Section: Anesthesiology

Original Research Article

COMPARATIVE STUDY OF EFFICACY OF INTRATHECAL FENTANYL, DEXMEDETOMIDINE AND FENTANYL-DEXMEDETOMIDINE COMBINATION AS ADJUVANTS TO 0.5% HYPERBARIC BUPIVACAINE FOR LOWER LIMB ORTHOPAEDIC SURGERY

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Abstract

Background: Lower limb surgeries use local, neuraxial, or general anaesthesia, with neuraxial blockade being preferred. Adjuvants such as dexmedetomidine and fentanyl improve spinal anaesthesia. This study aimed to assess the efficacy of intrathecal fentanyl, dexmedetomidine, and a combination of fentanyl-dexmedetomidine as an adjuvant to 0.5% hyperbaric bupivacaine in lower-limb orthopaedic surgery. **Material and Methods**: This prospective randomised study was conducted from October 2020 to October 2022, involving 84 patients undergoing lower-limb orthopaedic surgeries. Eighty-four patients were divided into three groups: Group BF, Group BD, and Group BDF, each consisting of 28 patients. Baseline vital parameters, such as pulse rate, respiratory rate, non-invasive blood pressure (NIBP), electrocardiogram (ECG), and pulse oximetry (SpO2), were recorded. Sensory block was evaluated using temperature perception, and pain was assessed using a visual analogue scale. **Results**: The study found that the maximum sensory level reached was T10 in 35.7% of BF cases, 53.6% of BD cases, and 39.3% of BDF cases, with significant differences in the time to reach T10, two-segment regression, modified Bromade III, and motor block regression. Dexmedetomidine added to bupivacaine significantly lowered postoperative VAS scores in all groups, with a significant reduction in the BD group compared to BF and BDF groups. Nausea was present in 10.7% of the BF cases, none of the BD cases, and 7.1% of the BDF group. Other complications include vomiting, bradycardia, and hypotension. **Conclusion**: Dexmedetomidine combined with bupivacaine offers faster sensory and motor analgesia, better haemodynamic stability, and intermediate postoperative analgesia, making it suitable for lower limb orthopaedic surgeries.

INTRODUCTION

Lower limb surgeries can be performed under local, neuraxial, or general anesthesia, with neuraxial blockade being the preferred method.[1] Lidocaine is the preferred local anesthetic due to its rapid onset and motor block; however, it has limitations and has been linked to transient neurologic symptoms and cauda equina syndrome.[1] Postoperative pain is a significant issue with local anesthetic drugs because of their limited duration of effect, necessitating additional postoperative analgesic administration. Combining local anesthetics with other analgesics, including opioids, can increase duration and pain relief, but also side effects.[1]

Some drugs have been used as adjuvants in spinal anesthesia to extend the duration of analgesia and reduce opioid use, including α2 agonists, neostigmine, vasoconstrictors, etc.[2] Clonidine and dexmedetomidine are two α2 agonists that act via pre- and post-synaptic α2 receptors.[2] Dexmedetomidine has gained widespread use for anesthesia and analgesia due to its sedative, anxiolytic, analgesic, neuroprotective, and anesthetic-sparing effects.[2] Dexmedetomidine, alongside other drugs, has been employed to extend

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the duration of analgesia in subarachnoid, epidural, and caudal blocks.[3] Fentanyl, a synthetic opioid with a central mode of action, is widely used for pain control. Intrathecal fentanyl is commonly added to local anesthetics to enhance anesthesia and analgesia. It has been shown to improve spinal anesthesia and reduce side effects related to anesthetic drugs.[3]

Both dexmedetomidine and fentanyl have been used as adjuvants to local anesthetics in various surgeries to provide superior pain relief and improve block duration.[4-6] A specific study demonstrated better efficacy of dexmedetomidine for lower limb surgeries.[7] The exact mechanism by which dexmedetomidine prolongs sensory and motor blockade remains unclear.[8] Dexmedetomidine is a highly selective α2-adrenergic receptor agonist that produces analgesia by suppressing the release of C-fiber transmitters and hyperpolarizing post-synaptic neurons.[8] Previous studies comparing dexmedetomidine with other drugs like clonidine, fentanyl, and sufentanil have reported a reduced need for postoperative analgesics, more stable hemodynamics, and a longer duration of sensory and motor block.[9] Additionally, in orthopedic surgeries of the lower limbs, dexmedetomidine has shown better results compared to fentanyl.[9]

Opioids in local anaesthetic solutions can cause side effects, such as pruritus and respiratory depression. Dexmedetomidine, a selective α2-agonist, is evaluated as a neuraxial adjuvant due to its stable hemodynamic conditions and prolonged postoperative analgesia. The FDA has approved this treatment for ICU patients. However, the mechanism underlying this prolongation is not well understood. Low doses of both dexmedetomidine and fentanyl can reduce adverse effects.

