ORIGINAL RESEARCH

Evaluation of effectiveness of two different Doses of Clonidine as an Additive to Intrathecal Isobaric Levobupivacaine in Patients Undergoing Infraumbilical Surgeries

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ABSTRACT
Background: To evaluate two different doses of clonidine as an additive to intrathecal isobaric levobupivacaine in Patients Undergoing Infraumbilical Surgeries.
Materials & methods: A total of fifty individuals between the ages of 30 and 55 were enrolled. Complete demographic and clinical information for every individual was gathered. Patients with ASA grades I/II who were scheduled for elective infraumbilical operations under spinal anesthesia were eligible. Every outcome was recorded into a Microsoft Excel spreadsheet, which was then analyzed statistically using SPSS.
Results: The mean age of subjects in group A was 45.4 years, while that of subjects in group B was 39.5. The majority of the subjects in both research groups were male.
Conclusion: Adding 30 µg of clonidine as an adjuvant can safely extend postoperative analgesia duration compared to 15 µg alone.
Keywords: Clonidine, infraumbilical surgery, Levobupivacaine.

INTRODUCTION

Adjuvants are agents possessing little effect by themselves, but potentiate the actions of other drugs when given at thesame time. Whether administered into the CSF in conjunction with a local anesthetic or alone, a variety of medications may exert a direct analgesic effect on the spinal cord and nerve roots,or prolong the duration of sensory and motor blockade. As such, the co-administration of these agents oftenallows for a reduction in the required dose of local anesthetic. [1]Many adjuvants have been added to local anesthetics such as clonidine, dexmedetomidine, dexamethasone, and fentanyl. One additive of particular interest that consistently prolongs local anesthetics' duration has been clonidine. However, at the clinically studied doses of 1 µg.kg−1 and 2 µg.kg−1, the use of clonidine is associated with bradycardia, sedation, and hypotension as side effects.[2,3] Till now, there has been a paucity of studies evaluating the effect of different doses of clonidine in

supraclavicular brachial plexus block in children and there is no study evaluating the effect of the use of a lower dose of 0.5 μg.kg−1 on the brachial plexus block characteristics using bupivacaine as a local anesthetic.[4]Clonidine, the first congener of alpha-2 adrenergic receptor agonist, is mainly used as antihypertensive in the clinical medicine.[5] However, it has also been used for drug detoxification, pain relief and sedation.[6] The role of systemic and intrathecal clonidine in acute post-operative pain has recently been well-established. However, there is an increasing evidences from animal and the human studiesthat clonidine may be effective in the prevention and management of chronic pain as well. [7]Chronic pain is continuous, long-term pain of more than 12 weeks or after the time when healing would have been thought to have occurred in pain after trauma or surgery. [8]Intrathecal anesthesia and epidural anesthesia are the most popular regional anesthesia techniques used for lower-limb orthopedic surgeries.[9] Spinal anesthesia is a safe, reliable, and inexpensive technique with the advantage of providing surgical anesthesia and prolonged postoperative pain relief, and it also blunts autonomic, somatic, and endocrine responses to surgical stimulus.[10] For decades, lidocaine had been the local anesthetic of choice for spinal anesthesia. However, its use was limited due to short duration of action and its implication in transient neurologic symptoms and cauda equina syndrome following intrathecal injection.[11] Till recently, hyperbaric bupivacaine 0.5% was the only drug used for spinal anesthesia in India after the discontinuation of lidocaine. Levobupivacaine does not provide prolonged duration of postoperative analgesia; hence, clonidine is used in combination which has been found to prolong postoperative analgesia but has produced significant perioperative hypotension and bradycardia. [12] Hence, this study was conducted to evaluate two different doses of clonidine as an additive to intrathecal isobaric levobupivacaine in Patients Undergoing Infraumbilical Surgeries.

MATERIALS & METHODS

A total of fifty individuals between the ages of 30 and 55 were enrolled. Complete demographic and clinical information for every individual was gathered. Patients with ASA grades I/II who were scheduled for elective infraumbilical operations under spinal anesthesia were eligible. There were two trial groups, each with 50 patients, as follows: Group A received 0.5% isobaric levobupivacaine (3 mL) with 15 μg of clonidine, while Group B received the same dose with 30 μg of clonidine. Blood samples were tested for baseline hemodynamic and biochemical profiles. The Visual Analog Scale (VAS) was used to assess postoperative outcomes. On a pain scale from 0 to 10, 0 signifies no pain and 10 symbolizes the most excruciating suffering. Patients getting rescue analgesia with a VAS score greater than three. Hemodynamic variables were constantly examined during and after operation. Every outcome was recorded into a Microsoft Excel spreadsheet, which was then analyzed statistically using SPSS.

RESULTS

The mean age of subjects in group A was 45.4 years, while that of subjects in group B was 39.5. The majority of the subjects in both research groups were male. The average time of onset of sensory block among subjects in groups A and B was 7.13 minutes and 2.74 minutes, respectively; when compared, significant outcomes were found. Significant results were found when comparing the time for maximum sensory blocking and the duration of analgesia between the 2 study groups.

