Comparison of Postoperative Analgesic Effect of Dexmedetomidine and Morphine as an Adjuvant to Intrathecal Bupivacaine in Infraumbilical Surgeries: A Randomised Clinical Trial

MURUGAPPAN ABHINAYA[1], RAMAMURTHY BALAJI[2], KARUNAKARAN MULLAINAYAKI[3], ANAND PUSHPARANI[4], GUNSEELAN MIRUNALINI[5]

ABSTRACT

Introduction: Regional anaesthesia is the standard technique for lower limb infraumbilical procedures. To provide a better analgesic profile, adjuvants are added to local anaesthetics to enhance their action. Opioids have been used as an adjuvant for a long-time. With evolving pharmacology, various drugs satisfy the criteria of being an adjuvant. One such drug is Dexmedetomidine, a novel alpha-2 agonist.

Aim: To compare the duration of analgesia of intrathecal Morphine and Dexmedetomidine as an adjuvant to bupivacaine in a subarachnoid block for lower limb infraumbilical surgeries.

Materials and Methods: In this randomised clinical, double-blinded study conducted in a multispecialty hospital over the period of June 2020 to February 2021, 70 patients were randomly divided into two groups: Group M received Morphine 125 µg, and Group D received dexmedetomidine 5 µg as an adjuvant to 15 mg of 0.5% hyperbaric bupivacaine. The primary outcome was to compare the duration of postoperative analgesia. The secondary results assessed the block characteristics, haemodynamic parameters, rescue analgesic consumption, sedation score, and side-effects like bradycardia, hypotension, nausea, vomiting, pruritus, and respiratory depression. Data was spread in an Excel sheet and descriptive analysis done.

Normally distributed continuous variables were compared using a Student's t-test, and discrete variables were compared using a Chi-square test. A p-value of <0.05 was considered significant.

Results: Both groups were similar with respect to age, sex, body mass index, American Society of Anaesthesiologists grading, and duration of surgery. The duration of analgesia was 956.97±120.043 minutes in group M and 392.83±50.354 minutes in group D (p-value <0.001). The total consumption of paracetamol was 1984.71±499.111 mg in group M and 3543.86±406.17 mg in group D. The onset and regression were significantly faster in group D. There was significant hypotension and bradycardia up to the 40th minute and an increase in heart rate, respiratory rate, and mean arterial pressure between 5-7 hours in group D. The sedation score was more in group D for the initial two hours. Postoperatively, the incidence of nausea, vomiting, and pruritus was more in group M.

Conclusion: It can be concluded that 125 µg of intrathecal morphine is a better adjuvant to spinal bupivacaine, providing excellent postoperative analgesia compared to 5 µg of intrathecal dexmedetomidine. However, dexmedetomidine had more incidence of hypotension, bradycardia, and sedation when compared to morphine intrathecally.

INTRODUCTION

Pain is an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage-Revised International Association for the Study of Pain (IASP) definition of pain (2020). Pain affects the patient's day-to-day activities, both physical and psychosocial [1]. Lower limb surgeries are usually performed using subarachnoid block and assessed using the Bromage scale [2]. Later modifications were made in the forthcoming years with drugs administered, their volume, the management of side-effects, and spinal anaesthesia emerged as a successful and safe form of anaesthesia. This dates to the history of spinal anaesthesia. It was found that there was a significant reduction in the rate of mortality and morbidity with neuraxial anaesthesia alone or in conjunction with general anaesthesia [3].

In order to provide a better analgesic profile, adjuvants are added to local anaesthetics to enhance their action. The onset and duration of intrathecal opioids depend on their lipophilic or hydrophilic nature. Morphine is a hydrophilic drug. An intrathecal opioid with higher hydrophilic nature [4] stays longer in the cerebrospinal fluid, spreads

in the cephalad direction, and exhibits delayed central action, especially more hydrophilic opioids like morphine. With evolving pharmacology, there are various drugs that satisfy the criteria of being an adjuvant. One such drug is dexmedetomidine, a novel alpha-2 agonist. It causes sedation and analgesia is because of the drug's interaction with receptors located in the locus coeruleus, and immense number of these receptors are also found in the spinal cord, especially at the substantia gelatinosa in the dorsal horn [5].