Aim

This study aimed to assess the efficacy of intrathecal fentanyl, dexmedetomidine, and a combination of fentanyl-dexmedetomidine as an adjuvant to 0.5% hyperbaric bupivacaine in lower-limb orthopaedic surgery.

MATERIALS AND METHODS

This prospective randomised study was conducted from October 2020 to October 2022, involving 84 patients aged 18-60 years undergoing lower-limb orthopaedic surgeries under spinal anaesthesia. The institutional ethics committee approved the study, and informed consent was obtained before initiation.

Inclusion Criteria

Adult patients who required lower limb surgery under spinal anaesthesia, ASA grade I or II classifications, aged between 18 and 60 years of either sex and weight within the range of 50 to 80 kg and a height between 150 and 180 cm, were included.

Exclusion Criteria

Patients undergoing emergency surgeries, particularly those with cardiovascular diseases, coagulopathy, known contraindications for spinal anaesthesia, drugs such as fentanyl, dexmedetomidine, and bupivacaine, pregnant women, and individuals with psychiatric disorders, who should be carefully evaluated for alternative anaesthesia methods due to potential risks and contraindications associated with spinal anaesthesia in these cases were excluded.

The spine was examined, and the L3–L4 space was identified. The patients were kept nil orally for 6 hours before surgery. Eighty-four patients were divided into three groups by random allocation using the closed envelope method, with each group having a constant total volume of 3 ml in constant. **Group BF:** 28 patients received 0.5% hyperbaric bupivacaine 12.5 mg [2.5 ml] plus fentanyl 25 mcg (0.5 ml). **Group BD:** 28 patients received 0.5% hyperbaric bupivacaine 12.5 mg [2.5 ml] plus dexmedetomidine (10 µg (0.1 ml) plus 0.4 ml normal saline. **Group BDF:** 28 patients received 0.5% hyperbaric bupivacaine 12.5 mg [2.5 ml] plus dexmedetomidine 5 mcg (0.05 ml) plus fentanyl 12.5 mcg (0.25 ml) plus 0.2 ml of normal saline.

We recorded and documented baseline vital parameters including pulse rate, respiratory rate, non-invasive blood pressure (NIBP), electrocardiogram (ECG), and pulse oximetry (SpO2). Intravenous access was established using an 18G cannula under aseptic precautions, and fluids were administered. A subarachnoid block was performed with a 25 G Quincke's needle at the L3–L4 space using a midline approach while the patient was in the left lateral position. Motor blockade was assessed using the Bromage scale, ranging from no block (inability to raise extended legs, knees, and feet) to three complete blocks. Sensory block was evaluated based on temperature perception, and pain was measured using a visual analogue scale.

Statistical Analysis

Descriptive statistics: Mean and standard deviation were calculated for each case. The normality of distribution was tested using the Shapiro-Wilk test, and ANOVA was applied if data were normally distributed. Otherwise, it is analysed as the data were analysed below by Statistical Package for Social Sciences - SPSS statistical package. The Kruskal-Wallis test was used to compare groups, and pairwise comparisons were performed with non-parametric tests, such as the Mann-Whitney test.

RESULTS

Eighty-four patients were divided into three groups: bupivacaine–fentanyl (BF), bupivacaine (BD), and bupivacaine–fentanyl–dexmedetomidine (BDF). The mean age of the BF group was 47.4 years, BD was 46.9 years, and BDF group was 47.8 years, which was statistically insignificant (p=0.964).

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Approximately 60.7% of the patients in the BF group, 57.1% in the BD group, and 64.3% in the BDF group were males, which was not statistically significant (p=0.861).

