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Research Article

Comparative analysis of injection clonidine and injection dexmedetomidine added to injection bupivacaine for spinal anaesthesia in lower abdominal surgeries

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ABSTRACT

Background: Efficacy of sub-arachnoid block can be improved by addition of various adjuvants to local anesthetics. Intrathecal administration of clonidine or dexmedetomidine has improved the quality of spinal anesthesia in terms of longer duration of post-operative analgesia with comparatively lesser side effects. In present study we compared the onset and duration of motor and sensory block, hemodynamic effects, post-operative analgesia and adverse effects of clonidine and dexmedetomidine used intrathecally with bupivacaine.
Methods: Present study was conducted in 150 patients (ASA class I and II) undergoing lower abdominal surgeries. Patients were randomly divided into three group's viz. B, C and D. Group B received bupivacaine (12.5 mg), group C received clonidine (30 µg) with bupivacaine and group D received dexmedetomidine (5 µg) with bupivacaine. Volume of administered drug was set at 3ml in all the groups. The onset time to reach peak sensory and motor block level, regression time to sensory and motor block, hemodynamic changes and side effects if any were assessed and recorded.
Results: In our study we observed that there was no significant difference in patient demography and duration of surgical procedure. The time to onset of sensory blockage was similar in all the three groups but time to onset of motor block was shorter in group C and D compared to group B. Total duration of sensory and motor block was significantly higher in group D compared to group C and B. The duration of sensory block in group D was 139.58+14.49, in group C it was 122.46+18.55 and in group B it was 100+13.43 minutes. The duration of motor block in group D was 250.40+27.33, in group C it was 229.28+23.68 and in group B it was 175.64+17.41 minutes.
Conclusions: It was concluded that though both clonidine and dexmedetomidine prolonged duration of sensory and motor block of Bupivacaine, Dexmedetomidine is better in terms of longer duration of action.

Keywords: Bupivacaine, Clonidine, Dexmedetomidine, Spinal anesthesia, α-2 adrenoceptor agonist

INTRODUCTION

Despite advances in knowledge of pathophysiology, pharmacology and the development of more effective techniques for the management of peri-operative analgesia, many patients continue to experience distressing pain in post-operative period.[1] Uncontrolled post-operative pain may activate the sympathetic nervous system which may increase myocardial oxygen consumption leading to development of various morbidity and mortality like myocardial ischemia and infarction.[2,3]

Intrathecal use of hyperbaric bupivacaine 0.5% is an appropriate for surgeries of short duration and may lead to early analgesic intervention in post-operative period. There are many studies done to improve the effect and duration of spinal anesthesia by using various drugs as an

adjuvant to hyperbaric bupivacaine.[4,5] In search of adjuvants that prolong the duration of analgesia with lesser side effect, various drugs as opioids, α agonists and midazolam have been tried with local anaesthetics.[1]. Dexmedetomidine and clonidine both are α_2 agonist drugs. Dexmedetomidine is a potent highly selective α_2 agonist and it has an α_2 / α_1 ratio eight time higher than clonidine. Clonidine has antihypertensive effect as well as ability to potentiate the effect of local anesthetics. It can provide pain relief by an opioid independent mechanism.[6]

The aim of our study was to compare the efficacy and safety of intrathecal administration of dexmedetomidine and clonidine added to hyperbaric bupivacaine in lower abdominal surgeries.

METHODS

After obtaining approval from the hospital Ethical committee, along with the written and informed consent at GMCH, 150 adult of either sex were enrolled in this prospective randomized and double blinded study. Belonging to ASA class I and II posted for lower abdominal surgeries.

Inclusion criteria

- Patients age between 18 to 60 years.
- ASA I-III
- Scheduled for lower abdominal surgeries

Exclusion criteria

Patients with contraindication to regional anaesthesia, coagulopathy history of significant disease like ischemic heart disease, hypertension, severe liver and renal disease were excluded from the study.

