



ISSN (E): 2277- 7695

ISSN (P): 2349-8242

NAAS Rating: 5.03

TPI 2020; 4(8): 147-150

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[www.thepharmajournal.com](http://www.thepharmajournal.com)

Received: 22-07-2015

Accepted: 24-08-2015

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## Effects of added intrathecal clonidine on spinal anaesthesia with bupivacaine 0.5 percent: A comparative controlled clinical study

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### Abstract

**Aim:** To evaluate the efficacy and adverse effects of small dose clonidine 75µg added to 0.5% hyperbaric bupivacaine administered intrathecally in patients undergoing elective.

**Material and method:** In the premedication room pulse rate, BP, Respiratory rate and SpO<sub>2</sub> were noted. An IV line was secured. Preloading done with Ringer lactate (15-20 ml/kg) over 20-30 mints. In the Operation theatre appropriate equipment for airway management and emergency drugs were kept ready. Patient was shifted from the premedication room to Operation theatre. The horizontal position of the operating table was checked and the patient was placed on it. Noninvasive blood pressure, SpO<sub>2</sub>, ECG leads were connected to the patient. Preoperative base line systolic and diastolic BP, PR, SpO<sub>2</sub> and RR were recorded.

**Result:** The mean weight for group BC (study) was 51.14±4.82 and for group B (control) was 50.68±4.61. By using 2 independent sample t-tests, p-value was 0.627. Since the p-value is > 0.05 therefore there is no significant difference between weights (kg) in group "BC" and "B". Sex wise comparison of demographic parameters in group "BC" (study) and group "B" (control). We have done our study for lower abdominal surgeries. The patients included in the present study were only female patients in both the groups i.e. group BC and group B.

**Conclusion:** The addition of 75µg of Clonidine to 2ml of 0.5% hyperbaric Bupivacaine provide late onset of sensory and motor block, excellent surgical anaesthesia with relative hemodynamic stability, good sedation, prolonged post-operative analgesia and reduces the postoperative analgesic requirements. Clonidine provides maximum benefit and minimum side effects.

**Keywords:** Intrathecal clonidine, spinal anaesthesia, bupivacaine

### Introduction

Anaesthesia is considered an American invention, although innovations of such significance can hardly have arisen spontaneously [3]. Eternally mankind has suffered pain of various kinds, but the individual's well-being was not considered genuinely, until the need for surgical treatment of disease arose. Attempts at relieving pain were previously sporadic [4].

Subarachnoid block is a widely practiced technique. It is easy to perform and provides faster onset along with effective sensory and motor block [5]. Bupivacaine produces long duration spinal anaesthesia which is useful in various surgical procedures without transient neurological symptoms (TNS). Since the initial introduction, the use of vasoconstrictors to prolong spinal anaesthesia has caused controversy among few clinicians for its possible adverse effect on spinal cord blood supply [6]. Apart from the vasoconstrictors like epinephrine and phenylephrine, opioids like fentanyl have also been used to prolong the duration of spinal anaesthesia and to provide post-operative analgesia as well [1-3]. These adjuvants also have their own side effects and limitations [7]

Apart from the obvious humanitarian reasons, post-operative pain is also associated with many respiratory, cardiovascular, gastrointestinal, neuroendocrine and psychological adverse responses which also contribute to increased morbidity and mortality of any operation [8]. The traditional approach to post-operative analgesia is to begin therapy when surgery is completed and pain is experienced. Recent evidence points to advantages of administering potent analgesic or nerve

block techniques prior to surgical stimulation. This is what the popular concept of preemptive analgesia [9]

However unlike spinal opioids, clonidine does not produce pruritus and respiratory depression. It also claim prolongs the sensory blockade and reduces the requirement of post-operative

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analgesics. This study was designed to evaluate the efficacy and adverse effects of small dose clonidine 75µg added to 0.5% hyperbaric bupivacaine administered intrathecally in patients undergoing elective lower abdominal surgeries.

### Material and method

This study was conducted at the Krishna institute of medical sciences and hospital, Karad between October 2008 – August 2010. This study was done after Ethical committee approval and written informed consent obtained from all the patients included in this study.

