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**Research Article**

# COMPARISON OF ANALGESIC EFFICACY OF INTRATHECAL CLONIDINE AND FENTANYL AS AN ADJUVANT TO LOW DOSE HYPERBARIC BUPIVACAINE IN ELECTIVE CAESAREAN SECTIONS

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**ABSTRACT**

***Background and Aims:*** Use of various adjuvants to local anaesthetics for spinal anaesthesia is a well known modality to provide prolonged duration of post operative analgesia. We designed this study to evaluate and compare the analgesic efficacy of intrathecal clonidine and fentanyl as an adjuvant to low dose hyperbaric bupivacaine (7.5 mg).

***Methods:*** Fifty patients of American Society of Anaesthesiologists physical status grade I/II, posted for elective lower segment caesarean section (LSCS) under spinal anaesthesia, were randomly allocated in two groups using chit in box method. Group A received 7.5 mg of 0.5% hyperbaric bupivacaine (1.5 ml) + fentanyl 25µg (0.5 ml) and Group B received 7.5 mg of 0.5% hyperbaric bupivacaine (1.5 ml) + clonidine 45µg (0.3 ml) + 0.2ml normal saline. We observed the duration of post operative analgesia as primary outcome variable and secondary outcome variables included onset and duration of motor and sensory block, haemodynamics and adverse effects.

***Results:*** The mean duration of analgesia was significantly ($P$ <0.001) longer in clonidine group (212.24 $\pm$ 44.34 min) as compared to the fentanyl group (175.12 $\pm$ 28.27 min).

***Conclusion:*** Intrathecal Clonidine (45mcg) when used as an adjuvant to low dose of 0.5% hyperbaric bupivacaine (7.5mg) provides prolonged post-operative analgesia along with longer duration of two segment regression as compared to fentanyl (25µg) with low dose of 0.5% hyperbaric bupivacaine (7.5mg) without any significant adverse effects and hemodynamic alteration.



## INTRODUCTION

Spinal anaesthesia is most preferred mode of providing anaesthesia for obstetrics and gynaecological surgery as it provides good operating conditions with excellent muscle relaxation, but even with long acting local anaesthetic like bupivacaine, the duration of postoperative analgesia is often inadequate. To combat this limitation, various intrathecal adjuvants are being used to provide better post operative pain control. α2 adrenergic agonists & opioids have both analgesic and sedative properties when used as an adjuvant in regional anaesthesia [1], [2], [3]. Stable hemodynamics and decreased oxygen demand due to enhanced sympatho-adrenal stability make them very useful pharmacologic agents [4], [5]

Intrathecal clonidine prolongs post operative analgesia by hyperpolarizing Aδ and C fibre in the substantia gelatinosa of the spinal cord. [6] Low-dose clonidine has good analgesic efficacy with a low incidence of adverse effects.[7] The use of intrathecal opioids like fentanyl as an adjuvant to local anaesthetics potentiates post operative analgesia without prolonging the motor blockade but associated with adverse effects like respiratory depression, pruritis, nausea vomiting, hemodynamic instability, urinary retention etc. [8]

We designed this study to evaluate and compare the analgesic efficacy of intrathecal clonidine and fentanyl as an adjuvant to low dose hyperbaric bupivacaine (7.5 mg) in elective lower segment caesarean section (LSCS). We observed duration of post operative analgesia as primary outcome variable and characteristics of spinal block, haemodynamics and adverse effects as secondary outcome variables.

## MATERIAL AND METHODS

This hospital based, randomized, double blinded and comparative study was conducted at a tertiary care centre after approval from the Institutional Ethics Committee and written informed consent from all patients.

Fifty patients aged between 20 to 40 years with American Society of Anaesthesiologist (ASA) physical status grade I or II, undergoing elective lower segment caesarean section under

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spinal anaesthesia were selected for this study. All the patients were evaluated thoroughly in pre anaesthetic check-up including history, general physical examination and necessary blood investigations. Patients with any contraindication to spinal anaesthesia and having any chronic illness were excluded from study. After taking written informed consent, fifty patients were randomized into two groups of twenty five patients using chit in box method. Both the patient and the anaesthetist were blinded to the drug used. The anaesthetist giving spinal anaesthesia was different from the anaesthetist who was involved in the post-spinal observations.

After checking fasting status, patients were shifted in operation theatre. A multipara monitoring for electrocardiogram (ECG), non invasive blood pressure (NIBP), heart rate (HR) and oxygen saturation (SpO2) was established and baseline vitals were recorded. Preloading was done with Ringer's lactate 15-20 ml/kg over 10 minutes. Under all aseptic measures, spinal anaesthesia was given at the L2-L3/L3-L4 interspace in left lateral decubitus position with 25 G spinal needle. A total of 2 ml study drug was injected intrathecally according to the allocated group.

