

Effect of Dexmedetomidine as an Adjuvant to Levobupivacaine in Spinal Anaesthesia for Infraumbilical Surgeries

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Abstract

Spinal anaesthesia is the preferred mode of anaesthesia for infraumbilical surgeries. Levobupivacaine is an isomer of racemic bupivacaine. Various adjuvants have been added to the local anaesthetics to prolong its effect. In present study, we have studied different doses of dexmedetomidine used as an adjuvant to levobupivacaine in spinal anaesthesia. *Background:* This study aims to investigate the effect of intrathecal administration of different doses of dexmedetomidine on the onset and duration of sensory and motor block, haemodynamic alterations and adverse effects produced by spinal levobupivacaine. *Methods:* 75ASA I-II patients with age group 18-70 years (weight 50-70 kg) undergoing infraumbilical surgeries were randomized to one of the three groups. Every patient received 3.3 ml of drug intrathecally that consisted of 15 mg (3 ml of 0.5%) preservative free levobupivacaine containing either 0.3 ml normal saline (Group L) as control group, dexmedetomidine 15 µg (Group LD1) or dexmedetomidine 30 µg (Group LD2). Onset and duration of sensory and motor block, maximum sensory level achieved, sedation levels, haemodynamic parameters and adverse effects were recorded. Analysis of data between groups was performed using one way analysis of variance test (ANOVA test), student t-test and chi-square test (whichever was applicable). *Results:* Dexmedetomidine significantly shortens the onset of sensory and motor block and prolonged the time to two segment regression and regression of motor block to modified Bromage 0. In addition group LD2 had higher sedation scores. There was higher incidence of hypotension, bradycardia and respiratory depression in group LD2. *Conclusion:* Intrathecal dexmedetomidine in a dose of 15 µg significantly prolongs the anaesthetic effects of intrathecal levobupivacaine without significant side effects. So, 15 µg is the preferred dose of dexmedetomidine over 30 µg, when used as an adjuvant to levobupivacaine in spinal anaesthesia.

Keywords: Dexmedetomidine; intrathecal; levobupivacaine; α_2 adrenoceptor agonist.

How to cite this article:

Sofia Jaswal, Anil Ohri, Manoj Kumar Panwar et al. Effect of Dexmedetomidine as an Adjuvant to Levobupivacaine in Spinal Anaesthesia for Infraumbilical Surgeries. Indian J Anesth Analg. 2019;6(2):684-688

Introduction

Spinal anaesthesia is the preferred mode of anaesthesia in patients undergoing infraumbilical surgeries [1]. Levobupivacaine is a long acting, amide local anaesthetic that is the S (-) isomer of the racemic bupivacaine [1,2]. Levobupivacaine has

demonstrated less affinity and strength of depressant effects on myocardium and central nervous system vital centers [3-9]. Dexmedetomidine, a highly selective α_2 adrenoceptor agonist, is used in combination with local anaesthetics for sedation and analgesia [10,11,12]. It can offer significant postoperative pain relief with fewer side effects

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Received on 04.02.2019, **Accepted on** 06.03.2019



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[13-25]. It has been reported to improve the quality of intrathecal and epidural anaesthesia. The purpose of present study is to evaluate the effects of intrathecal levobupivacaine 15 mg alone and levobupivacaine mixed with dexmedetomidine 15 µg and 30 µg in patients undergoing infraumbilical surgeries.

