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Original Research Article

To Compare Isobaric Levobupivacaine with Fentanyl and Dexmedetomidine for Spinal Blockade Onset, Duration, Hemodynamic Parameters, and Adverse Effects

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Abstract

Aim: The aim of the study to compare a combination of isobaric Levobupivacaine with fentanyl and dexmedetomidine for the characteristics of spinal blockade with respect to onset, duration and hemodynamic parameters and side effect. **Methods:** This was a prospective, randomized, and double blinded clinical comparative study conducted in the Department of Anaesthesia and Critical Care, Patna Medical College and Hospital, Bihar, India, from Jan 2018 to July 2018. The study population consisted of 150 adult patients who were classified as American Society of Anesthesiologists (ASA) physical status I or II, undergoing elective lower limb orthopaedic surgery under spinal anesthesia. The study participants were randomly divided into three groups.Group A: 0.5% Levobupivacaine Isobaric 2.5ml+ 0.5ml normal saline (total volume is upto 3.0 ml). Group F: 0.5% Levobupivacaine Isobaric 2.5ml + 25mug fentanyl (test solution will diluted with normal saline to total volume of 3.0ml). Group D: 0.5% Levobupivacaine isobaric 2.5ml +5 mcg dexmedetomidine (test solution will diluted with normal saline to total volume of 3.0 ml. **Result:** The mean time for onset of sensory block was 10.69 ±4.16 min in the saline group and 8.41±2.93 min in the dexmedetomidine group and 2.31±1.19 min in the fentanyl group. The mean time taken to achieve maximum sensory block in group A was 15.72±4.91 min, in group D was 13.28±3.51 min and in group F it was 5.38±1.92 min so maximum sensory block was achieved earlier in group. The mean duration of sensory block in group A was 114.47±7.12min, and in group F was 162.11±12.74min., and in group D was 205.12±6.41 min. The mean onset time of motor block in group A was 11.14±3.98 min, in group D it was 8.97±3.31 min, in group F it was 3.41 ±1.33 min. Onset of motor block occurred earlier in the fentanyl group. In the present study there was a significant difference in duration of motor block across the three groups with p value <0.001. In group A mean duration of motor block was 162.04±6.30 min, and in group D was 254.26±6.59 min and in group F it was 187.74±11.64 min. **Conclusion:** Dexmedetomidine group has longer onset of and duration of sensory block and effective postoperative analgesia and fewer side effects as compared to fentanyl group.

Keywords: postoperative analgesia, sensory block, dexmedetomidine, fentanyl

Introduction

Spinal anaesthesia is most valuable mode of anesthesia for lower limb orthopaedic surgeries because of its simplicity, ease of administration and absence of side-effects of general anesthesia. It provides effective sensory and motor blockade.[1] Different drugs used for spinal anaesthesia are lidocaine, bupivacaine, tetra Caine, mepivacaine,ropivacaine, levobupivacaine, chloroprocaine.[2] Levobupivacaine, the pure S(-) enantiomer of racemic bupivacaine, is a new long – acting local anaesthetic that has recently been introduced in the clinical practice and seems to be alternative to bupivacaine because of its significantly decreased cardiovascular and central nervous system toxicity.[3] Moreover the regression of motar block is significantly more rapid after levobupivacaine than bupivacaine, which may be advantageous for early ambulation after surgery.[4] There is very little experience as yet with the use of levobupivacaine. Various additives were added over time to the local anaesthetics to increase the duration of analgesia. Dexmedetomidine has been used to local anaesthesia in the intrathecal route and has significant effect on the onset and duration of spinal anesthesia.[5] Nalbuphine, a mixed agonist- antagonist opioid produce analgesia without the undesirable side effects of a mu-agonist.[6] Intrathecal opioids, like Fentanyl added to local anesthetics enhance analgesia without intensifying motor and sympathetic block, and make it possible to achieve successful anesthesia inspite of the use of a low dose local anesthetics.[7] 0.5%Levobupivaciane has not been extensively investigated in orthopedic surgeries and the published clinical studies are small despite its higher safety profile. Levobupivacaine causes less cardiovascular and neurological events. Onset of sensory and motor block is hastened with Hyperbaric Levobupivacaine compared to Isobaric Levobupivacaine. Increased protein binding and higher clearance explains cardiostability of Levobupivacaine.[8] Fentanyl is a synthetic opioid with central action, which is used widely for pain control. Intrathecal fentanyl is usually added to other local anesthetics to increase anesthesia and analgesia. It has improved spinal anesthesia and reduced the anesthetic drug related side effects including pruritus, nausea and vomiting.[9] Dexmedetomidine and fentanyl have been used as adjuvant to local anesthetics in different surgeries to provide superior analgesia and to improve the duration of the block.[10]

