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# TO ASSESS THE ANALGESIC EFFICACY OF ORAL CLONIDINE VS INTRATHECAL CLONIDINE ADDED AS AN ADJUVANT TO 0.5% HYPERBARIC BUPIVACAINE IN CESAREAN SECTION-A PROSPECTIVE RANDOMIZED DOUBLE BLINDED STUDY

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## Abstract

**Aims**: We aimed to compare the analgesic efficacy of oral clonidine vs intrathecal clonidine added as an adjuvant to 0.5% hyperbaric bupivacaine spinal anesthesia in cesarean section

**Materials and Methods**: A prospective randomized double blind controlled studyenrolled 50 patients for elective caesarean sections under spinal anesthesia and were allocated into 2 groups (25 each) after fulfilling the inclusion and exclusion criteria. Group O received 0.5% hyperbaric bupivacaine 2cc(10mg) plus 0.5 cc NS intrathecally and 200µg oral clonidine was given 90 mins before spinal anesthesia and group I received 0.5 % Hyperbaric bupivacaine 2cc(10mg) + 45 µg (0.5cc) of clonidine intrathecally with oral vitamin c tablets 90 mins before spinal anesthesia.

**Results:** Both the groups had comparable demographics in age, height,weight, BMI. There was a statistically significant difference in terms of duration of analgesia between the two groups. Duration of analgesia was prolonged more in Group I than in Group O with a p value 0.0001.There was a statistically significant difference in terms of onset of sensory and motor blockade which was faster in Group I than in Group O. (P=0.0001). There was a statistically significant difference in terms of duration of sensory and motor blockade which was prolonged in Group I than in Group O. (P=0.0001). There was a significant reduction in pulse rate and hypotensive episodes encountered with Group O than Group I which was statistically significant. The sedation, fetal well being and adverse effects were all comparable between the two groups.

**Conclusion:** Intrathecal clonidine when added as an adjuvant to hyperbaric bupivacaine prolongs the duration of analgesia, sensory and motor block than oral clonidine without significant adverse effects.

**Key words:** Clonidine, spinal anesthesia, Cesarean sections.

## INTRODUCTION

Spinal anaesthesia has become the preferred anaesthesia for cesarean section and it is simple to perform, economical, produces rapid onset and adequate muscle relaxation.[1]

However, spinal anaesthesia is associated with adverse effects like hypotension, bradycardia, respiratory depression etc. The incidence of adverse effects can be decreased by reducing the dosage of local anaesthetic used for Spinal anaesthesia, which can be accomplished by adding adjuvants like opioids, neostigmine, clonidine.[1]

Opioids such as morphine, fentanyl and sufentanil have been used as adjuvants to spinal anaesthesia. Although they ensure superior quality of analgesia, they are associated with many side effects such as pruritis, nausea, vomiting, urinary retention and respiratory depression.[2]

Clonidine is a selective partial agonist for alpha 2 receptors. Intra thecal clonidine has a substantial antinociceptive effect by its action on alpha 2 receptors on the dorsal horn of spinal cord produces dose dependent analgesia and it has been used successfully as a sole analgesic for pain relief in labour and for post operative pain treatment after cesarean section. [3]

Oral administration of clonidine results in complete absorption and peak plasma concentration occurs 1-3 hours after administration .The drug is highly lipid soluble, easily crosses the blood brain barrier and therefore interacts with alpha adrenergic receptors at spinal and supraspinal sites within the CNS. [4]

Studies comparing oral and intrathecal clonidine in lower limb surgeries had been done previously.[5] But, thorough literature search revealed the lack of study comparing oral and intrathcal clonidine in parturients. So, this study is conducted to compare the analgesic effects of oral clonidine and intrathecal clonidine as an adjuvant to hyperbaric bupivacaine under spinal anesthesia for cesarean section.

## AIM

To compare oral clonidine with intrathecal clonidine as an adjuvant to hyperbaric bupivacaine in cesarean section for post operative analgesia.

## OBJECTVES

**PRIMARY OBJECTIVE:** To assess, the duration of analgesia

**SECONDARY OBJECTIVE:** To assess,Onset and duration of sensory block and motor block, Hemodynamic changes, Level of sedation, Fetal wellbeing (Apgar score), Any significant adverse effects with the study drugs used.(Nausea, vomiting, shivering, pruritis)

## MATERIALS AND METHODS

After institutional ethical committee approval a randomization done by computer generated random number table, double- blinded study was conducted. A total number of 50 parturient of ASA grade II of age group between 18-40 years undergoing elective LSCS, who satisfied all the inclusion criteria were enrolled in the study after taking informed valid written consent.

**Study period**: January 2021 to July 2022

**Study design**: Prospective Randomized double blinded clinical trial.

**Inclusion Criteria**

- ASA physical statusII.
- Age 18-40 years.
- Singleton pregnancy
- Informed, written and valid consent.

**Exclusion Criteria:**

- Obstetric complications such as Placenta previa, Abruptio placenta and Preeclampsia
- Spinal deformity such as kyphoscoliosis
- BMI greater than 35kg/$m^2$
- Height less than 140 cm or greater than180 cm
- Women with Hypertensive disorders, Cardiovascular disorders, Deep vein thrombosis
- Allergy to study drugs.

