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**Original research article**

# A study to compare the influence of buprenorphine and clonidine when either drug was injected intrathecally as an adjuvant to bupivacaine in infra umbilical surgeries

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**Abstract**

Intrathecal Clonidine is being extensively evaluated as an alternative to neuraxial opioids for control of pain and has proven to be a potent analgesic, free of at least some of the opioids related side effects.

It was not unexpected that Clonidine, an alpha 2 adrenergic agonist, had beneficial effect of improved quality of intraoperative analgesia, and in last two decades several studies have demonstrated that Clonidine administered spinally or epidurally has potent antinociceptive action through an alpha adrenergic mediated mechanism in the dorsal horn of the spinal cord. This action exists for both somatic and visceral pain.

Intrathecal Clonidine potentiates the effect of intrathecal local anesthetics. It has been used as a sole agent as well as admixed with opioids along with local anaesthetics in labour analgesia and infra-umbilical surgeries.

Thus, the fastesr onset of action of local anaesthetiacs, rapid establishment of both sensory and motor blockade, prolonged duration of analgesia in to post-operative period, stable cardiovascular parameters makes $\alpha_2$ agonists like clonidine and Dexmedetomedine very effective adjuvants in regional anaesthesia.

Buprenorphine has been and is, till date popular as an additive for the provision of a prolonged period of postoperative pain relief when used along with Bupivacaine intrathecally.

The present study was thus undertaken to compare the effects of Buprenorphine (75 µg) added to 15 mg of 0.5% Bupivacaine to that of Clonidine (37.5 µg) added to the same.

**Keywords:** Buprenorphine, clonidine, intrathecally, adjuvant, bupivacaine, infra umbilical surgeries

## Introduction

Spinal anesthesia is the fastest, predictable and reliable form of anaesthesia for infra umbilical surgeries [1]. Spinal anaesthesia with Bupivacaine for lower abdominal and lower limb surgeries is used undisputedly far and wide as the procedure of choice, which provides sensory and motor block, creating optimal working conditions for surgeons. It also provides some pain relief in initial postoperative period.

However, insufficient duration of anesthesia and inadequate postoperative analgesia with local anaesthetics like Bupivacaine solely is unable to provide an extended duration of anaesthesia or postoperative analgesia. Visceral pain is an important component of many clinical pain states [2]. Deep pain associated with viscera is, different from somatic cutaneous pain.

Alternative anaesthetic techniques to prolong the duration of anesthesia and provide postoperative analgesia, like epidural or combined spinal epidural, may be time consuming and require technical expertise [3]. (Staphen Strabel *et al.* 2004).

In order to maximize duration of anesthesia and postoperative analgesia, a number of agents, (adjuvants) are added to local anaesthetic.

Sedation, stable hemodynamics and an ability to provide smooth and prolonged postoperative analgesia are the main desirable qualities of an adjuvant in neuraxial anaesthesia [4].

For many years, Vasopressors have been used to prolong the duration of various local anaesthetics in subarachnoid block. As a result of vasoconstriction, the absorption of local anaesthetic is delayed, and the effect of the local anaesthetic is allowed to continue at the local site [5].

Experimental studies have shown that both opioids and alpha 2 adrenergic agonists administered intrathecally, are able to relieve visceral pain[2]. Synergistic action between several analgesic drugs and local anaesthetics has been demonstrated.

In the 17th century English physician Thomas Sydenham wrote: "Among the remedies which it has pleased Almighty God to give man to relieve his suffering, none is so universal and as efficacious as opium."

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Despite their nearly universal ability to alleviate pain, opioids have a number of unpleasant, even life threatening side effects like nausea and vomiting, tolerance, pruritus, urinary retention, and respiratory depression [6].

The identification of opioid receptors has opened new horizons in pain management, Yaksh and Rudy, in 1976, were the first investigators to demonstrate direct opioid analgesia at the spinal cord level [7].

Opioid added to local anaesthetic for spinal anaesthesia was first introduced into clinical practice in 1979 with intrathecal morphine as a forerunner. Neuraxial administration of opioids along with local anaesthetics improves the quality of intraoperative analgesia and also provides postoperative pain relief for longer duration [8].

With demonstration of μ opioids receptors in substantia gelatinosa of spinal cord, the deficiency of inadequate duration of anaesthesia of local anaesthetics is overcome by addition of opioids like Morphine, Fentanyl, Buprenorphine, Sufentanil etc.

