ORIGINAL ARTICLE

Indian Journal of Anesthesia and Analgesia
Volume 11 Number 4 October - December 2024
DOI: http: //dx.doi.org/10.21088/ijaa.2349.8471.11424.2

Comparison of Two Different Doses of Dexmedetomidine as an Adjuvant in Spinal Anaesthesia to Bupivacaine for Abdominal Hysterectomy

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How to cite this article:
Yash Patel, Bina P Butala, Sarla Baria, *et al*. Comparison of Two Different Doses of Dexmedetomidine as an Adjuvant in Spinal Anaesthesia to Bupivacaine for Abdominal Hysterectomy. Ind J Anesth Analg. 2024; 11(4):185-191.

Abstract

Background and Aim: Lower abdominal surgeries today are done preferentially under subarachnoid block. The relatively short duration of analgesia is a limiting factor which is overcome by adding an adjuvant to intrathecal bupivacaine.Adjuvants have been helpful in induction of early ambulation but at the cost of their associated adverse effects. We aimed to compare two different doses of dexmedetomidine as adjuvant to 0.5% hyperbaric Bupivacaine in abdominal hysterectomy.

Material and Methods: It was a prospective, double-blind study among 60 patients posted for abdominal hysterectomy under spinal anaesthesia. The patients were randomly allocated to 2 groups (Group D1 and Group D2) of 30 each. Group D1 received hyperbaric Bupivacaine (15 mg) with Dexmedetomidine (5 µg). Group D2 received hyperbaric bupivacaine (15 mg) with Dexmedetomidine (10 µg). The onset time of sensory and motor block, regression time of sensory and motor block, duration of analgesia, hemodynamic parameters were recorded both intra and postoperatively. The primary efficacy parameters were to determine the onset and duration of sensory block, motor block and duration of postoperative analgesia. Secondarily any associated hemodynamic changes and adverse effects of Dexmedetomidine were also recorded.

Results: Onset of sensory block was 3.16 ± 0.37 minutes in Group D2 as compared to 4.80 ± 0.74 minutes in Group D1 with total duration of sensory block as 355.35 ± 11.83 minutes in Group D2 and 257.77 ± 18.43 minutes in Group D1. Similarly, the onset of motor block was 4.12 ± 0.34 minutes and 4.74 ± 0.71 minutes, with total duration of motor block as 324.67 ± 22.15 minutes and 225.41 ± 17.20 minutes in Group D2 and in Group D1 respectively. Duration of analgesia was360.19 ± 16.38 minutes with Dexmedetomidine 10 µg but 302.06 ± 17.36 minutes in Dexmedetomidine 5 µg group.

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Received on: 17.05.2024

Accepted on: 18.06.2024

Conclusions: Addition of 10 µg of Dexmedetomidine to 0.5% hyperbaric Bupivacaine 15mg (3 mL) in spinal anaesthesia significantly decreases the onset time, prolongs the duration of both sensory and motor blockade, improves the quality of postoperative analgesia with better hemodynamic stability as compared to bupivacaine with 5 µg Dexmedetomidine

Keywords: Bupivacaine, Dexmedetomidine, Postoperative analgesia, Subarachnoid block

INTRODUCTION

Anaesthesiologists constantly strive to offer the best possible anaesthetic technique with emphasis on minimum adverse effects and satisfactory perioperative analgesia. A pain free and stress-free postoperative period helps in early mobilization and recovery of patients thereby reducing morbidity.

Spinal subarachnoid block is still the first choice anesthesia in lower abdominal and lower limb surgeries because it blunts the "stress response" to surgery and decreases intraoperative blood loss and the incidence of postoperative thromboembolic events.[1] However, postoperative pain control is a matter of concern with spinal anaesthesia using only local anaesthetics as analgesic effect lasts for a relatively short duration. Various adjuvants such as opioids, epinephrine, neostigmine, magnesium, ketamine, and clonidine have been used with intrathecal local anaesthetics in attempts to prolong analgesia and reduce the incidence of adverse effects.[2,3]

Recently, α_2 adrenergic receptor agonists have gained popularity as an important adjuvant in anaesthetic practice.[4] They cause stimulation of prejunctional inhibitory α_2-Adrenoreceptors and thus have a sympatholytic effect. Inhibition of central neural transmission in the dorsal horn by pre and post sympathetic neurons. They also have direct sympatholytic effect on spinal preganglionic sympathetic neurons.