***Group A (n=25):*** Patients received 7.5 mg of 0.5% hyperbaric bupivacaine (1.5 ml) + fentanyl 25µg (0.5 ml)

***Group B (n=25):*** Patients received 7.5 mg of 0.5% hyperbaric bupivacaine (1.5 ml) + clonidine 45µg (0.3 ml) +0.2ml normal saline.

The patients were placed in supine position with a 15° head down tilt immediately after spinal injection to achieve desired level of block at $T_{10}$ level. Vitals were recorded. The patients were given 4.0 L/min of oxygen by face mask.

Sensory block was assessed at 2 minutes interval by pin prick method along midclavicular line on both sides using 25G hypodermic needle until the highest level of block was achieved and the required time was recorded. The onset of sensory block was defined as the time from the subarachnoid injection of the study drug to the time taken to achieve $T_{10}$ dermatomal level sensory block. Grading of sensory blockade was done by 3 point scale (0- sharp pain; 1-touch sensation only and 2- not even touch sensation). Regression of sensory block was defined as the time taken for 2 dermatomal regressions from the highest level of sensory block achieved. Motor block was assessed by modified Bromage score. Onset of motor block was defined as the time taken from drug injection to the time taken to achieve complete motor block (modified Bromage score-3). Duration of motor block was the time elapsed from the maximum to the lowest modified Bromage score (3-0).

Intraoperative monitoring of pulse rate, SpO2, blood pressure, ECG and saturation was done at every 2 minutes till 10 minutes, then at 10 minutes interval till the completion of surgery. Hypotension was defined as mean arterial pressure > 20% decrease in baseline values, treated with inj.ephedrine in incremental doses. Bradycardia was defined as heart rate < 50/min, treated with inj. atropine 0.4-0.6 mg i.v. in incremental doses.

In post operative period, pain was assessed by VAS (0-10) and sedation was assessed by a four point sedation scale (1- eyes open spontaneously; 2 -eyes open to speech; 3-eyes open when shake and 4-unarousable) at 30 min interval up to the 6 hours after the surgery or till the demand of first rescue analgesia. Duration of analgesia was defined as time from subarachnoid injection to the first dose of rescue analgesia which was given when VAS was 4. Any side effects such as nausea, vomiting, hypotension and bradycardia were noted and managed.

***Sample size*** was calculated to be 16 subjects in each of the two group at alpha-error 0.05 & study power 80% assuming expected difference in mean duration of analgesia to be 54.3 min. & SD 52.3 (as per our pilot study).We enrolled 25 subjects in each group for study purpose.

***Statistical analysis*** was performed with the SPSS, version 21 for Windows statistical software package (SPSS inc., Chicago, IL, USA). The Categorical data was presented as numbers (percent) and were compared among groups using Chi square test. The quantitative data was presented as mean and standard deviation and was compared by student t-test. Probability was considered to be significant if less than 0.05.

## RESULTS

Both the groups were comparable with respect to age, weight, height and ASA physical status. [Table 1]

**Table 1** Distribution of demographic variables

| Variables | Group A (n=25) | Group B (n=25) | *P* | Significance |
|---|---|---|---|---|
| Age (years) | 24.88±3.23 | 25.24 ±3.64 | 0.713 | NS |
| Weight (kg) | 57.04±5.34 | 57.12±5.31 | 0.958 | NS |
| Height (cm) | 159.52±0.80 | 157.56 3±0.64 | 0.690 | NS |
| ASA(I/II) | 23/2 | 24/1 | >0.05 | NS |
| Duration of surgery (min) | 33.68 + 4.57 | 32.20 + 5.24 | >0.05 | NS |

Values presented as mean±SD, Group A- fentanyl; Group B-clonidine.ASA American Society of Anaesthesiologist .SD-standard deviation

The duration of analgesia (time to first rescue analgesia) was significantly ($P$<0.001) prolonged in group B (212.24 4±4.34 min) as compared to Group A (175.12 2±8.27 min). [Table 2]

**Table 2** Characteristics of spinal block

| Variables | Group A | Group B | *P* | Significance |
|---|---|---|---|---|
| Onset of sensory block (min) | 2.54±1.14 | 2.45±1.24 | 0.791 | NS |
| Duration of sensory block (min) | 80.56±20.93 | 95.04±24.96 | 0.031 | S |
| Onset of motor block (min) | 2.62±1.08 | 2.40± 0.82 | 0.422 | NS |
| Duration of motor block (min) | 93.8±16.72 | 97.72±11.66 | 0.341 | NS |
| Duration of analgesia (min) | 175.12 ±28.27 | 212.24±44.34 | <0.001 | HS |

