Original Research Article

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How Efficacious Intrathecal Dexmedetomidine with Levobupivacaine in Lower Limb Surgeries: A Comparative Study

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Abstract

Background and Aim: Studies and research are ongoing to find appropriate adjuvants to intrathecal 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 (REF).

Settings and Design: After approval from hospital ethical committee a randomized double blind study was conducted among 60 healthy American Society of Anesthesiologist ASA I and II patients, scheduled for lower limb surgeries. The study was conducted over 1 year at SRMSIMS.

Materials and Methods: Spinal block was administered in L3 and L4 intervertebral space, using 0.5% Levobupivacaine 12mg. Adjuvants were added in group 1, Dexmedetomidine 5mcg, and in group 2, Dexmedetomidine 10 mcg. Anaesthetic level achieved was T10. Onset time to achieve sensory, motor blockade, their regression time was noted. Hemodynamic changes and requirement for other analgesic drug was also noted.

Results: 60 patients were enrolled in our study, the data was recorded and analyzed using statistical analysis.

Conclusion: To conclude, Levobupivacaine with Dexmedetomidine, gives better result for intra as well as for postoperative regional anaesthesia without any adverse effects.

Keywords: Adjuvants; Intrathecal; Levobupivacaine; Dexmedetomidine Clonidine.

Introduction

Subarachnoid blockadeis the commonly used regional anaesthetic technique for lower limb surgery, because of the advantages of being economical and easy to administer. Its dis-advantages of short duration of action and lack of post-operative analgesiahas started new researches for the search of such intrathecal compounds, which can provide good relaxation, least hemodynamic disturbances and prolonged analgesia. Surgical anaesthesia requires dense sensory block and usually moderate to dense motor block. To achieve this, concentrated local anaesthetic preparations are required. Levobupivacainea long-acting local anaesthetic, pharmacological structure similar to that of Bupivacaine with larger safety margin and less neurotoxic and cardiotoxic side effects, is new in the list of local anaesthetic. Intrathecal α-2 agonistsprolong the duration of action of local anaesthetics and reduce the required dose. Clonidine, an α2-agonist, produces vasoconstriction and antinociception from α2 stimulation of receptors in dorsal horn cells of spinal cord, widely accepted as adjuvant for spinal anaesthesia. Dexmedetomidine, a highly selective α2 adrenergic agonist, α2/α1 selectivity 8 times higher than that of Clonidine is the new drug to be used as the adjuvant.

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Aims & Objectives

To investigate the influences of Dexmedeto-midine added to Levobupivacaine ononset and duration of sensory and motor block, duration of analgesia, hemodynamic changes, adverse effect of drugs, if any.

Material & Methods

After approval from hospital's ethical committee, we took 60 patients for our study in our institute aged 18 years – 55 years, ASA I-II from Oct 13 - Feb14 for lower limb surgeries for interlocking of tibia. It was designed in the form of a prospective randomized double blind study. We excluded ASA III / IV, patients with BMI > 30 and <20, patients withuncontrolled or labile hypertension, Heart block, dysarrythmia, on cardiac medication therapy (adrenergic receptor antagonist, Beta blocker, CCB or ACE inhibitor), Addiction to narcotics, Any contraindication to spinal anaesthesia and H/O drug allergy to the drugs, we are using.

After full general physical and laboratory examination, Complete Blood Count, Fasting Blood Sugar, S. Urea, S. Creatinine, S. electrolytes, PT/PTT, ECG and CXR, the patients were admitted a day prior to surgery. We counseled the patients about the regional anesthesia and informed consent was taken.

Anxiolysis was done with Tab Alprazolam 0.25 mg night before and at 6 AM with sips of water.

In O.T, standard monitor's i.e. ECG, SpO_2, NIBP, HR were attached to the patients. All patients were preloaded with RL 500 ml. Ensuring all aseptic precautions, under local anaesthesia Lumbar Puncture was done with 27G Quincke spinal needle at L3-L4 space.

We injected the drug after ensuring free flow of clear CSF. O_2 through facemask was given to each patient. After following exclusion criteria, 60 patients were randomized into 2 groups by a computer generated list.

