

EFFECT OF DIFFERENT CONCENTRATIONS OF EPIDURAL DEXMEDITOMIDINE FOR POST-OPERATIVE ANALGESIAVaraprasad Raghupatruni¹, K. S. D. Ganesh²**HOW TO CITE THIS ARTICLE:**

Varaprasad Raghupatruni, K. S. D. Ganesh. "Effect of different Concentrations of Epidural Dexmedetomidine for Post-operative Analgesia". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 72, September 07; Page: 12587-12593, DOI: 10.14260/jemds/2015/1812

ABSTRACT: BACKGROUND: The aim of our study was to know the ideal epidural dose to achieve analgesia in the postoperative patients using different concentrations of epidural dexmedetomidine.

METHODS AND MATERIALS: Ninety patients of either sex, with age ranging from 25 years to 60 years were randomly selected and divided into three groups of thirty each. Group A received epidural 0.25% bupivacaine along with 25mcg of dexmedetomidine, Group B received epidural 0.25% bupivacaine along with 50mcg dexmedetomidine and Group C received epidural 0.25% bupivacaine along with 75 mcg dexmedetomidine. The duration of analgesia, sedation and cardiovascular stability were studied. **RESULTS:** Analgesia and sedation was more in Group C than the other two groups. Cardiovascular stability was good in groups A and B.

KEYWORDS: Dexmedetomidine, Epidural, Analgesia, Post-operative.

INTRODUCTION: Effective postoperative pain control is an essential component of the care of the surgical patient. Inadequate pain control, apart from being inhumane, may result in increased morbidity or mortality.^{1,2} Evidence suggests that surgery suppresses the immune system and that this suppression is proportionate to the invasiveness of the surgery.^(3,4) Good analgesia can reduce this deleterious effect. Data available indicate that afferent neural blockade with local anesthetics is the most effective analgesic technique. Next in order of effectiveness are high-dose opioids, epidural opioids and clonidine, patient controlled opioid therapy, and non-steroidal anti-inflammatory agents.⁽⁵⁾

The advantages of effective postoperative pain management include patient comfort and therefore satisfaction, earlier mobilization, fewer pulmonary and cardiac complications, a reduced risk of deep vein thrombosis, faster recovery with less likelihood of the development of neuropathic pain, and reduced cost of care.

The failure to provide good postoperative analgesia is multifactorial. Insufficient education, fear of complications associated with analgesic drugs, poor pain assessment, and inadequate staffing are among its causes.

Neuraxial anesthesia and analgesia provide solid analgesic effect by inhibiting nociceptive transmission from peripheral to central neuronal system.^{[6],[7]} However, their analgesic advantages might be limited by the short life of current local anesthetics (LAs), and, especially, be weakened during postoperative pain control.^[8]

METHODS AND MATERIALS: After obtaining institutional ethical committee approval and written consent from the ninety patients, they were randomly divided into three groups of thirty each. All the patients were pre-operatively assessed and the technic for study was explained to them. Patient's age ranging from 25 to 60 years, of either sex, belonging to ASA I and II and no contra-indications to epidural analgesia or the drugs were taken into consideration.

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The three groups were comparable in terms of baseline demographic parameters like age, sex, and weight. Basal haemodynamic parameters were comparable. Patients of ASA III and above, allergic to study drugs were excluded from the study. The surgical operations were abdominal and lower limb: i.e., general surgery, Obstetrics and gynaecology and orthopaedics. It was a double blind study, with one anaesthesiologist not involved in the study, preparing the drug and another anaesthesiologist observing the patient in the postoperative ward for analgesia, sedation and other complications. For infra-umbilical operations patients received combined spinal epidural analgesia whereas for supra-umbilical operations patients received general anaesthesia after an epidural catheter was inserted in the thoracic space.