**Method of Study:**

A Prospective Randomized, Double-blinded controlled trial was planned. 50 parturients in an academic institution are selected by computer generated randomization. Standard pre-operative data is collected prospectively for all patients who underwent elective caesarean section in our institution. All operations are carried out by obstetricians and anesthesia is standardized in all patients. All patients in the inclusion criteria undergo pre-anesthetic evaluation a day prior to surgery. Informed valid written consent is taken from all patients. Patients are instructed nil by mouth, 6 hours for solid food and 2 hours for clear liquids before surgery. The syringes were prepared by an investigator anaesthesiologist who is not included in the procedure, observation, or data collection. The observer anaesthesiologist as well as the patient are blinded to the drug injected. All patients belonging to the inclusion criteria are randomly allocated into following groups, each containing 25 parturients.

**Group O** (n = 25) received 0.5% hyperbaric bupivacaine 2cc plus 0.5ml NS plus 200µg oral clonidine.

**Group I** (n = 25) recived 0.5 % Hyperbaric bupivacaine 2cc plus 45 µg (0.5cc) of clonidine intrathecal.

Calculation to make 45 µg:One cc of Clonidine contains 150mcg. We have taken half cc of clonidine (75 mcg). Added 0.3 cc of Ns. Now each 0.1 cc contains 9mcg. We have taken 0.5 cc from that which contains 45 mcg of clonidine.

Parturients in **Group O** were given 200µg of clonidine orally with sips of water, 90 minutes before spinal anesthesia, by the investigator on the morning of surgery.Parturients in **Group I** were given Vitamin C tablets orally with sips of water, 90 minutes before spinal anesthesia, by the investigator on the morning of surgery.This was be done by investigator, who is not included in the procedure, observation or in data collection. In the operating room standard monitoring like electrocardiography, non-invasive blood pressure and oxygen saturation, heart rate was established and baseline values were noted.

18G IV cannula was inserted into a patent peripheral vein. Before conducting spinal anesthesia patients were preloaded with infusion of Ringer's lactate solution 10ml/kg body weight intravenously over 30 mins.All patients were premedicated with Inj. metaclopromide 10mg. Spinal anesthesia was given by 25 G spinal needle in sitting /lateral position through midline approach between L2-L3 or L3-L4 vertebral space. After making note of the clear flow of csf, parturients in **Group I** received 45µg of clonidine with 0.5% hyperbaric bupivacaine (2ml) intrathecally and Parturients in **Group O** received only 0.5% hyperbaric bupivacaine (2ml) with 0.5ml NS intrathecally.The type of study drug used was unknown to anesthesiologist administering the anesthesia or to the anesthesiologist who evaluated patient's response.

Parturients were placed in 15 degree left lateral position and Oxygen at 6 L/min with a face mask administered to all the parturient during the surgery. Surgery was started when sensory block reached T4.

Loss of sensation, and level of sensory block assessed with pin prick. Degree of motor block assessed by modified Bromage scale. NIBP, heart rate (PR), respiratory rate (RR) and oxygen saturation (Spo2) were monitored intra operatively at various intervals.

After the delivery of baby Inj. Oxytocin 10 IU was administered in the drip.

Apgar score was recorded at 1 and 5 mins after the birth of baby. Post operative analgesia was evaluated by determining the time interval between subarachnoid block and the first rescue analgesia.

**Parameters Observed**

**Duration of analgesia**: Assessed every 15 minutes post operatively by 10 cm Visual Analogue Scale (VAS). Time duration (minutes) was assessed from onset of sensory block to first request for rescue analgesic or VAS score 4 or more. Rescue analgesic injection Diclofenac sodium 1.5mg/kg will be given intramuscularly.

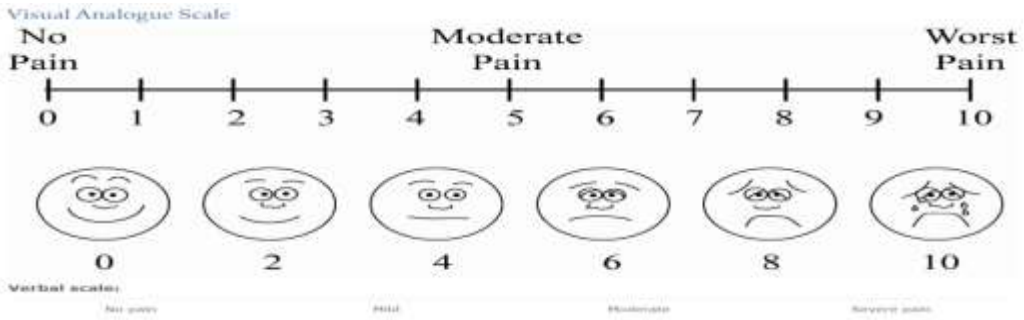


**Figure 1 Visual analogue scale**

**Onset of sensory block:** It is theinability to appreciate pin touching determined by pin prick method, till T6 level achieved.

**Onset of motor block:** It is theinability to raise extended leg and not able to move knee or feet (Modified bromage scale 3).

**Modified bromage scale:**

| | |
|---|---|
| Grade 0 | No motor block |
| Grade 1 | Inability to raise extended leg,able to move knee and feet |
| Grade 2 | Inability to raise extended leg and move knee, able to move feet |
| Grade 3 | Complete block of motor limb |

**Table 1: Modified bromage scale**

**Duration of sensory block**: It was assessed from onset of sensory block to regression of L1 dermatome by pin prick method.

**Duration of motor block:** It was assessed from onset of motor block to regression till grade 2 of modified bromage scale.

