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COMPARATIVE STUDY OF 0.5% LEVOBUPIVACAINE COMBINED WITH DEXMEDETOMIDINE VERSUS 0.5% BUPIVACAINE COMBINED WITH DEXMEDETOMIDINE INTRATHECALLY FOR ELECTIVE ORTHOPAEDIC SURGERIES

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ABSTRACT

Introduction:

Various adjuvants have been used with local anaesthetics in spinal anaesthesia to avoid intraoperative visceral and somatic pain and to provide prolonged postoperative analgesia. Dexmedetomidine, a new highly selective α2 agonist, is now being used as a neuraxial adjuvant. The aim of this study was to compare the onset and duration of sensory and motor block, haemodynamic effects, postoperative analgesia, and adverse effects of bupivacaine and levobupivacaine, in combination with dexmedetomidine, given intrathecally.

Patients and Methods:

70 patients of ASA physical status 1 & 2, scheduled for elective orthopaedic surgeries of lower limb were studied. Patients in group A (n=35) received 15 mg bupivacaine (volume 3 ml) plus 4 μg dexmedetomidine (volume 0.04 ml) i.e., a total volume of 3.04 ml intrathecally

and patients in group B (n=35) received 15 mg levobupivacaine (volume 3 ml) plus 4 μg dexmedetomidine (volume 0.04 ml) i.e., a total volume of 3.04 ml intrathecally.

Results:

Patients in levobupivacaine group (B) had a significantly longer onset (gr A→ 4.4±1.6 mins; gr B → 9.0±3.2 mins) and longer time to reach maximum motor block (gr A → 7.4±2.8 mins; gr B → 18.1±4.7 mins). Mean time of postoperative analgesia was also significantly longer in group B (gr A → 425.3±12.36 min; gr B → 444.1±12.27 mins) ,though duration of motor block was less (gr A → 406.4 ±12.98mins; gr B → 390.1±9.2 mins). Levobupivacaine was found to be haemodynamically sound during intraoperative period with less incidence of hypotension and more stable heart rate.

***Conclusion**:*

Intrathecal administration of either 15 mg bupivacaine or 15 mg levobupivacaine in combination with 4 μg dexmedetomidine was well tolerated and provided a rapid onset and prolonged duration of sensory and motor block with good operative condition in cases of elective orthopaedic operation of lower limbs, with the benifit of levobupivacaine and dexmedetomidine combination producing a significantly longer duration of postoperative analgesia, shorter duration of motor blockade and better intra operative haemodynamics.

Keywords:

Bupivacaine, Levobupivacaine, Dexmedetomidine, Intrathecally.

INTRODUCTION:

Regional anaesthesia due to its inherent benefits, has become common nowadays. In recent years levobupivacaine, the pure S(−) enantiomer of bupivacaine, has emerged as a safer alternative than its racaemic parent and is equally effective in spinal anaesthesia.[1,2,3,4]

A number of adjuvants, such as opioids, α2 agonists and others have been studied to prolong the effect of spinal anaesthesia.[5,6] The addition of fentanyl to hyperbaric bupivacaine improves the quality of intraoperative and early postoperative subarachnoid block, having disadvantages, such as pruritus and respiratory depression.[7] Intrathecal α2 agonists prolong the duration of action and reduce the required dose of local anaesthetic. The intrathecal use of

clonidine, a partial α2 adrenoceptor agonist, has been shown as an effective and safe procedure.[8,9]

Dexmedetomidine, a new highly selective α2 agonist, is under evaluation as a neuraxial adjuvant as it provides stable haemodynamic conditions, good quality of intraoperative and prolonged postoperative analgesia with minimal side effects.[8,10,11] Dexmedetomidine is an α2 receptor agonist and its α2/α1 selectivity is 8 times higher than that of clonidine.[12]

MATERIALS AND METHODS:

After obtaining approval from institutional ethical committee, this randomized, prospective, double blind, parallel group study was conducted in Department of Anaesthesiology at IPGMER, Kolkata in 70 patients of either sex, aged between 18 to 60 years, ASA physical status I & II, undergoing elective orthopaedic surgeries of lower limbs.

Patient's refusal to subarachnoid block, any contraindication to subarachnoid block including infection at the site of injection, autonomic dysfunction, coagulopathy, neurological disorders, stenotic heart diseases, spinal deformity, haemodynamically compromised patients, patients receiving β-blockers, chronic analgesic therapy or antiplatelet drugs or anticoagulants, and those having known allergy to study drugs were excluded from the study.

For sample size calculation, time to first administration of rescue analgesic was considered as the primary outcome measure. It was calculated that 35 subjects would be required per group in order to detect a difference of 8min in the parameter with 80% power and 5% probability of type I error. This calculation assumes a standard deviation of 12 minute in this parameter.