All the cases received a priming dose 16ml of 0.5% bupivacaine for lumbar epidural and 8ml of 0.5% bupivacaine for thoracic epidural. Group A patients received 4ml of 0.25% bupivacaine along with 25mcg of dexmedetomidine and Group B patients received 4ml of 0.25% bupivacaine along with 50mcg dexmedetomidine Group C patients received 4ml of 0.25% bupivacaine along with 75mcg of dexmedetomidine after the patients complained of pain: a VAS score of 5 or more. The parameters studied were heart rate, blood pressure, onset, intensity and duration of analgesia, sedation, nausea, vomiting pruritus and retention of urine. Visual Analogue Scale was followed for relief of pain, and Ramsay Score for sedation.

Criteria	Group A (30 Patients)	Group B (30 Patients)	Group C (30 Patients)
Age (Average)	39	37.5	38.5
Sex M:F	17:13	16:14	15:15
Weight (kgs)	58	61	53

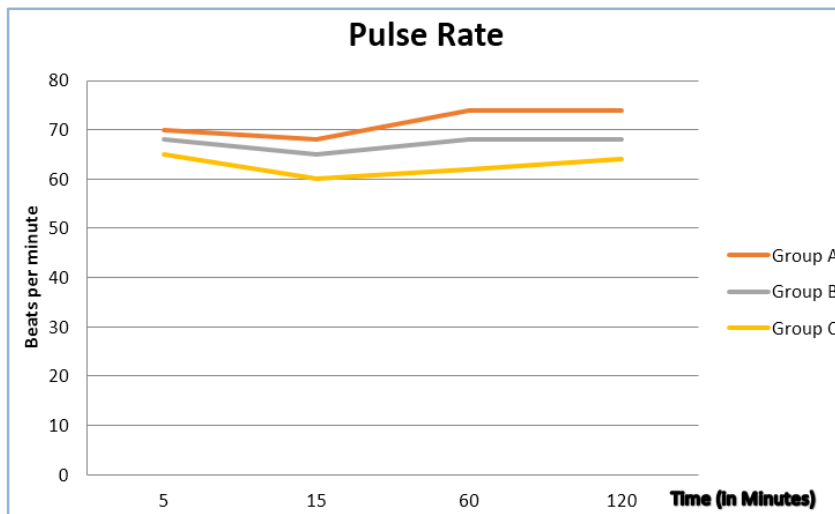
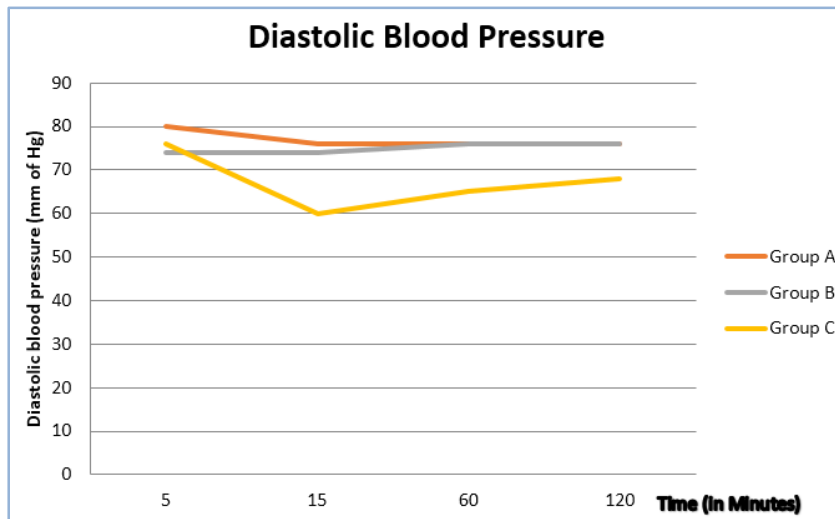
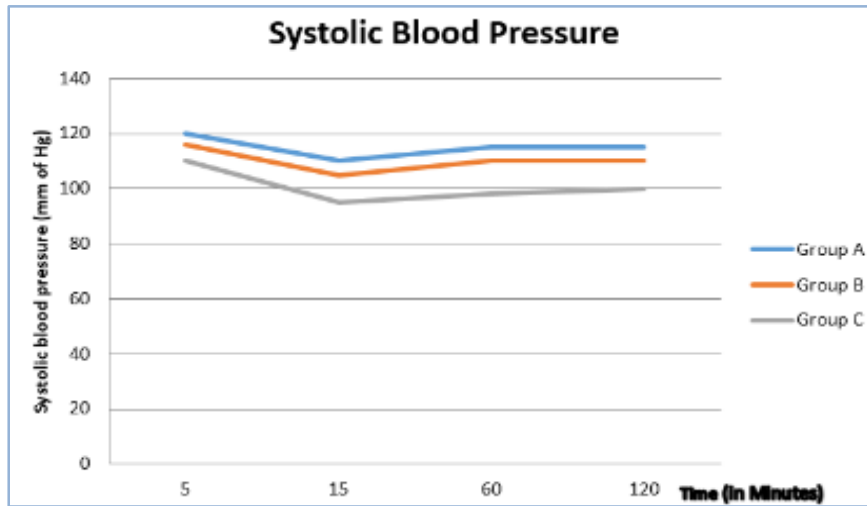
Table 1: Showing age and Sex distribution

