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ORIGINAL ARTICLE

Intravenous Dexmedetomidine enhances the Duration of Spinal Anesthesia with 0.5% Hyperbaric Bupivacaine in Lower Abdominal Surgeries

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ABSTRACT

Introduction: Spinal block is a preferred technique for most lower abdominal and lower limb surgeries. Lignocaine had been the local anesthetic of choice for decades in such surgeries. With the advent of adjuvants, now it has become possible to enhance the duration of spinal anesthesia. These adjuvants can be given intravenously or intrathecally. Intravenous clonidine and dexmedetomidine have been used in recent studies as adjuvant in spinal anesthesia with promising results. Dexmedetomidine is a more suitable adjuvant compared with clonidine due to its more selective alpha-2A receptor agonist activity.

Aims and objectives: To evaluate the effect of intravenous dexmedetomidine on spinal anesthesia with 0.5% bupivacaine in lower abdominal surgeries in terms of onset and duration of sensory and motor blockade and sensory regression.

Materials and methods: Sixty patients of American Society of Anesthesiologists grades I and II, 25 to 60 years of age, posted for elective lower abdominal surgeries under spinal anesthesia were included in the study and randomly allocated into computer-generated two groups. Group IV received intrathecal 0.5% bupivacaine heavy and intravenous infusion of dexmedetomidine 1 µg/kg over 20 minutes followed by 0.5 µg/kg/hour till the end of surgery. Patients in group III (control group) received intrathecal 0.5% bupivacaine heavy and intravenous normal saline as placebo.

Results: In groups IV and III, mean duration of analgesia was 209 ± 29.93 and 150.20 ± 3.46 minutes respectively. This increase in duration of analgesia in dexmedetomidine group was statistically significant. The mean duration of motor blockade was 189.48 ± 1.34 and 158.18 ± 3.27 minutes respectively. Injection diclofenac sodium 75 mg intramuscularly was used as rescue analgesic.

Keywords: Intravenous dexmedetomidine, Lower abdominal surgery, Postoperative analgesia, Sensory regression, Spinal anesthesia.

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INTRODUCTION

For lower abdominal and lower extremity surgeries, regional anesthesia with a local anesthetic is a preferred unique technique now. Various adjuvants, such as epinephrine, phenylephrine, magnesium sulfate, neostigmine, opioids, and clonidine, have been used to prolong the effect of the local anesthetic.[1-6] It has been shown recently that alpha-2 agonists clonidine and dexmedetomidine prolong the duration of local anesthetic bupivacaine.[2,7] Dexmedetomidine, a newer congener of clonidine and a dextro isomer of medetomidine, being more selective alpha-2 receptor agonist, possesses anxiolytic, sedative, analgesic, and sympatholytic properties.[8] Alpha-2 receptors are found at many sites throughout the body, including central nervous system (CNS) (brain and spinal cord) and peripheral tissues. In CNS, the highest densities of alpha-2 receptors are found in locus coeruleus, an important modulator of vigilance. Presynaptic activation of alpha-2 adrenoceptors in locus coeruleus inhibits the release of norepinephrine (NE), which results in sedative and hypnotic effects. Moreover, the locus coeruleus is the site of origin for descending medullospinal noradrenergic pathway. Stimulation of alpha-2 adrenoceptors in this area terminates the propagation of pain signals leading to analgesia. In spinal cord, stimulation of alpha-2 receptors at substantia gelatinosa of dorsal horn leads to inhibition of the firing nociceptive neurons and inhibition of the release of substance P. Furthermore, the alpha-2 adrenoceptors located at the nerve endings have a possible role in the analgesic mechanisms of alpha-2 agonists by preventing NE release. The spinal mechanism is the principal mechanism for the analgesic action of dexmedetomidine even though there is a clear evidence of both a supraspinal and a peripheral site of action.

AIMS AND OBJECTIVES

In this study, we have tried to investigate the effects of intravenous dexmedetomidine on spinal anesthesia

with 0.5% hyperbaric bupivacaine in lower abdominal surgeries in terms of:

- Evaluation of onset and duration of sensory blockade
- Evaluation of onset and duration of motor blockade
- Hemodynamic stability and sedation

This study was a randomized double-blind controlled study. Sixty patients of American Society of Anesthesiologist grades I and II with age between 25 and 60 years of both genders undergoing lower abdominal surgeries were included in the study.