In group 1, we used Levo Bupivacaine 0.5%, 12 mg + Dexmedetomidine 5 mcg, and in group 2, we used Levo Bupivacaine 0.5%, 12mg + 10mcg Dexmedetomidine. In group 2-0.3 ml, preservative free normal saline to make volume in all groups constant. The drug was prepared by a third observer, who was unaware about the study.

After the block, we assessed the time of sensory block up to T10 and grade 3 Bromage motor block before surgery. Zero was started at the time of subarachnoid block. Bromage 0-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 [3]. Vital signs (Pulse, B.P, ECG, SpO_2) were recorded preoperatively, then at 5 min interval intra-operatively until the end of surgery, then every 15 min, then 30 min.

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

We noted the time of recovery of S_1 dermatome and use of rescue analgesic drug.

Inj. Diclofenac 75 mg i.m. was administered for postoperative analgesia. We noted vital signs, response to pain and nausea. For nausea, Inj. Metoclopramide 10 mg i.v. was used, as a rescue drug.

Results

SPSS statistical software (16.0) was usedfor data analysis. In this study p value <0.05 have been considered as statistically significant. To calculate the sample size, a power analysis of α=0.05 and beta=0.80, showed that 30 patients per study group were needed. Data are expressed as mean and standard deviation. For comparing the three main groups Student t test was applied. For qualitative assessment chi square test was done. Demographic data's in both groups are comparable because p value is not significant (Table 1).

Table 1:

	Group-1 (N=30)	Group-2 (N=30)	P value
Hypotension	0	3	0.492
Bradycardia	3	2	1.00
Nausea	1	1	1.00
Vomiting	1	1	1.00

Table 1:

	Groups		
	Group1	**Group 2**	**p value**
Age in years(Mean ± SD)	46.6±6.91	39±15.47	0.403
Height in cm(Mean ± SD)	166.5±3.30	165±4.35	0.650
Weight in Kg(Mean ± SD)	68.25±3.11	63.5±2.72	0.086
BMI [Kg/M²]	24.57±0.165	23.35±0.65	0.176

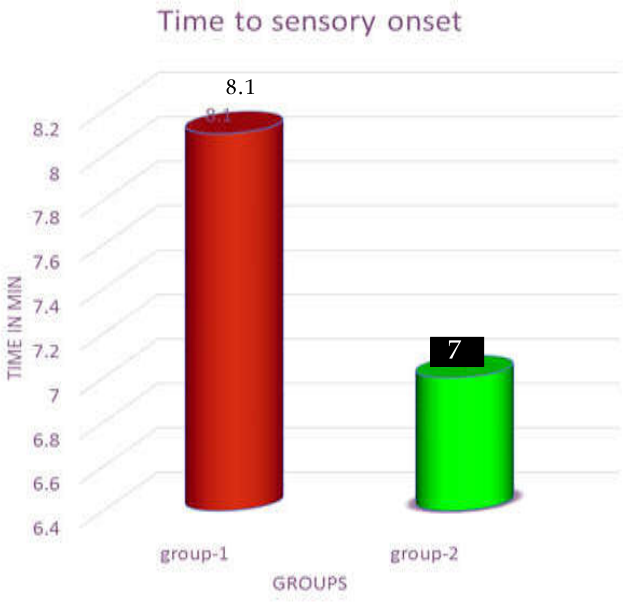


Fig. 2:

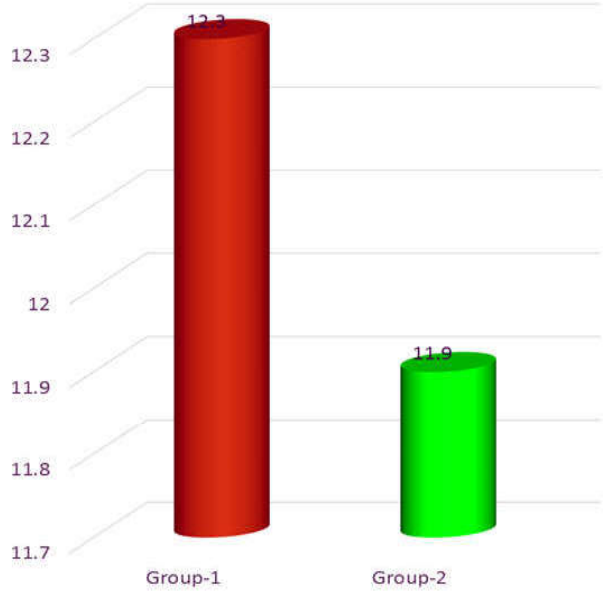


Fig. 3:

Table 2:

Groups	Group-1	Group-2	p value
Mean ± SD	8.1 ± 0.99	7.0 ± 1.05	<0.05
No of cases	30	30	

Table 3:

Groups	Group-1	Group-2	p value
Mean ± SD	12.3± 4.8	11.9 ± 3.4	<0.05
No of cases	30	30	

Demographic Data

All patients (n=60) completed the study. There was no statistically difference in patients demo-graphics.