After getting written informed consent, patients were allocated randomly to either group A or group B. Complete pre anaesthetic evaluation was performed in each patient including detailed history taking, thorough physical check-up, assessment of spine, airway examination and assessment of routine investigations, like complete haemogram, fasting blood sugar (FBS) and post prandial blood sugar(PPBS), serum urea, creatinine, ECG 12 leads & chest x-ray-PA View.

Patients were explained in details about the surgical procedure, anaesthesia technique and post operative monitoring. VAS scale was also explained to the patients.

Patients received ranitidine 150 mg orally, the night before operation and were kept at least 6 hours fasting before surgery.

Anaesthesia machine, airway equipment, drugs for resuscitation and general anaesthesia were kept ready in hand before starting the procedure. Monitoring included - continuous ECG,

pulse rate, oxyhaemoglobin saturation (SpO2), non-invasive blood pressure and respiratory rate.

After receiving the patients in the operation theatre, an intravenous line was established with an 18G intravenous cannula in a large vein and intravenous fluid was started with ringer's lactate solution 10-15ml /kg body weight, infused over 15 minutes.

Patients in group A received 15 mg bupivacaine (volume 3 ml) plus 4 μg dexmedetomidine (volume 0.04 ml) i.e., a total volume of 3.04 ml intrathecally and patients in group B received 15 mg levobupivacaine (volume 3 ml) plus 4 μg dexmedetomidine (volume 0.04 ml) i.e., a total volume of 3.04 ml intrathecally.

Randomly allocated coded syringes of drugs were prepared by an anaesthesiologist who did not perform subarachnoid block or record the outcome. Under strict aseptic precautions, with the patient in sitting posture, a 26G Quincke spinal needle was introduced into L3-L4 or L4-L5 interspace by midline approach and after confirming free flow of CSF, drug was administered at the rate of approximately 0.2 ml/sec without barbotage. Patient was placed supine soon after administration of intrathecal drug.

Time of onset of sensory block (detected by onset of tingling sensation) was noted. Upper level of sensory block was tested with a 22G blunt intramuscular needle at 5 minutes interval for the first 30 minutes, thereafter at every 10 minutes interval. Surgeons were allowed to proceed only when sensory block reached at least level of T10 or above. Thereafter sensory block was assessed at 10 minutes interval intraoperatively. Postoperatively sensory block was assessed at 30 minutes interval till 90 minutes and 15 minutes interval thereafter until requirement of rescue analgesic. Patients in whom dural puncture and adequate free flow of CSF could not be established or who did not show sensory blockade adequate for surgery was administered general anaesthesia and was dropped from the study.

Motor block was assesssed using Modified Bromage Scale (0= No motor paralysis, able to flex knee & ankle. 1= Unable to raise extended leg but able to flex knee. 2= Unable to flex knee but able to flex ankle. 3= Unable to move lower limb).[13] Time frame for assessment of motor block was same as for sensory block both intraoperative and postoperative period.

Haemodynamic parameters were monitored every 5 minutes for first 30 minutes and then at 10 minutes interval till the end of surgery and hourly thereafter till rescue analgesic was required. Bradycardia was managed by Inj. Atropine 0.5mg IV bolus. Hypotension was managed by Inj. Mephentermine 3-6mg IV bolus (titrated to patient response) along with fluids (both crystalloids and colloids).

Side effects like nausea, vomiting, hypotension, pruritus, retention of urine and respiratory depression were monitored.

Analgesia was assessed by visual analogue scale (VAS) score which is a linear pain scoring tool (0 -- no pain and 100 -- worst possible pain). Rescue analgesic was administered when VAS score > 40 or when patient requested for analgesia.

Considering the time of intrathecal injection as time zero, time to onset of sensory block, time taken to reach maximum sensory block, time to request for first rescue analgesic, time to onset of motor block, time to reach Bromage 3 and time of complete disappearance of motor block were recorded.

STATISTICAL ANALYSIS:

Statistical assessment of data were carried out using statistical software Statistica version 6 [Tulsa, Oklahoma: StatSoft Inc., 2001] GraphPad Prism version 5 [San Diego, California: GraphPad Software Inc., 2007].

For variables with normal distribution of inter group comparisons, Student's Unpaired t-Test and for variables, not showing normal distribution, Mann-Whitney U test were used. Within group comparisons in repeated measurements was performed with Variance Analysis. Comparisons between two categorical variables were performed with Fisher's exact test and Chi square test. p value < 0.05 was considered to be statistically significant.

RESULTS:

After approval from institution ethical committee this prospective randomized study was conducted. All the patients were monitored postoperatively and were discharged from the post-anaesthesia care unit (PACU) when the patients were fully conscious and haemodynamically stable. The patients remained haemodynamically and neurologically stable for the remainder of their hospital stay and were discharged thereafter. Demographic profile shows no significant statistical difference with respect to age, BMI, ASA physical status and duration of surgery (Table 1).