Lipophilic opioids such as Buprenorphine, methadone or naloxone exert their effects predominantly on tissues near the site of injection [9].

Central neuraxial opioids, intrathecal as well as epidural, offer the perceived benefit of selective analgesia without sensory or motor blockade. However, side effects such as potentially catastrophic delayed respiratory depression have prompted further research to develop non opioids analgesics with less worrisome side effects [10]. According to Stoelting [11], patients receiving intrathecal opioids should be under close surveillance for adequacy of breathing.

Intrathecal Clonidine is being extensively evaluated as an alternative to neuraxial opioids for control of pain and has proven to be a potent analgesic, free of at least some of the opioids related side effects [12].

It was not unexpected that Clonidine, an alpha 2 adrenergic agonist, had beneficial effect of improved quality of intraoperative analgesia, and in last two decades several studies have demonstrated that Clonidine administered spinally or epidurally has potent antinociceptive action through an alpha adrenergic mediated mechanism in the dorsal horn of the spinal cord. This action exists for both somatic and visceral pain [13].

Intrathecal Clonidine potentiates the effect of intrathecal local anesthetics. It has been used as a sole agent as well as admixed with opioids along with local anaesthetics in labour analgesia and infra-umbilical surgeries [14].

Thus, the fastesr onset of action of local anaesthetiacs, rapid establishment of both sensory and motor blockade, prolonged duration of analgesia in to post-operative period, stable cardiovascular parameters makes $\alpha_2$ agonists like clonidine and Dexmedetomedine very effective adjuvants in regional anaesthesia.

Buprenorphine has been and is, till date popular as an additive for the provision of a prolonged period of postoperative pain relief when used along with Bupivacaine intrathecally.

The present study was thus undertaken to compare the effects of Buprenorphine (75 μg) added to 15 mg of 0.5% Bupivacaine to that of Clonidine (37.5 μg) added to the same.

**Aims and Objectives:**

To study and compare the influence of Buprenorphine 75 μg and Clonidine 37.5μg when either drug was injected intrathecally as an adjuvant to 15mg of 0.5% Bupivacaine in infra umbilical surgeries.

**Materials and Methods**

It was a prospective randomized clinical trial.

After obtaining approval from institutional ethical committee, and taking written informed consent, 100 ASA grade I and II adult patients, of either sex undergoing elective or emergency infra umbilical surgeries, predicted to last from 60-180 min, [15] under spinal anesthesia were divided in to two groups of 50 each.

**Inclusion criteria**

1. ASA grade I and II patients.
2. Patients undergoing elective or emergency infra umbilical surgeries.
3. Age between 18-60 years.
4. Height more than 150 cm.

**Exclusion criteria**

1. Patients on treatment with alpha 2adrenergic antagonists and opioids.
2. ASA grade III or IV patients.
3. Patients with cardiovascular, neurological, respiratory, renal or endocrine diseases, Psychiatric illness.
4. Patients with height <150cms.
5. Contraindication to spinal anaesthesia like bleeding disorders, local infection.
6. Patients with spinal deformities.
7. History of sensitivity to local anaesthetics or opioids.

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8. Patients not willing for spinal anesthesia.
9. Pregnant patients.
10. Patients with hypertension, diabetes mellitus, disorders of liver, CVS, RS.
11. Patients with severe anaemia, emergency hypovolemic patients

Detailed history and preanaesthetic checkup was done for all patients. Minimum necessary investigations like hemogram, blood grouping, Bleeding and Clotting time, Urine analysis and Random blood glucose were done from every patient. Electrocardiogram, Chest X-ray and other investigations like LFT, KFT, and Coagulation profile were done in all patients above 45 years or as and when required according to history, clinical examination in younger patients too.
All patients were explained about the procedure and informed consent was taken. Patients were explained how to read VAS scale for pain and informed of feeling of tingling, warmth or heaviness that may be felt after the injection.
All patients were kept nil orally for six hours prior to surgery [15].
Vitals were noted in preanaesthetic room. No premedication was given to any patient. On operation table, baseline monitoring devices ECG, SpO2, noninvasive blood pressure were attached to patient.
Pulse rate, systolic blood pressure, diastolic blood pressure, respiratory rate, oxygen saturation and VAS were noted before giving subarachnoid block. A wide bore 18-20 G intravenous canula was inserted in to peripheral vein of an arm, and patient preloaded with 10 ml/kg of Ringer Lactate solution over 30 min.
With operation table in neutral position, and under all aseptic precautions, lumbar puncture was done in L3-4 interspace in sitting position with 25G Quincke spinal needle. L3-4 interspace was identified by line between the upper boarders of iliac crests passing through the spinous process of L4 or interspace between L4-5. After obtaining free flow of CSF, the proposed drug was injected slowly (1 ml/ 7seconds) [16] as per group allotment as follows-
**Group C:** 15 mg hyperbaric Bupivacaine 0.5% (3 ml) + 37.5 µg Clonidine (0.25ml) (50 patients)
**Group B:** 15 mg hyperbaric Bupivacaine 0.5% (3 ml) + 75 µg Buprenorphine (0.25ml) (50 patients)