The mean weights of the BF group were 66.9 kgs, the BD group was 66.8 kgs, and the BDF group was 66.3 kgs, which was statistically insignificant (p=0.738). The mean height in the BF group was 155 cm, BD was 150.2 cm, and the BDF group was 149.6 cm, which was statistically insignificant (p=0.505). Approximately 78.6% of the BF group, 78.6% of the BD group, and 85.7% of the BDF group had ASA grade II, which was statistically insignificant (p=0.734). The maximum sensory level reached was T10 in 35.7% of BF, 53.6% of BD, and 39.3% of BDF cases, which was statistically significant (p=0.01). [Table 1]

The mean duration of surgery was 105.9 minutes in the BF group, 108.07 minutes in the BD group and 108.78 minutes in the BDF group, respectively, and the difference was statistically insignificant (p=0.346). The time to reach the T10 level was 5.0 minutes in the BF cases, 4.2 minutes in the BD group, and 4.6 minutes in the BDF group, which was statistically significant (p=0.027). The time for two-segment regression in the BF group was 10.0 minutes in the BF group, 13.46 minutes in the BD group and 10.5 minutes in the BDF group, which was statistically significant (p<0.0001).

The mean time to reach modified Bromage III was 7.78 minutes in the BF group, 6.25 minutes in the BD group and 7.57 minutes in the BDF group, which was statistically significant between the three groups (p<0.0001). The mean time to regression of motor block to modified Bromage I was 138.6 minutes in the BF group, 144.96 minutes in the BD group and 140.4 minutes in the BDF group, which was statistically significant (p=0.017). [Table 2]

Nausea was present in 10.7% of the patients in the BF group, none in the BD group, and 7.1% in the BDF group. The other complications included vomiting, bradycardia, and hypotension. [Table 3]

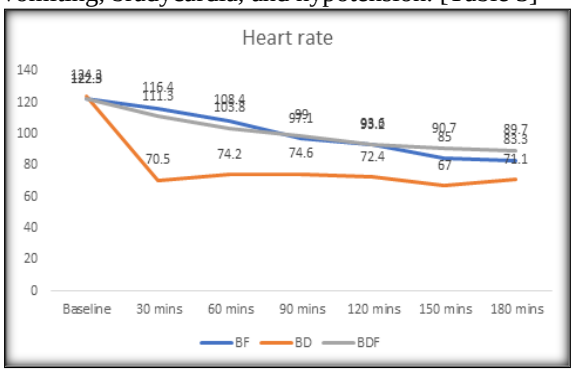

Figure 1: Heart rate between three groups

There was a statistically significant difference in baseline and at all follow-up time intervals except baseline, and the BD group had a significantly lower heart rate than the other two groups. [Figure 1]

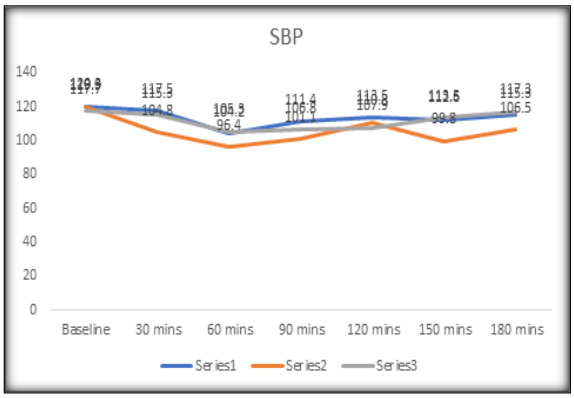

Figure 2: Systolic blood pressure between three groups

There was a statistically significant difference in systolic blood pressure between the BD, BF, and BDF groups at all-time intervals except the baseline. The BD group had comparatively lower systolic blood pressure (Figure 2).