**Foetal wellbeing**: Is assessed in both groups by APGAR scores at one minute and five minutes after birth of the baby.

**Level of sedation** is assessed by Campbell's score:

Campbell sedation score: 1-Wide awake, 2-Awake and comfortable, 3-Drowsy and difficult to arouse, 4-Unarousable.

**Hemodynamic parameters**: Pulse, Mean arterial pressure, were recorded at 90,60 and 30 minutes before spinal, just after spinal and 5 minutes, 10 minutes, 15 minutes, 30 minutes, 45

minutes, 60 minutes 90 minutes,120 minutes and thereafter hourly, after administration of Spinal anesthesia.

**Side effects**: Nausea, vomiting, pruritus, respiratory depression, shivering etc if noted, and treated with appropriate medication. Incidences of nausea and vomiting wasscored on a scale of 0 to 2 (0=None, 1=Nausea without vomiting, 2=vomiting). Urinary retention cannot be assessed as every patient will be catheterized in situ for 24 hours. All measurements and assessments were recorded by an anaesthesiologist who is unaware of the medication.Any complications related to the technique or the study drugs used was recorded and managed properly.

**Statistical Analysis:** Data were entered in MS Office Excel and were analysed using Statistical Package for Social Sciences (SPSS) version 24.0.

**Statistical Test:** Categorical variables were summarized as frequencies and variables. Continuous variables were summarized as mean and standard deviation, median inter quartile range.Categorical variables between the groups were compared using Chi-square test. The comparison of normally distributed continuous variables between the groups were analysed using T-test and Mann Whitney test. P value <0.05 will be considered as statistically significant.

## RESULTS

50 parturients aged between 18-40 years, of ASA grade II undergoing Ceserean section under spinal anaesthesia were included in the study.Parturients were divided into 2 groups using computer generated randomization table.Group O (n = 25) received 0.5% hyperbaric bupivacaine 2cc plus 0.5ml NS plus 200µg oral clonidine tablets.Group I (n = 25) received 0.5 % Hyperbaric bupivacaine 2cc plus 45 µg of clonidine intrathecal plus vitamin C tablets.
Following are the observations of this prospective randomized double blind study.

### DEMOGRAPHIC PROFILE

### COMPARISON OF AGE

**Table 2: Comparison of age distribution of the study participants between the two study groups (n=50)**

| Age | Group | | | Fisher's Exact Test | |
|---|---|---|---|---|---|
| | Oral | Intrathecal | Total | $\chi 2$ | P Value |
| 18-25 Years | 12 (48.0%) | 18 (72.0%) | 30 (60.0%) | 4.089 | 0.133 |
| 26-30 Years | 11 (44.0%) | 7 (28.0%) | 18 (36.0%) | | |
| 31-35 Years | 2 (8.0%) | 0 (0.0%) | 2 (4.0%) | | |

| Age | Group | | | Fisher's Exact Test | |
|---|---|---|---|---|---|
| | Oral | Intrathecal | Total | $\chi 2$ | P Value |
| Total | 25 (100.0%) | 25 (100.0%) | 50 (100.0%) | | |

Fisher's exact test was used to explore the association between 'Group' and 'Age'.

Among the parturients undergoing cesarean section under intrathecal bupivacaine with clonidine as an adjuvant, There was no significant difference between oral group and intrathecal group in terms of distribution of Age ($\chi 2 = 4.089$, $p = 0.133$).

**COMPARISON OF HEIGHT**

**Table 3: Comparison of height distribution of the study participants between the two study groups (n=50).**

| Height (cm) | Group | | t-test | |
|---|---|---|---|---|
| | Oral | Intrathecal | t | p value |
| Mean (SD) | 155.08 (4.97) | 154.80 (4.96) | 0.200 | 0.843 |
| Median (IQR) | 157 (152-159) | 154 (151-159) | | |
| Min - Max | 145 - 163 | 145 – 164 | | |

Parametric test (t - test) was used to explore the association between 'Group' and 'Height'.Among the parturients undergoing cesarean section under intrathecal bupivacaine with clonidine as an adjuvant, the mean height in oral and intrathrecal group was 155.08 (4.97) and 154.80 (4.96) respectively. There was no significant difference between oral group and intrathecal group in terms of distribution of Height($t = 0.200$, $p = 0.843$).

**COMPARISON OF WEIGHT**

**Table 4: Comparison of weight (Kg) distribution of the study participants between the two study groups (n=50).**

| Weight (Kg) | Group | | t-test | |
|---|---|---|---|---|
| | Oral | Intrathecal | T | p value |
| Mean (SD) | 55.40 (4.19) | 57.48 (4.74) | -1.644 | 0.107 |
| Median (IQR) | 55 (51-59) | 58 (54-60) | | |
| Min - Max | 49 - 62 | 49 - 65 | | |

Parametric test (t - test) was used to explore the association between 'Group' and 'weight'.Among the parturients undergoing cesarean section under intrathecal bupivacaine with clonidine as an

adjuvant, the mean weight in oral and intrathrecal group was 55.40 (4.19) and 57.48 (4.74) respectively. There was no significant difference between oral group and intrathecal group in terms of distribution of weight (t = -1.644, p = 0.107).