These alpha agonist have sedative, anxiolytic and analgesic properties which are beneficial in clinical use. As compared to opioid adjuvants they also cause minimal respiratory depression, pruritis and urinary retention. Dexmedetomidine has an affinity for the α_2 receptor more than 7 times greater than clonidine with a shorter distribution and elimination half-life. These properties make dexmedetomidine an attractive option to use as adjuvants in spinal anaesthesia.[5,6]

AIM

This study aims to compare two different doses of Dexmedetomidine as intrathecal adjuvants to Spinal anaesthsia in women undergoing Abdominal hysterectomy for benign indications. assessing the duration of analgesia and peri-operative events for 24 hours comprised the secondary objectives.

MATERIAL AND METHODS

After obtaining approval from Institutional Review Committee, a comparative study was conducted at the setting of an operating room and post-anaesthesia care unit of a teaching hospital. Informed written consent was taken from participants during pre-anaesthetic checkup performed a day before surgery. Women admitted to our hospital for undergoing elective abdominal hysterectomy for benign indications were the source of our participants.

All the participants were thoroughly informed about the importance of immediate reporting of pain to receive analgesics. Specifically, they were instructed to notify any discomfort, anxiety, nausea, and pain during surgery.

PATIENT CRITERIA

Patients willing to give consent, age between 18-40 years and those who met with American society of anesthesiology (ASA) grade I or II were included in the study. Patients with following conditions were excluded-Patients refusing to involve in the study, Patients with American society of anesthesiology (ASA) grade III or IV, Patients with congenital coagulopathy or anatomical abnormalities, Patients with coagulopathy or those on anti-coagulant treatment, Patients with history of allergy to study drug, Patients with infection at the site of injection and Patients with neurological and psychiatric disorders.

SETTINGS AND DESIGN

Sample size was calculated using epi info software version 7, assuming that power is 80 % and alpha-error was 0.05 and the percentage of unexposed with outcome is 5% so sample size is 58, so we included 60 patient for this study. We randomly divided sample population in two groups of 30, Group D1 and Group D2 each group having of Dexmedetomidine Hydrochloride 5 µg (Group D1) and 10µg (Group D2) as an adjuvant to Bupivacaine 15mg.

Using all aseptic conditions, spinal anaesthesia was performed in a sitting position at the level of L3–L4 through a midline approach using a 25-gauge Quincke spinal needle. The time of intrathecal injection was be noted, and monitoring of clinical parameters, VAS, and any side effects were observed. The onset of sensory block was assessed bilaterally in the midclavicular line by assessing the changes in pinprick sensation with hypodermic needle until no sensation is achieved at dermatome level T10.

Normal sensation, grade 0

Blunted sensation, grade 1

No sensation,

Grade 2; will be taken at the onset of the sensory block.

The highest dermatome level of sensory block and time taken to achieve the highest level of sensory block was noted. The onset of motor block was assessed till complete motor block (grade 3) is achieved, according to the Bromage scale in the limbs. Duration of motor block was assessed by the time taken to regress from maximum Bromage motor block to scale 0.

Visual analogue scale for pain: pain to be assessed using a standard 10 visual analogue score (VAS).

VAS Numeric Pain Distress Scale was recorded before the start of the procedure and postoperative until the patient demands IM/IV analgesia.

assessment of sedation will be done using the Ramsay Sedation Scale. Intra-operative monitoring of pulse, spo2, NIBP and ECG was done every 5 min for the first 30 min, every 10 min for the next 60 min, every 15 min upto 150 min, and every 60 min thereafter till the completion of the surgical procedure.

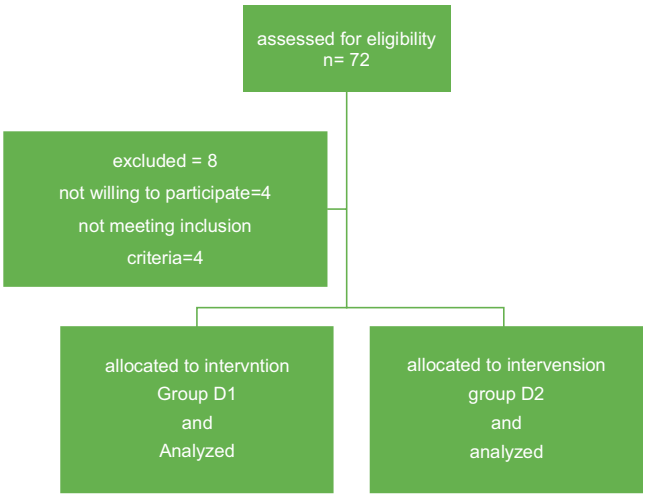
Postoperative non-invasive monitoring of vitals will be done four hourly.

