e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2022; 14(11); 80-87

Original Research Article

Intrathecal Dexmedetomidine and Fentanyl as an Adjuvant to Isobaric Levobupivacaine for Lower Limb Orthopaedic Surgery: A Comparative Study

Vishal Vaibhaw[1], Niraj Narain Singh[2], Kumar Rohit[3], Niraj Kumar[4]

[1]Assistant Professor, Department of Anesthesiology, ESIC Medical College, Bihta, Patna, Bihar, India

[2]Associate Professor, Department of Orthopaedic, ESIC Medical College, Bihta, Patna, Bihar, India

[3]Senior Resident, Department of Orthopaedic, ESIC Medical College, Bihta, Patna, Bihar, India

[4]Senior Resident, Department of Anesthesiology, ESIC Medical College, Bihta, Patna, Bihar, India

Received: 25-09-2022 / Revised: 15-10-2022 / Accepted: 30-10-2022
Corresponding author: Dr. Niraj kumar
Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to compare the efficacy and safety of 25 mcg of fentanyl vs 5 mcg dexmedetomidine as an adjuvant in 0.5% of 3ml of isobaric levobupivacaine in lower limb orthopaedic surgery.

Methods: The present study was conducted in the Department of Anesthesiology, ESIC Medical College Bihta, Patna, Bihar, India for the period of one year . The study participants were randomly divided into three groups. The study population consisted of 90 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. 90 patients with age between 20 to 60 yrs of either sex, ASA 1 and 2and Patient posted for elective lower limb orthopaedic surgeries were include in this study.

Results: In the present study, male dominated in all the three groups as compared to females. The patients were more in ASA I as compared to ASA II. The mean time for onset of sensory block was 11.04 ±4.21 min in the saline group and 8.76±2.99 min in the dexmedetomidine group and 2.28±1.42 min in the fentanyl group. The mean time taken to achieve maximum sensory block in group A was 16.18±4.83 min, in group D was 14.16±3.42 min and in group F it was 5.52±1.67 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.

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.

Keywords: Subarachanoid block, Levobupivacaine**,** dexmedetomidine, fentanyl

This is an Open Access article that uses a fund-ing model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0) and the Budapest Open Access Initiative (http://www.budapestopenaccessinitiative.org/read), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Subarachnoid blockade is the most commonly used regional anesthetic technique for lower limb surgery. Various adjuncts are being used with local anesthetics for prolongation of intraoperative and postoperative analgesia. However, there use is thwarted either due to the adverse effects of adjuvants or unreliable postoperative analgesia.

Most of the clinical studies about the intrathecal α2 adrenergic agonist are related to clonidine. [1] Dexmedetomidine, a highly selective α2 adrenergic agonist has evolved as a panacea for various applications and procedures in the perioperative and critical care settings. [2] It is also emerging as a valuable adjunct to regional anesthesia and analgesia, where gradually evolving studies can build the evidence for its safe use in central neuraxial blocks. [3]

Spinal anesthesia is the most commonly used technique for lower limb orthopaedic surgeries as it is very economical and easy to administer. However, postoperative pain control is a major problem because spinal anesthesia using only local anesthetics is associated with relatively short duration of action, and thus early analgesic intervention is needed in the postoperative period. A number of adjuvants, such as Clonidine and Midazolam, and others have been studied to prolong the effect of spinal anesthesia. [4]

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 cardio stability of Levobupivacaine. [5]

Regression of motor block occurs earlier with Levobupivacaine as compared to Bupivacaine. A common problem during lower limb orthopaedic surgeries under spinal anesthesia is post-operative pain intrathecally opioids act synergistically with local anaesthetics. [4] They improve the quality of intraoperative anaesthesia, permit lower doses of local anesthetics, provide faster onset of surgical block and prolong the duration of postoperative analgesia.