Time to Sensory Onset

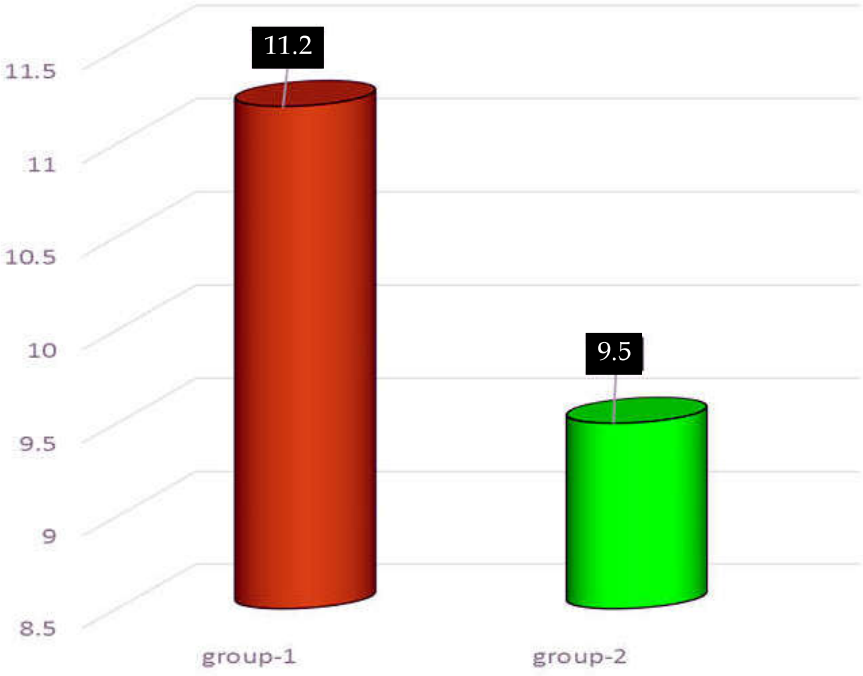
- The time to sensory onset in group-1 was 8.1± 0.99 min and in group-2 was 7.0±1.05 min
- Thus, the time of sensory onset was shortest in group-2 compared to group-1, which was statistically significant (p<0.05).

Time to motor block

- The time to motor block in group-1 was 12.3± 4.8 min and in group-2 was 11.9±3.4 min.
- Thus, the time of motor block was shortest in group-2 compared to group-1. (p value <0.05)

Table 4:

Groups	Group-1	Group-2	p value
Mean ± SD	11.2 ± 1.13	9.5 ± 1.08	0.00
No of cases	30	30	



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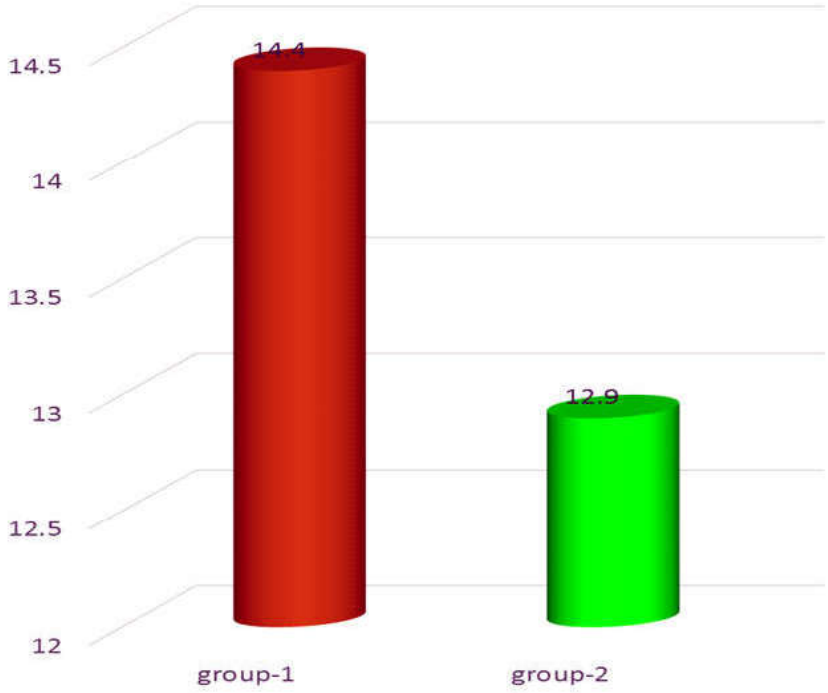