Type of Operation	Group A	Group B	Group C
General Surgery	13	14	12
Obst & Gyn	09	10	07
Orthopaedics	08	06	11

Table 2: Showing Distribution of Operations

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Table 3: Showing clinical parameters at 5, 15, 60 and 120 mins.



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	Group A	Group B	Group C
Intensity (VAS)	5-7	4-6	<3
Duration (Mins)	230±8	340±9	425±22

Table 4: Showing Quality and Duration of Analgesia in Different Groups

	Group A	Group B	Group C
Sedation	0-1	1-2	3-4

Table 5: Showing Sedation Scale

Complication	Group A	Group B	Group C
PONV	1	2	5
Pruritus	Nil	Nil	Nil
Retention of urine	-	-	-
Bradycardia	2	5	8
Hypotension	1	3	6

Table 6: Showing Misc. Complications

The retention of urine could not be assessed as most of the patients were catheterised.

DISCUSSION: The dosage of epidural dexmedetomidine is variable. So we studied on the different doses of the drug to know the ideal dose when given in the epidural space along with bupivacaine.

Dexmedetomidine is a clinically used anesthetic and belongs to high selective α_2 -adrenergic receptors (α_2 AR) against. Intravenous Dexmedetomidine exhibits synergism with regional anesthesia and facilitates postoperative pain control.^{[9],[10]} and has been accepted as a clinical anesthetic strategy.

Pre-clinic evidences showed that neuraxial Dexmedetomidine produces antinociception by inhibiting the activation of spinal microglia and astrocyte.^{[11],[12]} decreasing noxious stimuli evoked release of nociceptive substances,^[13] and further interrupting the spinal neuron-glia cross talk and regulating the nociceptive transmission under chronic pain condition.^[14] Thus, Dexmedetomidine might be an interesting adjuvant for neuraxial anesthesia and analgesia to decrease intra- and postoperative anesthetic consumption and prolong the postoperative analgesic duration, but the potentially increased risk of bradycardia, hypotension and neurotoxicity should be taken into consideration in clinical settings. One recent meta-analysis reported the facilitatory effects of perineural Dexmedetomidine on neuraxial and peripheral nerve block.^[15] Another suggested beneficial effects of intravenous and intrathecal Dexmedetomidine in spinal anesthesia.^[16]

Dexmedetomidine is a better neuraxial adjuvant compared with clonidine for providing early onset and prolonged post-operative analgesia and stable cardiorespiratory parameters. A slight decrease in heart rate and mean arterial pressure was observed in both the groups, it never fell down to more than 20% of the baseline values.