Table 1: Time of onset of sensory and motor block (mins)

Time of onset	Group A	Group B	p-value
Sensory block	7.13	2.74	0.001 (Significant)
Motor block	3.57	3.17	0.3

Table 2: Time for maximum sensory blockage

Time for maximum sensory blockage	Group A	Group B
Mean	13.42	8.74
p-value	0.001 (Significant)	

Table 3: Duration of analgesia (mins)

Duration of analgesia	Group A	Group B
Mean	250.1	322.7
p-value	0.001 (Significant)	

DISCUSSION

Spinal anesthesia is a safe, reliable, and inexpensive technique for infraumbilical surgeries with the advantage of providing surgical anesthesia and prolonged postoperative pain relief. It also blunts autonomic, somatic, and endocrine responses to surgical stimulus. Till recently, hyperbaric bupivacaine 0.5% was the only drug used for spinal anesthesia after the discontinuation of lidocaine. Bupivacaine is available as a racemic mixture of its enantiomers, dextrobupivacaine and levobupivacaine. It has been found that D-enantiomer is the cause for

cardiotoxicity and the levobupivacaine (S-1-butyl-2-piperidylformo-2',6'-xylidide hydrochloride), the pure S (-) enantiomer, does not have the cardiotoxicity. Levobupivacaine has similar pharmacodynamic properties to racemic bupivacaine but a documented reduced central nervous system and cardiovascular toxicity. Traditionally, the dose of levobupivacaine used for spinal anesthesia is 15 mg. Levobupivacaine has been introduced in India in 2012 and is available as 0.5% isobaric 4 mL ampoules for intrathecal use. It is known that a single injection of levobupivacaine will not produce a prolonged duration of postoperative analgesia.[13] Hence, this study was conducted to evaluate two different doses of clonidine as an additive to intrathecal isobaric levobupivacaine in Patients Undergoing Infraumbilical Surgeries.In the present study, the mean age of subjects in group A was 45.4 years, while that of subjects in group B was 39.5. The majority of the subjects in both research groups were male. A study by Krishna K et al, assess the efficacy 15 µg and 30 µg of intrathecal clonidine along with 3 mL of 0.5% isobaric levobupivacaine in comparison with plain 0.5% isobaric levobupivacaine.Seventy-five patients posted for elective lower-limb orthopedic surgeries were randomly divided into three groups with 25 patients in each group as L (levobupivacaine 0.5%), LC-15 (levobupivacaine 0.5% + clonidine 15 µg), and LC-30 (levobupivacaine 0.5% + clonidine 30 µg). All the patients were given spinal anesthesia using the study drugs, and various parameters were monitored.The three groups were compared statistically using analysis of variance and Student's t-test (independent samples t-test). $P < 0.05$ was considered statistically significant.There was a statistically significant difference among the three groups with respect to the onset of time for maximum sensory blockade and duration of analgesia. A statistically significant difference was noted among the three groups with respect to the onset of time for maximum motor blockade.[14]

In the present study the average time of onset of sensory block among subjects in groups A and B was 7.13 minutes and 2.74 minutes, respectively; when compared, significant outcomes were found. Significant results were found when comparing the time for maximum sensory blocking and the duration of analgesia between the 2 study groups.Another study by Maheshwari et al, 90 cases of emergency caesarean section of more than 37 weeks gestation with ASA physical status class 2 under spinal anaesthesia were randomly divided into three groups of 30 patients each. In all groups we assessed onset, two segment regression and requirement of analgesic in post-operative period, level of motor block by modified bromage scale and sedation by Campbell sedation score. Maternal and foetal hemodynamic was monitored as well. Group A (n = 30) 10 mg of 0.5% (2 ml) isobaric levobupivacaine + 15 mcg clonidine (0.5 ml). Group B (n = 30) 10 mg of 0.5% (2 ml) isobaric levobupivacaine + 30 mcg clonidine (0.5 ml). Group C (n = 30) 10 mg of 0.5% (2 ml) isobaric levobupivacaine + 45 mcg clonidine (0.5 ml). Normal saline was used to make volume of clonidine upto 0.5 ml.Onset of sensory block was highest in group A with significant difference (P value <0.0001) in all three groups. Two segment regression time (in minutes) was highest in group C with significant difference (P value <0.0001) in all three groups. There was fall in systolic blood pressure (SBP) <80% of baseline was found in 0 (0.00%), 10 (33.33%) and 22 (73.33%) patients in group A, B and C respectively while fall in HR <80% of baseline was found in 0 (0.00%), 1 (3.33%) and 19 (63.33%) patients. Sedation score was 1 in 30 (100%) patients in group A, it was 1 in 10 (33.33%), 2 in 20 (66.67%) in group B while it was 1 in 5 (16.77%), 2 in 10 (33.33%) and 3 in 15 (50%) patients in group C.Spinal anaesthesia performed with isobaric 0.5% levobupivacaine with 30 mcg clonidine (Group B) provides better haemodynamic stability, early onset of sensory and motor blockade, decreased requirement of post-operative analgesia.[15]Ackerman et al. did a retrospective chart review of 15 patients where intrathecal clonidine alone or in combinations with other opioid was used in a variety of chronic pain patients. All patients received trial of single-shot with or without short-term infusion of clonidine. They found that 10 of 15 patients reported a significant pain relief (>50% decrease in visual analog scale (VAS) scores) with the initial trial and received long-term therapy. Initially 70% patients responded to clonidine alone (75-950 µg/day) before requiring a second drug. Intrathecal clonidine in combination with intrathecal opioids provided long-term benefit lasting up to 24 months in 20% of patients who had previously failed intrathecal opioid monotherapy.[16]Clonidine was found to be a valuable adjuvant for peripheral nerve blocks when used as an additive to local anesthesia. The beneficial effect of clonidine was reported to be present with all tested local anesthetics in a meta-analysis by Pöpping et al.[17]Pöpping et al. concluded that adding clonidine to long or intermediate-acting local anesthetics prolonged the duration of analgesia, along with increased motor block duration. The dose of clonidine in this study ranged from 30 µg to 300 µg and the side effects (hypotension and sedation), were seen with the dose above 150 µg in adult patients.

CONCLUSION

Adding 30 µg of clonidine as an adjuvant can safely extend postoperative analgesia duration compared to 15 µg alone.

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