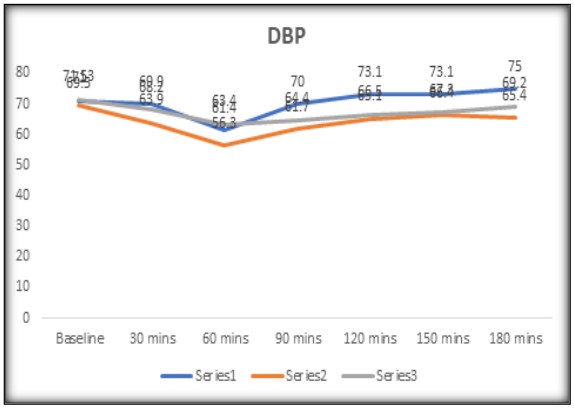

Figure 3: Diastolic blood pressure between three groups

There was a statistically significant difference in diastolic blood pressure at baseline at all-time intervals except at baseline. The BD group had comparatively lower blood pressure. [Figure 3]

There was a statistically significant difference in the VAS scores at all-time intervals. The BD group had lower VAS scores. Marginal significance was BF > BDF > BD. [Table 4]

Table 1: Demographic data of the study population

		BF	BD	BDF	P value
Age in years		47.4 ± 11.5	46.9 ± 11.5	47.8 ± 11.1	0.964
Sex	Male	17 (60.7)	16 (57.1)	18 (64.3)	0.861
	Female	11 (39.3)	12 (42.9)	10 (35.7)	
Weight (kgs)		66.9 ± 3.5	66.8 ± 3.4	66.3 ± 2.0	0.738

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Height (cm)		155.0 ± 2.7	150.2 ± 19.6	149.6 ± 25.8	0.505
ASA	I	6 (21.4)	6 (21.4)	4 (14.3)	0.734
	II	22 (78.6)	22 (78.6)	24 (85.7)	
Maximum sensory level reached	T4	0	3 (10.7)	3 (10.7)	0.01
	T6	9 (32.1)	1 (3.6)	1 (3.6)	
	T8	9 (32.1)	9 (32.1)	13 (46.4)	
	T10	10 (35.7)	15 (53.6)	11 (39.3)	

Table 2: Various findings among the three groups

	BF	BD	BDF	P value
Duration of Surgery	105.9 ± 10.2	108.07 ± 6.95	108.78 ± 5.02	0.346
Time to Reach T10 Level	5.0 ± 0.9	4.2 ± 1.1	4.6 ± 1.1	0.027
Time for two-segment regression sensory level	10.0 ± 1.0	13.46 ± 2.27	10.5 ± 1.4	0.000
Time to reach modified Bromage III	7.78 ± 1.1	6.25 ± 1.45	7.57 ± 1.62	0.000
Time to regression of motor block to modified Bromage I	138.6 ± 7.7	144.96 ± 7.58	140.4 ± 9.7	0.017

Table 3: Complications in the study population

Complications	BF n (%)	BD n (%)	BDF n (%)
Nausea	3 (10.7)	0	2 (7.1)
Vomiting	3 (10.7)	0	2 (7.1)
Bradycardia	0	5 (17.9)	2 (7.1)
Hypotension	1 (3.6)	5 (17.9)	3 (10.7)
Shivering	3 (10.7)	2 (7.1)	0

Table 4: VAS score data for the study population

VAS (hourly)	BF	BD	BDF	P value
4th	4.07 ± 0.64	3.79 ± 0.74	3.95 ± 0.79	0.04
8th	4.14 ± 0.87	3.87 ± 0.74	3.99 ± 0.47	0.04
12th	4.15 ± 0.87	3.80 ± 0.80	3.90 ± 0.72	0.01
24th	4.05 ± 0.87	3.77 ± 0.74	3.83 ± 0.52	0.02
Overall	4.10 ± 0.75	3.80± 0.77	3.91 ± 0.65	0.02

DISCUSSION

Spinal anaesthesia is simple to perform, uses small doses of drugs, offers rapid onset of action, and is a reliable surgical anaesthetic with good muscle relaxation. These advantages are sometimes offset by the relatively short duration of action and complaints of postoperative pain when the effect wears off. The efficacy of local anaesthetics can be enhanced using adjuvants, such as opioids, α2 agonists, magnesium, neostigmine, and ketamine. Prolonging the duration of the spinal block is desirable for long procedures and postoperative pain relief. Kim et al. observed that a fentanyl dose greater than 25 µg intrathecally produced no benefit in terms of the duration of analgesia. However, fentanyl 25 µg intrathecally with low-dose bupivacaine improved postoperative analgesia and haemodynamic stability.[10] Conversely, dexmedetomidine 3 µg with bupivacaine produced a shorter onset of motor blockade and prolonged motor and sensory block duration with haemodynamic stability and lack of sedation.[11] Gupta et al. observed that 5 µg dexmedetomidine with ropivacaine provided excellent postoperative analgesia with minimal side effects, and 5 µg dexmedetomidine seems to be an attractive alternative as an adjuvant to spinal bupivacaine. Intrathecal dexmedetomidine in doses of 10 µg and 15 µg significantly prolongs the anaesthetic and analgesic effects of spinal bupivacaine in a dose-dependent manner.[12,13]