Materials and Methods

The study was conducted in ASA I-II patients with age group 18-70 years (weight 50-70 kg) undergoing infraumbilical surgical procedures like vaginal hysterectomy, lower limb or hip surgeries and inguinal hernia repair after obtaining informed consent from the patients and approval from the ethical committee of Indira Gandhi Medical College, Shimla. Uncooperative patients and those with the history of allergy to amide local anaesthetics, bleeding or coagulation abnormalities, peripheral neuropathy, raised intracranial pressure, demyelinating central nervous disorders, local sepsis, spinal deformities, psychiatric diseases and valvular heart diseases are excluded from the study. Patients were randomly divided into three groups each of 25 patients. A detailed history was taken and physical examination was done. All patients were premedicated with tablet alprazolam 0.25 mg per orally a night before surgery. In the operating room monitoring was started with heart rate, non invasive blood pressure, pulse oximeter and electrocardiogram. Intravenous line was secured with 18 gauge cannula and intravenous infusion was started with crystalloid fluids. 26 gauge quincke needle was inserted L3-L4 interspace in sitting position under all aseptic conditions. Patients allocated to group L received 15 mg (3 ml of 0.5%) preservative free levobupivacaine + 0.3 ml normal saline as control group, patients allocated to group LD1 received 15 mg (3 ml of 0.5%) preservative free levobupivacaine + dexmedetomidine 15 µg + 0.15 ml normal saline and the patients allocated to group LD2 received 15 mg (3 ml of 0.5%) preservative free levobupivacaine + dexmedetomidine 30 µg. Drug was given slowly over 1-2 minutes. Level of sensory block was checked bilaterally by pin prick method with 23 gauge hypodermic blunt needle. The onset of sensory block was assessed from the time of injecting drug into subarachnoid space till complete analgesia at the level of T10. The dermatomal level was tested every 2 minutes until the highest level was stabilized for four consecutive tests. Maximum level achieved was noted. After that sensory level assessment was continued every 10 minutes till there was two segment regression of the block. The onset of motor block was assessed every 2 minutes

till complete motor block was achieved as per Modified Bromage Scale (1- total motor block, 2- patient can only move his/her feet, 3- patient can move his/her knees, 4- patient can lift his/ her leg but cannot hold the position, 5- No hip function, patient can lift and hold his/her leg for 10 seconds, 6- No motor block). The degree of sedation was measured with a four point verbal rating scale (1- no sedation, 2- light sedation, 3- somnolence, 4- deep sedation). Intraoperative blood pressure (systolic blood pressure, diastolic blood pressure, mean arterial pressure), heart rate and peripheral oxygen saturation (SpO₂) were measured every 3 minutes for first 30 minutes, then every 5 minutes for next 30 minutes and every 10 minutes for next 1 hour. Vitals of all the patients were monitored for 2 hours after giving spinal anaesthesia. Hypotension (mean blood pressure recording less than 20% of baseline) if any was treated with the help of intravenous fluid bolus and incremental doses of vasopressor agent mephentermine 6 mg i.v. If bradycardia (heart rate less than 50 beats per minute) occurred, it was treated with injection atropine 0.6 mg i.v. Respiratory depression (if RR < 8 breath/min or SpO₂ < 90%) was treated with oxygen supplementation. Nausea, vomiting, shivering or any other side effect was followed up post operatively for 24 hours and treated upon. For post operative pain injection tramadol 100 mg i.m. was given as rescue analgesia and then repeated four hourly if needed (maximum daily dose 400 mg/day). Analysis of the data between groups was performed using one way analysis of variance test (ANOVA test), student t-test and chi-square test (whichever was applicable). p < 0.05 was considered statistically significant.

Results

75 patients were enrolled in this study. The spinal technique was easy in all the patients and the recovery from spinal block was uneventful. The demographic data was comparable in all the three groups (Table 1). The baseline parameters were statistically similar in all the three groups (Table 2). As shown in Table 3, intrathecal dexmedetomidine fastened the time for the onset of sensory block (p = 0.046), time for onset of motor block (p = 0.043), time for two segment regression (p = 0.00) and duration of motor block (p = 0.00). The maximum level of sensory block achieved was significantly higher in groups receiving dexmedetomidine (p = 0.00). In group L maximum level of sensory block reached was T₆ (range T₅-T₉). Most of the patients in group LD1 achieved a

maximum sensory block level of T₅ (range T₄-T₆). In group LD2, most of the patients had a maximum sensory block level of T₄ (range T₃-T₆). The time to achieve maximum sensory level was not different statistically among the three groups (p=0.457). All patients in group L had a sedation score 1. Maximum patients in group LD1 had a sedation score 2 (range 1-3), and in group LD2 had a sedation score of 3 (range 2-4). The difference was highly significant (p-value <0.05). While comparing the changes in mean arterial pressure in all the three groups, there was no statistically significant difference in the readings at all the time intervals (p>0.05). As shown in Table 4, none of the patients

in any of the three groups experienced nausea and shivering. None of the patients in group L and LD1 experienced bradycardia. 24% patients in group LD2 experienced bradycardia (p= 0.001) and were treated with i.v. atropine. 12% patients in group L, 56% patients in group LD1 and 68% patients in group LD2 developed hypotension (p= 0.00) and were treated with i.v. mephentermine. The doses of i.v. atropine and mephentermine required was more in the group LD2 as compared to group LD1 and L. None of the patients in group L, 8% patients in group LD1 and 52% patients in group LD2 developed respiratory depression and was treated with oxygen supplementation. (p= 0.000).

