

# Oral Clonidine Premedication and its effect on Subarachnoid block: A Randomised Study

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## ABSTRACT

**Background:** Oral clonidine has been reported to prolong the sub arachnoid block and postoperative analgesia. The study was conducted to evaluate the effectiveness of oral clonidine as premedication on subarachnoid block. **Methods:** 100 patients of aged 20-60 years (ASA-1 and ASA-2 ) undergoing infraumbilical surgeries were included in this prospective, double blind randomized study. Patients divided in to two ( n = 50 ) groups. Group I patients receiving oral clonidine 150 µg one hour before surgery and Group II patients receiving oral placebo. Post-op motor block and pain was assessed by using Bromage Scale and Visual Analogue Scale respectively. Statistical analysis used: Both groups were compared by using paired t test. **Results:** the onset of sensory block in group II 4.40±0.11 min. Vs 3.58±0.10 min. in group I (p < 0.001) , the onset of motor block 5.47±0.12 min. in group II Vs 5.37±0.15 min. in group I (p < 0.001). the duration of sensory block in group II 154.8±13.01 min VS 211.1±10.37min. of group I duration of motor block 138.9±12.5 min. in group II VS 184.2±11.31 min. of group I. (p< 0.001). Total duration of Analgesia for group I 399.46 ± 6.12 vs 149.92 ± 4.14 for group I (P < 0.001). **Conclusion:** Clonidine as oral premedication hastens the onset of sensory block, motor block and increases duration of sensory and motor block as well as total duration of analgesia.

**Keywords:** Analgesia, Clonidine, Premedication.

## INTRODUCTION

Pain is a complex, subjective experience comprising both physical and emotional components.<sup>[1]</sup> Post-operative pain increases the possibility of post-surgical complications, raises the cost of medical care and importantly interferes with recovery and return to normal activities of daily living. The adequate post-operative pain relief will reduce the incidence of pulmonary complication, allowing the patient to take deep breath and cough effectively; it will also allow early ambulation thus preventing deep vein thrombosis. Any method of post-operative analgesia must meet three basic criteria: it must be effective, safe and feasible. Clonidine is a selective α<sub>2</sub> agonist is an imidazoline derivative with peak plasma concentration within 60 to 90 minutes. Clonidine inhibits presynaptic release of nor-epinephrine as well as suppress central noradrenergic activity.<sup>[2]</sup>

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## MATERIALS AND METHODS

Total number of 100 patients of ASA grade I and II of either sex belonging to the age group of 20-60 years and scheduled to undergo infra umbilical surgeries were included in the study after obtaining written and informed consent. Intradermal bupivacaine sensitivity was carried out.

**Group I (50 nos cases):** Patient receiving oral clonidine 150µg administered by the recovery room sister one hour (60 Min) before surgery.

**Group II (50 nos cases):** Patient receiving oral placebo administered by the recovery room sister one hour (60 Min) before surgery.

Before arrival in operation theatre, patients were premedicated with oral clonidine 150µg or oral placebo as per the group distribution. I.V. line was established with 18 G IV cannula. Pulse rate, NIBP, respiratory rate, O<sub>2</sub> saturation (by pulse oxymetry) and ECG status (by cardiac monitor) recorded 15 minutes before LP were taken as preoperative baseline values based on which intra and post operative complications were diagnosed.

Patients back was draped with sterile autoclaved towels, only exposing lumbosacral area. Antiseptic dressing was done with Betadine, followed by spirit. After drying up of spirit, the interspace L3-L4 was identified. The LP needle with its stylet was inserted

in the respective interspace exactly in the midline, with the bevel of the needle parallel to midline (so as to split the fibers, rather to cut) just below the upper border of lower vertebra.

The position of the tip of the needle was confirmed by looking for the free flow of CSF on removal of the stylet. The syringe loaded with the respective drugs was attached to the hub of the L.P. needle. The drug was injected at the rate of 0.2 ml/sec. After injection of the drug a little amount of CSF was drawn into the syringe to reconfirm the position of the tip of the needle. The time of injection was noted.

Patient was immediately turned to supine position. PR, BP, RR, O<sub>2</sub> saturation were checked immediately and thereafter. SBP, DBP, MAP and HR measured and noted at 5 min, 10 min, 15 min, 30 min, 45 min, 60 min, 75 min, 90 min, 105 min and 120 min interval.

