravenous fentanyl in doses of 0.05 mg was administered. Oxygen was delivered by a facemask 5 $L.min^{-1}$ to all patients throughout the procedure. Administration of any medication apart from the study protocol and occurrences of complications and side effects were recorded.

Sedation and monitoring were performed by the same anesthesiologist in all cases but assessments were performed by an individual who was blinded to the study drug. Surgeons were asked about their satisfaction with neuromuscular relaxation during the procedure. The following parameters were measured continuously: heart rate (HR), respiratory rate (RR), mean arterial pressure (MAP), hemoglobin oxygen saturation ($SpO_2$). The recorded data were analyzed and averaged over the following time intervals: before injection of study drug (baseline), at least 3 min later from the first injection of study drug, after epidural administration of bupivacaine and every 10 minutes from the start to the end of surgery (at which the infusions were discontinued). RSS and VAS was assessed during epidural catheter implantation, intraoperative period (VAS was assessed until RSS reached to score 4), the post-anesthesia care unit at the $30^{th}$ and the $60^{th}$ minutes. The patients were transferred to ward when RSS was 2 point. A 12-h follow up was made to assess the analgesic requirements of the patients and ask their willingness to undergo a repeat procedure with the same anesthetic regimen in the future if required.

Statistical analysis: Statistical analyses were performed using Statistica for Windows version 10.0 software. Results were expressed as members of occurrences, percentages and mean ± SD. With a 2-sided type I error of 5 % and study power at 80%, the number of patients required in each group to demonstrate a difference between groups was 25. Repeated measures analysis of variance was used to compare continuous variables. The difference in continuous parameters such as patient characteristics, preoperative data and amount of supplemental analgesic were analyzed using one-way analysis of variance or Kruskal Wallis test for non-parametric quantitative data. A p values less than 0.05 was considered significant.

## RESULTS

In all patients the study was completed without any serious complication. The study groups were comparable regarding to ASA physical status, demographic characteristics, initial vital signs, maximum analgesia level and duration of operation (Table 1).

**Figure 1**

Table 1: Patient demographics, preoperative and operative data.

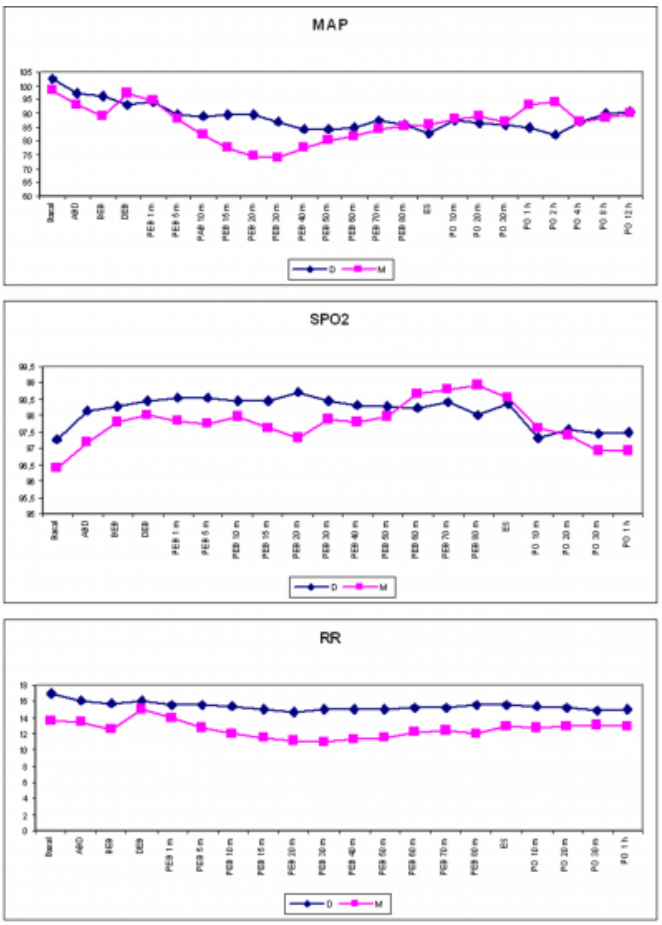
| Parameter | Group D | Group M |
|---|---|---|
| ASA I (%) | 26 (86.7%) | 23 (76.6%) |
| Age (yr) | 42.36 ± 13.14 | 46.32 ±11.03 |
| Weight (kg) | 74.00 ± 11.24 | 69.16 ± 9.55 |
| Height (cm) | 171.33 ± 7.83 | 170.16 ± 5.88 |
| MAP (mmHg) | 102.27 ± 11.74 | 98.20 ± 13.80 |
| HR (beat.min$^{-1}$) | 77.36 ± 13.43 | 71.60 ± 11.07 |
| $SpO_2$ (%) | 97.27 ± 1.68 | 96.40 ± 1.82 |
| RR (min$^{-1}$) | 16.87 ± 3.63 | 16.13 ± 3.32 |
| Max analgesia level (T) | 9.27 ± 1.23 | 9.15 ±1.12 |
| Duration of operation (min) | 42.80 ±11.60 | 40.60 ± 6.97 |