In our study, we compared the effects of intrathecally administered fentanyl and dexmedetomidine with bupivacaine and bupivacaine on the time of onset, duration, haemodynamic profile, and side effects. The patients in the three groups did not show any statistically significant differences in age, sex, weight, ASA of Anesthesiologists classification, and type of surgery. Mazy et al.'s study showed that group DF's sensory block to the T10 level was faster. The motor block extended for approximately 6 hours without intergroup differences. Motor recovery precedes sensory recovery, in which patients may move their legs but tolerate surgery. The authors concluded that intrathecal dexmedetomidine 10 µg and bupivacaine 20 mg with or without fentanyl 25 µg were suitable for long orthopaedic procedures within 6 hours. The addition of fentanyl does not prolong the sensory and motor block characteristics of dexmedetomidine.[14] This was like our study wherein all the parameters studied favoured the use of dexmedetomidine alone as the combination with fentanyl did not hasten the onset or prolong the duration. However, in contrast to our study and many others, Mazy et al. found an earlier onset with the combination.[14]

Sun et al. conducted a systematic review and meta-analysis of randomised controlled trials to compare the effects of dexmedetomidine (Dex) and fentanyl as adjuvants to local anaesthetics in spinal anaesthesia.[15] The result of our study showed that the onset of sensory block was faster in the dexmedetomidine group compared to fentanyl and

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the combined groups. These differences were statistically significant. In contrast, several other studies in the meta-analysis showed no significant difference in the onset of sensory block between the two groups $p > 0.05$.[16-18]

In our study, the onset of both sensory and motor blocks was faster in the BD group than in the BF and BDF groups. This difference was statistically significant, indicating that the combination of both drugs did not hasten onset. Other studies have compared the onset time of motor block with dexmedetomidine and fentanyl as local anaesthetic adjuvants for intrathecal injection. The result showed that there was no significant difference between the two groups $p > 0.05$.[16,17,19] Our study time to reach the peak sensory level of T10 was less in the BD group than in the BF and BDF groups, and this difference was statistically significant ($p = 0.028$, $p < 0.05$). In contrast, a cumulative analysis of similar studies reported the time to peak sensory level, with 320 and 319 patients in the Dex and fentanyl groups, respectively, and the two groups had no significant differences ($p > 0.05$).[16,17,19]

In our study, the time taken for 2-segment regression in the dexmedetomidine group was significantly longer than that in the fentanyl and combined groups, indicating that the duration of the sensory block was longer with dexmedetomidine. Basuni et al. reported in the Dex group, it was 73.9 ± 13.9, and in the Fentanyl group, it was 64.9 ± 11.3, which was statistically significant in the duration of sensory block. Gupta et al. reported that in the Dex group, it was 4.9 ± 0.92, and in the fentanyl group, it was 5.1 ± 0.82, which was statistically significant for the duration of the sensory block. The duration of stable sensory block of the dexmedetomidine group was significantly higher than that of the fentanyl group; the difference was statistically significant $p < 0.01$.[16,19]

In our study, as the time to regression of motor block to modified Bromage I was significantly delayed in the BD group compared to the BF and BDF groups ($p = 0.017$), it can be concluded that dexmedetomidine provided a longer duration of motor block and that the addition of fentanyl was not advantageous. Similarly, Basuni et al. reported in the Dex group was 73.3 ± 8.5, and in the Fentanyl group was 64.2 ± 11.9, which was statistically significant ($p<0.01$). Mahendru et al. reported in the Dex group was 273.3 ± 24.6, and in the Fentanyl group was 196 ± 26.8, which was statistically significant ($p<0.01$). Gupta et al. reported a value of 421 ± 21 in the Dex group. In the Fentanyl group, it was 149.3 ± 18.2, which was statistically significant in the time to regression of motor block to modified Bromage I ($p<0.01$). The studies showed that dexmedetomidine as an adjuvant of local anaesthetics significantly prolonged the duration of sensory and motor block compared with fentanyl.[16,17,19]