Preoperative

All patients were thoroughly investigated a day prior to surgery and instructed to keep fasting for 6 hours and received tab alprazolam 0.5 mg and tab ranitidine 150 mg orally the night before surgery. All procedure including VAS (visual analogue scale) was explained in detail and its use in measuring post-operative pain.

Intraoperative

On arrival in operating room, an 18 gauge intravenous cannula was inserted and standard monitoring including pulse oximetry, ECG leads, NIBP were attached. All patients were preloaded with ringer lactate solution, 10-15 ml per kg body weight. Baseline parameters like heart rate, oxygen saturation and non-invasive mean BP were noted. Patients were randomly divided in three groups of 50 each.

Group B: 0.5% bupivacaine 12.5 mg + normal saline (total volume 3 ml)

Group C: 0.5% bupivacaine 12.5 mg+ clonidine 30 µ gm

Group D: 0.5% bupivacaine 12.5 mg+ dexmedetomidne 5 µ gm.

Study solution were prepared in 5 ml syringe by an anesthesiologist who then handed them over in a coded form to the attending anaesthesiologist blinded to the nature of drugs given to him/her. SAB was performed with strict aseptic precautions at L_{3-} L_4 intervertebral space using 25 G quinke spinal needle with patients in sitting position. Study drugs solution (3ml) was injected as per groups allocated. Patient was made supine immediately following the block. Anaesthetic performing the block recorded the following data:

- Patients were monitored for heart rate, mean blood pressure, spo_2 every 5 minute after injection for 30 minute and then every 15 minutes. Any drop in heart rate below 60/min was treated with intravenous atropine 0.01 mg/kg body weight and any drop In mean blood pressure below 20% of basal reading was treated by fluid bolus and 6 mg intravenous increment of ephedrine.

- Assessment of sensory blockage: The onset of sensory blockage was defined as the time between injection of intrathecal drug and the absence of pain at T_{10} dermatome. This is assessed by sterile 25 gauge blunt needle pinprick along the mid-clavicular line bilaterally every 2 min till T_{10} level was achieved, than every 5 min for 20 min, than after every 15 minutes. The time from Intrathecal injection to two segment sensory regression, sensory regression to S_1 dermatome were noted (duration of sensory blockage).

- Assessment of motor blockage: Motor blockage was assessed according to modified bromage score (0-3). Time for motor block onset was defined as score (3) and complete motor block recovery as score (0).

Bromage scale

- 0 - the patient is able to move the hip, knee and ankle.
- 1 - the patient is unable to move the hip, but is able to move the knee and ankle.
- 2 - the patient is unable to move hip and knee but is able to the ankle.
- 3 - the patient is unable to move the hip, knee and ankle.

Pain score assessed with VAS between 0-10 were recorded 5 min before intrathecal injection, after the start of surgery and subsequently every 15 min till surgery was over.

- Duration of pain relief (effect analgesia) was defined as the time from spinal injection to 1st request for rescue analgesic or VAS >3, rescues analgesic given was intravenous injection of diclofenac sodium 75 mg.
- All duration were calculated in relation to spinal injection.
- Patient sedation was recorded according to de kock sedation scale.
    - Patient somnolent but responding verbal command,
    - Patient somnolent, not responding to verbal commands but responding to manual stimulation.
    - Patient somnolent not responding to verbal commands or manual stimulation.
- Incidence of nausea, vomiting were recorded.

Post-operative

Sensory block regression were assessed every 15 minutes after completion of surgery till the time of regression of two segments in maximum block in the post anaesthetic care unit along with VAS score. Any patient showing VAS more than or equal to 3 was given a dose of intravenous diclofenec 75 mg. The amount required by the patient in the next 24 hours was recorded in all the groups. Motor recovery (modified bromage score of zero) was noted.