Data were presented as n or mean ± SD

There were significant declines in HR and MAP values compared to baseline in both groups but the difference between groups was not significant ($p>0.05$). Atropine requirements between the groups were not significant. MAP was significantly reduced in one patient in both groups and treated with ephedrine. The variations in $SpO_2$ and respiratory rate were negligible in both groups (Figure 1).

**Figure 2**

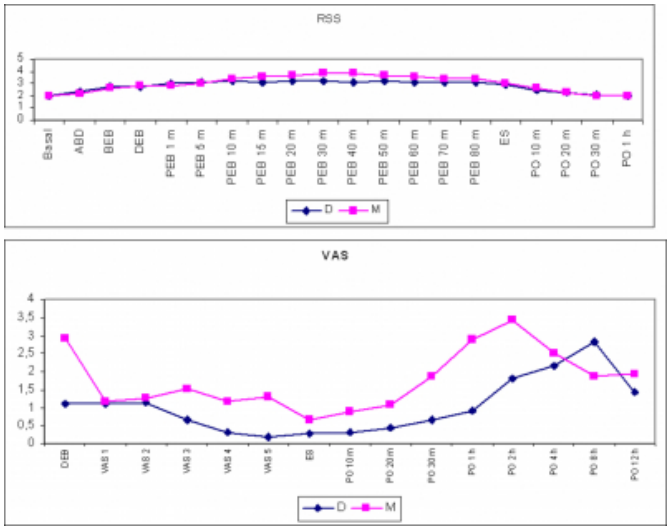
Figure 1: Cardiorespiratory variables during the intraoperative period. Mean values of mean arterial pressure, heart rate, SpO values, respiratory rate in determined times. ABD: after bolus drug, BEB: before epidural block, DEB: during epidural block, PEB: postepidural block, ES: end of surgery, PO: postoperative period.




RSS were significantly higher in group M during the intraoperative period and dose reduction of the drug was required in 16 patients. In group D only one patient required dose adjustment. There were no differences between treatment groups at postoperative 30 $^{th}$ and 60 $^{th}$ min in respect to sedation scores. VAS during epidural catheter implantation and the intraoperative period was decreased significantly in both groups. The patients receiving dexmedetomidine presented lower VAS values in the post-anesthesia care unit but the difference between groups throughout the postoperative period was not significant (Figure 2). No patient required supplemental fentanyl.

**Figure 3**

Figure 2: Comparison the level of sedation according RSS and intensity of pain according toVAS.




The number of patients (n=24 in group D, n=20 in group M) and surgeon (n=22 in group D, n=13 in group M) who revealed a good satisfaction from anesthetic technique were similar. The time to first analgesic requirement was significantly longer ($p<0.01$) in group D (487.27 ± 201.25 min and 278.54 ± 153.48 min respectively). No other side effects or administration of medication other than those in the study protocol were recorded.