This study compares 5 µg of dexmedetomidine with 125 µg of morphine intrathecally to prolong the analgesic action of bupivacaine given intrathecally in orthopaedic lower limb surgeries. Adjuvants to bupivacaine in subarachnoid block for lower limb infraumbilical surgeries. The primary objective was to compare the duration of analgesia. The secondary objectives were to compare the motor and sensory onset and regression time, haemodynamic parameters, sedation score, quantity of rescue analgesic needed in the first 24 hours, Visual Analogue Scale (VAS) score at 4, 8, 12, and 24 hours, and the incidence of side-effects (bradycardia, hypotension, nausea, vomiting, pruritus, respiratory depression).

MATERIALS AND METHODS

This study was a randomised clinical trial conducted over a period of nine months between June 2020 and February 2021 on patients who underwent infraumbilical surgeries requiring spinal anaesthesia at SRM Medical College Hospital and Research Centre, Chennai, Tamil Nadu, India. After Institutional Ethics Committee (IEC) approval (2995/IEC/2021), CTRI registration (CTRI/2022/09/045775) and obtaining informed written consent for participation in the study, patients were recruited.

Inclusion criteria: Patients in the age group of 18-65 years with ASA Grade-I and II were included in the study.

Exclusion criteria: Patients with any contraindication for spinal anaesthesia were excluded from the study.

Sample size: According to the study by Qi X et al., [6], the standard deviations were s1=1.35 and s2=2.3, with a study power of 80%. Using the formula:

$$n = 2 \, Sd^2 \, \{Z(1-\alpha/2)+Z(1-\beta)\}^2/d^2$$

The calculated value of N was 28. Study included 35 patients in each group for the study. Initially, during the study design, a sample size of 64 was derived, but after starting the study, we rounded up 70 cases for the study was taken.

Patients were allocated to two groups based on computer-generated random assignments before the start of the study ([Table/Fig-1] CONSORT). Both the patients and operators (anaesthetists, intraoperative and postoperative observers, and recorders) were unaware of the group allocation. A third person not involved in the study prepared the medication solution. Group M, received 15 mg of 0.5% hyperbaric bupivacaine with 125 µg of preservative-free Morphine. Group D, received 15 mg of 0.5% hyperbaric bupivacaine with 5 µg of Dexmedetomidine. The volume of drug administered was made to 3.1 mL in both groups. Electrocardiography, pulse oximetry (SpO_2), and Non Invasive Blood Pressure (NIBP) were connected to the patient, and baseline values were documented. Under all aseptic precautions, the subarachnoid block was administered in a sitting position with a 25-gauge Quincke needle at the L3-L4/L4-L5 space by a midline approach. All groups received 15 mg of 0.5% hyperbaric bupivacaine with their respective adjuvants in 5 mL syringes.
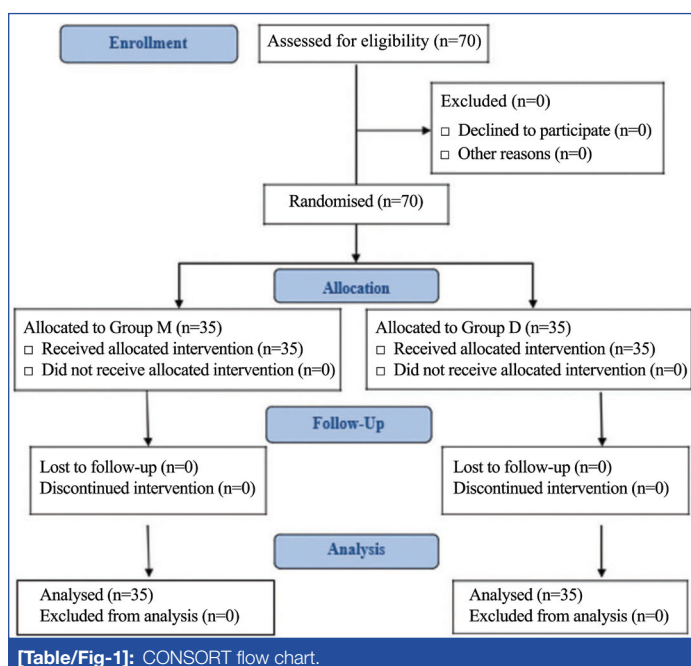
[Table/Fig-1]: CONSORT flow chart.