In our study, the reduction was seen throughout 30 to 180 min in all groups, although this was significant only in the BD group compared to the other groups. Systolic blood pressure was significantly reduced from 5 min to 90 min intraoperatively in both the dexmedetomidine and dexmedetomidine + fentanyl groups compared with that in the control group ($p < 0.05$). There was a significant reduction in intraoperative diastolic blood pressure from 5 min to 20 min in the dexmedetomidine and dexmedetomidine + groups compared to the control group ($p < 0.05$). Our study only showed a statistically significant reduction in SBP and DBP in the BD group. Mohamed et al. found that there was a significant reduction in pulse rate starting at 20 minutes until 120 minutes in the dexmedetomidine + fentanyl group and starting at 20 minutes until 60 minutes in the dexmedetomidine group in comparison to the control group ($p < 0.05$).[20]

The postoperative VAS scores were significantly lower in the BD group than in the other groups. The mean VAS scores were 4.36 ± 0.83, 2.57 ± 1.17 and 4.78 ± 0.96, respectively, in the BF, BD, and BDF groups assessed at 4th, 8th, 12th, and 24 hours post-operatively, showing that dexmedetomidine added to bupivacaine significantly lowered the postoperative VAS scores. However, in the study by Mohamed et al., the mean VAS scores showed a reduction in both the dexmedetomidine group and the dexmedetomidine + fentanyl group in comparison to the control group ($p<0.05$) with no significant difference between the dexmedetomidine and dexmedetomidine + fentanyl groups.[20] In our study, nausea and vomiting were not observed in any of the cases in the BD group, while bradycardia and hypotension were observed in five patients in the BD group. This was not statistically significant, like the findings of other studies.[16,17,19]

CONCLUSION

Our study showed that dexmedetomidine added to bupivacaine provides a faster onset of sensory and motor analgesia with a longer duration of action than a combination of fentanyl and both drugs. Patients in the BD group had a higher incidence of hypotension and bradycardia. Better haemodynamic stability was observed in the BDF group. Postoperative analgesia was intermediate with BDF compared to that with BD and BF. The BDF combination can be preferred for lower limb orthopaedic surgeries as it has intermediate postoperative analgesia, intermediate motor and sensory blockade, and reduced side effects compared to the BD group. The BDF combination is as effective as intrathecal adjuvants for lower limb orthopaedic surgeries.

REFERENCES

1. Faiz SH, Rahimzadeh P, Sakhaei M, Imani F, Derakhshan P. Anesthetic effects of adding intrathecal neostigmine or magnesium sulphate to bupivacaine in patients under lower