Epidural administration of these drugs is associated with sedation, analgesia, anxiolysis, hypnosis and sympatholysis. The faster onset of action, rapid establishment of both sensory and motor blockade, prolonged duration of analgesia in the post-operative period, dose-sparing action of

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local anaesthetics and stable cardiovascular parameters make these agents a very effective adjuvant in regional anaesthesia.^{17,18,19}

Onset of postoperative pain was significantly early in the group A than group B or group C, with the need for supplementary analgesic in group A.²⁰ The cardiovascular stability was better in group A and B than group C. Eight patients had bradycardia and six patients had hypotension in group C which was treated with atropine and phenylephrine respectively. A study ZA Zang et al,²¹ with low dose epidural dexmedetomidine i.e. 0.5mcg/Kg, in thoracic epidural for postoperative analgesia after nephrectomy, showed analgesia lasted for four hours, which is similar to our study.

Post-operative analgesia with 75mcg epidural dexmedetomidine is lacking. Sedation and bradycardia were seen with 75mcg dexmedetomidine given for lower limb surgeries.²²

In a randomized study with human beings using lidocaine and dexmedetomidine alone or in association, it has been observed decreased EEG delta wave, blood pressure and heart rate in the group receiving dexmedetomidine alone. In the group receiving the association of both drugs it has been observed longer anesthetic effect and decreased analgesic doses for postoperative pain relief.²³

CONCLUSION: Since sensitivity to a drug depends on numerous factors, the search for an ideal dose is endless. We found that epidural dexmedetomidine 50mcg does give satisfactory analgesia and sedation with minimal side effects.

REFERENCES:

1. Sharrock NE, Cazan MG, Hargett MJ, Williams-Russo P, Wilson PD, Jr Changes in mortality after total hip and knee arthroplasty over a ten-year period. *Anesth Analg*. 1995; 80:242–248.]
2. Katz J, Jackson M, Kavanagh BP, Sandler AN. Acute pain after thoracic surgery predicts long-term post-thoracotomy pain. *Clin J Pain*. 1996; 12:50–55.
3. Pollock RE, Lotzova E, Stanford SD. Mechanism of surgical stress impairment of human perioperative natural killer cell cytotoxicity. *Arch Surg*. 1991; 126:338–342.
4. Lennard TW, Shenton BK, Borzotta A, Donnelly PK, White M, Gerrie LM, Proud G, Taylor RM. The influence of surgical operations on components of the human immune system. *Br J Surg*. 1985; 72:771–776.
5. Kehlet H. Modification of response to surgery and anesthesia by neural blockade: clinical implications. In: Cousins MT, Bridenbaugh PO, editors. *Neural Blockade in Clinical Anesthesia and Management of Pain*. 3rd ed. Philadelphia: Lippincott; 1998.
6. EkatoDRAMIS G (2001) Regional anesthesia and analgesia: their role in postoperative outcome. *Current topics in medicinal chemistry* 1: 183–192.
Doi: 10.2174/1568026013395236.
7. Tziavrangos E, Schug SA (2006) Regional anaesthesia and perioperative outcome. *Current opinion in anaesthesiology* 19: 521–525. Doi: 10.1097/01.aco.0000245278.22658.1e.
8. Becker DE, Reed KL (2012) Local anesthetics: review of pharmacological considerations. *Anesthesia progress* 59: 90–101; quiz 102–103.
9. Adams R, Brown GT, Davidson M, Fisher E, Mathisen J, et al. (2013) Efficacy of dexmedetomidine compared with midazolam for sedation in adult intensive care patients: a systematic review. *British journal of anaesthesia* 111: 703–710. Doi: 10.1093/bja/aet194.