Hemoglobin, Packed cell volume, Bleeding time, clotting time, Renal function test, Blood sugar, ECG, Chest x-ray and Platelet count were done. Patients who satisfied the inclusion criteria were explained about the nature of the study and the anaesthetic procedure. Written informed consent was obtained from all patients included in the study.

In the premedication room pulse rate, BP, Respiratory rate and SpO<sub>2</sub> were noted. An IV line was secured. Preloading done with Ringer lactate (15-20 ml/kg) over 20-30 mints. In the Operation theatre appropriate equipment for airway management and emergency drugs were kept ready. Patient was shifted from the premedication room to Operation theatre. The horizontal position of the operating table was checked and the patient was placed on it. Noninvasive blood pressure, SpO<sub>2</sub>, ECG leads were connected to the patient. Pre operative base line systolic and diastolic BP, PR, SpO<sub>2</sub> and RR were recorded. The anesthesiologist performed the SAB and made observations in all the patients involved in the study. A midline lumbar puncture was performed at L3-L4 interspace using a 25G Quincke needle in lateral recumbent position. Following free flow of clear CSF, anaesthetic solution was injected slowly in both the groups. Then patient was placed in supine position. The time of intrathecal injection was considered as 0 and following parameters were observed.

### Result

Proposed work was done in a comparative controlled clinical study manner carried out on patients posted for elective lower abdominal surgery. The mean age for group BC (study) was 25 ±2.35 and for group B (control) was 24.84± 2.46. By using 2 independent sample t-test, p-value was 0.74. Since the p-value is > 0.05 therefore there is no significant difference between age (years) in group “BC” and “B”. The mean weight for group BC (study) was 51.14±4.82 and for group B (control) was 50.68±4.61. By using 2 independent sample t-tests, p-value was 0.627. Since the p-value is > 0.05 therefore there is no significant difference between weights (kg) in group “BC” and “B”. Sex wise comparison of demographic parameters in group “BC” (study) and group “B” (control). We have done our study for lower abdominal surgeries. The patients included in the present study were only female patients in both the groups i.e. group BC and group B. The mean duration for loss of knee jerk in group “BC” (study) was 54.54±20.90 and for group “B” (control) was 46.07±13.09. By using 2 independent sample t-tests, p-value was 0.031. Since the p-value is < 0.05 hence there is significant difference between duration for onset of loss of knee jerk in group “BC” and group “B”. Loss of knee jerk being the first clinical sign of onset of sub arachnoid block is indicative of the onset of regional block. This signifies that addition of Clonidine to bupivacaine delays onset of spinal subarachnoid block as compared to use of plain bupivacaine.

The mean duration for onset of loss of sensation to pain, temperature in group “BC” (study) was 2.95±1.23 and for group “B”(control) was 2.58±0.86. By using 2 independent sample t-tests, p-value was 0.090. Since the p-value is > 0.05, there is no significant difference between onset of loss of sensation to pain, temperature in group “BC” and group “B”. On the other hand, the mean duration for onset of loss of sensation to touch and pressure in group “BC” (study) was 5.36±1.97 and for group “B” (control) was 4.69±1.63. By using 2 independent sample t-tests, p-value was 0.069. Since the p-value is > 0.05 there is no significant difference between onset of loss of sensation to touch and pressure in group “BC” and group “B”.

This signifies that there is no statistically significant effect on onset of sensory block with addition of Clonidine to bupivacaine compared to plain bupivacaine solution used for subarachnoid block. The mean time for onset of motor block in group “BC” (study) was 9.22±2.40 and for group “B” (control) was 8.31±1.77. By using 2 independent sample t-tests, p-value was 0.037. Since the p-value is < 0.05 there is significant difference between time for onset of motor block in group “BC” and group “B”.