Immediately after the injection, patients were made to lie down in a supine position. The completion of the injection was taken as time zero for the induction of anaesthesia. An anaesthesiologist blinded to the group allocation and study drug recorded the observations.

The sensory level was monitored every minute for the initial 10 minutes, every five minutes for the next 20 minutes, and every 30 minutes thereafter until the end of the surgery using spirit-soaked gauze. The time for the onset of sensory blockade was noted. Motor blockade was assessed using the Bromage scale:

- Grade 0: No weakness, full power.

- Grade 1: Able to flex knees but unable to raise legs.

- Grade 2: Only foot movements.

- Grade 3: Complete paralysis.

The time taken to achieve Bromage Grade 3 was noted as the time for the onset of motor block. Sedation score was assessed as per modified Ramsay sedation score at the start of the surgery, hourly for the first 4 hours, and then every 4 hours until 24 hours. Visual Analog Scale (VAS) scores were also assessed at 4, 8, 12, and 24 hours.

Patients did not receive any premedication. All patients were preloaded with 10 mL/kg of Ringer lactate solution through an 18-gauge intravenous (IV) cannula half an hour prior to the procedure.

STATISTICAL ANALYSIS

All statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS, Version 25.0) for Microsoft Windows. Descriptive statistics, including mean, standard deviation, and frequency, were included. To compare categorical data, the Chi-square test was used, and for non categorical data, the Student's t-test was used. Non normally distributed data were analysed using the Mann-Whitney U test. The results were expressed with a 95% confidence interval. A p-value of <0.05 was considered statistically significant.

RESULTS

Both groups were similar with respect to age, sex, body mass index, American Society of Anaesthesiologists grading, and duration of surgery [Table/Fig-2].

Parameters	Group M	Group D	p-value
Age (Mean±SD) (years)	37.43±10.167	36.89±10.183	0.824*
Sex			
Male	26	24	0.597*
Female	9	11	
Weight (Mean±SD) (kg)	71.23±7.175	71.63±6.62	0.809*
Height (Mean±SD) (cms)	165. 66±7.436	166. 69±8.256	0.586*
BMI (Mean±SD) (kg/m²)	25.814±2.2639	25.426±2.0991	0.459*
ASA I	7	8	0.7656*
ASA II	28	27	
Duration of surgery (Mean±SD) (minutes)	56.33±17.22	50±13.65	0.1198*

[Table/Fig-2]: Comparison of demographic and duration of surgery.
Age, height, weight and duration of surgery analysed using Student's t-test; ASA and sex were analysed using Chi-square test; *=not significant, †=significant, ‡=highly significant

The onset of sensory blockade (from the time of injecting the drug into the subarachnoid space to the loss of pinprick sensation) in group M was significantly delayed compared to group D. The onset of motor blockade in group M (time taken to achieve Bromage Grade-3) was also significantly delayed compared to Group D [Table/Fig-3]. The duration of analgesia in group M patients was prolonged almost three times compared to group D patients, which was taken as the time to the first request for rescue analgesia.

VAS scores was noted at 4, 8, 12, and 24 hours in the present study. Scores were considerably higher in group D at the 4th and 8th hour. The difference was statistically significant with a p-value of 0.01 for both time points [Table/Fig-4].

Variables	Group M	Group D	p-value
Onset of sensory blockade (min)	5.17±0.618	2.4±0.497	<0.001‡
Onset of motor blockade (min)	6.83±0.857	3.71±0. 86	<0.001‡
Sensory blockade regression to S2 (hrs)	6.63±0.91	6.03±0.707	0.003‡
Motor blockade regression to Bromage 0 (hrs)	5.46±0.741	5±0.728	0.011†
Time for first rescue (duration of postop analgesia)	956.97±120.043	392.83±50.354	<0.001‡
Total amount of rescue analgesic-paracetamol (mg)	1984.71±499.111	3543.86±406.17	<0.001‡

[Table/Fig-3]: Comparison of block onset characteristic.
*=not significant; †=significant; ‡=highly significant

VAS	Group M	Group D	p-value
4 hrs	0.6±0.55	1.14±1.089	0.01†
8 hrs	1.57±0.884	2.15±0.99	0.025†
12 hrs	2.6±0.775	2.485±.701	0.582*
24 hrs	3.06±0.338	3±0.686	0.696*

[Table/Fig-4]: Comparison of VAS Score.
*=not significant; †=significant; ‡=highly significant

Sedation was monitored and documented as per Ramsay sedation score [Table/Fig-5].