**Intra-operative monitoring:** The upper level of sensory block was tested immediately for by loss of sensation to pinprick from below upwards. Since all the patients underwent lower limb surgery, sensory blockade was considered to have begun when the sensory block reached T10. Onset of Motor block was calculated from time of intrathecal injection till Bromage scale-I.<sup>[3]</sup> The highest level of sensory block was noted and this was considered as the height of the block. Those cases where spinal blockade proved to be a failure right from the beginning were excluded from the study. Duration of sensory block was taken from the time of onset of sensory block till the level regression to T12. Duration of motor block was taken from the time of onset of motor block till regression to Bromage scale-IV.<sup>[3]</sup> Total duration of analgesia is taken from the onset of sensory block till the patient receiving rescue analgesia at VAS score 3.<sup>[4]</sup>

#### **The following complications were looked for:**

- Hypotension was said to be significant when MAP is less by 30% of baseline value. This was managed by increasing the drip rate of IVF initially. If hypotension persisted ephedrine hydrochloride was given intravenously in increments of 5 mg. simultaneously 100% O<sub>2</sub> was administered through face mask and leg end of the table raised.

- Bradycardia was considered when PR fell below 60/min and treated with injection Atropine sulphate i.v. in 0.6 mg increments as required.
- Nausea and vomiting if occurred treated accordingly.
- Dry mouth both subjective as well as objective was looked for.
- Hypoxia (O<sub>2</sub> sat <90%) or arrhythmia (if any) was noted and treated as necessary.
- Respiratory depression (RR < 10/min) - if associated with hypoxia was treated with O<sub>2</sub> administration.
- Sedation score was monitored as per Ramsay sedation score.<sup>[5]</sup>

**Post-operative monitoring:** All the above mentioned parameter (PR, BP, RR, O<sub>2</sub> sat) were monitored and all the above mentioned complications were looked for in addition to urinary retention.

When a patient complained of pain or requested for additional analgesia at pain score 3, injection. Diclofenac Sodium 75 mg was given deep I.M. and that particular patient left the study. Patients were reassessed between 3rd & 8th postoperative day for development of any neurological complication.

#### **Statistics**

The findings were presented as mean with standard deviation. There were no dropouts. Data were summarized using "paired t test". SPSS v17 software was used for data analysis.

#### **Motor block evaluation:**

Bromage scale - was defined by Bromage P.R. in 1965, to evaluate the degree of motor blockade

**Grade I:** Complete block - unable to move, knee, toes & feet. ;

**Grade II:** Almost complete block - unable to move knees, but can flex toes.

**Grade III:** Partial block - Just able to flex knees with free movement of the toes.

**Grade IV:** None - Full flexion of knees, feet & toes with flexion of hip.

## **RESULTS**

As per demographic profile the average age was 41.28 years in group I and 40.54 years in group II, average height being 165.62cm in group I and 165.10cm in group II and lastly average weight was 52.92kg in group I and 52.98 kg in group II. Both groups were comparable in age, height and weight.

**Table 1: Comparison of SBP, DBP, MAP and HEART RATE of both Group (I & II)**

	Group-I				Group-II			
	SBP (mmHg)	DBP (mmHg)	MAP (mmHg)	HR Per Minute	SBP (mmHg)	DBP (mmHg)	MAP (mmHg)	HR Per Minute
Baseline	124	76	92	86	126	82	97	82
At 5 min.	124	80	95	86	112	78	89	86
At 10 min.	128	76	93	84	118	76	90	84
At 15 min.	104	78	87	88	124	76	92	80
At 30 min.	110	78	89	90	126	82	97	80
At 45 min.	116	76	89	86	120	84	96	84
At 60 min.	122	84	97	76	120	78	92	80
At 75 min.	124	84	97	78	126	74	91	88
At 90 min.	118	86	97	82	124	76	92	90
At 105 min.	118	72	87	76	120	80	93	86
At 120 min.	124	70	88	80	118	80	93	88

**Table 2: Onset of action and duration of block**

Group	Onset of action (in min.) (m±SD)		Duration of block (in min.) (m±SD)	
	Sensory	Motor	Sensory block	Motor block
I	3.58±0.10	5.37±0.15	211.1±10.37	184.2±11.31
II	4.40±0.11	5.47±0.12	154.8±13.01	138.9±12.5

Onset of sensory and motor action: Though the onset of sensory action in group II is 4.40 min. Vs 3.58 min. in group I and they were statistically significant (p < 0.001) and the onset of motor block is 5.47 min. in group II as comparison to 5.37 min. in group I and are statistically significant, p < 0.001.

