Original Article

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Comparison of Intrathecal Adjuvants with Levobupivacaine in Lower Limb Surgeries

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Abstract

Background and Aim: Studies and research are ongoing to find appropriate adjuvants tointrathecal local anaesthetic agents to make them more effective and economical. In view of the same we undertook a study with Levobupivacaine,being a newer agent with more cardiac stability and compared the outcomes with 3 adjuvants.

Settings and Design: After approval from the hospital ethical committee, a randomized double blind study was conducted among 90 healthy, American Society of Anesthesiologists ASA I and II patients, scheduled forlower limb surgeries.The study wasdone over a period of one year.

Materials and Methods: Spinal block was administered in L3 and L4 intervertebral space, using 0.5% Levobupivacaine 12mg. Adjuvants added in group 1- Fentanyl 25 mcg, in group 2- Dexmedetomidine 10mcg and in group 3 - Clonidine 30mcg. Anaesthetic level achieved was T10. Onset time to achieve sensory, motor blockade, and their regression time was noted. Hemodynamic changes and requirement for other analgesic drugs was also noted.

Results: 90 patients were enrolled in our study. The data was recorded and analysed using statistical analysis.

Conclusion: To conclude, Levobupivacaine with Dexmedetomidine, gavebetter result for intra and postoperativeregionalanaesthesia without any adverse effects.

Keywords: Adjuvants; Intrathecal; Levobupivacaine; Dexmedetomidine; Fentanyl; Clonidine.

Introduction

Spinal anaesthesia is an accepted technique for lower limb surgeries. Anaesthesiologists are searching for such compounds for intrathecal use which can provide good relaxation, less hemodynamic disturbances and prolonged analgesia. Levobupivacaine (an Sisomer of Bupivacaine) is the most recent such addition [1]. It has less adverse CVS and CNS side effects. Studies on using adjuvants with Levobupivacaine are relatively few.Adding adjunct allows reduction in dose of Levobupivacaine and provides CVS stability.

Fentanyl and Clonidine are being used in spinal anaesthesia to improve the quality of anaesthesia blockade and for prolongation of post operative analgesia [2].

A newer alpha 2 agonist, Dexmetodomidine, is on theway to be added in the list of adjuvants. In our study, we compared the effects of various adjuvants added to Levobupivacaine.

Material and Methods

After approval from hospital's ethical committee, we selected 90 patients in our institute, aged 18 years – 55 years. Patients with American Society of Anaesthesiologists (ASA) physical status I and II, posted for lower limb surgeries,closed procedures (e.g. Tibia and Femur interlocking,arthroscopies) during the period between Oct 2013 to Feb 2014, were selected through closed envelope technique. Design of the study was a prospective randomized double blind study. We excluded, patients with American Society of Anaesthesiologists (ASA) physical status III / IV/V; patients with BMI > 30 and <20; patients on any alpha adrenergic blocker drugs e.g. Prazosin, and H/O drug allergy to the drugs, used in the

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study. Completegeneral physical examination and laboratory examination (completeblood count, fasting blood sugar, S.Urea, S.Creatinine, S.electrolytes, PT/ PTT,ECG and CXR)weredone to rule out any abnormality. The patients were admitted, one day prior tosurgery. They werecounseled about the regional anesthesia and informed consent was taken.

Tab Alprazolam 0.25 mg was prescribed night before and at 6 AM, on the day of surgery,with sips of water, to allay anxiety.For aspiration prophylaxis, Inj. Ondansetron 4mg IV was givenhalf an hour before the surgery.