**COMPARISON OF BMI**

**Table 5: Comparison of BMI ($Kg/m^2$) distribution of the study participants between the two study groups (n=50).**

| BMI ($Kg/m^2$) | Group | | t-test | |
|---|---|---|---|---|
| | Oral | Intrathecal | t | p value |
| Mean (SD) | 23.09 (2.08) | 24.07 (2.64) | -1.458 | 0.152 |
| Median (IQR) | 23.24 (22.31-24.13) | 23.37 (22.21-25.97) | | |
| Min - Max | 18.82 - 26.94 | 19.63 - 29.49 | | |

Parametric test (t - test) was used to explore the association between 'Group' and 'BMI'.Among the parturients undergoing cesarean section under intrathecal bupivacaine with clonidine as an adjuvant, the mean BMI in oral and intrathrecal group was 23.09 (2.08) and 24.07 (2.64) respectively. There was no significant difference between oral group and intrathecal group in terms of distribution of BMI (t = -1.458, p = 0.152).

**COMPARISON OF DURATION OF ANALGESIA**

**Table 6: Comparison of VAS score of the study participants between the two study groups (n=50) over time.**

| VAS | Group | | P value for comparison of the two groups at each of the timepoints (Wilcoxon-Mann-Whitney Test) |
|---|---|---|---|
| | Oral | Intrathecal | |
| | Mean (SD) | Mean (SD) | |
| 0 Minutes | 0.00 (0.00) | 0.00 (0.00) | - |
| 1 Minutes | 0.00 (0.00) | 0.00 (0.00) | - |
| 5 Minutes | 0.00 (0.00) | 0.00 (0.00) | - |
| 10 Minutes | 0.00 (0.00) | 0.00 (0.00) | - |
| 15 Minutes | 0.00 (0.00) | 0.00 (0.00) | - |

| VAS | Group | | P value for comparison of the two groups at each of the timepoints (Wilcoxon-Mann-Whitney Test) |
|---|---|---|---|
| | Oral | Intrathecal | |
| | Mean (SD) | Mean (SD) | |
| 30 Minutes | 0.00 (0.00) | 0.00 (0.00) | - |
| 45 Minutes | 0.00 (0.00) | 0.00 (0.00) | - |
| 60 Minutes | 0.00 (0.00) | 0.00 (0.00) | - |
| 90 Minutes | 0.00 (0.00) | 0.00 (0.00) | - |
| 120 Minutes | 0.00 (0.00) | 0.08 (0.40) | 0.337 |
| 180 Minutes | 2.88 (0.53) | 2.32 (0.99) | 0.028 |
| 240 Minutes | 5.52 (1.23) | 2.92 (0.28) | <0.001 |
| 300 Minutes | 3.60 (1.22) | 4.64 (1.38) | 0.004 |
| 360 Minutes | 2.88 (0.60) | 4.24 (1.79) | 0.003 |
| **P Value for change in VAS over time within each group (Friedman Test)** | <0.001 | <0.001 | |
| **Overall P Value for comparison of change in VAS over time between the two groups (Generalized Estimating Equations)** | - | | |

**Table 7: A comparison of mean analgesia of the study participants between the two study groups (n=50).**

| Analgesia Duration | Group | | Wilcoxon-Mann-Whitney U Test | |
|---|---|---|---|---|
| | Oral | Intrathecal | W | p value |
| Mean (SD) | 236.80 (9.88) | 316.80 (24.62) | 0.000 | <0.001 |

| Analgesia Duration | Group | | Wilcoxon-Mann-Whitney U Test | |
|---|---|---|---|---|
| | Oral | Intrathecal | W | p value |
| Median (IQR) | 240 (230-240) | 300 (300-340) | | |
| Min - Max | 210 - 260 | 280 – 360 | | |

Wilcoxon-Mann-Whitney Test test was used to compare the two groups in terms of VAS score at each of the timepoints. Friedman test was used to explore the change in VAS score over time within each group. Generalized Estimating Equations method was used to explore the difference in change in VAS score between the two groups over time.

Among the parturients undergoing cesarean section under intrathecal bupivacaine with clonidine as an adjuvant, the mean duration of analgesia was 236.80 ± 9.88 mins with oral clonidine group and 316.80 ± 24.62 mins with intrathecal clonidine group. This difference was statistically significant with (P <0.05).

## COMPARISON OF ONSET OF SENSORY BLOCKADE

**Table 8: Comparison of onset of sensory blockade of the study participants between the two study groups (n=50).**

| Time Of Onset: Sensory (Minutes) | Group | | Wilcoxon-Mann-Whitney U Test | |
|---|---|---|---|---|
| | Oral | Intrathecal | W | p value |
| Mean (SD) | 2.76 (0.60) | 1.88 (0.44) | | |
| Median (IQR) | 3 (3-3) | 2 (2-2) | 546.500 | <0.001 |
| Min - Max | 1 - 3 | 1 - 3 | | |

Wilcoxon-Mann-Whitney Test test was used to compare the two groups in terms of onset of sensory blockade.The time of onset of sensory blockade was faster in intrathecal group with mean value of 1.88 (0.44), when compared to oral group which had mean value of 2.76 (0.60).There was a significant difference between the two groups (W = 546.500, p = <0.001).

## COMPARISON OF ONSET OF MOTOR BLOCKADE

**Table 9: Comparison of onset of motor blockade of the study participants between the two study groups (n=50).**

| Time Of Onset: Motor (Minutes) | Group | | Wilcoxon-Mann-Whitney U Test | |
|---|---|---|---|---|
| | Oral | Intrathecal | W | p value |
| Mean (SD) | 3.84 (0.37) | 2.88 (0.44) | 570.500 | <0.001 |
| Median (IQR) | 4 (4-4) | 3 (3-3) | | |
| Min - Max | 3 - 4 | 2 - 4 | | |

Wilcoxon-Mann-Whitney Test test was used to compare the two groups in terms of onset of motor blockade.The time of onset of motor blockade was faster in intrathecal group with mean value of 2.88 (0.44), when compared to oral group which had a mean value of 3.84 (0.37).There was a significant difference between the two groups (W = 570.500, p = <0.001).