Table 1: Demographic data & Duration of Surgery

	A	**B**	**p value**
Age	40.09± 10.99	42.94±9.27	0.244
BMI	21.96±1.74	21.67±1.56	0.456
Sex(M/F)	18/17	18/17	1.000
ASA(1/2)	25/10	23/12	0.797
Duration of surgery	100±12.13	100±13.51	0.788

Table 2 :Time of onset of sensory and motor block, time to reach peak sensory and motor block

	A	B	**p value**
Onset of sensory block	1.7±0.7	1.6±0.6	0.698
Time to reach peak sensory block height	12.9±3.04	13.9±3.45	0.203
Onset of motor block	4.4±1.6	9.0±3.2	**0.000**
Tme to reach max motor block	7.4±2.8	18.1±4.7	**0.000**

Onset of sensory block, and time to reach peak sensory block height was not significant between groups. However onset of motor block with time to reach maximum motor block was significantly more in levobupivacaine group.

Figure 1: Intraoperative Heart Rate

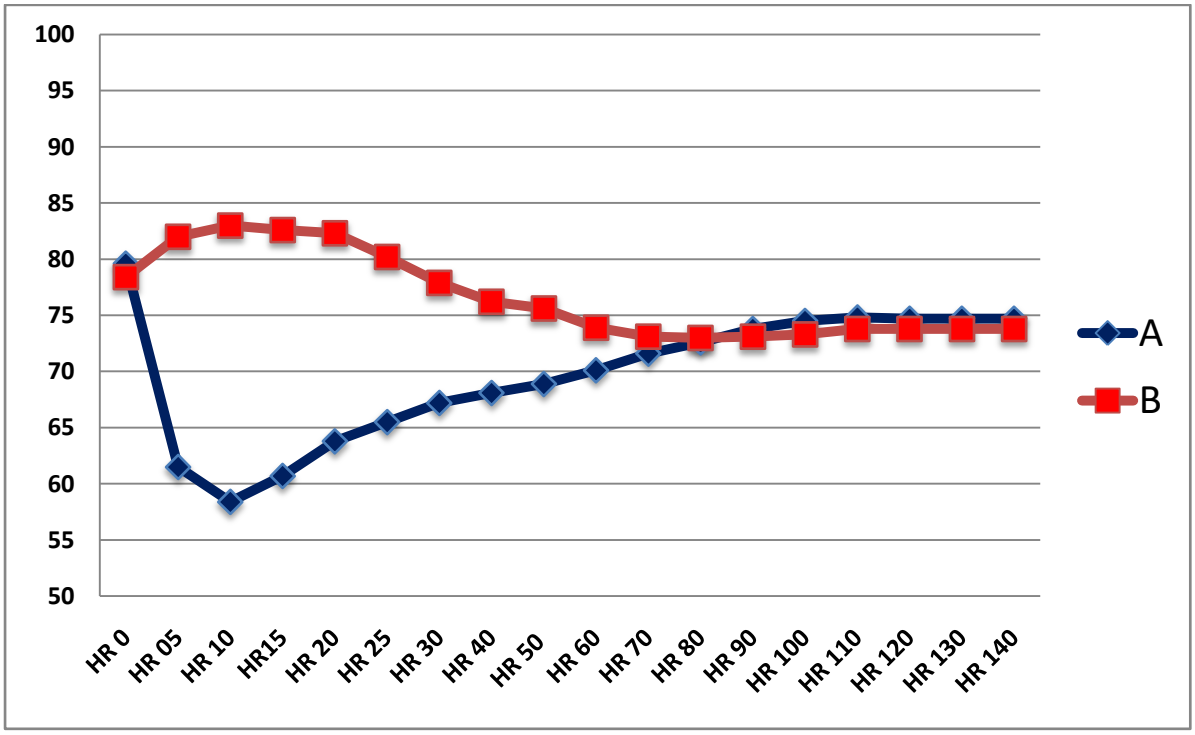


Figure 2: Intraoperative SBP

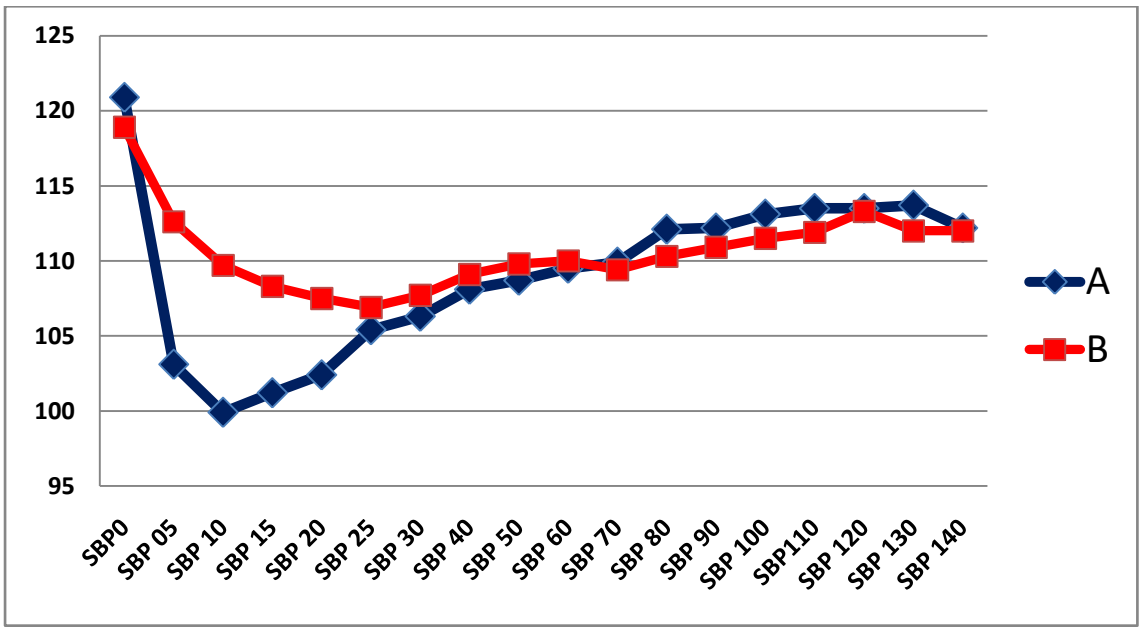


Figure 3: Intraoperative DBP

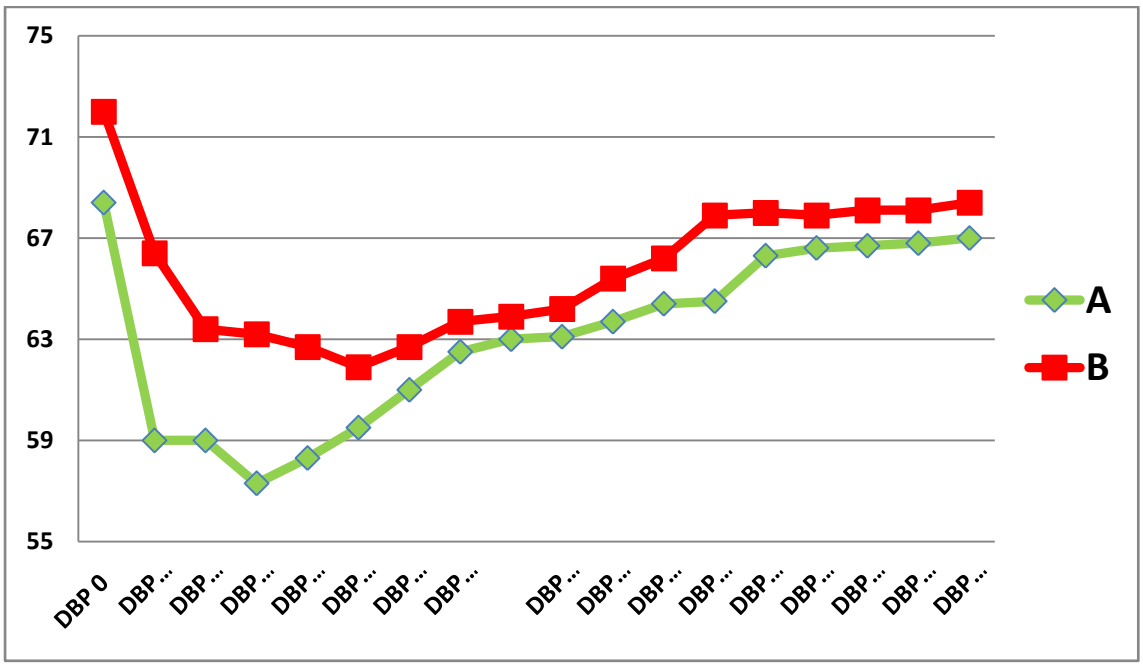
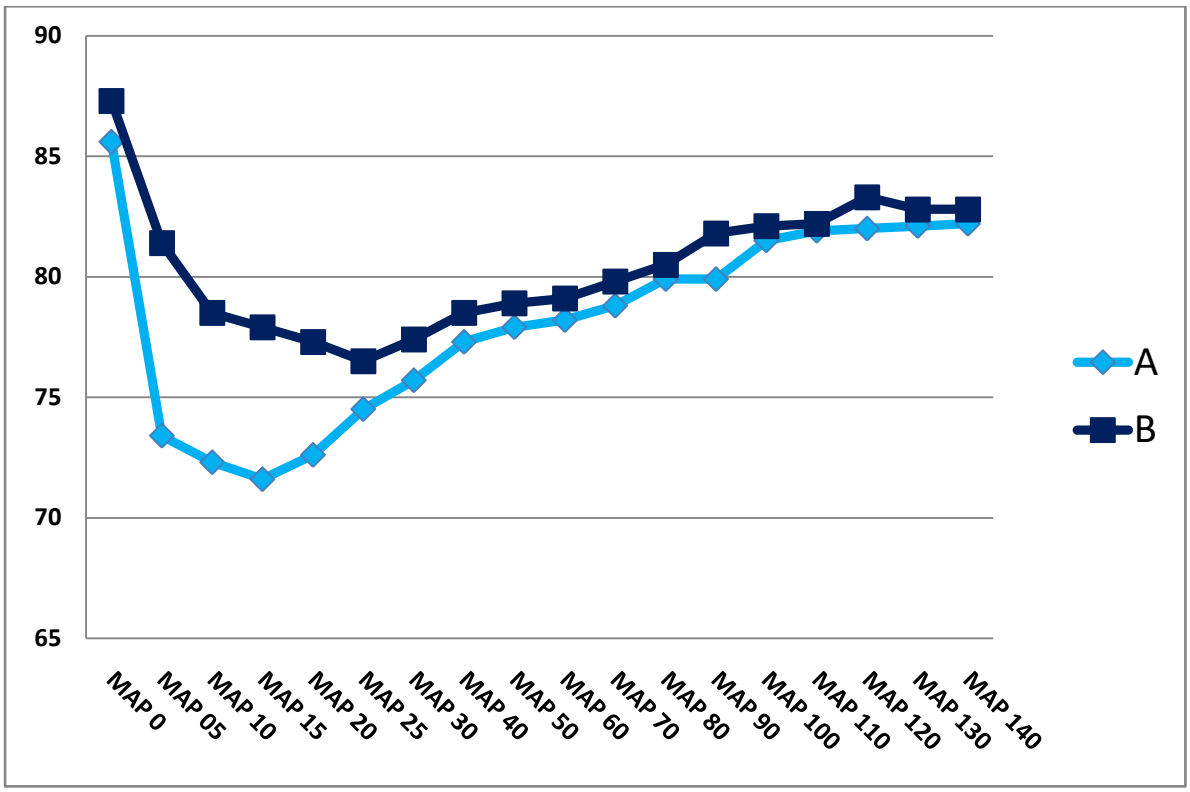