In operation room, standard monitors,i.e., ECG, SPO_2, NIBP, HRf were attached to the patients. All patients were preloaded with RL 500 ml. After ensuring all aseptic precautions, and local skin infiltration of 2 ml of 2% Lignocaine, lumbar puncture was done with 27G Quincke spinal needle at L3-L4 space. A third observer injected the drug after ensuring free flow of clear CSF. Oxygen through facemask was given to each patient.After following

Bromage Zero	the patient has free movement of legs and feet
Bromage 1	the patient is just able to flex knee with free movement of feet.
Bromage 2	the patient is unable to flex knee, but free movement of feet.
Bromage 3	the patient is unable to move the leg and feet

exclusion criteria, 90 patients were randomized into 3 groups by a computer generated list.

Ingroup 1-Levobupivacaine 0.5% 12 mg + 25 mcg Fentanyl, ingroup 2-Levobupivacaine 0.5%12mg + 10mcg Dexmedetomidine andin group 3-Levobupivacaine 0.5% 12mg +Clonidine 30mcg were administered.In group2- 0.4 mland in group 3-0.3mlpreservative freenormal saline was added to make volume in all groups the same.The drug was prepared by the third observer,who was unaware about the study.

After the block, the time of sensory block up toT10 and grade 3Bromage motor block was assessed before the start of surgery[3]. Time was set at zero when the subarachnoid block was administered.

Hypotension[SBP fall> 30% from baseline or < 90mm Hg] and bradycardia [HR<50 bpm] were noted. The other adverse effects viz. nausea, vomiting, shivering, pruritus, sedation and respiratory depression were noted.

Time of recovery of S_1dermatome and complete recovery from motor block, i.e. Bromage 0 was also noted.Vital parameters were also noted.

Results

SPSS statistical software(16.0) was usedfor data analysis. In this study p value< 0.05 has been considered as statistically significant. To calculate the sample size, a power analysis of α=0.05 and β=0.80, showed that 30 patients per study group were needed. Datas are expressed as mean and standard deviation. For comparing, the two main groups,

Table 1: Comparison of demographic data amongst groups

	Group1	Group 2	Group 3	p value		
				B/T group 1 and 2	B/T 2 and 3	B/T 1 and 3
Age in years	46.6±6.91	39±15.47	38.2±9.76	0.403	0.928	0.127
Height in cm	166.5±3.30	165±4.35	161±1.29	0.650	0.320	0.076
Weight in Kg	68.25±3.11	63.5±2.72	61.75±2.13	0.086	0.432	0.05
BMI[Kg/M²]	24.57±0.165	23.35±0.65	23.67±1.05	0.176	0.772	0.104

Abbreviation-B/t-Between

Student t test was applied. For qualitative assessment, Chi Square test was done.

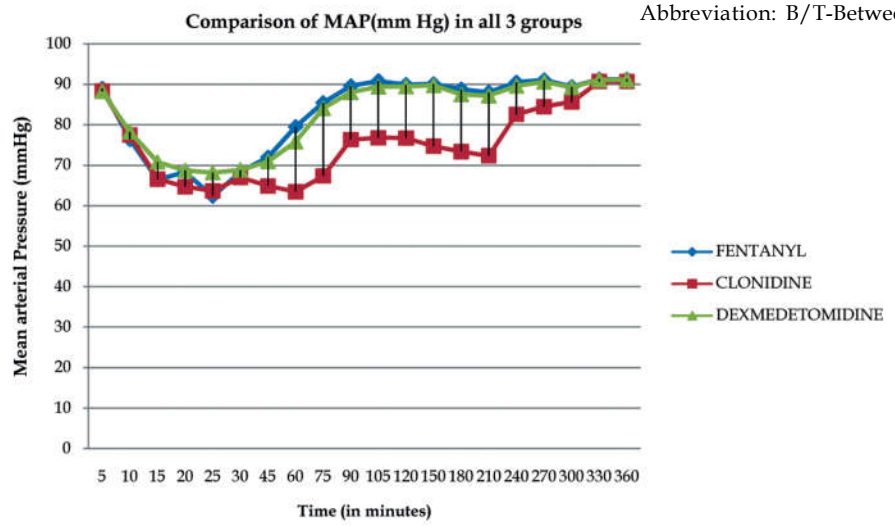
Demographic data, in all groups are comparable, because p value is not significant.