## COMPARISON OF DURATION OF SENSORY BLOCKADE

**Table 10: Comparison of duration of sensory blockade of the study participants between the two study groups (n=50).**

| Sensory Duration (Minutes) | Group | | Wilcoxon-Mann-Whitney U Test | |
|---|---|---|---|---|
| | Oral | Intrathecal | W | p value |
| Mean (SD) | 155.60 (7.12) | 179.60 (6.11) | 2.500 | <0.001 |
| Median (IQR) | 160 (150-160) | 180 (180-180) | | |
| Min - Max | 140 - 170 | 170 - 190 | | |

Wilcoxon-Mann-Whitney Test test was used to compare the two groups in terms of duration of sensory blockade.The duration of sensory blockade was more prolonged in intrathecal group with mean value of 179.60 (6.11) when compared to oral group with mean value of 155.60 (7.12). There was a significant difference between the two groups (W = 2.500, p = <0.001).

## COMPARISON OF DURATION OF MOTOR BLOCKADE

**Table 11: Comparison of duration of motor blockade of the study participants between the two study groups (n=50).**

| Motor Duration | Group | | Wilcoxon-Mann-Whitney U Test | |
|---|---|---|---|---|
| | Oral | Intrathecal | W | p value |

| Motor Duration | Group | | Wilcoxon-Mann-Whitney U Test | |
|---|---|---|---|---|
| | Oral | Intrathecal | W | p value |
| Mean (SD) | 154.40 (7.12) | 166.80 (5.57) | 71.000 | <0.001 |
| Median (IQR) | 150 (150-160) | 170 (160-170) | | |
| Min - Max | 140 - 170 | 150 - 170 | | |

Wilcoxon-Mann-Whitney Test test was used to compare the two groups in terms of duration of motor blockade.The duration of motor blockade was more prolonged in intrathecal group with mean value of 166.80 (5.57) when compared to oral group which had a mean value of 154.40 (7.12). There was a significant difference between the two groups Duration (W = 71.000, p = <0.001).

## COMPARISON OF HEMODYNAMIC PARAMETERS

## COMPARISON OF BLOOD PRESSURE

**Table 12: Comparison of mean arterial pressure (mm hg)of the study participants between the two study groups (n=50).**

| MBP (mmHg) | Group | | P value for comparison of the two groups at each of the timepoints (Wilcoxon-Mann-Whitney Test) |
|---|---|---|---|
| | Oral | Intrathecal | |
| | Mean (SD) | Mean (SD) | |
| Baseline | 74.84 (6.02) | 75.52 (5.46) | 0.648 |
| 30 Minutes Before Spinal | 74.80 (5.61) | 75.28 (5.83) | 0.846 |
| 1 Minute Before Spinal | 71.20 (4.96) | 77.64 (5.87) | <0.001 |
| 0 Minutes | 72.84 (5.33) | 78.68 (6.05) | <0.001 |
| 1 Minutes | 70.88 (4.60) | 75.40 (5.55) | 0.003 |
| 5 Minutes | 67.36 (3.99) | 70.04 (5.60) | 0.067 |
| 10 Minutes | 68.96 (3.03) | 70.12 (5.13) | 0.654 |
| 15 Minutes | 75.00 (4.41) | 73.64 (4.50) | 0.267 |

| MBP (mmHg) | Group | | P value for comparison of the two groups at each of the timepoints (Wilcoxon-Mann-Whitney Test) |
|---|---|---|---|
| | Oral | Intrathecal | |
| | Mean (SD) | Mean (SD) | |
| 30 Minutes | 76.40 (5.32) | 77.00 (5.21) | 0.586 |
| 45 Minutes | 78.68 (4.54) | 77.08 (5.30) | 0.407 |
| 60 Minutes | 80.16 (6.34) | 77.88 (6.01) | 0.196 |
| 90 Minutes | 81.16 (5.76) | 78.64 (5.73) | 0.173 |
| 120 Minutes | 80.08 (5.16) | 77.16 (6.06) | 0.082 |
| 180 Minutes | 81.12 (5.02) | 80.20 (6.08) | 0.572 |
| 240 Minutes | 82.44 (4.19) | 81.48 (5.54) | 0.466 |
| 300 Minutes | 83.76 (4.04) | 83.64 (6.11) | 0.884 |
| 360 Minutes | 84.56 (3.55) | 84.08 (5.22) | 0.733 |
| **P Value for change in MBP (mmHg) over time within each group (Friedman Test)** | <0.001 | <0.001 | |
| **Overall P Value for comparison of change in MBP (mmHg) over time between the two groups (Generalized Estimating Equations)** | <0.001 | | |

Wilcoxon-Mann-Whitney Test test was used to compare the two groups in terms of MAP (mmHg) at each of the timepoints. Friedman test was used to explore the change in MAP (mmHg) over time within each group. Generalized Estimating Equations method was used to explore the difference in change in MAP (mmHg) between the two groups over time.

Among the parturients undergoing cesarean section under intrathecal bupivacaine with clonidine as an adjuvant, there was a statistically significant difference at 1 min before spinal anesthesia between group O (mean=71.20, SD=4.96), group I (mean=77.64,SD=5.87), at $0^{th}$ min O (mean=72.84, SD=5.33), group I (mean=76.68,SD=6.05) and 1 min after spinal anesthesia

between group O (mean=70.88,SD=4.60 ), group I (mean=75.4,SD=5.6 ) with a p value of <0.05.