Material and methods

This was a prospective, randomized, and double blinded clinical comparative study conducted in the Department of Anaesthesia and Critical Care, Patna Medical College and Hospital**,** Bihar, India, from Jan 2018 to July 2018, after taking the approval of the protocol review committee and institutional ethics committee.

We evaluate the effect, hemodynamic stability and adverse effects of using intrathecal dexmedetomidine and fentanyl as an adjuvant to Isobaric Levobipivacaine for lower limb orthopaedic surgery. The study participants were randomly divided into three groups.

The study population consisted of 150 adult patients who were classified as American Society of Anesthesiologists (ASA) physical status I or II, undergoing elective lower limb orthopaedic surgery under spinal anesthesia. 150 patients with age between 20 to 61 yrs of either sex, ASA 1 or 2and Patient posted for elective lower limb orthopaedic surgeries were include in this study. Patients who had History of allergy to study drugs and Patients using alpha 2-adrenergic receptors antagonists, calcium channel blockers, angiotensin-converting enzyme inhibitor were exclude from the study.

Methodology

All patients were preloaded with Ringer lactate solution 10ml/kg over 15 minutes before the spinal anaesthesia. The base line heart rates, systolic, diastolic and mean Blood pressure, SpO2 respiratory rate, were recorded. Then after Subarachnoid Block, all the parameters like pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, SPO2, respiratory rate, level of sensory block, grade of motor block, sedation scale at every 1 minute for 5 minutes; then every 5 minutes till 30 minutes and then every 15 min up to 2 hrs and then after every 30 min till the end of surgery. In the postoperative period following paramerters are observed pulse, systolic blood pressure, diastolic blood pressure, mean arterial pressure, SPO2, VAS, 1st rescue analgesic requirement, total analgesic requirement in 24 hr period, sedation scale and side effect were recorded immediately in postoperative recovery room, 0.5 hr, 1 hr, 1.5 hr, 2 hr, 3 hr, 4 hr, 8 hr, 12 hr, 18 hr, 24 hr period.

- Group A: 0.5% Levobupivacaine Isobaric 2.5ml+ 0.5ml normal saline (total volume is upto 3.0 ml).
- Group F: 0.5% Levobupivacaine Isobaric 2.5ml + 25mug fentanyl (test solution will diluted with normal saline to total volume of 3.0ml).
- Group D: 0.5% Levobupivacaine isobaric 2.5ml +5 mcg dexmedetomidine (test solution will diluted with normal saline to total volume of 3.0 ml.

Sensory anesthesia assessed by loss of sharp sensation to pinprick test in the midclavicular line. Motor blockade was determined using Modified Bromage scale.