## DISCUSSION

The present randomized, double-blinded study demonstrated that loading dose of 1 μg.kg $^{-1}$ dexmedetomidine followed by 0.5 μg.kg $^{-1}$ h $^{-1}$ infusion provided a good and stable sedative effect during epidural anesthesia and manifested a longer time to first analgesic requirements in patients undergoing inguinal hernioraphy. Loading dose of 0.04 μg.kg $^{-1}$ midazolam followed by 0.04 μg.kg $^{-1}$ h $^{-1}$ infusion resulted in higher sedation scores in patients whose the heavy sedation was not necessary. Cardiovascular stability and respiratory function were well maintained in both study groups.

During surgical procedures, both under- and over- sedation carry inherent risk, the former increases the likelihood of recall and agitation-induced sympathetic activation, and the latter, excessive depression of vital physiologic functions ([6]) . It's important to distinguish the sedation scales used to assess the sedation during surgical procedures rather than in patients in intensive care units, because the aim of intraoperative sedation is to provide calmness more than decrease the level of consciousness ([7,8]) .

Selection of sedation agents largely depends on physician preference. A wide variety of centrally-active drugs are used to provide sedation, anxiolysis, and amnesia. There is a growing interest in the use of alpha-2 adrenoceptors agonists as sedatives. Dexmedetomidine is a currently used agent because of its short half-life, sedation, analgesic properties and favorable cardiorespiratory effects ([9]) . It's sympatholytic effect is manifested by decreases in arterial blood pressure, heart rate and norepinephrine release ([9,10,11]) .

It has been previously reported that the use of dexmedetomidine in colonoscopy ([1]) , intravenous sedation ([12]) , awake craniotomy ([13,14]) , carotid endarterectomy ([15]) , fiberoptic intubation ([16]) and intravenous regional anesthesia ([17]) provided satisfactory sedation, intra- and post-operative analgesia and hemodynamically stable perioperative period. However, only a limited number of reports describe the use of a-2 receptor agonists for intraoperative sedation during regional anesthesia. Systemically administration of dexmedetomidine may prolong the duration of spinal anesthesia depending on activation of a-2 adrenoceptors. Supplemention of intravenous dexmedetomidine during spinal anesthesia may be beneficial to overcome the discomfort of the patients especially in prone position ([18]) . In comparison to propofol, dexmedetomidine achieved similiar levels of sedation with a slower onset and offset of sedation, comparable respiratory changes and more stable hemodynamic parameters. Blood pressure and heart rate decreased in both groups of our patients but were not significant between groups. These decreases were not only depending on the drug infusions but also decreased sympathetic reflex and release from anxiety.

As previously reported, dexmedetomidine may provide better analgesia for postsurgical pain compared with widely used drugs ([19,20]) . Although the patient satisfaction with their procedure is impacted by multiple variables, intra and post-operative pain control is the primary determinant. Regional anesthesia may be somewhat painful itself and require analgesic medication ([21]) . Dexmedetomidine administration also reduced the discomfort during epidural catheter replacement and postoperative analgesic requirements in our patients. Therefore, it may be advantageous for the recovery and satisfaction point of view. It was considered that, dexmedetomidine, in addition to its sedative effect is a good analgesia-sparing agent.

In conclusion, during epidural anesthesia loading dose of μg.kg $^{-1}$ dexmedetomidine followed by continuous infusion

of 0.5 μg.kg $^{-1}$ h $^{-1}$ may be beneficial for the providing stable sedation, hemodynamics and respiration together with the good postoperative analgesia. Efficacy of intravenous dexmedetomidine during intra-operative period needs to be researched in a large number of patients.