**COMPARISON OF PULSE RATE**

**Table 13: Comparison of pulse rate (bpm) of the study participants between the two study groups (n=50).**

| Pulse Rate (BPM) | Group | | P value for comparison of the two groups at each of the timepoints (Wilcoxon-Mann-Whitney Test) |
|---|---|---|---|
| | Oral | Intrathecal | |
| | Mean (SD) | Mean (SD) | |
| Baseline | 79.44 (7.65) | 79.76 (10.39) | 0.816 |
| 30 Minutes Before Spinal | 76.44 (10.48) | 84.72 (12.25) | 0.014 |
| 1 Minute Before Spinal | 77.88 (14.05) | 87.80 (10.34) | 0.006 |
| 0 Minutes | 80.76 (11.97) | 87.24 (12.28) | 0.077 |
| 1 Minutes | 80.24 (11.89) | 86.00 (11.61) | 0.077 |
| 5 Minutes | 78.24 (10.52) | 84.96 (11.44) | 0.039 |
| 10 Minutes | 77.44 (10.08) | 84.64 (9.87) | 0.020 |
| 15 Minutes | 79.40 (8.56) | 84.16 (8.88) | 0.051 |
| 30 Minutes | 70.60 (6.50) | 81.12 (8.62) | <0.001 |
| 45 Minutes | 70.48 (7.90) | 80.68 (8.32) | <0.001 |
| 60 Minutes | 72.92 (6.99) | 83.32 (9.44) | <0.001 |
| 90 Minutes | 74.80 (6.21) | 83.12 (10.28) | 0.003 |
| 120 Minutes | 76.80 (8.26) | 81.84 (9.96) | 0.095 |
| 180 Minutes | 81.88 (7.81) | 84.84 (8.62) | 0.264 |
| 240 Minutes | 83.20 (7.41) | 87.36 (7.94) | 0.089 |
| 300 Minutes | 88.28 (6.65) | 88.84 (8.02) | 0.823 |
| 360 Minutes | 91.04 (6.22) | 92.08 (7.51) | 0.689 |

| Pulse Rate (BPM) | Group | | P value for comparison of the two groups at each of the timepoints (Wilcoxon-Mann-Whitney Test) |
|---|---|---|---|
| | Oral | Intrathecal | |
| | Mean (SD) | Mean (SD) | |
| P Value for change in Pulse Rate (BPM) over time within each group (Friedman Test) | <0.001 | <0.001 | |
| Overall P Value for comparison of change in Pulse Rate (BPM) over time between the two groups (Generalized Estimating Equations) | <0.001 | | |

Wilcoxon-Mann-Whitney Test test was used to compare the two groups in terms of pulse rate (bpm) at each of the timepoints. Friedman test was used to explore the change in pulse rate (bpm) over time within each group. Generalized Estimating Equations method was used to explore the difference in change in pulse rate (bpm) between the two groups over time.

Among the parturients undergoing cesarean section under intrathecal bupivacaine with clonidine as an adjuvant, there was a significant reduction in pulse rate in oral clonidine group when compared to intrathecal group and was statistically significant ($p < 0.05$).

The two groups differed significantly in terms of Pulse Rate (bpm) at the following timepoints: 30 Minutes before Spinal, 1 Minute before Spinal, 5 Minutes, 10 Minutes, 30 Minutes, 45 Minutes, 60 Minutes, 90 Minutes.

**COMPARISON OF SEDATION**

**Table 14: Comparison of campbells sedation score of the study participants between the two study groups (n=50).**

| Campbell's Sedation Score | Group | | P value for comparison of the two groups at each of the timepoints (Wilcoxon-Mann-Whitney Test) |
|---|---|---|---|
| | Oral | Intrathecal | |
| | Mean (SD) | Mean (SD) | |

| Campbell's Sedation Score | Group | | P value for comparison of the two groups at each of the timepoints (Wilcoxon-Mann-Whitney Test) |
|---|---|---|---|
| | Oral | Intrathecal | |
| | Mean (SD) | Mean (SD) | |
| 30 Minutes Before Spinal | 1.00 (0.00) | 1.00 (0.00) | - |
| 1 Minute Before Spinal | 1.00 (0.00) | 1.00 (0.00) | - |
| 0 Minutes | 1.00 (0.00) | 1.00 (0.00) | - |
| 1 Minutes | 1.00 (0.00) | 1.00 (0.00) | - |
| 5 Minutes | 1.08 (0.28) | 1.00 (0.00) | 0.161 |
| 10 Minutes | 1.08 (0.28) | 1.00 (0.00) | 0.161 |
| 15 Minutes | 1.12 (0.33) | 1.00 (0.00) | 0.081 |
| 30 Minutes | 1.16 (0.47) | 1.08 (0.28) | 0.628 |
| 45 Minutes | 1.16 (0.47) | 1.12 (0.33) | 0.973 |
| 60 Minutes | 1.16 (0.47) | 1.16 (0.47) | 1.000 |
| 90 Minutes | 1.12 (0.33) | 1.16 (0.47) | 0.973 |
| 120 Minutes | 1.12 (0.33) | 1.24 (0.60) | 0.629 |
| 180 Minutes | 1.08 (0.28) | 1.20 (0.50) | 0.380 |
| 240 Minutes | 1.08 (0.28) | 1.08 (0.28) | 1.000 |
| 300 Minutes | 1.04 (0.20) | 1.00 (0.00) | 0.337 |
| 360 Minutes | 1.00 (0.00) | 1.00 (0.00) | - |
| **P Value for change in Campbell's Sedation Score over time within each group (Friedman Test)** | 0.004 | <0.001 | |

| Campbell's Sedation Score | Group | | P value for comparison of the two groups at each of the timepoints (Wilcoxon-Mann-Whitney Test) |
|---|---|---|---|
| | Oral | Intrathecal | |
| | Mean (SD) | Mean (SD) | |
| Overall P Value for comparison of change in Campbell's Sedation Score over time between the two groups (Generalized Estimating Equations) | - | | |