Sedation score	Group M	Group D	p-value
At the start of surgery	3.0±0.2	2.7±0.2	0.1*
1 hrs	2±0	2.77±0.731	<0.001‡
2 hrs	2.03±0.169	3.06±0.765	<0.001‡
3 hrs	2.11±0.323	2.23±0.426	0.208*
4 hrs	2.17±0.453	2.17±0.453	1*
8 hrs	2.37±0.77	2.03±0.169	0.022†
12 hrs	3.09±0.284	2.97±0.296	0.105*
16 hrs	2±0.000	2±0.000	1*
20 hrs	3±0.000	3±0.000	1*
24 hrs	2±0.000	2±0.000	1*

[Table/Fig-5]: Comparison of Ramsay sedation Score.
*=not significant: †=significant; ‡=highly significant

Patients in group D were calmer during surgery with lower sedation scores in the 1st and 2nd hours compared to those in group M. The difference between the groups in the initial two hours with respect to sedation was found to be statistically significant. Although the sedation score was significantly higher in the dexmedetomidine group, none of the patients had a score of more than three requiring oxygen support. The need for rescue analgesics was significantly higher in the dexmedetomidine group compared to the morphine group. Group D had a significantly higher heart rate in the 5th to 7th hours compared to Group M. On statistical analysis of postoperative Mean Arterial Pressure (MAP) up to 24 hours using an unpaired t-test, there was an increase in MAP in the 5th and 7th hours in both Group M and Group D [Table/Fig-6,7]. No significant fall in saturation was observed during the observation period [Table/Fig-8]. Throughout the observation period, there was no significant difference between the groups with respect to respiratory rate except during the 5th, 6th, and 7th hours postoperatively [Table/Fig-9]. No major complications requiring treatment were observed in either group. Eight patients in group D experienced bradycardia, while this was observed in only one patient in group M. Among the study population, 28.90% of patients in group D had intraoperative hypotension, while 14.3% experienced this complication in group M. There was a significant difference between the two groups regarding nausea and pruritus [Table/Fig-10].

HR-post op	Group M	Group D	p-value
3 hrs	78.74±2.616	78.74±2.616	1*
4 hrs	78.29±2.652	78.29±2.652	1*
5 hrs	77.51±3.476	82.4±6.831	<0.001‡
6 hrs	77.17±2.955	90.57±11.753	<0.001‡
7 hrs	76.34±2.98	85.69±13.018	<0.001‡
8 hrs	78.54±3.776	77.86±2.788	0.39*
9 hrs	78.37±3.172	78.37±3.172	1*
10 hrs	77.63±2.669	77.63±2.669	1*
12 hrs	78.685±3.419	79.23±3.671	0.522*
14 hrs	76.94±2.645	77.09±2.79	0.818*
16 hrs	79.6±4.772	79±3.413	0.547*
18 hrs	79.23±4.833	79.74±5.249	0.673*
20 hrs	79.4±5.653	79.37±3.353	0.978*
22 hrs	80.29±5.954	80.06±4.795	0.859*
24 hrs	76.83±2.728	77.23±3.059	0.565*

[Table/Fig-6]: Comparison of heart rate between the groups.
*=not significant; †=significant: ‡=highly significant