Figure 4: Intraoperative MAP (mm Hg)



Levobupivacaine group was found to be haemodynamically sound during intra operative period with less incidence of hypotension and more stable heart rate.

Table 3: Duration of analgesia and motor block

	A	B	**p value**
Duration of analgesia(mins)	425.3±12.36	444.1±12.27	**0.00**
Duration of motor block(mins)	406.4±12.98	390.1±9.2	**0.00**

Median duration of effective analgesia was significantly longer in group B patients (445 minutes) than group A patients (420 minutes). However, group A had a significantly longer duration of motor blockade (405 minutes) compared to group B (390 minutes), as seen by time to reach Modified Bromage score of 0.

Figure 6: Duration of analgesia

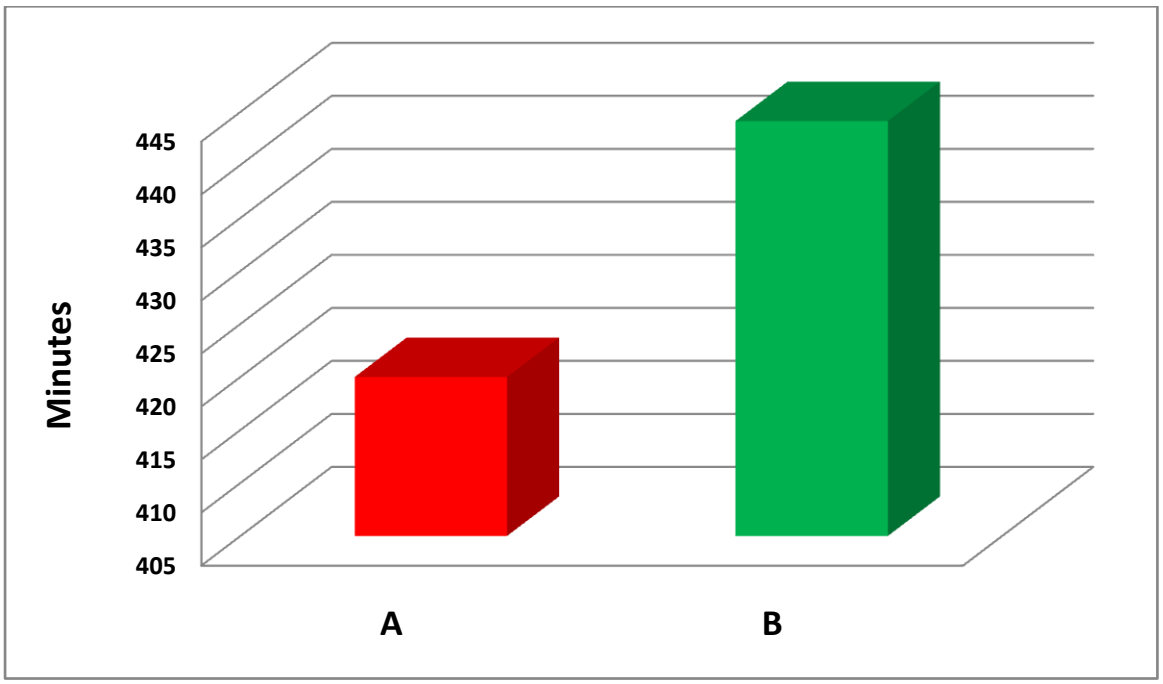
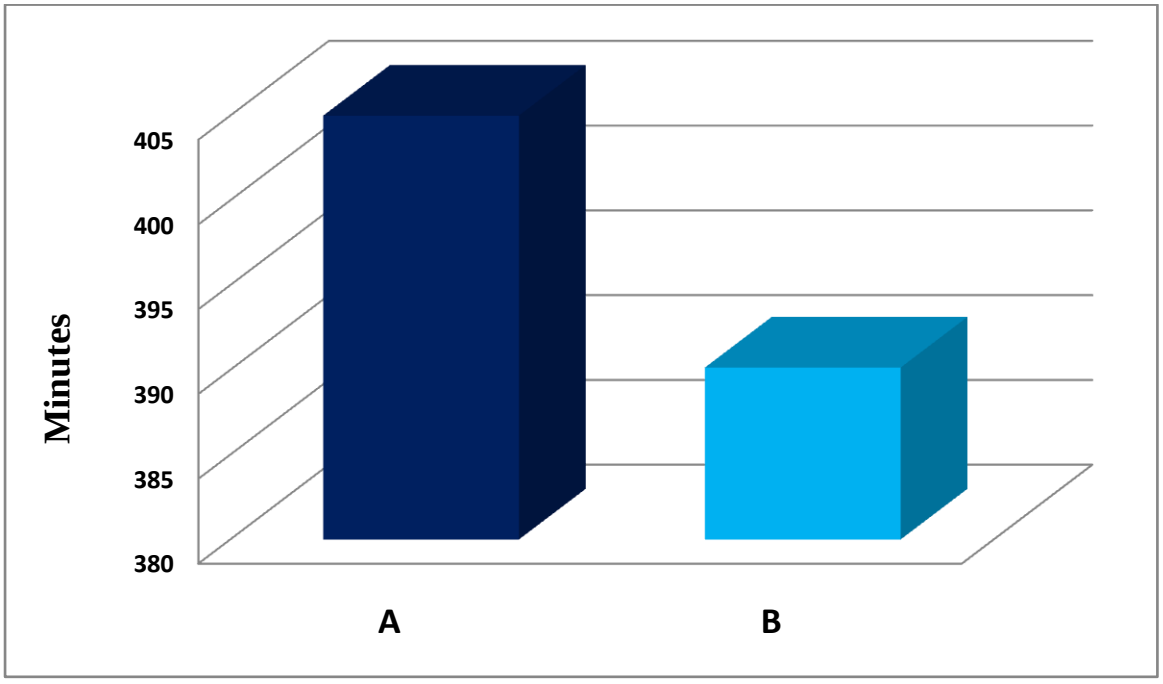


Figure 7: Duration of motor blockade



There was no significant difference in the incidence of postoperative nausea vomiting between groups. None of the patients of either group experienced any kind of sedation, pruritus or respiratory depression in postoperative period.

DISCUSSION:

Aim of this study was to compare analgesic efficacy and duration of motor blockade of bupivacaine dexmedetomidine combination and levobupivacaine dexmedetomidine combination in subarachnoid route in patients undergoing elective orthopaedic surgery of lower limb.

Using levobupivacaine and bupivacaine Gulec et al[14] and Sahin et al[15] did not find any significant statistical difference in the time of onset of sensory block. However time taken was longer compared to our study as they did not use any adjuvant. In a meta-analysis on dexmedetomedine, F W Abdallah et al[16] had shown dexmedetomidine to acceleralate the onset when combined with local anaesthetic agents. This finding is corroborated by Guler et al[3] who also found no significant statistical difference in onset of sensory block with levobupivacaine fentanyl and bupivacaine fentanyl combinations.

Mantouvalou et al[17], Vanna et al[8], did not find any statistically significant difference in peak sensory block height. However, Guler et al[3] and Erdil et al[4] found lower peak sensory block height with levobupivacaine (combined with fentanyl), whereas Sahin et al[15] found higher peak block height with levobupivacaine.

There wasn't any statistically significant difference between two groups regarding time to reach peak sensory block height. This is corroborated by the similar findings of Mantouvalou et al[17] and Gulec et al[14]. However, Guler et al[3] reported less time taken by levobupivacaine to reach peak sensory block height using fentanyl in combination.