Exclusion Criteria

Patients using alpha-2 adrenergic agonists, calcium channel blockers, angiotensin-converting enzyme inhibitors, neurological disorders, allergy to study drug, coagulation disorders, spine deformities, and pregnancy were excluded from this study.

MATERIALS AND METHODS

After getting approval from the Ethics Committee, 60 patients were selected and randomly allocated in computer-generated two groups of 30 each. After an informed written consent, patients were kept nil orally from the midnight prior to surgery. Tab. alprazolam (0.01 mg/kg) was given orally to the patients in the evening prior to surgery. An intravenous line with 18 gauge cannula was established on the previous day at bedtime. Patients were rehydrated with Lactated Ringer's solution 30 minutes before the procedure. Noninvasive blood pressure, electrocardiogram monitor, and pulse oximeter were connected to all patients in the operating room and baseline readings recorded. All the patients and anesthesiologists were blinded to the treatment groups and all recordings were taken by anesthesiologist blinded to randomized schedule. Two milliliters of Inj. dexmedetomidine was diluted in 48 mL of normal saline to have the concentration of drug 4 µg/mL in it. Infusion was prepared by an independent senior resident who was not involved in subsequent phases of the study. Thus, both the resident conducting the case and the patient were not aware of the assigned group in all the cases.

Table 1: Modified Bromage scale

Grades	*Criteria*	*Degree of block*
I	Free movement of legs and feet	None
II	Just able to flex knees with free movement of feet	Partial 33%
III	Unable to flex knees, but with free movement of feet	Partial 66%
IV	Unable to move legs or feet	Complete paralysis

Group IV received intravenous dexmedetomidine at the rate of 1 µg/kg/hour for first 10 minutes as loading dose and after 10 minutes at the rate of 0.5 µg/kg/hour as maintenance dose. Group III received normal saline in equal amounts.

Onset of analgesia was assessed by loss of pinprick (22G blunt needle) every 30 seconds till the level of T10 dermatome was reached. The highest level of analgesia was also assessed at 10 minutes. Motor blockade was assessed by modified Bromage scale (Table 1) every 2 minutes for the first 10 minutes. Duration of sensory blockade was assessed by two-segment regression and analgesia was assessed from onset of subarachnoid block to time of requirement of rescue analgesia. Duration of motor block was noted. Vital parameters were monitored. Side effects, such as bradycardia, hypotension, and nausea were recorded. Duration of analgesia was defined as the time from subarachnoid block to visual analog scale >2 when rescue analgesia was administered (Fig. 1). Level of sedation was assessed using Ramsay level of sedation score (Table 2).

Student's unpaired t-test was applied for statistical analysis and $p < 0.05$ was considered statistically significant. Independent and identically distributed two sets of population were studied using unpaired t-test, and analysis was done using Statistical Package for the Social Sciences statistical software.

OBSERVATIONS

- Time of onset of analgesia in group IV was 2.26 ± 0.11, and in group III it was 2.5 ± 0.11, as shown in Table 3 with $p < 0.0001$.

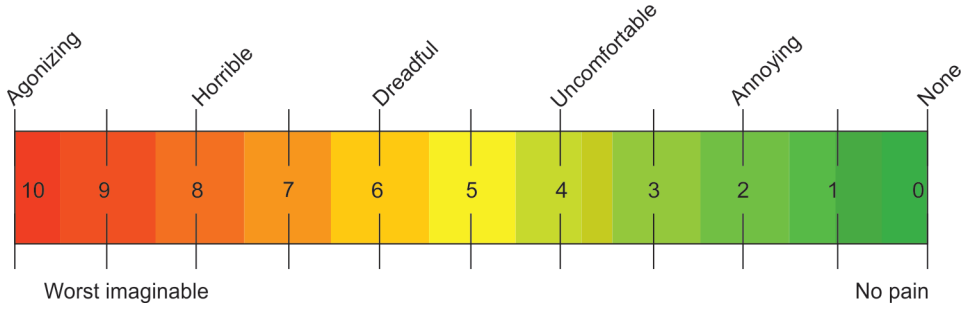

Fig. 1: Visual analog scale

Table 2: Ramsey level of sedation score

1	Patient anxious, agitated, or restless
2	Patient cooperative, oriented, and tranquil alert
3	Patient responds to commands
4	Asleep, but with brisk response to light glabellar tap or loud auditory stimulus
5	Asleep, sluggish response to light glabellar tap or loud auditory stimulus
6	Asleep, no response