Table 1: Demographic Data

Parameter		Group L	Group LD1	Group LD2	p-value
Age (years)	Mean ± S.D.	36.12 ± 15.40	39.36 ± 15.29	39.04 ± 10.95	0.669
Weight (Kg)	Mean ± S.D.	56.76 ± 5.98	57.76 ± 7.46	58.80 ± 8.03	0.608
Sex	Male	21	18	20	0.573
	Female	4	7	5	

Table 2: Baseline Parameters

Parameter	L	LD1	LD2	p-value
HR (bpm)	84.76 ± 14.27	87.68 ± 11.07	89.40 ± 8.98	0.368
SBP (mmHg)	127.44 ± 13.08	125.28 ± 11.63	132.04 ± 13.75	0.172
DBP (mmHg)	74.28 ± 7.36	75.60 ± 8.71	78.32 ± 8.61	0.218
MAP (mmHg)	93.32 ± 8.15	93.16 ± 7.52	95.72 ± 7.66	0.432
SpO ₂	95.96 ± 1.94	95.96 ± 1.90	95.56 ± 1.91	0.698

Table 3: Anaesthetic characteristics of spinal block

Parameter	L	LD1	LD2	p
Onset of sensory block (in minutes)	3.64 ± 0.91	3.60 ± 0.91	3.00 ± 1.16	0.046*
Time to achieve maximum sensory level (in minutes)	10.92 ± 2.27	11.52 ± 1.93	10.52 ± 3.88	0.457
Maximum level of sensory block achieved	T6 (T5-T8)	T5 (T4-T6)	T4 (T3- T6)	0.000**
Time for two segment regression (in minutes)	146.40 ± 17.82	216.20 ± 18.21	227.08 ± 26.46	0.000**
Onset of motor block (minutes)	4.80 ± 1.41	4.64 ± 1.41	3.76 ± 1.79	0.043*
Duration of motor block (minutes)	222.16 ± 36.37	340.60 ± 58.47	419.44 ± 72.52	0.000**
Sedation scores	1	2 (1-3)	3 (2-4).	0.000**

Table 4: Assessment of side effects

Parameter	Group L		Group LD1		Group LD2		P
	number	% age	number	% age	number	% age	
Nausea	0	0	0	0	0	0	NS
Bradycardia	0	0	0	0	6	24	0.001**
Hypotension	3	12	14	56	17	68	0.000**
Shivering	0	0	0	0	0	0	NS
Respiratory depression	0	0	2	8	13	52	0.000**

Discussion

This study compared different doses of intrathecal dexmedetomidine used as an adjuvant to levobupivacaine in spinal anaesthesia. The anaesthetic and analgesic effects of levobupivacaine were largely similar to those of bupivacaine at the same dose [3,4,5,6]. Intrathecal α_2 -adrenoceptor agonists as adjuvant drugs have been shown to decrease the required doses of local anaesthetics. Dexmedetomidine is highly selective α_2 -adrenoceptor agonist [15,17,18,20]. The $\alpha_2:\alpha_1$ activity of dexmedetomidine is 1620:1, as compared to 220:1 when contrasted against clonidine [10,13]. It potentiates local anaesthetics effects, prolongs postoperative analgesia, and has a dose dependent sedative effect without respiratory depression. Kalso et al. [23] reported that dexmedetomidine is a specific and selective α_2 agonist. It has an increased ratio of α_2 to α_1 activity of 1620:1, as compared to 220:1 when contrasted against clonidine. The largest dose of recorded intrathecal dexmedetomidine used in animal studies was 100 μg [10,13]. It was used in a sheep model, where a 7 day follow up showed no neurological deficits in the studied animals [13]. Intrathecal dexmedetomidine in combination with bupivacaine has been studied in human beings without any postoperative neurological deficit [13,22,25]. Maroof et al. used dexmedetomidine for epidural administration in a dose of 2 $\mu\text{g}/\text{kg}$ [26]. The results of our study showed that dexmedetomidine fastened the onset and prolonged the duration of sensory and motor block in a dose dependent manner. The maximum level of sensory block achieved is significantly higher in the groups using dexmedetomidine in a dose dependent manner but the time to reach the maximum sensory level was not different statistically among the three groups. The results of our study are in accordance with Basuni et al. [27], who in their study concluded that dexmedetomidine (3 μg) as an adjuvant to levobupivacaine (4 mg) fastened the onset of sensory block and prolonged the duration of sensory and motor blocks in spinal anaesthesia as compared to fentanyl (10 μg) in 60 patients undergoing knee arthroscopy. Al-Mustafa et al. [13] concluded in their study that the dexmedetomidine (5 μg and 10 μg) when used as an adjuvant to bupivacaine (12.5 mg) fastened the onset of sensory and motor block and prolonged the duration of sensory and motor block in a dose dependent manner in 66 patients undergoing urological procedures under spinal anaesthesia. The results of our study are also supported by Kanazi et al. [22], who concluded in their study that the supplementation