STATISTICAL ANALYSIS

Data was entered into MS excel sheet and analyzed using SPSS software. Qualitative data was described as frequency and percentage and analyzed using Chi Square test. Quantitative data was described as Mean and Standard Deviation and analyzed using an Unpaired t-test. P- value less than 0.05 considered as statistically significant.

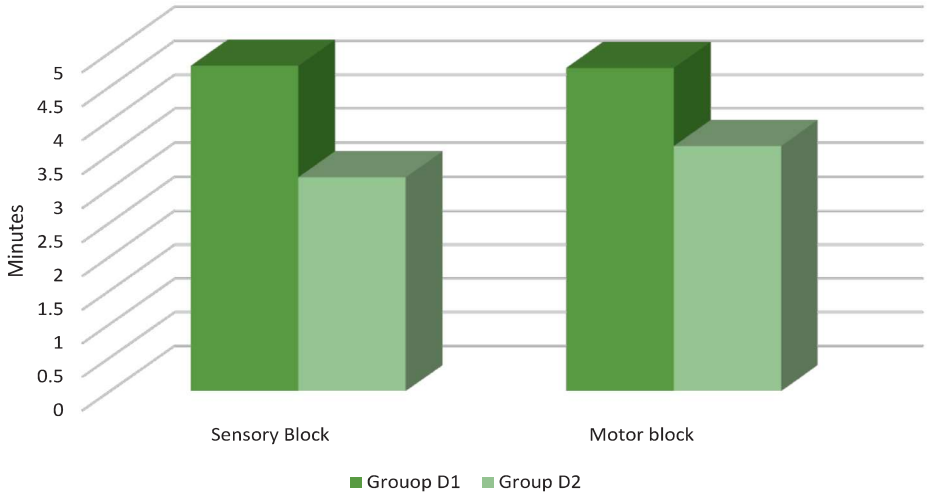
RESULTS

Seventy-two potentially eligible patients were examined in the study duration. Four patients were excluded because of not meeting inclusion criteria and Four patients denied the consent. Sixty patients were randomized in the study in whom SA was easily performed. There was no block failure and peak sensory block level reached the median of T4 in both groups.



The mean time of onset of sensory block in group D2 was 3.16 ± 0.37 min and in group D1 was 4.80 ± 0.74 min, which was significantly (p<0.001) faster in group 2. The mean onset of motor blockade was also statistically significant in group D2 (3.62 ± 0.26 min) as compared to group D1 (4.77 ± 0.71min)

chart 1 : onset of block



The mean duration of sensory block in Group D2 was 355.35 ± 11.83 minutes and in Group D1 was 257.77 ± 18.43 minutes. Mean duration of motor recovery in Group D2 was 324.67 ± 22.15 minutes and Group D1 was 225.41 ± 17.20 minutes which was also statistically significant (p<0.001).

Though there were statistically significant variations over time within a group, vital parameters (HR, SBP, DBP, MAP, and RR) remained comparable between study groups at all assessment time points, namely at 0, 5, 10, 15, 30, and 120 minutes into the operation. These data have been shown in the table.

Table 1: Hemodynamic parameters. Data represented as Mean±SD

Time interval	Heart rate		Systolic bp		Diastolic bp	
	Group D1	Group D2	Group D1	Group D2	Group D1	Group D2
0	82.12 ± 1.5	83.06 ± 1.6	114.38 ±3.29	115.06 ± 3.0	82.25 ± 1.5	81.90 ± 1.3
5	79.12 ± 1.8	78.67 ± 1.8	110.51 ± 3.6	115.06 ± 3.0	78.25 ± 2.3	75.93 ± 3.0
10	75.66 ± 3.0	73.51 ± 2.9	108.12 ± 2.8	108.51 ± 2.8	76.80 ± 3.0	74.12 ± 3.3
15	75.12 ± 2.7	70.32 ± 3.1	106.03 ± 2.3	106.29 ± 2.0	72.19 ± 3.6	67.83 ± 4.7
20	73.25 ± 2.8	72.54 ± 3.2	102.06 ± 2.1	101.77 ± 2.4	70.64 ± 3.8	63.90 ± 4.1
30	75.48 ± 3.0	73.54 ± 3.8	104.70 ± 1.8	101.74 ± 1.3	73.93 ± 3.9	67.22 ± 5.1
120	77.25 ± 3.0	81.64 ± 3.7	114.4 ± 3.1	114.45 ± 2.6	84.25 ± 2.0	82.09 ± 4.7