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10. Abdallah FW, Abrishami A, Brull R (2013) The facilitatory effects of intravenous dexmedetomidine on the duration of spinal anesthesia: a systematic review and meta-analysis. *Anesthesia and analgesia* 117: 271–278. Doi: 10.1213/ane.0b013e318290c566.
11. Li SS, Zhang WS, Ji D, Zhou YL, Li H, et al. (2013) Involvement of spinal microglia and interleukin-18 in the anti-nociceptive effect of dexmedetomidine in rats subjected to CCI. *Neuroscience letters*.
12. Degos V, Charpentier TL, Chhor V, Brissaud O, Lebon S, et al. (2013) Neuroprotective effects of dexmedetomidine against glutamate agonist-induced neuronal cell death are related to increased astrocyte brain-derived neurotrophic factor expression. *Anesthesiology* 118: 1123–1132. Doi: 10.1097/aln.0b013e318286cf36.
13. Liu YL, Zhou LJ, Hu NW, Xu JT, Wu CY, et al. (2007) Tumor necrosis factor- α induces long-term potentiation of C-fiber evoked field potentials in spinal dorsal horn in rats with nerve injury: the role of NF- κ B, JNK and p38 MAPK. *Neuropharmacology* 52: 708–715. Doi: 10.1016/j.neuropharm.2006.09.011.
14. Liu L, Ji F, Liang J, He H, Fu Y, et al. (2012) Inhibition by dexmedetomidine of the activation of spinal dorsal horn glia and the intracellular ERK signaling pathway induced by nerve injury. *Brain Res* 1427: 1–9. Doi: 10.1016/j.brainres.2011.08.019.
15. Abdallah FW, Brull R (2013) Facilitatory effects of perineural dexmedetomidine on neuraxial and peripheral nerve block: a systematic review and meta-analysis. *British journal of anaesthesia* 110: 915–925. Doi: 10.1093/bja/aet066.
16. Niu XY, Ding XB, Guo T, Chen MH, Fu SK, et al. (2013) Effects of intravenous and intrathecal dexmedetomidine in spinal anesthesia: a meta-analysis. *CNS neuroscience & therapeutics* 19: 897–904.
17. Selim MF, Elnabtity AM, Hasan AM. Comparative evaluation of epidural bupivacaine-dexmedetomidine and bupivacaine-fentanyl on Doppler velocimetry of uterine and umbilical arteries during labor. *J Prenat Med*. 2012; 6:47–54.
18. Bajwa SJ, Arora V, Kaur J, Singh A, Parmar SS. Comparative evaluation of dexmedetomidine and fentanyl for epidural analgesia in lower limb orthopedic surgeries. *Saudi J Anaesth*. 2011; 5:365–70.
19. Bajwa SJ, Kaur J, Bajwa SK, Bakshi G, Singh K, Panda A. Caudal ropivacaine-clonidine: A better post-operative analgesic approach. *Indian J Anaesth*. 2010; 54:226–30.
20. Samy Elsayed Hanoura, Rabei Hassanin and Rajvir Singh. Intraoperative conditions and quality of postoperative analgesia after adding dexmedetomidine to epidural bupivacaine and fentanyl in elective cesarean section using combined spinal-epidural anesthesia. *Anesth Essays Res*. 2013 May-Aug; 7(2): 168–172. doi: 10.4103/0259-1162.118947.
21. XZ_Zang_YMXu_XGCui_YPGuo_WZLi_Low_dose_epidural_dexmedetomidine_improves_thoracic_epidural_anaesthesia_for_nephrectomy_Anesthesia_and_Intensive_Care_Vol_42_Issue_2.
22. Manjunath Thimmappa, Ravi Madhusudhana, Somasekharan Potli, Dinesh Kartik – *World Journal of Pharmacy and Pharmaceutical Sciences* Vol 3 Issue 4, 1218-1230
23. Fukushima K, Nishimi Y, Mori K et al - The effect of epidural administered dexmedetomidine on central and peripheral nervous system in man. *Anesth Analg*, 1997; 84:S292.

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