MAP-post op	Group M	Group D	p-value
3 hrs	92.4±3.327	92.4±3.327	1*
4 hrs	90.31±2.908	90.57±2.627	0.699*
5 hrs	91.83±4.495	96.37±8.616	0.007‡
6 hrs	92.26±3.951	99.51±9.416	<0.001‡
7 hrs	91.74±3.364	98.2±12.35	0.004‡
8 hrs	92.94±3.819	93.8±5.016	0.424*
9 hrs	90.09±3.275	90.26±3.372	0.83*
10 hrs	92.2±4.136	92.2±4.136	1*
12 hrs	91.51±3.883	91.83±4.069	0.737*
14 hrs	93.91±7.797	91.34±4.498	0.096*
16 hrs	92.31±4.136	92.63±3.905	0.763*
18 hrs	94.11±8.774	93.4±7.072	0.71*
20 hrs	93.69±7.36	93.89±6.57	0.905*
22 hrs	90.63±2.498	90.86±2.767	0.716*
24 hrs	91.29±5.534	91.29±5.222	1*

[Table/Fig-7]: Comparison of mean arterial pressure between the groups
*=not significant: †=significant: ‡=highly significant

SpO2-intraop	Group M	Group D	p-value
3 hrs	99.97±0.169	99.97±0.169	1*
4 hrs	99.91±0.284	99.86±0.355	0.46*
5 hrs	99.91±0.284	99.86±0.43	0.514*
6 hrs	99.83±0.382	99.77±0.426	0.557*
7 hrs	99.8±0.473	99.8±0.473	1*
8 hrs	99.83±0.453	99.74±0.561	0.484*
9 hrs	99.89±0.323	99.69±0.631	0.1*
10 hrs	99.71±0.622	99.83±0.514	0.405*
12 hrs	99.83±0.514	99.83±0.453	1*
14 hrs	99.91±0.284	99.83±0.514	0.391*
16 hrs	99.94±0.236	99.86±0.43	0.305*
18 hrs	99.94±0.236	99.89±0.323	0.4*
20 hrs	99.83±0.514	99.8±0.406	0.797*
22 hrs	99.89±0.323	99.91±0.284	0.695*
24 hrs	99.91±0.284	99.89±0.323	0.695‡

[Table/Fig-8]: Comparison of Saturation between the groups
*=not significant: †=significant: ‡= highly significant

RR-intra op	Group M	Group D	p-value
3 hrs	14.11±0.963	14.11±0.963	1*
4 hrs	13.57±0.85	13.57±0.85	1*
5 hrs	13.89±0.758	14.94±2.155	0.008‡
6 hrs	13.8±0.901	16.23±2.315	<0.001‡
7 hrs	13.91±0.887	15.23±2.402	0.003‡
8 hrs	14.09±0.951	14.34±1.494	0.393*
9 hrs	13.94±0.802	13.94±0.802	1*
10 hrs	13.8±0.901	13.83±0.923	0.896*
12 hrs	13.91±1.197	14.09±1.442	0.571*
14 hrs	14.17±1.706	14.09±1.56	0.827*
16 hrs	13.43±0.85	13.74±1.094	0.19*
18 hrs	14.49±1.946	15.49±2.748	0.083*
20 hrs	14.43±1.975	14.14±1.556	0.504*
22 hrs	13.66±0.802	13.71±0.957	0.813*
24 hrs	13.51±1.011	13.51±1.095	1*

[Table/Fig-9]: Comparison of respiratory rate between the groups
*=not significant: †=significant: ‡= highly significant

Complications		Group M n (%)	Group D n (%)	p-value
Bradycardia	Yes	1 (2.9%)	8 (22.9%)	0.012435
	No	34 (97.1%)	27 (77.1%)	
Hypotension	Yes	3 (14.3)	8 (22.9%)	0.1005
	No	32 (85.7%)	27 (77.1%)	
Nausea/Vomiting	Yes	4 (11.40)	0	0.039†
	No	31 (88.60)	35 (100.00)	
Pruritus	Yes	8 (22.90)	0	0.003‡
	No	27 (77.10)	35 (100.00)	
Respiratory Depression	Yes	0	0	x
	No	35 (100)	35 (100)	

[Table/Fig-10]: Comparison of postoperative complications
*=not significant: †=significant: ‡=highly significant; Values are mean±SD; #p-value are statistically significant <0.05

DISCUSSION

A wide variety of drugs have been used as additives in spinal anaesthesia, with opioids being the most common. However, their advantages come with complications like urinary retention, respiratory depression, pruritus, and an increase in postoperative nausea and vomiting. Alpha-2 agonists, as additives, are known to cause bradycardia and hypotension [6]. Intrathecal dexmedetomidine activates α2-adrenergic receptor, leading to strong analgesic properties through the inhibition of spinal α2-AR by intrathecal injection of dexmedetomidine, displaying strong analgesic properties via the inhibition of the spinal ERK1/2 signaling pathway. In-vitro experiments indicated that dexmedetomidine might act as a preventer of local anaesthetics-induced neurotoxicity when used together with local anaesthetics [7,8].