Duration of blockade: the duration of sensory block in group II was 154.8min. in comparison to 211.1min. of group I. Likewise duration of motor block is 138.9min. in group II as opposed to 184.2 min. of group I. this shows significant prolongation (p< 0.001).

**Table 3: Total duration of analgesia**

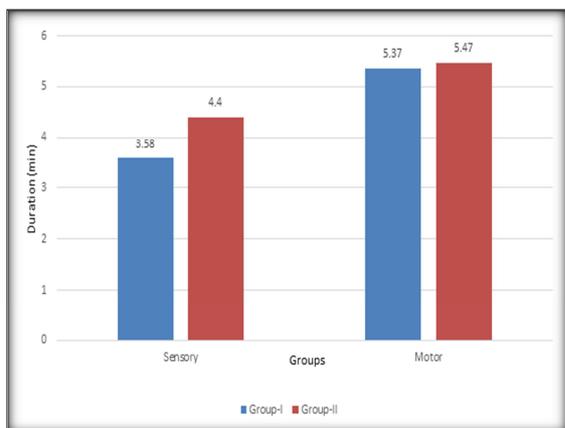
Group	Average duration(mean± SD) (in min)
I	399.46 ± 6.12
II	149.92 ± 4.14

Total duration of Analgesia is 399.46 for group I and 149.92 for group II. P value is highly significant (P < 0.001). On following 7 days postoperatively; none of the patients in either group developed any neurological complication.

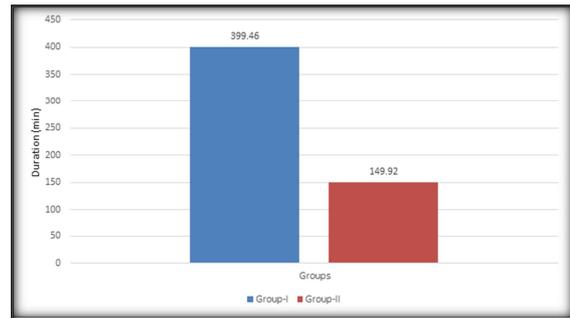
**Table 4: Intraoperative Complication**

Group	Sedation score			Dry mouth	Nausea & Vomiting
	1	2	3		
I	0	7	43	50	4
II	28	22	0	15	3

86% of patients were drowsy in group I. All the patients (100%) in group I experienced dry mouth where as it is 30% in Group II. 8% in group I and 6% in group II had nausea and vomiting.



**Figure 1: Onset of Sensory and Motor Blockade**



**Figure 2: Comparison of Total Duration of Analgesia between Group I & II**

## DISCUSSION

In 1898 spinal anesthesia was first used by Bier as a local anesthesia. The subarachnoid block has occupied an important place in the practice of anesthesia as it provides effective analgesia and adequate muscle relaxation and thus imparts optimal operating conditions with minimal physiological and biochemical alteration in the patients. But it has got some disadvantages, the most important being the short duration of action of lignocaine and longer latent period if Bupivacaine is used for block. As a result patient will have considerable discomfort in the postoperative period due to pain.

Various drugs are being used alone or in combination to increase the duration of spinal anaesthesia. Clonidine is a cheaper alternative in this regard with some acceptable side effects. In 1987 Jean P. Racle et.al.<sup>[6]</sup> studied the prolongation of isobaric bupivacaine with clonidine 150 mcg in spinal anesthesia. Clonidine is a selective partial agonist for  $\alpha_2$  adrenoreceptor and its role in regional anesthesia as an analgesia described by Gabriel et. Al,<sup>[7]</sup> in December 2001.

This  $\alpha_2$  agonist (clonidine) mediated antinociception might be due to blocking of transmission of pain information by activating presynaptic and postsynaptic  $\alpha_2$ -adrenoceptors in the spinal cord, which inhibit substance P release (Kuraishi Y, 1985),<sup>[8]</sup> and dorsal horn neuron firing respectively. Fielding S et.al.<sup>[9]</sup> described the Antinociceptive action of clonidine. According to Meire Nakamura et.al.<sup>[10]</sup> (1988), the Peripheral analgesic action of clonidine is mediated by release of endogenous enkephalin like substances. (Antinociception was due to involvement of interneurons causing primary afferent depolarization of cutaneous sensory fibres resulting in attenuation of pain as described by Zemlan).