Guler et al[3], Mantouvalou et al[17] and Gulec et al[14] reported significant statistical difference, with levobupivacaine taking a longer time for onset of motor blockade. However using these drugs alone shows a much greater time required than our study results. This result was corroborated by G E Kanazi et al[18] who showed a significant shorter onset of motor block when combined with dexmedetomidine.

There was significant statistical difference between two groups for time to reach maximum motor blockade. This is similar to the findings of Guler et al[3], Erdil et al[4], Gulec et al[14], and Turkmen et al[9], who all reported a statistically significant increase in time required by levobupivacaine for maximum motor block either used single or in combination.

In this study, duration of analgesia was significantly higher with levobupuvacaine than bupivcaine. Turkmen et al[9] demonstrated that mean duration of analgesia with levobupivacaine fentanyl combination was significantly higher than bupivacaine fentanyl combination. In our study, the duration of analgesia was higher since we used 15mg drug with dexmedetomidine compared to 7.5 mg drug used in their study. This is corroborated by

HA Nyagam et al[21], R Gupta et al[22] and SMA Ghanam et al[10], where dexmedetimidine was found to have increased period of analgesia, compared to fentanyl when used in combination. Also A Esmaoglu et al[20], Ayektas et al[23], Kanazi et al[18], SS Nehtra et al[24] and FW Abdullah et al[15] showed dexmedetomidine when combined to either bupivacaine or levobupivacaine, increased their duration of analgesia.

In our study, duration of motor blockade was significantly higher in bupivacaine than levobupivacaine. Guler et al[3] similarly found that motor blockade of levobupivacaine was significantly shorter than bupivacaine. They had used 10mg of drug with fentanyl, so the duration is less compared to our study. This is corroborated by HA Nyagam et al[21], R Gupta et al[22] and SMA Ghanam et al[10] where dexmedetomidine was found to have increased period of motor block ,compared to fentanyl when used in combination. Sahin et al[15] also found significantly less duration of motor block with levobupivacaine. However, Erdil et al[4], Mantouvalou et al[17], Turkmen et al[9] and Vanna et al[8] did not report any significant difference in duration of motor blockade.

Marked fall in heart rate was found in bupivacaine group in the initial 60 mins. The findings of our study relate well with those of Guler et al[3]. But Erdil et al[4], Misirlioglu et al[19] and Gulec et al[14] did not find any significant heart rate variations. Besides A Esmaoglu et al[20], Kanazi et al[18] concluded that dexmedetomidine didn't change heart rate when combined with either bupivacaine or levobupivacaine.

MAP fell marginally from baseline following intrathecal injection in both the groups, but a statistically significant change in MAP was found with group A patients having lower MAP than group B in initial period, which might point to better haemodynamic profile of levobupivacaine . In other time periods difference was not significant. Mantouvalou et al[17] and Gulec et al[14] demonstrated similar findings on MAP in their respective studies. Erdil et al[4] also found that with bupivacaine + fentanyl, MAP values were significantly lower than with levobupivacaine + fentanyl, from 10 mins to 30 mins after intrathecal injection.

Higher incidence of hypotension was found in group A compared to group B. In literature, Guler et al[3], Erdil et al[4], Mantouvalou et al[17] and Vanna et al[8] have all reported significantly higher incidence of hypotension when using bupivacaine in spinal anaesthesia, compared to levobupivacaine.

CONCLUSION:

From the above observations and analyses, we can conclude that intrathecal administration of either 15 mg bupivacaine or 15 mg levobupivacaine in combination with 4 μg dexmedetomidine is well tolerated and provide a rapid onset and prolonged duration of sensory and motor block with good operative condition in cases of elective orthopaedic surgeries of lower limbs, with the benefit of levobupivacaine and dexmedetomidine combination producing a significantly longer duration of postoperative analgesia, with a shorter duration of motor blockade and better intraoperative haemodynamics.

REFERENCES :

1. Burlacu CL, Buggy DJ. Update on local anaesthetics: focus on levobupivacaine. Ther Clin Risk Manag. 2008;4(2):381–92.

2. Glaser C, Marhofer P, Zimpfer G, Heinz MT, Sitzwohl C, Kapral S. levobupivacaine Versus Racaemic bupivacaine for Spinal Anaesthesia. Anesth Analg 2002;94(1):194-8.

3. Guler G, Cakir G ,Ulgey A, Ugur F, Cihangir B, Isin G. A Comparison of Spinal Anaesthesia with levobupivacaine and Hyperbaric bupivacaine for Cesarean Sections: A Randomized Trial. Open Journal of Anesthesiology 2012;2:84-9.

4. Erdil F, Bulut S, Demirbilek S, Gedik E, Gulhas N, Ersoy MO. The effects of intrathecal levobupivacaine and bupivacaine in the elderly. Anaesthesia. 2009;64(9):942-6.