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extremities surgeries. J Res Med Sci 2012;17. https://pubmed.ncbi.nlm.nih.gov/23825989/.
2. Shah A, Patel I, Gandhi R. Haemodynamic effects of intrathecal dexmedetomidine added to ropivacaine intraoperatively and for postoperative analgesia. Int J Basic Clin Pharmacol 2013; 2:26. https://doi.org/10.5455/2319-2003.ijbcp20130105.
3. Harsoor SS, Sudheesh K. Dexmedetomidine in anaesthesia practice: A wonder drug? Indian J Anaesth 2011; 55:323. https://doi.org/10.4103/0019-5049.84824.
4. Mohamed T, Susheela I, Balakrishnan B, Kaniyil S. Dexmedetomidine as adjuvant to lower doses of intrathecal bupivacaine for lower limb orthopaedic surgeries. Anesth Essays Res 2017; 11:681. https://doi.org/10.4103/aer.aer_243_16.
5. Khalifa OY, Saadalla AE. Influence of addition of dexmedetomidine or fentanyl to bupivacaine lumber spinal subarachnoid anaesthesia for inguinal hernioplasty. Anesth Essays Res 2017; 11:554. https://doi.org/10.4103/aer.aer_210_16.
6. Singh R, Farooq N, Sarkar A, Rasheed M, Choubey S. To evaluate the efficacy of fentanyl and dexmedetomidine as an adjuvant to ropivacaine in brachial plexus block: a double-blind, prospective, randomised study. Anesth Essays Res 2017; 11:730. https://doi.org/10.4103/aer.aer_30_17.
7. Mahendru V, Tewari A, Katyal S, Grewal A, Singh M, 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; 29:496. https://doi.org/10.4103/0970-9185.119151.
8. Yektaş A, Belli E. The effects of 2 μG and 4 μG doses of dexmedetomidine in combination with intrathecal hyperbaric bupivacaine on spinal anaesthesia and its postoperative analgesic characteristics. Pain Res Manag 2014; 19:75–81. https://doi.org/10.1155/2014/956825.
9. Gupta M, Gupta P, Singh DK. Effect of 3 different doses of intrathecal dexmedetomidine (2.5μg, 5μg, and 10 μg) on subarachnoid block characteristics: A prospective randomised double-blind dose-response trial. Pain Physician 2016; 19: E411-420. https://www.painphysicianjournal.com/current/pdf?article=MjYwMw%3D%3D&journal=95&utm_medium=email&utm_source=transaction.
10. Kim SY, Cho JE, Hong JY, Koo BN, Kim JM, Kil HK. Comparison of intrathecal fentanyl and sufentanil in low-dose dilute bupivacaine spinal anaesthesia for transurethral prostatectomy. Br J Anaesth 2009; 103:750–4. https://doi.org/10.1093/bja/aep263.
11. 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 blocks. Acta Anaesthesiol Scand 2006; 50:222–7. https://doi.org/10.1111/j.1399-6576.2006.00919.x.
12. Gupta R, Bogra J, Verma R, Kohli M, Kushwaha J, Kumar S. Dexmedetomidine as an intrathecal adjuvant for postoperative analgesia. Indian J Anaesth 2011; 55:347. https://doi.org/10.4103/0019-5049.84841.
13. Eid HE, Shafie MA, Youssef H. Dose-related prolongation of hyperbaric bupivacaine spinal anaesthesia by dexmedetomidine. Ain Shams J Anesthesiol. 2011; 4:83-95. https://www.semanticscholar.org/paper/Dose-Related-Prolongation-of-Hyperbaric-Bupivacaine-Eid-Shafie/d71f61399fd48cc61677c1f9ac5d3625ffcbdc94
14. Mazy A, Ghanem MA, Abd Elatif MSE, Basyoni YE. Spinal anaesthesia for lengthy lower limb orthopaedic surgeries: dexmedetomidine plus fentanyl versus dexmedetomidine. Ain-Shams J Anaesthesiol 2019;11. https://doi.org/10.1186/s42077-019-0024-z.
15. Sun S, Wang J, Bao N, Chen Y, Wang J. Comparison of dexmedetomidine and fentanyl as local anaesthetic adjuvants in spinal anaesthesia: A systematic review and meta-analysis of randomised controlled trials. Drug Des Devel Ther 2017; 11:3413–24. https://doi.org/10.2147/dddt.s146092.
16. Basuni AS, Ahmed Ezz HA. Dexmedetomidine as a supplement to low-dose levobupivacaine spinal anaesthesia for knee arthroscopy. Egyptian J Anaesth 2014; 30:149-53. http://doi.org/10.1016/j.egja.2013.11.003.
17. Mahendru V, Tewari A, Katyal S, Grewal A, Singh M, 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; 29:496. https://doi.org/10.4103/0970-9185.119151.
18. Nayagam H, Singh N, Singh H. A prospective randomised, double-blind study of intrathecal fentanyl and dexmedetomidine added to low-dose bupivacaine for spinal anaesthesia for lower abdominal surgeries. Indian J Anaesth 2014; 58:430. https://doi.org/10.4103/0019-5049.138979.
19. Gupta R, Verma R, Bogra J, Kohli M, Raman R, Kushwaha J. A Comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to bupivacaine. J Anaesthesiol Clin Pharmacol 2011; 27:339. https://doi.org/10.4103/0970-9185.83678.
20. Mohamed AA, Fares KM, Mohamed SA. Efficacy of intrathecally administered dexmedetomidine versus dexmedetomidine with fentanyl in patients undergoing major abdominal cancer surgery. Pain Physician 2012;15. https://pubmed.ncbi.nlm.nih.gov/22828688.