Result

The mean time for onset of sensory block was 10.69 ±4.16 min in the saline group and 8.41±2.93 min in the dexmedetomidine group and 2.31±1.19 min in the fentanyl group. The mean time taken to achieve maximum sensory block in group A was 15.72±4.91 min, in group D was 13.28±3.51 min and in group F it was 5.38±1.92 min so maximum sensory block was achieved earlier in group. Peak level of sensory block attained in the fentanyl group was T4 and the peak level of sensory block in dexmedetomidine group was T6 and in the saline group peak level was T8. So the highest sensory block was attained in the fentanyl group. The mean duration of sensory block in group A was 114.47±7.12min, and in group F was 162.11±12.74min., and in group D was 205.12±6.41 min. Prolong duration occur in the dexmedetomiine group. The prolongation of effect may result from synergism between local anaesthetic and alpha2 adrenoceptor agonist action. The mean onset time of motor block in group A was 11.14±3.98 min, in group D it was 8.97±3.31 min, in group F it was 3.41 ±1.33 min. Onset of motor block occured earlier in the fentanyl group. In the present study there was a significant difference in duration of motor block across the three groups with p value <0.001. In group A mean duration of motor block was 162.04±6.30 min, and in group D was 254.26±6.59 min and in group F it was 187.74±11.64 min. There was a significant difference in the pulse rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure from the 2 min to 20 min in the intraoperative period. In the postoperative time period the pulse rate, systolic blood pressure, diastolic blood pressure, mean blood pressure was not statistically significant with p value of >0.05. In regard, first analgesic requirement was prolonged in group D as compared to group A and group F and requirement of 24 hr analgesia was also found lower in the dexmedetomidine group, and however supplementary analgesia in the form of diclofenac 75 mg iv was required in group A only. No patient in any of the groups had side effects like shivering, pruritus, nausea vomiting, and no patient had episode of respiratory depression. There were 30 (60%) patients in the dexmedetomidine group had bradycardia while in the fentanyl group 4(8%) patients and in the saline

group 2 (4%) patients had bradycardia being statistically significant.

Table 1: Comparison of demographic parameters

Parameters	Group A (n=50)	Group D (n=50)	Group F (n=50)	P-value
Age (years) [mean±SD]	37.15±9.78	38.67±14.98	39.87±14.48	0.65 (NS)
Gender [No. (%)]				
Male	35 (70)	39 (78)	34 (68)	0.69(NS)
Female	15 (30)	11 (22)	16(32)	
ASA				
1	48 (96)	46 (92)	46 (92)	0.75 (NS)
2	2 (4)	4 (8)	4 (8)	
Weight (mean ±SD)	63.29±2.69	63.32±1.74	63.98±2.12	0.48(NS)
Height (mean ±SD)	159.12±2.61	159.81±2.84	159.19±3.18	0.58 (NS)
duration of surgery (mean ±SD)	90.87±16.74	97.18±18.36	99.49±13.13	0.051 (NS)

Table 2: Comparison of Sensory and Motor block parameters across three groups

Parameters	Mean ± SD						P-value
	Group A (n=50)		Group D (n=50		Group F (n=50)		
Onset of sensory block (in min)	10.69	4.16	8.41	2.93	2.31	1.19	< 0.001* (S)
Duration of sensory block (in min)	114.47	7.12	205.12	6.41	162.11	12.74	< 0.001* (S)
Onset of motor block (in min)	11.14	3.98	8.97	3.31	3.41	1.33	< 0.001* (S)
Duration of motor block (in min)	162.04	6.41	254.26	6.59	187.74	11.64	< 0.001* (S)
Time taken to achieve for maximum sensory block (in min)	15.72	4.91	13.28	3.51	5.38	1.92	< 0.001* (S)
Bromage Scale	[No. (%)]						
3: Inability to raise leg, flex knee or ankle or move toes	50	100	50	100	50	100	< 0.001 (S)

S: Significant

Table 3: Comparison of maximum sensory block attained in three groups

Maximum sensory block attained	Group A (n=50)	Group D (n=50)	Group F (n=50)	P-value*
T4 dense	0	0	3 (6)	< 0.001 (S)
T6 dense	0	7 (14)	35 (70)	
T8 dense	7 (14)	26 (52)	12 (24)	
T10 dense	43 (86)	17 (34)	0	

*Obtained using Chi square test; S: Significant

Table 4: Frequency distribution according to first analgesic requirement in patients – Post operative period

Post-operative first analgesic requirement	No. (%)
Group A	
Intraoperative	21(42))
Postoperative recovery	14(28)
0.5hr	15 (30)
Group D	
2 hr	2(4)
3 hr	10 (20)
4 hr	25 (50)
6 hr	13 (26)
Group F	
Postoperative recovery room	6(12)
0.5 hr	24(48)
1 hr	16 (32)
2 hr	4 (8)

Table 5: Frequency distribution according to total analgesic requirement in 24 hr – Postoperative period

Group / Number of doses in 24 hr.	No. (%)
Group A	
4	18 (36)
5	26 (52)
6	6 (12)
Group D	
1	3 (6)
2	46 (92)
3	1 (2)
Group F	
1	2 (4)
2	9 (18)
3	39 (78)