Table 3: Comparison of time of onset of analgesia

	Group IV (n = 30)	*Group III (n = 30)*	*p-value*
Time in minutes	2.26 ± 0.11	2.5 ± 0.11	<0.0001

p < 0.0001 considered highly significant

Table 4: Comparison of time of two-segment regression

	Group IV (n = 30)	*Group III (n = 30)*	*p-value*
Time in minutes	142.86 ± 1.49	93.27 ± 1.60	<0.0001

p < 0.0001 considered highly significant

Table 5: Comparison of duration of motor blockade

	Group IV (n = 30)	*Group III (n = 30)*	*p-value*
Time in minutes	189.48 ± 1.34	158.18 ± 3.27	<0.0001

p < 0.0001 considered highly significant

Table 6: Comparison of duration of analgesia

	Group IV (n = 30)	*Group III (n = 30)*	*p-value*
Time in minutes	209.72 ± 29.93	150.20 ± 3.46	<0.0001

p < 0.0001 considered highly significant

- Time of onset of motor blockade in group IV was 8.51 ± 0.11, and in group III it was 9.32 ± 0.08 with p < 0.0001.
- Comparison time of two-segment regression in both the groups is shown in Table 4. The time was prolonged in group IV (142.86 ± 1.49) than in group III (93.27 ± 0.08), which was statistically significant (p < 0.0001).
- Comparison of duration of motor blockade is shown in Table 5, which reveals the duration in group IV as 189.48 ± 1.34 and in group III as 158.18 ± 3.27 with p < 0.0001.
- Duration of analgesia (Table 6) was 209.72 ± 29.93 in group IV and 150.2 ± 150.20 ± 3.46 (p < 0.0001).

DISCUSSION

For the surgeries lasting for around 120 minutes, 0.5% bupivacaine is the drug of choice. Various drugs have been used intrathecally as adjuvants to further prolong the duration of spinal anesthesia, such as magnesium sulfate, neostigmine, midazolam, fentanyl, and clonidine. Opioids have been used extensively as adjuvant to spinal anesthesia but they may cause pruritus and respiratory depression.[9] Though alpha-2 agonist clonidine is in wide use as adjuvant through oral, intrathecal, and intravenous routs in spinal anesthesia,[2] recently a new alpha-2 agonist drug dexmedetomidine administered intravenously has been shown to be a better choice due to minimal side effects and better hemodynamic stability. It has also been approved by the Food and Drug Administration in 1999 as an analgesic and sedative in intensive care unit.[10,11] Alpha-2 adrenoceptor agonists have different alpha-1:alpha-2 selectivity. Clonidine is considered a partial alpha-2 agonist with an alpha-1:alpha-2 selectivity of 200, while alpha-1:alpha-2 selectivity of dexmedetomidine is 1620. So the affinity is eight times more than that of clonidine.[12,13] Intravenous dexmedetomidine prolongs duration of sensory and motor blockade of spinal anesthesia with bupivacaine.[14] Dexmedetomidine possesses more selective alpha-2 adrenoceptor agonist activity, especially for 2A subtype of this receptor than clonidine and thus makes it a more suitable sedative and analgesic adjuvant drug to spinal anesthesia.[10] Despite desired levels of sedation, there is limited respiratory depression which provides wide margin of safety.[15] Dexmedetomidine is thus used in epidural,[16] spinal,[17] and intravenous regional anesthesia. Dexmedetomidine has a biphasic cardiovascular response. An initial bolus of 1 µg/kg produces an increase in blood pressure and a reflex decrease in heart rate due to stimulation of peripheral alpha-2B receptors. This initial response lasts 5 to 10 minutes and is followed by a decrease in blood pressure below the baseline and a stabilization of heart rate. Both these effects are caused by the inhibition of the central sympathetic outflow overriding the direct stimulating effects.[18]