Clonidine increase both sensory and motor block of local anesthetics. The analgesic effect is mediated spinally through activation of post synaptic  $\alpha_2$  receptors in substantia gelatinosa of spinal cord. Dobrydnov et.al.<sup>[11]</sup> in their study in orthopaedic patient on post-operative pain relief following intrathecal or oral clonidine, found that addition of intrathecal clonidine prolonged analgesia and

decrease morphine consumption postoperatively more than oral clonidine.

Clonidine, has been extensively studied as an anesthetic adjuvant, which promotes sedation,<sup>[12]</sup> reduces hemodynamic responses to laryngoscopy and tracheal intubation,<sup>[13]</sup> improves perioperative hemodynamic stability and decreases analgesics and volatile anaesthetics requirements.<sup>[14-16]</sup> When spinally injected, it has no motor block properties and seems to decrease local anesthetics vascular absorption by reducing spinal blood flow, thus prolonging local anesthetics blockade, as confirmed by this study. This effect is probably due to a direct action of clonidine blocking Ad and C fibers stimuli conduction, increasing potassium conductance in isolated neurons and intensifying local anesthetics conduction block, as well as indirectly decreasing their absorption by a vasoconstrictor effect mediated by  $\alpha_2$  post-synaptic receptors

Reviewing the literature present study has got stimulus to evaluate the efficacy and safety of clonidine as a means of providing postoperative analgesia. We have also tried to find out that low dose (150 $\mu$ g) oral clonidine also prolong the pain free period without any side effect and excellent surgical analgesia.

As per our clinical study, 100 patients (ASA I and ASA II) selected (patient undergoing infra umbilical surgeries) and were divided into Group I and Group II.

**Group I (50 nos cases):** Patient receiving oral clonidine 150  $\mu$ g one hour (60 Min) before surgery

**Group II (50 nos cases):** Patient on oral placebo

The demographic profiles in both groups were comparable In our study average age in years was 41.28 and 40.54; average height in cm was 165.62 and 165.10; average weight in kg was 52.92 and 52.98 in Group I and Group II respectively.

In the present study the sensory onset was 3.58 minutes in the study group in comparison to 4.40 minutes in control group and Motor onset in study group was 5.37 minutes in comparison to 5.47 minutes of control group. p value being significant ( $p < 0.001$ ). The result of this study is similar to the study done by Baljit Singh Bajwa et.al.<sup>[17]</sup> in January 2017.

Total duration of analgesia was 399.46 min in group I in comparison to 149.92 min in group II. The result of this study is similar to the study done by Abdorrahman Tofighi Rad.<sup>[18]</sup> (P-value was highly significant,  $p < 0.001$ ).

Similar to our study B. S Sethi,<sup>[19]</sup> in 2007 also observed in the clonidine group (1 $\mu$ g/kg) duration of anaesthesia was significant longer than control group. In our study the sensory duration in group I was 211.1 minutes in comparison to 154.8 minutes of group II. Likewise motor duration was 184.2 minutes in group I as opposed to 138.9 minutes of group II. This shows significant prolongation ( $p$  value  $< 0.001$ ). This result is similar to other workers

who had prolonged bupivacaine spinal anaesthetic and tetracaine spinal anaesthesia by adding clonidine.

The prolongation of local anaesthetic block might be due to  $\alpha_2$  mediated presynaptic and post synaptic antinociceptive action G H Paalzow and L K Paalzow,<sup>[20]</sup> may also be due to supraspinal inhibition and due to vasoconstriction of spinal cord vasculature.

As per hemodynamic variations observed in our study is that, the peak reduction of mean arterial blood pressure in the clonidine group was comparatively lower than in the control group. The reason is probably by inhibiting noradrenaline release by clonidine. Similar effects have been observed by Dr. Subhendu Sarkar et. al.<sup>[21]</sup> in 2006.

Intraoperatively all the patients in study group were sedated, either drowsy or dozing intermittently. It offers additional benefits in spinal anaesthesia where supplemental intravenous sedation was required.

Other complications were dry mouth in all patients in group I, and vomiting in few patients in group I.<sup>[22]</sup>

## CONCLUSION

To conclude, oral clonidine is a boon in anaesthetic practice. More and more pioneering works are to be conducted to establish its promising role in other forms of regional anaesthesia besides spinal anaesthesia and other different forms of surgeries. clonidine as oral premedication produces higher incidence of moderate sedation, hastens the onset of sensory block and motor blockade. It prolongs the duration of sensory and motor blockade as well as total duration of analgesia. Also, not associated with any greater change in heart rate and blood pressure following spinal anaesthesia.

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