Nowadays, newer Phenylpiperidine compounds like fentanyl and sufentanil are being increasingly used to provide segmental analgesia. Being highly lipid soluble and having higher affinity for opioid receptors, these drugs provide quicker onset of the block, improve the quality of intraoperative anaesthesia and prolong postoperative analgesia with fewer side effects. [6]

Dexmedetomidine, a new highly selective α2-agonist, is under evaluation as a neuraxial adjuvant as it provides stable hemodynamic conditions, good quality of intraoperative and prolonged postoperative analgesia with minimal side effects. [7]

Dexmedetomidine has been approved by Food and Drug Administration (FDA) as a short-term sedative for mechanically ventilated intensive care unit (ICU) patients. Based on earlier human studies, it is hypothesized that intrathecal 5 µg dexmedetomidine would produce prolong postoperative analgesic effect with Hyperbaric Levobupivacaine in spinal anaesthesia with minimal side effect. [7-10]

The aim of the present study was to compare the efficacy and safety of 25 mcg of fentanyl vs 5 mcg dexmedetomidine as an adjuvant in 0.5% of 3ml of isobaric levobupivacaine in lower limb orthopaedic surgery.

Methods

The present study was conducted in the Department of Anesthesiology, ESIC Medical College Bihta, Patna, Bihar, India

for the period of one year. The study participants were randomly divided into three groups. The study population consisted of 90 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. 90 patients with age between 20 to 60 yrs of either sex, ASA 1 and 2 and Patient posted for elective lower limb orthopaedic surgeries were include in this study. In the proposed study, three groups have been considered with Saline, fentanyl and dexmedetomidine as adjuvants with the anaesthetic drug.

Inclusion Criteria:

1. Patient aged between 18 to 60yrs of either sex.
2. ASA 1 and 2.
3. Patient posted for elective lower limb orthopaedic surgeries.
4. Height 150-180 cm.
5. Weight 50-70 kg.

Exclusion Criteria:

1. History of allergy to study drugs.
2. Patient refusal.
3. Patients using alpha 2-adrenergic receptors antagonists, calcium channel blockers, angiotensin-converting enzyme inhibitor.
4. Patient having absolute contraindication to spinal anaesthesia.

Careful pre anaesthetic check-up was carried out in all patients with detailed clinical history, general and systemic examination. After checking the informed consent overnight fasting for 8-10hrs done. 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, SpO_2 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 upto 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, SpO_2, 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.

Results

Table 1: Comparison of demographic parameters

Parameters	Group A (n=30)	Group D (n=30)	Group F (n=30)	P-value
Age (years) [mean±SD]	36.01±8.21	37.09±13.03	36.16±13.27	0.500
Gender				
Male	20 (66.66)	23 (76.66)	18 (60)	0.505
Female	10 (33.34)	7 (23.34)	12(40)	

ASA				0.610
1	27 (90)	25 (83.34)	26 (86.66)	
2	3 (10)	8(16.66)	4 (13.34)	
Weight (mean ±SD)	65.25±2.58	65.35±1.64	65.95±2.02	0.450
Height (mean ±SD)	161.12±2.51	161.71±2.74	161.09±3.08	0.520
Duration of surgery (mean ±SD)	90.87±16.55	99.36±18.42	100.27±13.26	0.060

In the present study, male dominated in all the three groups as compared to females. The patients were more in ASA I as compared to ASA II.

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

Parameters	**Group A (n=30)**		**Group D (n=30)**		**Group F (n=30)**		**P-value**
Onset of sensory block (in min)	11.05	4.26	8.72	2.99	2.28	1.42	< 0.001
Duration of sensory block (in min)	115.63	7.15	206.17	6.42	163.32	12.74	< 0.001
Onset of motor block (in min)	11.21	3.77	8.89	3.64	3.55	1.39	< 0.001
Duration of motor block (in min)	161.04	6.42	253.29	6.62	186.88	11.16	< 0.001
Time taken to achieve for maximum sensory block (in min)	16.18	4.83	14.16	3.42	5.52	1.67	
Bromage Scale N (%)							
3: Inability to raise leg, flex knee or ankle or move toes	30	100	30	100	30	100	< 0.001