In our study, the age, gender, height, and weight distribution (demographic profile) were comparable between two groups. The mean maximum height of sensory block in dexmedetomidine group was T4–T6 compared with T6–T8 level in control group. The maximum height of the sensory blockade of the present study was in accordance with the study of Kaya et al[19] in both the groups. The mean duration of two-segment regression in dexmedetomidine and control group was 142.86 ± 1.49 and 93.27 ± 1.60 minutes respectively, and was in accordance with Kaya et al,[19] i.e., 145 ± 26 and 97 ± 27 minutes in dexmedetomidine and control groups respectively. This was also comparable with the study done by Gupta et al[9] where time taken for two-segment regression was significantly prolonged in dexmedetomidine group (124.35 ± 30.7) when compared with control group (98.54 ± 23.2), p < 0.05.

The mean duration of motor blockade in the present study was in accordance with the study of Al-Mustafa et al.[2] The mean duration of analgesia in the present study was comparable with Whizar et al[10] (208 ± 13.5 minutes with dexmedetomidine and 137 ± 129.97 minutes with

Table 7: Comparison of time of onset of motor blockade

	Group IV (n = 30)	*Group III (n = 30)*	*p-value*
Time in minutes	8.51 ± 0.11	9.32 ± 0.08	<0.0001

p < 0.0001 considered highly significant

control group), AlOweidi et al[20] (209.6 ± 25.9 minutes with dexmedetomidine and 149.4 ± 14.6 minutes with placebo group), and Gupta et al[9] (dexmedetomidine group 259.70 ± 46.84 minutes and control group 216.40 ± 31.43 minutes), p < 0.001.

Intravenous dexmedetomidine administration also reduces NE release and inhibition of sympathetic activity due to its supraspinal action, thus resulting in decreased heart rate and blood pressure. In dexmedetomidine group, there was a significant decrease in heart rate, whereas systolic, diastolic blood pressures and mean arterial pressure were comparable in both groups. The Ramsay sedation score was also higher in dexmedetomidine group as compared with control group.[21]

Observed Side Effects

Bradycardia was observed in 7 (23.33%) patients, hypotension in 2 (6.66%), and nausea in 1 (3.33%) patient in dexmedetomidine group, whereas in control group bradycardia in 2 (6.66%) patients, hypotension in 3 (10%) patients, and nausea in 1 (3.33%) patient.

RESULTS

The mean duration of analgesia in group 1 was 209.72 ± 29.93 minutes and in group II was 150.20 ± 3.46 minutes. The prolongation in duration of analgesia in dexmedetomidine group was statistically significant. The mean durations of motor blockade in groups I and II were 189.48 ± 1.34 and 158.18 ± 3.27 minutes respectively.

Comparison of time of onset of analgesia in group I was 2.26 ± 0.11 minutes and in group II was 2.5 ± 0.11 minutes as shown in Table 3, with p < 0.0001. Comparison of time of onset of motor blockade in both groups is as shown in Table 4. Onset of motor block in group I was 8.51 ± 0.11 minutes and group II was 9.32 ± 0.08, with p < 0.0001. Comparison of time of two-segment regressions in both groups is depicted in Table 5. Two-segment regression was prolonged in group I, which was 142.86 ± 1.49 and in group II was 93.27 ± 1.60, which was statistically significant. Comparison of duration of motor blockade in both groups as shown in Table 6 reveals the duration in group I as 189.48 ± 1.34 and group II as 158.18 ± 3.7, with p < 0.0001. Comparison of duration of analgesia is shown in Table 7. Duration of analgesia in group I was 209.72 ± 29.93 and that of group II was 150.20 ± 3.46; p-value was considered statistically significant.

Statistical Analysis

Statistical analysis was done using Student's unpaired t-test; p < 0.05 was considered statistically significant and p < 0.001 was considered statistically highly significant.

CONCLUSION

Observing the results in this study, we conclude that the use of intravenous dexmedetomidine as adjuvant to spinal anesthesia with 0.5% bupivacaine in lower abdominal surgeries was found to be promising in terms of increased duration of analgesia and motor blockade. Time of regression of sensory blockade was also prolonged with dexmedetomidine.

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