The present study aimed to compare the duration of analgesia of intrathecal morphine and dexmedetomidine as adjuvants to bupivacaine in a subarachnoid block for lower limb infraumbilical surgeries. In the current study, 125 µg of morphine was used as an additive to intrathecal hyperbaric bupivacaine. The duration of analgesia was 956.97±120.043 minutes in group M and 392.83±50.354 minutes in group D (p-value <0.001). In the study conducted by Ashfi S et al., they studied the effect of intrathecal morphine 150 µg with intrathecal dexmedetomidine 5 µg in 60 patients, and they found that the time to request rescue analgesia was longer with dexmedetomidine (408.83±45.2) compared to morphine 150 µg (286.88±30.0) [9].

The present study showed that the morphine group had a delayed onset of sensory and motor blockade, although the dosages used by them were different (2.5 µg dexmedetomidine and 250 µg morphine) and they performed the lumbar puncture procedure in the right lateral position in their study. In the study conducted by Kurhekar P et al., they compared 250 µg morphine and 2.5 µg dexmedetomidine as adjuvants in a subarachnoid block [10]. In their study, the sensory onset time to the T10 level was significantly earlier in the dexmedetomidine group, whereas the time to attain Bromage 3 was comparable between the groups. The reason may be that high water-soluble morphine takes time to get absorbed into the nerve fibers at the same time staying longer in the nerves, thereby prolonging the duration of action.

The first rescue analgesia, paracetamol, was given when the VAS score was more than 4. In the present study, paracetamol consumption was more than three times higher compared to the morphine group. The morphine group had more incidence of nausea, vomiting, and pruritus. Sedation score and respiratory rate were comparable between the groups. Patients in group D were calmer during surgery with sedation scores of 2.03±0.169 and 3.06±0.765 in the first postoperative hour compared to those in group M [Table/Fig-5]. This may be explained by the better analgesic profile of intrathecal morphine compared to dexmedetomidine. During the rest of the observation period, sedation was comparable between the groups and the patients were cooperative. Samal S et al., in their study, documented shivering as another significant complication in the morphine group, while this was not observed in the present study [11]. There was no incidence of respiratory depression in either of the groups, confirming the results of studies proving that respiratory depression is negligible with intrathecal morphine doses less than 300 µg.

A meta-analysis on intrathecal dexmedetomidine with bupivacaine is known to increase the duration of sensory block, motor block, and analgesia. It also appears to be safe with no increased risk of bradycardia or hypotension. It is also associated with decreased postoperative shivering [12,13]. Present study also proves that intrathecal dexmedetomidine is safe, and when compared to morphine, present study showed that morphine has a prolonged duration of action than dexmedetomidine.

Limitation(s)

The present study has the following limitations, like absence of a control group and the exclusion of elderly patients aged over 65 years, in whom side-effects can be more pronounced, was a lacuna. Continued patient-controlled spinal analgesia, where patients can be mobile while being pain-free under the vigilant supervision of an anaesthesiologist, will be a routine in the future.

CONCLUSION(S)

The study concludes that 125 µg of intrathecal morphine proves to be a better adjuvant, providing excellent postoperative analgesia compared to 5 µg of intrathecal dexmedetomidine when added to 15 mg of 0.5% hyperbaric bupivacaine in a subarachnoid block with stable haemodynamics. In the future, further studies are needed using various dosages of dexmedetomidine and morphine as additives to hyperbaric bupivacaine.