5. Elia N, Culebras X, Mazza C, Schiffer E, Tramèr MR. Clonidine as an adjuvant to intrathecal local anaesthetics for surgery: Systematic review of randomized trials. Reg Anesth Pain Med 2008;33:159-67.

6. Boussofara M, Carlès M, Raucoules-Aimé M, Sellam MR, Horn JL. Effects of intrathecal midazolam on postoperative analgesia when added to a bupivacaine-clonidine mixture. Reg Anesth Pain Med 2006;31:501-5.

7. Hunt CO, Naulty JS, Bader AM, Hauch MA, Vartikar JV, Datta S. Perioperative analgesia with subarachnoid fentanyl–bupivacaine for Cesarean delivery. Anesthesiology 1989;71:535-40.

8. Vanna O, Chumsang L, Thongmee S. Levobupivacaine and bupivacaine in spinal anaesthesia for transurethral endoscopic surgery. J Med Assoc Thai. 2006;89(8):1133-9.

9. Turkmen A, Moralar DG, Ali A, Altan A. Comparison of the Anaesthetic Effects of Intrathecal levobupivacaine plus fentanyl and bupivacaine plus fentanyl during Caesarean Section. Middle East J Anesthesiol. 2012;21(4):577- 82.

10. 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 Appl Sci 2009;6:882-7.

11. Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, Murshidi MM, Ammari BA, Awwad ZM. Effect of dexmedetomidine added to spinal bupivacaine for urological procedure. Saudi Med J 2009;30:365-70.

12. Bridenbaugh PO, Wedel DJ. The Lower Extremity: Somatic Blockade. In: Cousins MJ, Bridenbaugh PO, editors. Neural Blockade in Clinical Anaesthesia and Management of Pain. Philadelphia: Lippincott-Raven;1998:373–94.

13. Kalso E, Poyhia R, Rosenberg P. Spinal antinociception by dexmedetomidine, a highly selective alpha 2- adrenergic agonist. Pharmacol Toxicol 1991;68:140-3.

14. Gulec D, Karsli B, Ertugrul F, Bigat Z, Kayacan N. Intrathecal bupivacaine or levobupivacaine: which should be used for elderly patients?. J Int Med Res 2014;42(2):376-85.

15. Sahin AS , Türker G, Bekar A, Bilgin H, Korfal G. A comparison of spinal anesthesia characteristics following intrathecal bupivacaine or levobupivacaine in lumbar disc surgery. Eur Spine J. 2014 Mar;23(3):695-700.

16. Abdallah F W and Brull R. Facilitatory effects of perineural dexmedetomidine on neuraxial and peripheral nerve block: a systematic review and meta-analysis. British Journal of Anaesthesia 2013:1-11.

17. Mantouvalou M, Ralli S, Arnaoutoglou H, Tziris G, Papadopoulos G. Spinal anesthesia: comparison of plain ropivacaine, bupivacaine and levobupivacaine for lower abdominal surgery. Acta Anaesthesiol Belg. 2008;59(2):65-71.

18. Kanazi G E, Aouad M T, Jabbour-Khoury S I, Al Jazzar M D, Alameddine M M, Al-Yaman R, Bulbul M, Baraka A S. Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anaesthesiol Scand 2006; 50: 222—227.

19. Misirlioglu K, Sivrikaya G, Hanci A, Yalcinkaya A. Intrathecal low-dose levobupivacaine and bupivacaine combined with fentanyl in a randomised controlled study for caesarean section: blockade characteristics, maternal and neonatal effects. Hippokratia. 2013;17(3):262-7.

20. Esmaoğlu1 A, Turk S, Bayram A, Akın A, Uğur F, Ulgey A. The Effects of Dexmedetomidine Added to Spinal Levobupivacaine for Transurethral Endoscopic Surgery. Balkan Med J 2013; 30: 186-90.

21. Nayagam H A, Singh N R, Singh H S. A prospective randomised double blind study of intrathecal fentanyl and dexmedetomidine added to low dose bupivacaine for spinal anesthesia for lower abdominal surgeries. Indian J Anaesth 2014; 58(4): 430–5.

22. Gupta R, Verma R, Bogra J, Monica Kohli, Raman R, Kushwaha JK. A Comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to Bupivacaine. Journal of Anaesthesiology Clinical Pharmacology 2011;27(3):339-43.

23. Yektas A, Belli E. The effects of 2 μg and 4 μg doses of dexmedetomidine in combination with intrathecal hyperbaric bupivacaine on spinal anesthesia and its postoperative analgesic characteristics. Pain Res Manag 2014;19(2):75-81.

24. Nethra SS, Sathesha M, Dixit A, Dongare P A, Harsoor SS, Devikarani D. Intrathecal dexmedetomidine as adjuvant for spinal anaesthesia for perianal ambulatory surgeries: A randomised double-blind controlled study. Indian J Anaesth. 2015 Mar; 59(3): 177–81.