Time to achieve sensory level up to T10 dermatome level and time to achieve complete motor block i.e.Bromage grade 3 were found to be significantly longer in group 3. (p value< 0.05 shown in chart). Time for complete reversal of sensory block or regression time to S1 was significantly longerin group 2 approx 470±5.38 minutes [p<0.05]. Time for complete regain of motor block orBromage 0 was also significantly longerin group 2. There is no statistical difference, between the groups relative to baseline MAP and HR values.Study was done up to 480

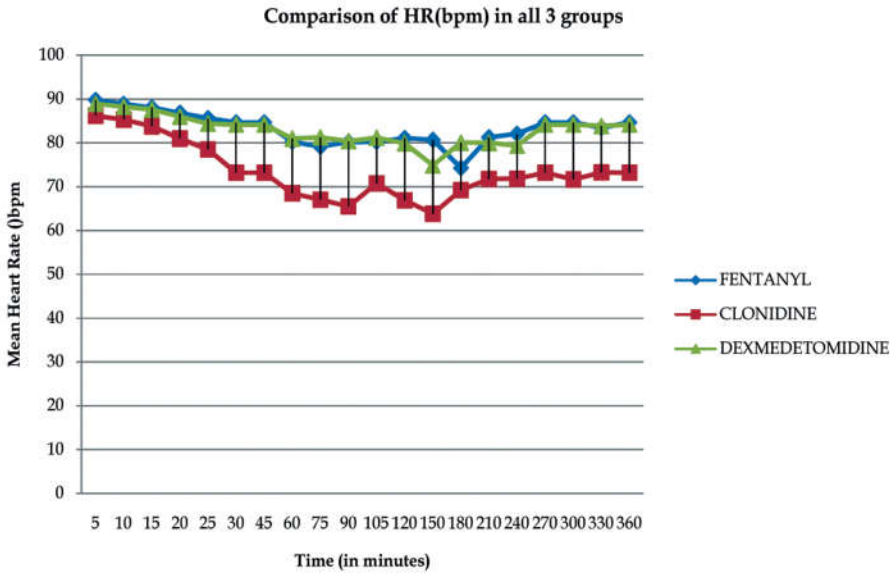
Table 2: Comparison of Spinal Block Characteristics amongst groups

	Group 1	Group 2	Group 3	p value B/T group 1 & 2	p value B/T Group2 & 3	p value B/T Group 1 & 3
Time to onset of sensory block	2.84±0.96	4.17±1.11	6.28±1.2	0.00	0.00	0.00
Time to onset of motor block	2.5±0.59	2.94±0.95	7.95±0.55	0.051	0.00	0.00
Time to achieve sensory level up to T10	5.25±0.87	5.04±0.84	7.94±1.02	0.396	0.000	0.00
Time to achieve Bromage3	6.12±0.80	6.17±0.67	8.44±0.78	0.746	0.00	0.00
Time to regression to S1	257.96±4.29	470±5.38	309±3.52	0.00	0.00	0.00
Time to achieve Bromage 0	215.73±4.36	422.33±5.24	286±7.070	0.00	0.00	0.00

Abbreviation: B/T-Between



Graph 1:



Graph 2:

minutes.

Although, group 3 showed slight fall in values, but that is not significant statistically.

Three patients in group 1, 4 patients in group 2 and 8 patients in group 3developed hypotension. It was managed with inj.Ephedrine and IVfluids[p >0.05]. Four patients in group 1, three patients in group 2 and six patients in group 3 developed bradycardia. It responded well to inj. Atropine 0.6 mg [p>0.05]. Only patients of group 1(Fentanyl) had pruritus, which was absent in Dexmedetomidine group. It was found to be significant [p<0.05]. Incidence of nausea, in all three groups were very low and statistically non significant. Mild sedation was significantly present,in group 2and 3 [p<0.05]

Discussion

Levobupivacaine is a

longer acting local anaesthetic, with pharmacological structure similar to Bupivacaine and with a larger safety margin. Levobupivacaine has less inotropic effects and produces less prolongation of QTc interval, than Bupivacaine.It also has less depressant effect on AV conduction and QRS duration. Glacer C. compared it with racemic Bupivacaine in elective hip replacement cases and demonstrated thatLevobupivacaine is less cardio and neurotoxic[4].