REFERENCES

[1] Raja SN, Carr DB, Cohen M, Finnerup NB, Flor H, Gibson S, et al. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. Pain. 2020;161(9):1976-82.
[2] Rasheed AM, Amirah MF, Abdallah M, Parameaswari PJ, Issa M, Alharthy A. Ramsay sedation scale and richmond agitation sedation scale: A cross-sectional study. Dimens Crit Care Nurs. 2019;38(2):90-95.
[3] Johnson RL, Kopp SL, Burkle CM, Duncan CM, Jacob AK, Erwin PJ, et al. Neuraxial vs general anaesthesia for total hip and total knee arthroplasty: A systematic review of comparative-effectiveness research. Br J Anaesth. 2016;116(2):163-76.
[4] Cummings K, Naguib MA. Opioid Agonist and Antagonists, In: Chapter 7. 5th edition. Stoeltings Pharmacology and physiology in anaesthetic practice. Philadelphia: Wolters Kulwer Health; 2015. Pp. 217-29.

[5] Gertler R, Brown HC, Mitchell DH, Silvius EN. Dexmedetomidine: A novel sedative-analgesic agent. Proc (Bayl Univ Med Cent). 2001;14(1):13-21.

[6] Qi X, Chen D, Li G, Huang X, Li Y, Wang X, et al Comparison of intrathecal dexmedetomidine with morphine as adjuvants in cesarean sections. Biol Pharm Bull. 2016;39(9):1455-60.

[7] Staikou C, Paraskeva A. The effects of intrathecal and systemic adjuvants on subarachnoid block. Minerva Anestesiol. 2014;80(1):96-112.

[8] Zhang H, Zhou F, Li C, Kong M, Liu H, Zhang P, et al. Molecular mechanisms underlying the analgesic property of intrathecal dexmedetomidine and its neurotoxicity evaluation: An in vivo and in vitro experimental study. PloS one. 2013;8(2):e55556.

[9] Ashfi S, Haque A, Kumar M, Lakra L. A comparative study of intrathecal hyperbaric bupivacaine 0.5% with morphine and dexmedetomidine in lower limb orthopedic surgeries: A double-blind randomized clinical trial. Anesth Essays Res. 2022;16(3):373-77.

[10] Kurhekar P, Kumar SM, Sampath D. Comparative evaluation of intrathecal morphine and intrathecal dexmedetomidine in patients undergoing gynaecological surgeries under spinal anaesthesia: A prospective randomised double blind study. Indian J Anaesth. 2016;60(6):382-87.

[11] Samal S, Pattnaik SK, Mohta A, Jena SK. Intrathecal dexmedetomidine versus morphine as adjuvant to bupivacaine in elective LSCS: A comparative study. Indian J Clin Anaesth 2016;3(4):607-10.

[12] Kumar S, Choudhury B, Varikasuvu SR, Singh H, Kumar S, Lahon J, et al. A systematic review and meta-analysis of efficacy and safety of dexmedetomidine combined with intrathecal bupivacaine compared to placebo. Cureus. 2022;14(12):e32425.

[13] Gehling M, Tryba M. Risks and side-effects of intrathecal morphine combined with spinal anaesthesia: A meta-analysis. Anaesth. 1259;64(6):643-51.

PARTICULARS OF CONTRIBUTORS:
1. Postgraduate Student, Department of Anaesthesiology, SRM Institute of Science and Technology, Chennai, Tamil Nadu, India.
2. Professor, Department of Anaesthesiology, SRM Institute of Science and Technology, Chennai, Tamil Nadu, India.
3. Postgraduate Student, Department of Anaesthesiology, SRM Institute of Science and Technology, Chennai, Tamil Nadu, India.
4. Professor, Department of Anaesthesiology, SRM Institute of Science and Technology, Chennai, Tamil Nadu, India.
5. Assistant Professor, Department of Anaesthesiology, SRM Institute of Science and Technology, Chennai, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Anand Pushparani,
F2, No. 16, Meenakshi Flats, Officers Colony, First Street, Adambakkam,
Chennai-88, Tamil Nadu, India.
E-mail: pushpa82_dr@yahoo.com

AUTHOR DECLARATION:
• Financial or Other Competing Interests: None
• Was Ethics Committee Approval obtained for this study?   Yes
• Was informed consent obtained from the subjects involved in the study?   Yes
• For any images presented appropriate consent has been obtained from the subjects.   NA