RESULTS

One hundred and fifty patients posted for lower abdominal surgeries were enrolled for the study. In our study all the groups were comparable with regards to demographic variables and there was no statistical significance found (Table 1). The time of onset of sensory block (to reach T10 level) was statistically insignificant in all the three groups (Table 2). Onset of motor block (time to reach Bromage score 3) was statistically significant between group B and C, as well as between group B and D but not between group C and D (Table 2). Difference between duration of sensory and motor block was statistically significant in all the three groups (Table 1 and 2). We found that the change in mean heart rate and mean blood pressure at various intervals from baseline in all three groups was statistically insignificant.

Table 1: Demographic profile.

Variable	Group B	Group C	Group D
Age	30±7.5	31±8.65	32±7.2
height	162±4.5	160±4.1	162±6.4
weight	60±24.5	57±21.4	59±22
Duration of surgery	95±26.6	84.4±25	83.6±24.5

Table 2: Characteristics of Spinal block.

Variable	Group B (Mean±SD)	Group C (Mean±SD)	Group D (Mean±SD)	P value
Time to reach T 10 sensory level (mins)	6.98± 0 .50	6.12±0.75	6.4±0.78	.0054
Time to reach Bromage score 3 (mins)	15.23±0.77	9.73±0.47	10.38±0.60	.0004
Time to S1regression (mins)	202.13±26.94	284.73±26.72	299.94±29.31	.0657
Regression time to Bromage score 0 (mins)	175.64±17.41	229.25±23.68	250.40±27.33	.00034
Time to two segment regression (mins)	100±13.43	122.46±18.55	139.58±14.49	.00065
Duration of analgesia (mins)	199.8±13.31	303.44±29.99	325.18±31.05	<.001

Table 3: Occurrence of side effect.

Number of patients (%)	Group B	Group C	Group D
Hypotension	05(10)	8(16)	5(10)
Bradycardia	0	0	5(10)
Respiratory depression	0	0	0
Shivering	9(18)	4(8)	3(6)
Nausea/vomiting	6(12)	2(4)	4(8)

Three patients in group B and D and five patients in group C received one dose of ephedrine. Two patients in group D required atropine. VAS values were observed to be less than 3 in all the three groups for complete duration of surgery and none required additional analgesics. Intra operative and post-operative nausea and

vomiting occurred in 6 patients in group B, 2 in group C and 4 patients in group D (Table 3).

DISCUSSION

For lower abdominal surgeries subarachnoid block (SAB) is widely used popular technique as it provides profound nerve block in a large part of body by simple injection of small amount of local anesthetic drug. An ideal local anesthetic agent used in spinal anesthesia should have rapid onset of action, intense analgesia, and adequate motor blockade, long duration of action, adequate post-operative analgesia and minimal cardiovascular changes.[1] Most anesthesiologist concern that reduced dose of local anesthetic may provide insufficient spinal block. Thus there have been many trials to reduce the dose of intrathecal local anesthetics and improve their block quality with co administration of additives such as clonidine and opioids. However, combine additives can induce their own side effects such as nausea/vomiting, pruritis, hypotension/brady cardia and excessive sedation.[7]

In our study we found that both dexmedetomidine and clonidine prolonged both sensory and motor blockade and reduced the need of rescue analgesia for first 24 post-operative hours. But administration of dexmeditomidine 5 µg added to intrathecal bupivacaine prolonged the duration of post-operative anesthesia significantly compared with addition of clonidine 30 µg.[8]

Intrathecal α_2 - adrenoceptor agonist produced analgesia by binding and depressing the release of presynaptic C fibres neurotransmitters and also by hyperpolarisation of postsynaptic dorsal horn neurons. This anti-nociceptive effect may explain the prolongation of the sensory block while prolongation of motor block may be due to binding of α_2- adrenoceptor agonists to motor neurons in the dorsal horn.[8] Dexmedetomidine is a more potent and selective α_2 adrenoceptor agonist than clonidine thereby enhance the therapeutic window of α_2 adrenoceptor agonists in the treatment of pain and overcome problematic adverse effects of clonidine.[7] The binding affinity of dexmedetomidine compared with clonidine is nearly 1:10 Thus it is hypothesized that 3 to 5 µg of intrathecal dexmedetomidine might be equipotent to 30 to 45 µg of intrathecal clonidine. Several studies have been done using different dosage of clonidine and dexmedetomidine to determine the most effective intrathecal administration with minimal side effects[1]. In our study, the intrathecal dose of dexmedetomindine selected was based on previous human studies where no neurotoxic effects have been observed.[9-11]