In our study we have included 50 patients in group “BC” and group “B”. Out of them 2 patients in group “B” did not show motor block. So, they were not included in our statistical analysis for the above parameter (motor block). This statistical analysis signifies that addition of Clonidine prolongs the duration of onset of motor block, however, the data indicates that addition of Clonidine has improved the success to achieve motor block in all the patients under study group as against failed motor block observed in two out of the 50 patients studied with plain bupivacaine. Although the number of patients studied is limited in this study, there is an indication that use of Clonidine with bupivacaine results in potentiation of local anaesthetic effect with resultant improved muscle relaxation compared to that with plain bupivacaine. The mean duration in hours of two segment regression for pain, temperature in group “BC” (study) was 1.65±0.42 and for group “B” (control) was 1.25±0.28. By using 2 independent sample t-tests, p-value was <0.001 hence there is very high significant difference between mean duration for loss of sensation to pain, temperature in group “BC” and group “B” with respect to sensory block in two segment regression. Similarly, the mean duration of two segment regression.

### Discussion

The subarachnoid block has occupied an important place in the anaesthetic practice, since the time it is known. It provides efficient analgesia and adequate muscle relaxation and thus imparts optimal operating conditions in the patient. Subarachnoid block is a commonly used anaesthetic technique for lower abdominal and lower limb surgery [10]. Bupivacaine produces long duration spinal anaesthesia but does not prolong post-operative analgesia adequately [11]. There has been a practice and growing interest in the use of adding vasoconstrictors like epinephrine and phenylephrine as well as opioids like fentanyl has also been used to prolong the duration of spinal anaesthesia and to provide extended post-operative analgesia but all these adjuvants have their own side effects and limitations. Another method, recently describe to prolong the duration of spinal anaesthesia is the administration of the α<sub>2</sub>- agonist intrathecally as an adjuvants to local anaesthetics. Clonidine an α<sub>2</sub>- agonist added to

subarachnoid local anaesthetics have been claimed to provide excellent surgical anaesthesia and increase both sensory and motor block of local anesthetic. In our study 75µg of Clonidine was added to 10mg (2ml) of 0.5% hyperbaric Bupivacaine and its efficacy as an adjuvant to subarachnoid Bupivacaine was studied in hundred patients undergoing elective lower abdominal surgeries. Patients in both the groups were age, sex and weight wise comparable.

In our study we found that, the addition of Clonidine to hyperbaric Bupivacaine intrathecally had prolonged the onset of loss of knee jerk and also delayed the recovery of knee jerk. This represents the block of very fine myelinated fibres. Knee jerk is regulated by large diameter myelinated afferent nerve fibres (Type Ia, II) originating in the central portion of the muscle fibres and small diameter myelinated efferent nerves fibres (α-motor neurons) supplying the polar contractile region of the muscle fibres. Stretch stimulates the muscle spindle, which activates Ia nerve fibres of the femoral nerve which synapses (without interneuron) at the level of L2 in spinal cord and excite the α-motor neurons.

Stimulation of the α-motor neurons thus cause the contractile ends of the muscle fibres to shorten and therefore deforming the endings and initiating impulses in the Ia fibres. This in turn can lead to reflex contraction of the muscle. Thus, muscle can be made to contract by stimulation of the α-motor neurons that initiate contraction by the stretch reflex. The sensitivity of nerve blockade to local anaesthetic drug is determined by diameter of the fibres as well as by fibre type. In general small diameter fibres are more sensitive than large diameter fibres and nonmyelinated fibres are blockade more easily than myelinated fibres. Moreover, frequency dependence of blockade makes smaller sensory fibres more vulnerable since they generate high frequency longer lasting action potentials than the motor fibres. According to "Erlanger and Gasser" classification the α motor fibres to muscle spindles, block first therefore, the knee jerk is the reflex which blocks first as well as recovers last.

In present study, there was no significant difference in the mean duration for onset of loss of sensation to pain, temperature as well as touch and pressure in both the groups. Hence, we found that the addition of Clonidine 75µg to 0.5% hyperbaric Bupivacaine 10mg (2ml) did not enhance the onset of sensory block. This correlated with the study done by Klimscha *et al.* 13 who studied intrathecally administered 0.5% Bupivacaine 5mg and 150µg Clonidine and without Clonidine and observed that there was no statistically significant difference between the two groups as regards to the onset time of sensory block at T-11 dermatome level. Acalvoschi Lurie *et al.* in his study found that there was no statistically significant difference in the onset time for sensory block for Clonidine 2µg/kg combined with Meperidine 1% 1mg/kg (3.9±0.9min) and meperidine alone 3.6 ±0.6 min). This concluded that findings of our study were well correlated with above studies.