Wilcoxon-Mann-Whitney Test was used to compare the two groups in terms of sedation at each of the timepoints. Friedman test was used to explore the change in sedation over time within each group. Generalized Estimating Equations method was used to explore the difference in change in sedation between the two groups over time.Among the parturients undergoing cesarean section under intrathecal bupivacaine with clonidine as an adjuvant, there was a no significant changes in sedation between the two groups.

**FETAL WELL BEING (COMPARISON OF APGAR SCORE)**

**At 1 minute**

**Table 15: Comparison of APGAR score at 1 minute after birth, between the two study groups (n=50).**

| APGAR (1 Minute) | Group | | Wilcoxon-Mann-Whitney U Test | |
|---|---|---|---|---|
| | Oral | Intrathecal | W | p value |
| Mean (SD) | 8.80 (0.41) | 8.80 (0.41) | 312.500 | 1.000 |
| Median (IQR) | 9 (9-9) | 9 (9-9) | | |
| Min - Max | 8 - 9 | 8 - 9 | | |

Among the parturients undergoing cesarean section under intrathecal bupivacaine with clonidine as an adjuvant, there was no significant change in APGAR score at 1 minute between the two study groups (p = 1.000).

**At 5$^{th}$ minute**

**Table 16: Comparison of APGAR score at 5th minute after birth, between the two study groups (n=50).**

| APGAR (5 Minutes) | Group | | Wilcoxon-Mann-Whitney U Test | |
|---|---|---|---|---|
| | Oral | Intrathecal | W | p value |
| Mean (SD) | 8.80 (0.41) | 8.80 (0.41) | 312.500 | 1.000 |
| Median (IQR) | 9 (9-9) | 9 (9-9) | | |
| Min - Max | 8 - 9 | 8 – 9 | | |

Among the parturients undergoing cesarean section under intrathecal bupivacaine with clonidine as an adjuvant, there was no significant change in APGAR score at 5th minute between the two study groups (p = 1.000).

**COMPARISON OF SIDE EFFECTS**

**Table 17: Comparison of side effects of the study participants between the two study groups (n=50).**

| Side Effects | Group | | | Fisher's Exact Test | |
|---|---|---|---|---|---|
| | Oral | Intrathecal | Total | $\chi 2$ | P Value |
| None | 20 (80.0%) | 19 (76.0%) | 39 (78.0%) | 0.359 | 1.000 |
| Shivering | 2 (8.0%) | 2 (8.0%) | 4 (8.0%) | | |
| Vomiting | 2 (8.0%) | 2 (8.0%) | 4 (8.0%) | | |
| Nausea | 1 (4.0%) | 2 (8.0%) | 3 (6.0%) | | |
| Total | 25 (100.0%) | 25 (100.0%) | 50 (100.0%) | | |

Fisher's exact test was used to explore the association between 'Group' and 'Side Effects'.There was no significant difference between the two groups in terms of distribution of Side Effects ($\chi 2$ = 0.359, p = 1.000).

## DISCUSSION

Subarachnoid block, also known as spinal anaesthesia, is a type of regional anaesthesia in which a local anaesthetic drug is injected into the subarachnoid space (CSF). The injection is commonly performed at the L2/3 or L3/4 space. It is the technique of choice for both elective and emergency cesarean deliveries because of its safety in pregnancy, simplicity and low dose of drug needed, adequate muscle relaxation, low placental transfer of drug, awake state of mother

for mother-baby bonding and early initiation of breast-feeding, faster recovery of gastrointestinal functions post-operatively, better postoperative analgesia, early mobilization and avoids polypharmacy.[6]

It also provides patients with a high level of acceptance and satisfaction. It also avoids the risk of aspiration, airway complications, neonatal respiratory depression, and many other difficulties associated with general anaesthesia.

Therefore, we planned adouble blind prospective randomized controlled trial at our institute to compare the efficiency of oral clonidine versus intrathecal clonidine as an adjuvant to bupivacaine in parturients scheduled for elective caesarean sections,keeping pharmacologic interactions and other features in mind.

**DEMOGRAPHIC PROFILE**

The current study's demographic profile was comparable to those of similar prior research and showed no statistical significance when compared.

**AGE:** All of the parturients were between the age of 18 and 40 years. Group O had a mean age of 25.28 years, while group I had a mean age of 24.20 years. Age incidences were equivalent and statistically insignificant. (P=0.2504)

**ANTHROPOMETRY**

Weight and Height of each patient was noted**.**

a. The mean weight in group O was 55.40 kg and in group I was 57.48 kg. Mean weight between the two groups was similar. (P>0.05).
b. The mean height in group O was 155.08 cm and group I was 154.80 cm. Mean height between the two groups was comparable. (P>0.05)**.**
c. The mean BMI in group O was 23.09kg/m2 and group I was 24.07kg/m2. Mean BMI between the two groups was comparable.(P>0.05)

In a study conducted by Mb Adegboye, IkKolawole, BO Bolaji[4]on post operative analgesia with oral clonidine as premedication in caesarean section: randomised double blind controlled study had no statistically significant (P>0.05) difference among two study groups in terms of demographic data like age, weight, height and BMI which is comparable with the findings of our study.