In our study all the demographic variables were comparable in all the three groups and did not hold any statistical significance, and this finding was in agreement with those of Jahanabee et al and Omprakash suthar et al.[1,8]

In our study time to reach T10 sensory level was minimum for clonidine (6.4±0.78) and maximum for bupivacaine (6.98±0.5). These findings were in agreement with studies done by Jahnabee Sarma et al and Kanazi et al but in study done by Omprakash suthar et al, it was maximum for dexmeditomidine group and lower for bupivacaine and clonidine.[1,8,9]

In our study time to reach bromage scale 3 was maximum for bupivacaine (15.33±0.77) and there was not much difference between clonidine (9.73±0.47) and dexmedetomidine (10.76±0.60), which was in accordance with the study done by Omprakash suthar et al[8], Jahnabee et al and Kanazi et al.[1,9] All studies revealed that time to reach Bromage scale 3 was maximum for bupivacaine and less for clonidine and dexmedetomidine.

In current study time to reach Bromage score 0 was longer with dexmedetomidine (250.40±27.33) as compared to clonidine group which was 229.28±23.68 minutes and with bupivacaine alone it was only 175.64±17.41 minutes. Our findings were in agreement with various studies done by Kanazi et al, Gunjan jain et al, Jahanabee et al and Omprakash Suthar et al.[1,8,9,12]

In our study two segment regression time was highest with dexmadetomidine (139.58±14.49) as compared to clonidine (122.46±18.55) and Bupivacaine alone (100±13.43). Time to S1 regression was found to be high in dexmedetomidine group (299.94±29.31) as compared to clonidine (284.73±26.72) and bupivacaine (202.13±26.94). In regard to regression time our study was in accordance with those studies conducted by Jahanabee et al, Omprakash suthar et al, Rampal singh et al and Kanazi et al.[1,8,9,13] They concluded that though both clonidine and dexmedetomidine prolonged duration of sensory block of bupivacaine, dexmedetomidine is better in terms of longer duration of action.

Duration of analgesia was found to be maximum with dexmedetomidine (325.18+31.05) in our study as compared to clonidine group (303.45+29.99) and least with bupivacaine alone which was 199.8+13.31). Similar results were observed by jahanabee et al, omprakash et al, rampal singh et al and gunjan jain et al in their studies.[1,8,13] In a study conducted by Hala E A Eid et al, shown significant prolongation of duration of spinal blockage by intrathecal administration of dexmedetomidine when added to hyperbaric bupivacaine.[12,14] Another recent study done by Solanki S L et al proved superiority of intrathecal dexmedetomidine in comparision with clonidine and fentanyl. It provided prolonged motor and sensory block and reduced demand of additional analgesics.[15]

There was no significant change in mean heart rate and blood pressure at various intervals from baseline, and this finding is in accordance with the study of G. E. Kanaji et al, Jahanabee et al, Gunjan Jain et al and Omprakash suthar et al.[1,8,9,12]

CONCLUSION

It is shown that relief of pain with subarachnoid blockage with the local anesthetic like bupivacaine alone is limited to the immediate post-operative period. When a combination of local anesthetic and α_2 adrenergic agonist is used, pain relief can be extended well into the post-operative period.

Based on the results of our study we concluded that, the addition of bupivacaine spinal block with intrathecal dexmedetomidine (5 µgram) and Clonidine (30 µgram) leads to significant faster onset of sensory and motor block. They also prolonged the duration of sensory and motor block than bupivacaine alone. Dexmedetomidine, a newer α_2 agoinsts seems to an better adjuvant to spinal bupivacaine which provide longer duration of sensory and motor block and post-operative analgesia when compared to clonidine with minimal hemodynamic alterations.

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