The mean segmental height for loss of sensation to pain/temperature and touch/ pressure was higher in Clonidine group in our study. Hence, we found that addition of Clonidine to hyperbaric Bupivacaine increases the spread of sensory level (level of thoracic segment). Vasoconstriction. Vasa nervorum are small arteries that provide blood supply to peripheral nerves. A decrease in blood flow through the vasa nervorum has been implicated in the low concentration of local anaesthetic to be achieved at nerve core fibers probably resulting in increase the duration of onset of motor block [11].

The mean duration for recovery of motor block was prolonged in group receiving intrathecal Clonidine in comparison to group receiving plain Bupivacaine. This correlated well with study by Wu Cl *et al.* 14 that increasing the dose of Clonidine (15µg, 30µg, 45µg) during hyperbaric tetracaine spinal anaesthesia increased the duration of motor blockade (48%, 70%, 74%) respectively. Juliao Mc *et al.* in their study found that addition of 30µg of Clonidine to intrathecal 0.5% Bupivacaine (15mg) increased the duration of motor blockade. De Negri *et al.* [12]. in their study found that addition of Clonidine 105µg with hyperbaric Bupivacaine 1% intrathecally prolonged the motor blockade. This is already explained that vasoconstriction caused by Clonidine leads to prolongs duration of action of local anaesthetic by decreasing its rate of removal thereby maintaining a relatively higher local anaesthetic concentration for a longer duration of time period which possibly potentiates the conduction block. In present study, the mean duration for subarachnoid analgesia was prolonged in Clonidine group comparison to control group. Therefore, we found that the addition of Clonidine to Bupivacaine significantly prolonged the duration of demand analgesia.

The present study correlated well with the study of Fogarty D *et al.* [13]. who concluded that addition of 75µg of Clonidine with 2.75ml of 0.5% hyperbaric Bupivacaine prolonged the duration of spinal block and the time to first analgesia (mean 278±93.2minutes) than with plain Bupivacaine (mean 61.9±23). In our study the incidence of hypotension was higher in group receiving Clonidine intrathecally but it could be easily managed with intravenous fluids and there was no significant difference in the requirement of vasopressors in both the groups. This was correlated by study of Wu Cl *et al.* who found that incidence of hypotension was more in 45µg group compared with 15µg and 30µg group combined with 10mg tetracaine intrathecally [14]. This correlated with the study by Dobrydnjov et al and Filos Kriton S *et al.* who found that increasing dose of Clonidine produces bradycardia. In our study incidence of sedation was higher in Clonidine group. Sedation commonly accompanies the use of Clonidine for regional anaesthesia, consistent with the known sedative/anaesthetic-sparing properties of alpha2 -adrenergic agonists by actions in the locus coeruleus [11] This brainstem nucleus is associated with a wide variety of physiologic regulatory processes, including regulation of sleep and wakefulness, and is inhibited by alpha2 -adrenergic agonists via a G-protein mediated mechanism that involves inhibition of adenylate cyclase. Actually in our study sedation caused by Clonidine is an anticipated beneficial effect, because of it patient remains calm and quiet during surgery as well as post-operatively. Pruritus, nausea, vomiting, respiratory depression, urinary retention and transient neurological symptoms did not occur in any of the patients included in our study [15].

## Conclusion

This study confirms the efficacy of 75µg of Clonidine as a safe adjuvant to 0.5% hyperbaric Bupivacaine in subarachnoid block for lower abdominal surgeries. The addition of 75µg of Clonidine to 2ml of 0.5% hyperbaric Bupivacaine provide late onset of sensory and motor block, excellent surgical anaesthesia with relative hemodynamic stability, good sedation, prolonged post-operative analgesia and reduces the postoperative analgesic requirements. Clonidine provides maximum benefit and minimum side

effects. It is recommended when prolongation of spinal anaesthesia is desired as, for example in patients scheduled for long, lower abdominal and lower extremity orthopedic procedures.

**Conflict of interest:** No conflict of interest

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