Both Buprenorphine and Clonidine were measured in an insulin syringe for accuracy[1] and added to Bupivacaine taken in a 5ml syringe. Intrathecal solutions were at room temperature. The total volume injected was 3.25 ml in both groups.
The time of drug injection was noted and recorded as 0.
After injection patient was turned supine slowly and given oxygen 4 lit /min by Venturi mask, following parameters of blockade characteristics and hemodynamic parameters were monitored and noted as follows-
1. Onset of sensory analgesia.
2. Onset of motor blockade.Time to achieve $T_{10}$ sensory level
3. Time to achieve maximum sensory level.
4. Time to achieve maximum motor blockade.
5. Time of two segment sensory regression.
6. Total duration of motor block.
7. Total duration of analgesia.
8. Quality of Anaesthesia.

The time of start of monitoring was taken from the time the drug was injected into the intrathecal space. (t=0),

**1. Onset of sensory analgesia**
This was subjectively assessed by patient complaining of sensation of tingling or warmth in his or her limbs, confirmed by decreased VAS score to pinprick of 5 or less at calf level (pinprick test) [15] and it was measured from injection of study drug in subarachnoid space to patient saying of sensation of tingling or warmth in his or her limbs, noted in seconds.

**2. Onset of motor block**
It was subjectively assessed by patient and confirmed by Modified Bromage Scale [1], is measured from the time of injection of drug in subarachnoid space till the onset of feeling of heaviness in legs and was noted in seconds.

**3. Time to achieve $T_{10}$ sensory level**
It was taken from time of intrathecal drug administration to attaining of $T_{10}$ sensory level. It was noted in minutes.

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**4. Time to maximum sensory level achieved**
The duration from injection of study drug and time to maximum cephalic sensory level achieved was noted in minutes. It was tested by pinprick with sterile 25G hypodermic needle. Patients were tested every 2 min for 10 min, every 5 min for 30 min or till starting of surgery, whichever was earlier.

**5. Maximum sensory cephalic level achieved**
Maximum sensory cephalic level achieved was assessed with 25G hypodermic needle, recorded as loss of sensation to pinprick.

**6. Time of maximum motor blockade**
This was the time interval between drug injection into intrathecal space and the minimum time at which maximum degree of motor blockade was achieved.
This was assessed by Modified Bromage scale, noted in minutes.
Modified Bromage Scale:
**Gr 0:** Pt. able to move hip, knee and ankle
**Gr I:** Able to move knee and ankle, cannot move hip.
**Gr II:** Able to move ankle, cannot move hip and knee.
**Gr III:** Unable to move hip, knee or ankle.

**7. Total duration of motor blockade**
It was taken from injection of study drug to regression of motor block to grade 0 and noted in minutes.

**8. The duration of surgery**
This was taken from surgical incision to skin closure.

**9. Time of two segment regression of sensory block**
It was calculated from the time of maximum sensory level achieved to the regression of sensory block by two dermatomes. It was assessed 60 min after spinal puncture or after completion of surgery and every 10 min until regression of sensory level by two dermatomes below maximum sensory level was attained.

**10. Quality of Anaesthesia**
During surgery, the surgeon was requested to assess the quality of anaesthesia by using the following four point scale. [17]
Grade 1: Excellent, Grade 2: Good, Grade 3: Inadequate and Grade 4: Poor

**11. Duration of analgesia**
It was measured from the time of sensory onset to the time of first rescue analgesic given to the patient, i.e. when patient showed VAS of 4 or more, noted in minutes. VAS was assessed on a 10 cm (100mm) pain scale on which 0 end indicates no pain 10 cm indicates worst possible pain. VAS recorded at 0 min as baseline, at 60 min after subarachnoid block, and after then along with vitals.