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### References

1. Jalowiecki P, Rudner R, Gonciarz M. Sole use of dexmedetomidine has limited utility for conscious sedation during outpatient colonoscopy. Anesthesiology 2005; 103 (2): 269-73.
2. Kamibayashi T, Maze M. Clinical uses of alpha-2 adrenergic agonists. Aneslhesiology 2000 ;93:1345-9.
3. Dyck JB, Shafer SL. Dexmedetomidine pharmacokinetics and pharmacodynamics.
Anaesthetic Pharmacology Review 1993; 238-45.
4. Taittonen MT, Kirveli OA, Aantaa R, Kanto JH. Effect of clonidine and dexmedetomidine
premedication on perioperative oxygen consumption and haemodynamic state. Br J Anaeslh
1997; 78:400-6.
5. Arian SR, Thomas JE. The efficacy, side effects, and recovery characteristics of
dexmedetomidine versus propofol when used for intraoperative sedation. Anesth Analg 2002;
95:461-6.
6. Nemethy M, Paroli L, Williams-Russo PC, Blanck TJ. Assessing sedation with regional
anesthesia: inter-rater agreement on a modified Wilson Sedation Scale. Aneslh Analg 2002;
94:723-8.
7. Avripas MB, Symthe MA, Carr A, Begle RL, Johnson MH, Erb DR. Development of an
intensive care unit bedside sedation scale. Ann Pharmacother 2001; 35(2): 262-3.
8. de Lemos J, Tweeddale M, Chittock D. Measuring quality of sedation in adult
mechanically ventilated critically ill patients. The Vancouver Interaction and Calmness Scale.
J Clin Epidemiol 2000; 53(9): 908-19.
9. Mantz J. Dexmedetomidine. Drugs of Today 1999;35(3):151-7.
10. Talke P,Chen R,Thomas B et al. The hemodynamic and adrenergic effects of perioperative
dexmedetomidine infusion after vascular surgery. Aneslh Analg 2000, 90: 834-9.
11. Hogue CW, Talke P, Stein PK et al. Autonomic nervous system responses during sedative
infusions of dexmedetomidine. Anesthesiology 2002; 97:592-8.
12. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic
properties of small-dose dexmedetomidine infusions. Aneslh Analg 2000; 90:699-705.
13. Ard J, Doyle W, Bekker A. Awake craniotomy with dexmedetomidine in pediatric
patients. J Neurosurg Aneslhesiol 2003; 15(3): 263-6.
14. Bekker AY, Kaufman B, Samir H, Doyle W. The use of dexmedetomidine infusion for awake craniotomy. Anesth Analg 2001; 92:1251-3.
15. Bekker Ay, Basile J, Golg M et al. Dexmedetomidine for awake carotid endarterectomy:
efficacy, hemodynamic profile, and side effects. J Neurosurg Anesthesiol 2004;!6(2): 126-35.
16. Scher CS, Gitlin MC. Dexmedetomidine and low-dose ketamine provide adequate
sedation for awake fibreoptic intubation. Can J Aneslh 2003; 50(6): 607-10.
17. Memis D, Turan A, Karamanlioglu B, Pamukcu Z, Kurt I. Adding dexmedetomidine to
lidocaine for intravenous regional anesthesia. Aneslh Analg 2004; 98:835-40.
18. Gunaydm B, Ozkose Z, Tarhan B. Intravenous dexmedetomidine sedation for spinal
anesthesia in the prone knee-chest position for lumbar laminectomy surgery. Turk J Med Sci
2004; 34:353-5.
19. Arian SR, Ruehlow RM, Uhrich TD, Ebert TJ. The efficacy of dexmedetomidine versus
morphine for postoperative analgesia after major inpatient surgery. Anesth Analg 2004;
98:153-8.
20. Alhashemi J, Kaki AM. Dexmedetomidine in combination with morphine PCA provides superior analgesia for Shockwave lithotripsy. Can J Anesth 2004; 51:342-7.
21. Helgeson LE. Sedation during regional anesthesia: inhalational versus intravenous. Curr Opin Anaesthesiol 2005; 18:534-9.

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