Fig. 5

Table 5:

Groups	Group-1	Group-2	p value
Mean ± SD	14.4 ± 1.83	12.9 ± 1.79	0.071
No of cases	30	30	

Time to achieve sensory level up to T10

- The time to achieved sensory level up to T10 in group-1 was 11.2±1.13 min and in group-2 was 9.5±1.08 min
- Thus, time to achieved sensory level up to T10 was shortest in group-2 compared to group-1, which was statistically significant.(p<0.05)

Time to Achieve Bromage 3

- The time to achieved bromage3 in group-1 was 14.4±1.83 min and in group-2was 12.9±1.79 min
- Thus, time to achieved bromage3 was shortest in group-2 compared to group-1, which was statistically non-significant (p>0.05).

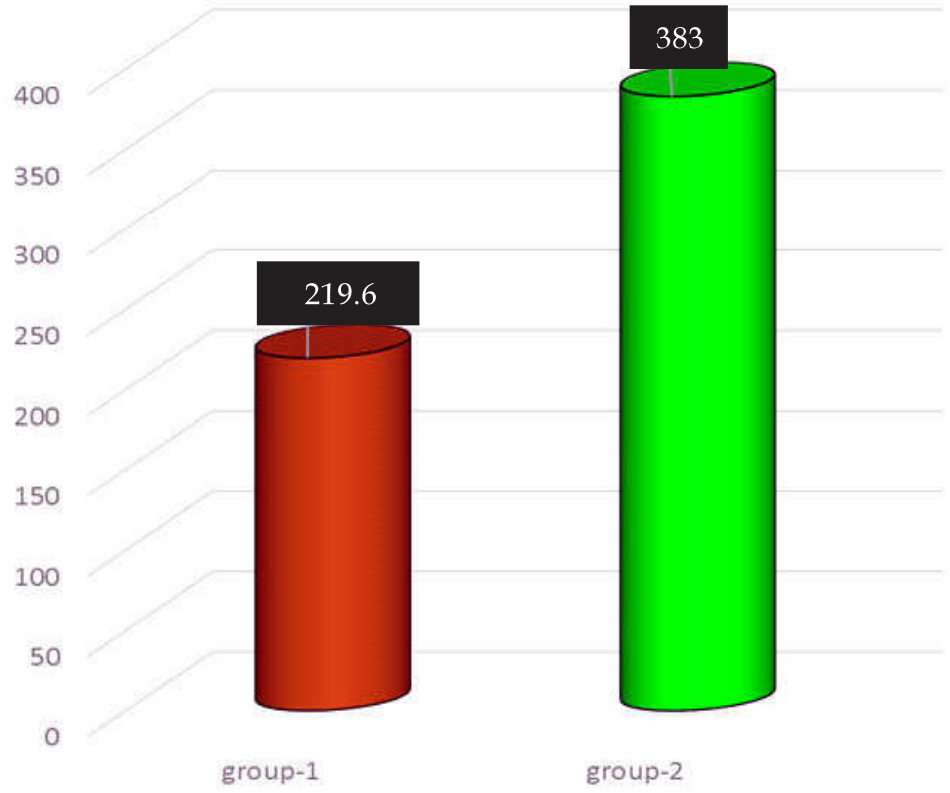

Fig. 6:

Table 6:

Groups	Group-1	Group-2	p value
Mean ± SD	297.9 ± 13.5	473.7 ± 15.2	0.000
No of cases	30	30	