A study conducted by Atasi Das, Sudipta Kumar Mandal, Susmita Bhattacharya[2]on post caesarean analgesia with intrathecal clonidine : a randomised, double blinded, controlled study found similar results in both groups in terms of patient characteristics, age, height, weight, BMI and was statistically insignificant which were correlating with our study findings.[7]

**DURATION OF ANALGESIA:** In our study the mean duration of analgesia was 236.80 ± 9.88 mins with oral clonidine group and 316.80 ± 24.62 mins with intrathecal clonidine group. This difference was statistically significant with (P = 0.0001).

Our study is comparable to that of Anjali Teresa Mathew Ollapally, Prithi Jainwho found that the mean duration of analgesia for lower limb orthopaedic surgery was 280 minutes for oral clonidine at a dose of 2.5 mcg/kg and 370 minutes for intrathecal clonidine at a dose of 75 mcg (P = 0.001).Compared to the oral clonidine group, the intrathecal clonidine group's analgesia lasted significantly longer.[8]

**ONSET OF SENSORY AND MOTOR BLOCKADE**

In our study the onset of sensory and motor blockade was 2.76 mins and 3.84 mins with oral clonidine group and 1.88 mins and 2.88 mins with intrathecal clonidine group. This difference was statistically significant with (P = 0.0001).So we affirm that intrathecal clonidine has faster onset of sensory and motor blockade than oral clonidine.

Our study is comparable with a study conducted by Anjali Teresa Mathew Ollapally, Prithi Jain for lower limb orthopaedic surgery. The authors have concluded that the onset of sensory and motor blockade was faster in intrathecal group 1-1.9 mins 2-2.9 mins than oral clonidine group 2-2.9 mins 3-3.9 mins which was statistically significant.[9]

**DURATION OF SENSORY BLOCK**

In our study the duration of sensory blockade was 155.6 ±7.12 mins with oral clonidine group and 179.60±6.11 with intrathecal clonidine group. This difference was statistically significant with (P = 0.0001).We conclude that intrathecal clonidine prolongs the duration of sensory blockade more than oral clonidine.

Bonnet F et alshowed in his study of orthopaedic surgeries that intrathecal clonidine but not oral clonidine prolonged the duration of sensory block. This is in contradiction to the findings in our study.

**DURATION OF MOTOR BLOCK**

In our study the duration of motor blockade was 154.40±7.12 mins with oral clonidine group and 166.80±5.57 with intrathecal clonidine group. This difference was statistically significant with (P = 0.0001).we conclude that intrathecal clonidine increases the duration of motor blockade more than oral clonidine.

**HEMODYNAMIC CHANGES**

In our study, baseline heart rate and mean arterial pressure recorded preoperatively was comparable in each group. Bradycardia in spinal anesthesia, particularly with clonidine as an additive is a worrisome side effect. But, we did not observe any significant bradycardia with the addition of clonidine. Two parturients in oral clonidine group and one in intrathecal clonidine group had bradycardia that resolved on its own. However, there was a significant reduction in pulse rate in oral clonidine group when compared to intrathecal group and was statistically significant ($p < 0.05$).

**SEDATION**

The degree of sedation was compared between the groups. Only 3 patients in oral clonidine group had sedation in which 2 of them had grade 2 campbells score. 1 patient had grade 3 campbells score. This was comparable with intrathecal clonidine group where 2 patients had grade 2 sedation and one patient had grade 3 sedation. But this was statistically insignificant. However, all patients who were administered clonidine experienced mild sedation and were easily arousable.

**Fetal wellbeing**

The Apgar score was comparable between oral clonidine and intrathecal clonidine groups. APGAR scores at one minute and 5 minutes after birth were comparable in both groups. There was no difference in neonatal outcome.This was similar to Allen TK, Mishriky BM, Klinger RY, Habib ASfor post caesarean analgesia where authors concluded that intrathecal clonidine has no impact on neonatal outcome.

**SIDE EFFECTS**

8% of the parturients in oral clonidine group had shivering and vomiting. 4% of the parturients had nausea. 8% of the parturients in intrathecal clonidine group had shivering, nausea and vomiting.There was no significant difference between the two groups in terms of distribution of side effects.[10]

**Limitation of our study**: were that,

1) It was a hospital based study hence demography does not represent population atlarge.
2) Hemodynamic changes like hypotension and reduction in heart rate which are the adverse effects of clonidine are most commonly seen after spinal anesthesia.
3) We have taken fixed doses of clonidine for both oral and intrathecal route, according to previous studies.

## CONCLUSION

In conclusion, the addition of clonidine as an adjuvant to hyperbaric bupivacaine in subarachnoid block prolongs duration of analgesia.I conclude that (45 mcg) of intrathecal clonidine added to hyperbaric bupivacaine in subarachnoid block has proved to be a better adjuvant than oral clonidine (200mcg) in prolonging the duration of analgesia, duration of sensory and motor blockade and hastens the onset of sensory and motor blockade, with good neonatal outcome and without significant adverse effects.

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