Availability of relatively few studies of Levobupivacaine with adjuvants prompted us to compare effects of adding different adjuvants to Levobupivacaine. Fentanyl as an intrathecal adjuvant, is being used for years. The addition of Fentanyl 15mcg demonstrated sparing effect on requirement of Levobupivacaine with least hemodynamic variations[2]. It was found in some studies that time taken for maximum sensory and motor block was shorter in Bupivacaine + Fentanyl group in caesarean sections than in Levobupivacaine + Fentanyl group[5]. Fentanyl group showed shorter anesthesia phase than Dexmedetomidinegroup but was associated with side effects like pruritus.

Dexmedetomidine, a novel α_2 agonist potentiates local anaesthetic action, prolongs postoperative analgesia and has dose dependent sedative effect.The stimulation of α_2 receptor, decreases calcium entry into nerve terminals, which may contribute to its inhibitory effect on neurotransmitter releaseleading to its various effects such as hypotension, brady cardia, sedation and analgesia[6,7,8]. Studies by Shubhi M. et al and collegues have shown the prolongation of spinal block by intrathecal 5mcg and 10 mcg, Dexmedetomidine has no effect on BP or HR[9,10]. Keshav and his collegues used Dexmedetomidine 10 mcg with intrathecal Bupivacaine without significant hypotension[11]. Al Mustafa et al, added 5 and 10 mcg Dexmedetomidine to intrathecal Bupivacaine 12.5 mg for urological procedures.They noted shorter onset and prolonged duration of block without significant side effects[12]. We did not get statistically significant hypotension in our study, as we were using Levobupivacaine, which as discussed earlier has least cardiotoxiceffects.Also by its nature Local anaesthestics reduce BP by decreasing the sympathetic outflow.But the intrathecal local anaesthetics, already producemaximum blockade of sympathetic outflow so intrathecalDexmedetomidine does not have scope to lower down BP. This explains, the absence of large variations in haemodynamic profiles in our study even if we used large amount of drug intrathecally[13,14]. Group 2 showed more prolongation of anaesthesia blockade than other groups.

Clonidine, a selective partial α_2 agonist is successfully being used to prolong sensory and motor block of local anaesthetics.Its effect is mediated through the activation of postsynaptic α_2 receptors in substsansiagelatinosa of spinal cord. Sethi et al and collegues demonstrated prolongation of the effect of intrathecal Bupivacaine by addition of Clonidine in gynaecological surgeries [15]. In our study, Group 3 developed same height of block after little duration of time($p<0.05$), but the effect did not last for a longer duration in comparison to Dexmedetomidine group. Niemi et al, used very high concentration of Clonidine intrathecally [3mcg/kg], which resulted in profound hypotension[16]. Van Tuijl I et al showed significant out come when used Clonidine in a very low concentration [15mcg][17]. We used very low dose 30mcg Clonidine, which had no significant effect on HR and BP butwith mild sedation. The effect of Clonidine lasted less than the Dexmedetomidine group but longer than the Fentanyl group.

So, to conclude, Levobupivacaine with Dexmedetomidine provides a better choice for intraoperative an aesthesia as well as for postoperative analgesia without any adverse effects.

Conclusion

There is a constant search for intrathecal adjuvant which can prolong the blockwithout causing hemodynamic disturbances.In our study, Dexmedetomidine group showed significant prolongation of spinal block than other groups without causing significant hemodynamic disturbances.

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