The mean time for onset of sensory block was 11.04 ±4.21 min in the saline group and 8.76±2.99 min in the dexmedetomidine group and 2.28±1.42 min in the fentanyl group. The mean time taken to achieve maximum sensory block in group A was 16.18±4.83 min, in group D was 14.16±3.42 min and in group F it was 5.52±1.67 min so maximum sensory block was achieved earlier in group. The mean duration of sensory block in group A was 115.63±7.15min, and in group F was 163.32±12.74min., and in group D was 206.17±6.42 min. Prolong duration occur in the dexmedetomidine 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 11.04±4.21 min, in group D it was 8.76±2.99 min, in group F it was 2.28 ±1.42 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 161.04±6.42 min, and in group D was 253.29±6.62 min and in group F it was 186.88±11.16 min.

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

Maximum sensory block attained	**Group A (n=30)**	**Group D (n=30)**	**Group F (n=30)**	**P-value**
T4 dense	0	0	2 (6.66)	< 0.001
T6 dense	0	5 (16.66)	22 (73.34)	
T8 dense	5 (16.66)	15 (50)	6 (20)	
T10 dense	25 (83.34)	10 (3.34)	0	

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.

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

Post-operative first analgesic requirement	No. (%)
Group A	
Intraoperative	12(40)
Post-operative recovery	9 (30)
0.5hr	9 (30)
Group D	
2 hr	2 (6.66)
3 hr	6 (20)
4 hr	14 (46.66)
6 hr	8 (26.66)
Group F	
Postoperative recovery room	3 (10)
0.5 hr	13 (43.34)
1 hr	9 (30)
2 hr	5 (16.66)

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

Post-operative first analgesic requirement	No. (%)
Group A	
4	10 (33.34)
5	15 (50)
6	5 (16.66)
Group D	
1	2 (6.66)
2	25 (83.34)
3	3 (10)
Group F	
1	3 (10)
2	5 (16.66)
3	22 (73.34)

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.

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.

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 the mean time for onset of sensory block was 11.04 ±4.21 min in the saline group and 8.76±2.99 min in the dexmedetomidine group and 2.28±1.42 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. Nayagam HA et al (2014) [13] 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 200915 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 statistically insignificant with p value of 0.12. [8]

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 [8] (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 115.63±7.15min, and in group F was 163.32±12.74min., and in group D was 206.17±6.42 min. Prolong duration occur in the dexmedetomiine group. 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 [14] in 2013 also stated the prolongation of the block in the dexmedetomidine.

In our study the mean onset time of motor block in group A was 11.04±4.21 min, in group D it was 8.76±2.99 min, in group F it was 2.28 ±1.42 min. 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.

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) [4] 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)19 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 201314 and R. Ahmed et.al in 2009. [15]

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 [16] 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 [17] Total morphine doses in 24 hours was significantly lower in the dexmedetomidine group as compared to fentanyl and control groups ($P < 0.05$). In the present study no patient had episode of respiratory depression. Vidhi Mahendru et al in 2013, [18] Rajani Gupta et al 2011 [4] in both the studies there was no evidence of respiratory depression. [19] 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 200915 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. [8]

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. Our study showed that the use of intrathecal dexmedetomidine as an adjuvant to Levobupivacaine seems it to be an attractive alternative to fentanyl and clonidine for long duration surgical procedures due to its profound intrathecal anesthetic and analgesic properties combined with minimal side effects. However, prolonged duration of motor blockade with dexmedetomidine may be undesirable for short‑term surgical procedures or ambulatory surgeries.