A statistically significant difference in duration wof complete analgesia was observed between the wtwo groups Group II 360 ± 20.6 minutes and Group I 302.67± 17.36 minutes.(Table 2)

Table 2: Mean Comparison of Various Parameters

Variables	Group D1	Group D2	P value
Mean time of onset of the sensory block	4.80 ± 0.74	3.16 ± 0.37	<0.001
Mean time of onset of the motor block	4.74 ± 0.71	4.12 ± 0.34	<0.001
Mean duration of sensory block	257.77 ± 18.43	355.35 ± 11.83	<0.001
Mean duration of motor block	225.41 ± 17.20	324.67 ± 22.15	<0.001
Duration of analgesia	302.06 ± 17.36	360.19 ± 16.38	<0.001
Rescue analgesia	298.03 ± 16.81	359.06 ± 16.11	<0.001

Intraoperative Visual Analogue Score was <3 in both the groups, at the end of 4 hours postoperatively, it was 2.51 and 3.51 in Group D2 and Group D1 respectively. But at the end of 6 hours VAS was 2.67 and 3.7 in Group D2 and Group D1 wwrespectively where rescue medication was started for Group D1. Twelve hours postoperatively the scores were 6.3 and 6.8 in Group D2 and Group respectively. VAS values were significantly lower wup to 3 and 6 hours postoperatively in Group D2 implying patients had better pain relief in the postoperative period than in Group D1. (Table 3)

Table 3: Postop Vas Score

Time	Group D1	Group D2
4 hr	3.51 ± 1.20	2.51 ± 1.12
6 hr	3.70 ± 1.29	2.67 ± 1.11
12 hr	6.82 ± 1.23	6.30 ± 1.14

Group II, 15.52% patient experienced hypotension, 12.51% had bradycardia, 3.25% had nausea/vomiting and 3.20% shivering when compared to Group I in which 6.25 had hypotension, 12.5% had bradycardia, 3.25% had nausea/vomiting and 15% had shivering (Table 4). There was no respiratory depression and sedation in both the groups.

Table 4: Adverse effects

Adverse effect	Group D1	Group D2
Bradycardia	5	4
Hypotension	2	5
Sedation (Ramsay hunt score >2)	0	0
Nausea/vomiting	1	0
Shivering	5	4
Respiratory depression	0	0

DISCUSSION

α-2-adrenoceptor agonists are being currently explored in anaesthetic field for their sedative, analgesic, sympatholytic, anaesthetic-sparing and favorable haemodynamic properties. Dexmedetomidine, is one such agonist having a relatively high α2/α1-activity ratio (1620:1) as compared to clonidine (220:1). It's also unique that it lacks respiratory depressant action, and conscious sedation making it therapeutically a useful and safe adjunct.[2,4] Intrathecal α-2 agonists like clonidine are used as adjuvants to local anesthetics to potentiate the effects of local anesthetics and allow a decrease in required dose without causing respiratory depression.[5] Intrathecal α-2 adrenergic agonists have antinociceptive action for both somatic and visceral pain.[6-10]

Dexmedetomidine is an alpha-2 agonist and it was approved by FDA in 1999 for use in humans as a short term medication for sedation/analgesia in the intensive care unit.