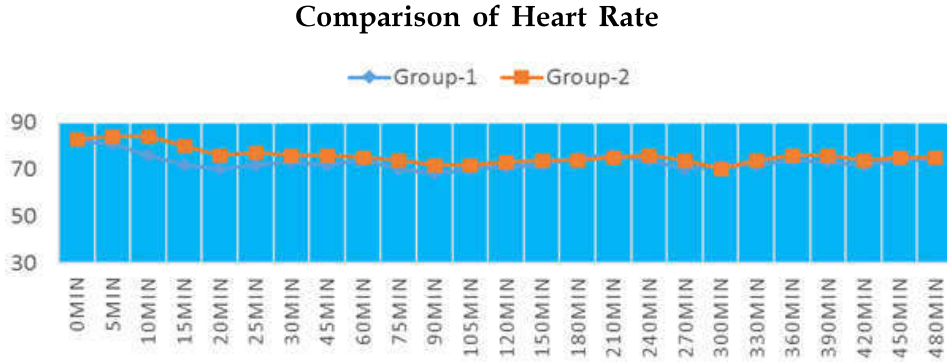

Fig. 7:

Time to Regression to S1

- The time to Regression to S1 in group-1 was 297.9± 13.5 min and in group-2 was 473.7± 15.2 min.
- Thus, the Regression to S1 was greater in group-2 compared to group-1, which was statistically significant. ($p<0.05$).

Time to achieve Bromage

- The time to achieved Bromage 0 in group-1 was 219.6±7.35 min and in group-2 was 383.8 ± 7.85 min.
- Thus, the time to achieved Bromage 0 was greater in group-2 compared to group-1, which was statistically significant ($p<0.05$).

Heart Rate

There was no statistically significant difference ($p \geq 0.05$) in heart rate amongst the groups.

Mean Arterial Blood Pressure

Mean Arterial Blood pressure started falling after 5min in both groups, but was no statistically significant difference in between groups.

Oxygen Saturation

- Oxygen saturation was similar in all the two groups
- There was no statistically significant difference

Table 7:

Groups	Group-1	Group-2	p value
Mean ± SD	219.6 ± 7.35	383.8 ± 7.85	0.00
No of cases	30	30	

Comparison of Mean Arterial Pressure

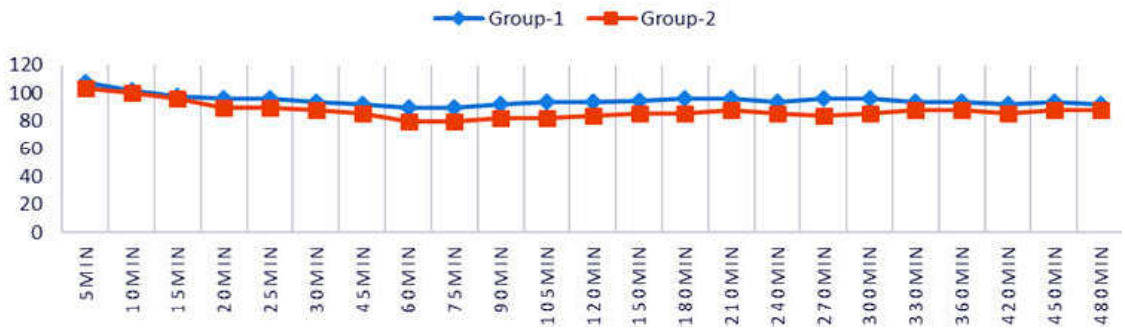

Fig. 7:

Table 8:

Adverse Effects	Group-1 (n=30)	Group-2 (n=30)	p value
Hypotension	0	3	0.492
Bradycardia	3	2	1.00
Nausea	1	1	1.00
Vomiting	1	1	1.00

Side Effects

- Among the side effects, hypotension was common in group-2 than in group-1
- Bradycardia was seen in both groups
- Nausea and vomiting was less in both groups

The characteristics of spinal block were summarized in Table 2. Time to reach T6 and Time to reach Bromage grade 3 were significantly late in Dexmedetomidine group. Regression time to S1 and Bromagein these patients who received supplemental anaesthesia was analyzed. This requirement was mainly at the time of puncture, $p<0.05$. So a significant number of patients in group 1 received supplemental anesthesia.6 patients in group 1 and 9 patients in group 2 developed hypotension. It was managed with Inj. Mephenteramine and ivfluids [$p >0.05$].