Discussion

In this study we compared the 5-mcg dose of dexmedetomidine with 25 mcg dose of fentanyl administered to the Isobaric Levobupivacaine. There were very few studies that compared both the doses simultaneously with Isobaric Levobupivacaine; we have compared and discussed our results with various other studies using similar adjuvants in same doses but in combination with various local anaesthetic as well in various surgeries. The values of the demographic variables were comparable between the three groups. Onset of sensory block defined as time taken to attain the T12 dermatomal level. Our study showed mean time for onset of sensory block was 10.59 ±4.16 min in the saline group and 8.41±2.93 min in the dexmedetomidine group and 2.31±1.19 min in the fentanyl group. So, onset of sensory block occurred earlier in the fentanyl group Mohamad Kamal et al in 2017[11] found that the onset of sensory block was 3.22±0.69 min in the group F and 3.90±0.94 min in the group D with p value highly significant p <0.001. Shelly Rana[12] in 2017 stated that the earlier onset with fentanyl can be attributed to its lipophilic properties. The lipophilic opioids rapidly

traverse the dura mater, where they are sequestered in the epidural fat and enter the systemic circulation; they also rapidly penetrate the spinal cord where they binds opioid receptors within the white matter as well as dorsal horn receptors and eventually enter the systemic circulation as they are cleared from the spinal cord. Al Ghanem et al 2009[13] found the onset time for sensory block was upto T10 level and it was 7.5±7.4 min in dexmedetomidine group and 7.4±3.3 min in fentanyl. The mean time taken to achieve maximum sensory block in group A was 15.72±4.91 min, in group D was 13.28±3.51 min and in group F it was 5.38±1.92 min so maximum sensory block was achieved earlier in group F. Nayagam HA et al (2014)[14] found that the mean time for peak sensory levels was (11.88 ± 2.156) min in fentanyl group and in dexmedetomidine group it was (12.92 ± 3.131) min. The difference between the two means was statistically significant. ($p<0.05$). Al Ghanem et al in 2009[13] studied and found that time to reach the maximum sensory block was around 19.34±2.87 min in the dexmedetomidine group and 18.39±2.46 min in the fentanyl group which was stastistically insignificant with p value of 0.12.

Peak level of sensory block attained in the fentanyl group was T4 and the peak level of sensory block in dexmedetomidine group was T6 and in the saline group peak level was T8. So, the highest sensory block was attained in the fentanyl group. Ghanem M Subhi et al [13] (2009) found out that highest sensory level was T6 in the Dexmedetomidine group and in the fentanyl group it was around T8 level. The mean duration of sensory block in group A was 114.47±7.12min, and in group F was 162.11±12.74min., and in group D was 205.12±6.41 min. Prolong duration occur in the dexmedetomiine group. The prolongation of effect may result from synergism between local anaesthetic and alpha2 adrenoceptor agonist action. Ahmed Basuni et al[15] in 2013 also stated the prolongation of the block in the dexmedetomidine.

In our study mean onset time of motor block in group A was 11.14±3.98 min, in group D it was 8.97±3.31 min, in group F it was 3.41 ±1.33 min. Onset of motor block occured earlier in the fentanyl group. Mohamad Kamal et al in 2017[11] found that onset of motor block was 3.74±0.57 min in the group F and 4.44±0.91 min in the group D with p value<0.001. In the present study there was a significant difference in duration of motor block across the three groups with p value <0.001. In group A mean duration of motor block was 162.04±6.30 min, and in group D was 254.26±6.59 min and in group F it was 187.74±11.64 min. Mahendru et al (2013) [16] found that duration of motor block was (161.5±19.8 min) in saline group. (196.0 ± 26.8) min in group fentanyl and (198.7±26.4 min) in clonidine, (273.3 ± 24.6) min in the dexmedetomidine group (P<0.0001). Dr Rayees Ahmad et al 2016[17] found duration of motor block in the fentanyl group was around 152.90 ±8.31 min and in the dexmedetomidine group it was around 419.70±16.85 min.(p<0.001).