of bupivacaine spinal block (12 mg) with a low dose of intrathecal dexmedetomidine (3 μg) or clonidine (30 μg) produces a significantly shorter onset of motor block and a significantly longer sensory and motor block than bupivacaine alone without any significant hemodynamic instability or sedation in 60 patients undergoing transurethral resection of prostate or bladder tumor under spinal anaesthesia. Al-Ghanem et al. [25], concluded that 5 μg dexmedetomidine seems to be alternative as adjuvant to spinal 10 mg isobaric bupivacaine in surgical procedures. It prolonged the duration of anaesthesia with minimal side effects and excellent quality of analgesia. Eid et al. [10] concluded that intrathecal dexmedetomidine in the doses of 10 μg and 15 μg significantly prolong the anaesthetic and analgesic effects of spinal hyperbaric bupivacaine (3 ml of 0.5%) in a dose dependent manner. They found a dose dependent increase in dexmedetomidine action resulting in significant reduction of the 24 hour analgesic requirement in patients who were given 15 μg . In our study, the maximum sensory level achieved was more in the group using 30 μg dexmedetomidine (group LD2) with a level of T₃ in 2 patients. Sedation scores were more in the patients receiving 30 μg dexmedetomidine (group LD2) as compared to 15 μg dexmedetomidine (group LD1) when used with 15 mg levobupivacaine intrathecally. Side effects like hypotension, bradycardia, respiratory depression were more in the group using 30 μg dexmedetomidine (group LD2).

Conclusion

Dexmedetomidine shortens the time of onset and prolongs the duration of sensory and motor block. 15 μg dexmedetomidine is an attractive alternative as an adjuvant to spinal levobupivacaine in surgical procedures especially in those that need quite long time with minimal side effects and excellent quality of spinal analgesia.

References

1. Mantouvalou M, Ralli S, Arnaoutoglou H, Tziris G, Papadopoulos G. Spinal anesthesia: Comparison of plain ropivacaine, bupivacaine and levobupivacaine for lower abdominal surgery. *Acta Anaesth. Belg.* 2008;59:65-71.
2. Kokki H, Ylonen P, Heikkinen M, Reinikainen M. Levobupivacaine for pediatric spinal anesthesia. *Anesth Analg.* 2004;98:64-67.
3. Burlacu CL, Buggy DJ. Update on local anesthetics:

- focus on levobupivacaine. *TherClin Risk Manag.* 2008;4(2):381-92.
4. Foster RH, Markham A. Levobupivacaine: A review of its pharmacology and use as a local anaesthetic. *Drugs.* 2000;59(3):551-579.
 5. Leone S, Cianni SD, Casati A, Fanelli G. Pharmacology, toxicology, and clinical use of new long acting local anesthetics, ropivacaine and levobupivacaine. *Acta biomed.* 2008;79:92-105.
 6. Onur O, Sibel AM, Mustafa A, Mehmet Y. Comparison of the effects of intrathecal different dosage of levobupivacaine in elective day-case arthroscopy of the knee. *M.E.J. Anesth.* 2010;20(5):703-708.
 7. Glaser C, Marhofer P, Zimpfer G, Heinz MT, Sitzwohl C, Kapral S, Schindler I. Levobupivacaine versus racemic bupivacaine for spinal anesthesia. *AnesthAnalg.* 2002;94:194-98.
 8. Fattorini F, Ricci Z, Rocco A, Romano R, Pascarella MA, Pinto G. Levobupivacaine versus racemic bupivacaine for spinal anaesthesia in orthopaedic major surgery. *Minerva anesthesiol.* 2006;72:637-44.
 9. Lee Y, Kee WD, Fong SY, Liu JT, Gin T. The median effective dose of bupivacaine, levobupivacaine, and ropivacaine after intrathecal injection in lower limb surgery. *AnesthAnalg.* 2009;109:1331-34.
 10. Eid HE, Shafie MA, Youssef H. Dose-related prolongation of hyperbaric bupivacaine spinal anesthesia by dexmedetomidine. *Ain Shams Journal of Anesthesiology.* 2011;4(2):83-92.
 11. Sudo RT, Maia JA, Sudo GZ. Anesthetic-sparing effect of dexmedetomidine on spinal anesthesia induced by isobaric solution of levobupivacaine. *Anesthesiology.* 2003;99: 936.
 12. MaiaJAC, Sudo GZ, Sudo RT. Dexmedetomidine prolongs spinal anaesthesia induced by levobupivacaine 0.5% in guinea-pigs. *J Pharm Pharmacol.* 2005;57(11):1415-20.
 13. Mustafa M. Effect of dexmedetomidine added to spinal bupivacaine for urological procedures. *Soudi Med J.* 2009;30(3):365-70.
 14. Lawrence CJ, Delange S. Effect of a single pre-operative dexmedetomidine dose on isoflurane requirements and peri-operative haemodynamic stability. *Anaesthesia.* 1997;52:736-44.
 15. Memis D, Turan A, Karamanlioglu B, Pamukcu Z, Kurt I. Adding dexmedetomidine to lidocaine for intravenous regional anesthesia. *Anethanal.* 2004; 98(3):835-40.
 16. Yazbek-Karam VG, Aouad MM. Perioperative use of dexmedetomidine. *Middle East J Anaesthesiol.* 2006; 18(6):1043-58.
 17. Ramsay M, Kuterman D. Dexmedetomidine as a total intravenous anesthetic agent. *Anesthesiology* 2004;101:787-90.
 18. Jordan VS, Pousman RM, Sanford MM, Thorborg PA, Hutchens MP: dexmedetomidine overdose in the perioperative setting. *Ann pharmacother.* 2004;38(5):803-807.
 19. Ingersoll-Weng E, Manecke G, Thistlethwaite P. dexmedetomidine and cardiac arrest. *Anesthesiology.* 2004;100:738-39.
 20. Fukushima K, Nishimi Y, Mori K, Takeda J. Effect of epidurally administered dexmedetomidine on sympathetic activity and postoperative pain in man. *AnesthAnalg.* 1996;82:S121.
 21. Eisenach J, Shafer S, Bucklin B, Carswell J. Pharmacokinetics and pharmacodynamics of intraspinal dexmedetomidine in sheep. *Anesthesiology.* 1994;80:1349-59.
 22. Kanazi GE, Aouad MT, Jabbour-Khoury SI, AL Jazzar, Alameddine MM, Al-Yaman R, Bulbul M, Baraka AS. Effect of Low dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. *Actaanesthesiolscand.* 2006;50: 222-27.
 23. Kalso E, Poyhia R, Rosemberg P. Spinal Antinociceptive by dexmedetomidine, a highly selective α_2 adrenergic agonist. *Pharmacoltoxicol* 1991;68:140-43.
 24. Post C, Gordh T, Minor G, Archer T, Freedman J. Antinociceptive effects and spinal cord tissue concentrations after intrathecal injection of guanfacine or clonidine into rats. *Anesthanalg.* 1987;66:317-24.
 25. Al-Ghanem SM, Massad IM, Al-Mustafa MM, Al-Zaben KR, Qudaisat IY, Qatawneh AM, Abu- Ali HM. Effect of adding dexmedetomidine versus fentanyl to intrathecal bupivacaine on spinal block characteristics in gynecological procedures: A double blind controlled study. *Am j applsci.* 2009; 6:882-87.
 26. Maroof M, Khan SA, Jain D, Khan RM, Maroof SM. Evaluation of effect of dexmedetomidine in reducing shivering following epidural anesthesia. *Anesthesiology.* 2004;101:495-496.
 27. Basuni AS, Ezz HAA. Dexmedetomidine as supplement to low dose levobupivacaine spinal anesthesia for knee arthroscopy. *Egyptian Journal of Anaesthesia.* 2014;30:149-53.