In our study, addition of dexmedetomidine (5 μg and 10 μg) to hyperbaric bupivacaine 15 mg intrathecally produced a rapid onset of sensory and motor block, prolonged the sensory and motor block and the time to first analgesic requirement significantly in a dose dependent manner. It also maintained stable hemodynamics with minimal side effects.

in our study, both groups were comparable with respect to demographic profile, The primary outcome of present study was early onset and increased duration of both sensory and motor block along with prolonged postoperative analgesia following addition of 10 mcg Dexmedetomidine to 15 mg of 0.5% hyperbaric Bupivacaine in spinal anaesthesia. In the present study, there was statistically significant difference with regard to onset of sensory and motor block between both the groups with faster onset in following addition of 10 mcg Dexmedetomidine. Our results correlate with studies done by, Deepika Shukla et al.[8], Al-Mustafa

et al[11] and Sheriff A Abdelhamid et al.[12]

A study by Shukla D et al[8] concluded that there was no significant difference in the mean values of heart rate and mean arterial pressures between dexmedetomidine group (10 µg) and plain bupivacaine group. Administration of a α-2 agonist via an intrathecal or epidural route provides an analgesic effect without severe sedation. This effect is due to sparing of supraspinal CNS sites from excessive drug exposure, resulting in robust analgesia without heavy sedation.[9,10] In our study there was no statistically significant differences in the sedation scores between three group.

The maximum motor block achieved in both groups as per modified Bromage scale was 4, and there was no statistically significant difference between groups in this regard. Time to reach maximum motor block, however, showed a progressive and statistically significant decline with 10 µg dose of dexmedetomidine. Kanazi et al.[13] showed that supplementation of bupivacaine with low dose intrathecal dexmedetomidine (3.0 mcg) produced significantly shorter onset of motor block and prolongation of sensory and motor block than bupivacaine plain group. Al-Mustafa et al.[11]conducted a study on 66 patients undergoing urological procedures randomized to three groups normal saline, dexmedetomidine 5.0 mcg, and dexmedetomidine 10.0 mcg by intrathecal route in addition to spinal bupivacaine 12.5 mg. They found that the maximum motor block was reached in the shortest time with 10.0 mcg dexmedetomidine. Our study results are thus in conformity with these reports although, admittedly, the absolute differences are small.

VAS scoring is a standard technique for evaluating postoperative analgesia, and we also used the same method in our study at appropriately spaced out intervals. the mean duration of postoperative analgesia was substantially longer in the 10.0 µg group 360 min than 302 minutes in the 5.0 µg group. This hour gain in analgesia duration is not large but may be important from the patient's perspective. Halder et al.[14] documented similar differences. In their study in the setting of lower limb orthopedic surgery in trauma patients, mean duration of analgesia was 242 minutes with 10.0 µg of adjuvant dexmedetomidine compared to 227 minutes with 5.0 µg.

Though there were variations over time, vital parameters (HR, SBP, DBP, MAP, and RR) remained comparable between study groups at all assessment time points. Similar findings have been reported in other studies with intrathecal dexmedetomidine as adjuvant to bupivacaine.[15]

Bradycardia, hypotension, and postoperative nausea were encountered in a few subjects. However, the figures were comparable between groups and no serious or unexpected events were encountered. When administered intrathecally. The Ramsay sedation score in fact did not exceed 2 in any subject which is reassuring from the safety point of view. Thus, dexmedetomidine is safe as an adjuvant to spinal anesthesia with bupivacaine. The safety aspect is corroborated in multiple other studies.

Exact mechanisms, by which α2-adrenoceptor agonists prolong the duration of sensory and motor block, and the duration of analgesia, are not well understood. Local anesthetics exert their action after binding to voltage gated sodium channels whereas α2-adrenoceptor agonists exert their action by binding to pre-synaptic C fibers and post-synaptic dorsal horn neurons. Possibly, these agents inhibit the release of C fiber transmitters and hyperpolarize the post-synaptic dorsal horn neurons.[16,17] Potential local anesthetic toxicity may be reduced by using α2-adrenoceptor agonists that can prolong sensory and motor blocks and reduce local anesthetic requirement. Interestingly, in addition to subarachnoid block as in our study, dexmedetomidine as adjuvant has been researched in various other regional blocks (axillary, paravertebral, infraclavicular brachial plexus, or interscalene) and shows promising results in most situations.[18]

The main limitation of the study was that it involved only healthy adults and the effect in older patients with cardiovascular morbidities are not known. Secondly, total analgesic consumption in 24 hours was not noted.

CONCLUSION

Addition of 10 µg of Dexmedetomidine to 0.5% hyperbaric Bupivacaine 15mg (3mL) in spinal anaesthesia significantly decreases the onset time, prolongs the duration of both sensory and motor blockade, improves the quality of postoperative analgesia with better hemodynamic stability as compared to bupivacaine with 5 µg Dexmedetomidine.

Conflicts of Intrests: None declared by the authors.

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