In the present study there was a significant difference in the pulse rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure from the 2 min to 20 min in the intraoperative period. In the postoperative time period the pulse rate, systolic blood pressure, diastolic blood pressure, mean blood pressure was not statistically significant with p value of >0.05. Khan A L et al (2015)[18] inferred that the heart rate at all intervals was lower in dexmedetomidine group when compared to fentanyl group. Rao et.al in 2015[19] found that the significant decrease in the pulse rate was observed in the dexmedetomidine group as compared to the fentanyl and control. Ahmed Sobhy Basuni et al (2013)[15] found that blood pressure was comparable in the two groups throughout the surgery. 2 patients in group F showed intraoperative period

hypotension. Mohamad Kamal et al in 2017[11]stated that hypotension occur in both the groups but the value was not statistically significant in using the intravenous vasopressor therapy.

Mechanism of sedation in the dexmedetomidine group is due to action on the sleep promoting pathway. In the present study both intraoperative and postoperative period dexmedetomidine contribute to sedation scale 2. Rajani Gupta R et al (2011)[20] stated that the mean sedation score was (3.8±0.5) in group dexmedetomidine as compared to (2.2±0.53) in group fentanyl (P<0.05). Rayees Ahmad R et al (2016)[17] found the mean sedation score for group dexmedetomidine was (3.40 ± 0.49) and in fentanyl was (2.16 ± 0.37), (P <0.001). There was no significant difference between the three groups in the respiratory rate. Similar to Ahmed Sobhy Basuni et al in 2013[15] and R. Ahmed et.al in 2009.[17] In regard, first analgesic requirement was prolonged in group D as compared to group A and group F and requirement of 24 hr analgesia was also found lower in the dexmedetomidine group, and however supplementary analgesia in the form of diclofenac 75 mg iv was required in group A only.

Aamir Laique Khan et.al in 2015[18] studied that the time for first analgesic requirement in the dexmedetomidine group was (280±7.84) min and in the fentanyl group it was (173.88±8.12) min after the starting of surgery which was highly significant with p value of (<0.001).

Farhad Safari, et al in 2016[21] total morphine doses in 24 hours was significantly lower in the dexmedetomidine group as compared to fentanyl and control groups (P < 0.05).

Ayman Eskander et al in 2017[22]found that the postoperative analgesic requirement in first 24 hr was significantly lower in the dexmedetomidine and the fentanyl group compared to the control group and it was significantly lower in the dexmedetomidine group than fentanyl group (p< 0.05).

In the present study no patient had episode of respiratory depression. Vidhi Mahendru et al in 2013,[16] Rajani Gupta et al 2011[20] in both the studies there was no evidence of respiratory depression. In the present study no patient in any of the groups had side effects like shivering, pruritus, nausea vomiting, similar to Ahmed Sobhy Basuni et al 2013.Al Ghanem et al in 2009[13] stated that that 2 (5%) patients in the dexmedetomidine group and 4(10%) patients in the Fentanyl group had nausea and vomiting with p value of 0.401, no patient in the dexmedetomidine group got pruritus and 5 patients in the fentanyl group had pruitu.

Gupta R et al (2011)[20] studied intrathecally dexmedetomidine and fentanyl as adjuvant to Bupivacaine in lower abdominal surgeries. In group dexmedetomidine only one patient had Nausea and no patient had vomiting while in group fentanyl two patients had nausea and one patient had vomiting. One patient in the fentanyl group had pruritus. In the present study 30 (60%) patient in the dexmedetomidine group had bradycardia while in the fentanyl group 4(8%) patients and in the saline group 2 (4%) patients had bradycardia being statistically significant. However there was no episode of bradycardia found Mohamad Kamal et al in 2017[11] studies. Ghanem et al in 2009[13] stated that side effect of bradycardia was less because small dose of intrathecal dexmedetomidine was used in their study.

In our study, 37 patients in the fentanyl group had episode of hypotension. Which was treated with inj mephentermine 3 mg in incremental doses. The maximum hypotension occur in the F Ahmad R et al (2016)[17] studied they found that 14(28.0%) patients in group fentanyl and 8 (16.0%) patients in group dexmedetomidine had hypotension.

Conclusion

Dexmedetomidine group has longer onset of and duration of sensory block and effective postoperative analgesia and fewer side effect as compared to fentanyl group.

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