Two patients in group 1 and 3 patients in group 2 had persistent hypotension. Five patients in group 1 and 4 patients in group 2 developed bradycardia. It responded well to inj. Atropine 0.6 mg [p>0.05]. Only patients of group 1 had pruritus, which is absent in Dexmedetomidine group. It was found to be significant [p>0.05]. Incidence of nausea in both groups are almost very low and non-significant.

Discussion

Levobupivacaine is a longer acting with pharmacological structure similar to Bupivacaine with larger safety margin. Levobupivacaine had less inotropic effect and produced less prolongation of QTc interval than Bupivacaine. It also had less depressant effect on AV conduction and QRS duration. Feyzi Celik et. al. compared the anaesthetic and hemodynamic effects of intrathecally administered Levobupivacaine and Bupivacaine in combination with Fentanyl in hip surgery. They found the onset of sensory block and the time to two segment regression wassimilar between the two groups. In the Levobupivacaine group, the time to onset of motor block was longer and the motor block regression time was shorter than that of Bupivacaine group. They proposed that Levobupivacaine may be a good alternative to Bupivacaine.

Glacer C. compared it with Racemic Bupivacaine in elective hip replacement cases and demonstrated that Levobupivacaine is less cardiotoxic and neurotoxic [4].

Studies of adding intrathecal adjuvants in Levobupivacaine are very less. Dexmedetomidine, a novel $\alpha 2$ agonist is on its way to be added in the list of adjuvants. It potentiates local anaesthetic action, prolongs postoperative analgesia and has dose dependent sedative effect. The stimulation of $\alpha 2$ receptors decreases calcium entry into nerve terminals, which may contribute to its inhibitory effect on neurotransmitter release, leading to its various effects such as hypotension, bradycardia, sedation and analgesia [6,7,8]. Vidhi Mahendru et. al. found significantly longer sensory and motor block times, when 5 μg Dexmedetomidine was added to Bupivacaine than Fentanyl and Clonidine was added.

Studies have shown that prolongation of spinal block by intrathecal 5mcg and 10mcg Dexmedetomidine with no effect on hemodynamics. Hala et. al. opined that addition of 5mcg and 10 mcg Dexmedetomidine to intrathecal Bupivacaine, prolonged the analgesic effect of drug in dose dependent manner. With 5mcg Dexmedetomidine, the mean duration of analgesia achieved was 240 min and with 10 mcg Dexmedetomidine the mean duration of analgesia was 520 min.

No hemodynamic instability or other side effects were noted in either group. Keshav et. al. used 5 and 10 mcg Dexmedetomidine with intrathecal Bupivacaine. It showed dose dependent shortening of onset of block and prolongation of block accordingly.

In our study we used 5mcg and 10 mcg of spinal Dexmedetomidine without premedication with any type of Benzodiazepines. Onset of sensory block was also shortened which was dose dependent. Addition of Dexmedetomidine to Levobupivacaine prolonged the sensory andmotor block duration in patients subjected to lower limb surgery under spinal anaesthesia.

Aliye Esmaoglu et. al. found sensory and motor block onset times were shorter and regression of the sensory block to S1 dermatome and Bromage 0 were longer, when 3 μg Dexmedetomidine was added to Levobupivacaine, no statistically significant differences between groups in terms of blood pressure and heart rate.

Feroz Ahmad Dar et. al. investigated the effect of adding Dexmedetomidine to intrathecal Bupivacaine on the onset time and duration of motor and sensory blocks and found sensory and motor block onset times were similar but durations were prolonged without any significant adverse effects.

Dipak L. Raval, Minaxi Chaudhary compared intrathecal Bupivacaine with either Dexmedetomidine or Clonidine, found onset time of sensory and motor block is decreased in Dexmedetomidine.

Conclusion

Levobupivacaine, which has similar anaesthetic properties to Bupivacaine, being more cardio stable, may be a good alternative anaesthetic to Bupivacaine.

Dexmedetomidine precipitated the onset time of sensory and motor block and it prolonged duration of sensory and motor block significantly when used with Levobupivacaine in spinal anaesthesia in a dose dependent manner.

Because of the absence of significant adverse effect, we endorse the addition of Dexmedetomidine to spinal anaesthesia with Levobupivacaine when prolongation of spinal anaesthesia is desired.

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