References

1. Elia N, Culebras X, Mazza C, Schiffer E, Tramèr MR. Clonidine as an adjuvant to intrathecal local anesthetics for surgery: systematic review of randomized trials. Regional anesthesia and pain medicine. 2008 Mar 1;33(2):159-67.
2. Grewal A. Dexmedetomidine: new avenues. Journal of anaesthesiology, clinical pharmacology. 2011 Jul;27(3):297.
3. Mantz J, Josserand J, Hamada S. Dexmedetomidine: new insights. European Journal of Anaesthesiology| EJA. 2011 Jan 1;28(1):3-6.
4. Verma R, Kohli M, Kushwaha J, Gupta R, Bogra J, Raman R. A Comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to Bupivacaine. J Anaesthesiol Clin Pharmacol 2011; 27 (3):339.
5. Borgeat A, Aguirre J. Update on local anesthetics. Curr Opin Anaesthesiol 2010;23(4):466–471.
6. Motiani P, Chaudhary S, Bahl N, Sethi a K. Intrathecal sufentanil versus fentanyl for lower limb surgeries - a randomized controlled trial. J Anaesthesiol Clin Pharmacol 2011; 27 (1):67–73.
7. Jamliya RH, Deshmukh V, Rajesh C, Maliwad J, Shah BJ, Shah MH. Effect of adding dexmedetomidine in intrathecal bupivacaine versus intrathecal bupivacaine alone on spinal block characteristics in orthopaedic lower limb procedures [A Comparative

Study]. Res J Pharm Biol Chem Sci 2013;4(1):1340–1346.
8. 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. American journal of applied sciences. 2009;6(5):882.
9. Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AKS, Murshidi MM, Ammari BA, Awwad ZM, et al. Effect of dexmedetomidine added to spinal bupivacaine for urological procedures. Saudi Med J 2009;30(3):365–370.
10. Kanazi GE, Aouad MT, Jabbour-Khoury SI, Al Jazzar MD, Alameddine MM, Al-Yaman R, et al. Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anaesthesiol Scand 2006;50(2):222–227.
11. Kamal MH, Ibrahim JH, Saaed AA, Zayed MS, Magdy M. Comparison of Intrathecal Dexmedetomidine and Fentanyl as Adjuvants to Levobupivacaine in Parturients Undergoing Elective Cesarean Sections. Med J Cairo Univ 2017;85 (2):593–600.
12. Shelly MP. Editorial I: Dexmedetomidine: a real innovation or more of the same? British Journal of Anaesthesia. 2001 Nov 1;87(5):677-8.
13. Nayagam HA, Ratan Singh N, Shanti Singh H. 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):430–435.
14. Basuni AS, Ezz HAA. Dexmedetomidine as supplement to low-dose levobupivacaine spinal anesthesia for knee arthroscopy. Egypt J Anaesth 2014;30(2):149–153.
15. Ahmad R. A Comparative Study of Intrathecal Low Dose Bupivacaine and Dexmedetomidine with Low Dose Bupivacaine and Fentanyl. IOSR J Dent Med Sci 2016;15(4):09–17.
16. Khan AL, Singh RB, Tripathi RK, Choubey S. A comparative study between intrathecal dexmedetomidine and fentanyl as adjuvant to intrathecal bupivacaine in lower abdominal surgeries: A randomized trial. Anesth essays Res 2015;9(2):139–148.
17. Safari F, Aminnejad R, Mohajerani SA, Farivar F, Mottaghi K, Safdari H. Intrathecal Dexmedetomidine and Fentanyl as Adjuvant to Bupivacaine on Duration of Spinal Block in Addicted Patients. Anesthesiol Pain Med 2016;6(1):1–8.
18. Mahendru V, Tewari A, Katyal S, Grewal A, Singh Mr, Katyal R. A comparison of intrathecal dexmedetomidine, clonidine, and fentanyl as adjuvants to hyperbaric bupivacaine for lower limb surgery: A double blind controlled study. J Anaesthesiol Clin Pharmacol 2013; 29 (4):496.
19. Al-Khafaji D. K. H., Al-Quzwiny K. Y. H., & Al-Daami Q. J. Analytical Implication of Cardiac Biomarkers in Patients with Acute Ischemic Stroke: A Cross-Section Study. Journal of Medical Research and Health Sciences. 2022; 5(8): 2145–2152.