Values presented as mean±SD, Group A- fentanyl; Group B-clonidine.,.SD-standard deviation., NS-non significant, S-significant, HS- highly significant

The onset of both sensory and motor block was comparable in both the groups ($P$>0.05). [Table 2] Mean time of duration of motor block was 93.8±16.72 minutes in Group A and 97.72±11.66 minutes in Group B, which was not significant statistically (p>0.05). [Table 2]

During intraoperative period, HR, SBP and DBP were comparable in both the group ($P$>0.05). Hypotension occurred in 5 patients in group B as compared to only 3 patients in group A. Bradycardia was observed in 4 patients in group B as

compared to only 2 patients in group A, but it was not significant statistically . ($P$>0.05)

**Table 3** Incidence of adverse effects

| Variables | Group A | | Group B | | *P* | Significance |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | | |
| Shivering | 2 | 8.0 | 2 | 8.0 | > .05 | NS |
| Nausea | 4 | 16.0 | 4 | 16.0 | > .05 | NS |
| Pruritis | 3 | 12.0 | 1 | 4.0 | >.05 | NS |
| Respiratory depression | 0 | 0.0 | 0 | 0.0 | - | - |

The sedation scores were comparable in both of the groups ($P$ >0.05). Regarding the incidences of adverse effects like nausea, shivering, pruritis, and respiratory depression, no significant differences ($P$ >0.05) were observed in both the groups.

## DISCUSSION

Various drugs are being used as intrathecal adjuvants with local anaesthetics to provide longer duration of post operative analgesia as well as to improve the quality of subarachnoid block to facilitate functional recovery of patients.[9] Although many studies have shown the prolongation of postoperative analgesia with both intrathecal clonidine and fentanyl when used as adjuvants to local hyperbaric bupivacaine in lower segment caesarean section, but none of them have used low dose of 0.5 % hyperbaric bupivacaine (7.5mg), as low dose of local anaesthetics reduces the level of spinal block, local anaesthetic toxicity and provides faster recovery, mobilization, better care of new born with satisfaction of mother and improves breastfeeding. We observed prolonged duration of post operative analgesia without any adverse effects, with intrathecal clonidine as compared to intrathecal fentanyl in this study. The synergistic action of both clonidine and local anaesthetic is responsible for profound analgesia and better quality of both sensory and motor blocks. [10]

In our study the mean duration of analgesia (demand of first rescue analgesia), in clonidine + bupivacaine group was 212 ± 44.34 min and in fentanyl bupivacaine group was 175 ± 28.27 min. ($P$ <0.001) This is in accordance with studies done by Md. Manowarul Islam *et.al* [11], Ranju singh *et.al* [12], Pooja chopra *et.al* [13] and Umesh K Dash *et.al*[14] All of these studies concluded a prolonged duration of analgesia with use of intrathecal clonidine as compared to fentanyl.

Onset of sensory block and motor block were comparable in both clonidine and fentanyl group ($P$ >0.05). Our results are similar to studies [13], [14], [15] The mean duration of motor block was comparable in both Fentanyl and clonidine group. ($P$ value >0.05). Similar observation was made by Ranju *et.al* [12] We observed that time taken for two segment regression was significantly prolonged in clonidine group ($P$= 0.031). Similar results were observed by Pooja chopra *et.al* [13] and Dhummansure *et.al* [15]

Regarding haemodynamic variables, no statistically significant difference was found between the two groups. ($P$ >0.05). Our results are in line with observations made in various other studies [13, 14, 16,] We observed that sedation scores were comparable between clonidine and fentanyl groups. ($P$ value>0.05) This correlates with the other studies. [13, 16]

The incidence of hypotension, bradycardia and sedation varies with the dose of intrathecal clonidine. It is mainly due to central alpha-2 agonistic activity. [17] Intrathecal clonidine in dosage of 45 µg with bupivacaine 7.5 mg used in our study had no clinically relevant side effects in terms of nausea, pruritis, shivering and respiratory depression ($P$ value>0.05) when compared to intrathecal fentanyl 25 µg. Similar results were obtained by Umesh k Dash *et.al* [14] while Ranju singh *et.al* [12] observed same findings in terms of shivering and respiratory depression ($P$ value>0.05), but observed significantly lower incidence of nausea and pruritis in clonidine group as compared to fentanyl group ($P$<0.001).

## CONCLUSION

Intrathecal clonidine (45mcg) when used as an adjuvant to low dose of 0.5% hyperbaric bupivacaine (7.5mg) provides prolonged post-operative analgesia along with longer duration of two segment regression as compared to fentanyl (25µg) with low dose of 0.5% hyperbaric bupivacaine (7.5mg) without any significant adverse effects and hemodynamic perturbation.

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