**12. Sedation score**
Level of sedation assessed with Ramsay sedation score, and noted along with vitals. Sedation was studied as a central effect of drug. The time of onset of sedation after injection of drug was noted and sedation graded by Ramsay sedation scale-

**Ramsay sedation score**

| Score | Criteria |
|---|---|
| I | Patient is anxious, agitated and restless or both |
| II | Patient is co-operative oriented and tranquil. |
| III | Patients respond to verbal commands only. |
| IV | Patient exhibit brisk response to glabellar tap or loud auditory stimulus. |
| V | Patient exhibit sluggish response to glabellar tap or loud auditory stimulus. |
| VI | Patient exhibit no response. |

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**Results**

**Table 1:** Showing Distribution of Patients According To Age and Sex

| Age (In years) | Clonidine group | | Buprenorphine group | |
|---|---|---|---|---|
| | Male | Female | Male | Female |
| 18-30 | 14(28%) | 0(0%) | 14(28%) | 2(4%) |
| 31-40 | 10(20%) | 5(10%) | 8(16%) | 1(2%) |
| 41-50 | 7(14%) | 6(12%) | 6(12%) | 9(18%) |
| 51-60 | 7(14%) | 1(2%) | 9(18%) | 1(2%) |
| | 38(76%) | 12(24%) | 37(74%) | 13(26%) |
| Total | 50 | | 50 | |
| Mean ± SD | 38.32±12.78 | | 39.56±13.94 | |
| t-value | 0.46 | | | |
| p-value | 0.60,NS,p>0.05 | | | |

The distribution of patients according to age and sex was found to be statistically insignificant amongst the two groups.
Mean age in group C was 38.32±12.78 yr and in group B, 39.56±13.94yr.
Sex ratio of 3.16:1 (male: female) in Clonidine group, and 2.8:1 in Buprenorphine group was found to be comparable for both the groups. (p>0.05)

**Table 2:** Showing Distribution of Patient According To Height

| Height (in cm) | Number of patients | |
|---|---|---|
| | Clonidine group | Buprenorphine group |
| 150-160 | 19(38%) | 18(36%) |
| 161-170 | 31(62%) | 32(64%) |
| Total | 50(100%) | 50(100%) |
| Mean ± SD | 163.18+4.71 | 160.28+23.36 |
| ⨪2-value | 0.04 | |
| p-value | 0.83,NS,p>0.05 | |

Mean height in Clonidine group was 163.18±4.7 cm, whereas it was 160.28±23.36 cm. in Buprenorphine group.
Maximum number of patients (62%) and (64%) had height in range of 160-170 cm. in Clonidine and Buprenorphine groups respectively. Mean height was found to be comparable between the groups.

**Table 3:** Showing Distribution of Patients According To Weight

| Weight (in kg) | Number of patients | |
|---|---|---|
| | Clonidine group | Buprenorphine group |
| 40-50 | 11(22%) | 6(12%) |
| 51-60 | 22(44%) | 21(42%) |
| 61-70 | 16(32%) | 22(44%) |
| 71-80 | 1(2%) | 1(2%) |
| Total | 50(100%) | 50(100%) |
| Mean ± SD | 57.06±8.03 | 58.70±6.22 |
| ⨪2-value | 2.44 | |
| p-value | 0.48,NS,p>0.05 | |

Distribution of patients according to the weight was also found to be statistically comparable between the groups.
Maximum number of patient's i.e.38 (76%) Clonidine group and 43 (86%) in Buprenorphine group were having weight in the range of 50-70 kg.

**Table 4:** Showing Distribution of Patients According To Type of Surgery

| Type of surgery | Number of patients | |
|---|---|---|
| | Clonidine group | Buprenorphine group |
| Abd. Hyst. / TAH with BSO/ Exploratory laparotomy | 5(10%) | 6(12%) |
| Vag. Hyst. / Vault repair | 6(12%) | 5(10%) |
| Eversion of sac | 8(16%) | 7(14%) |
| Appendectomy/ incisional hernia repair | 2(4%) | 2(4%) |
| Hernia repair surgeries | 15(30%) | 18(36%) |
| # shaft/ neck Femur, # Tibia/ fibula, | 15(30%) | 13(26%) |
| Total | 50(100%) | 50(100%) |

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Though randomly allocated, distribution of patients according to the type of surgery undergone by them was comparable amongst the groups. Surgeries of inguinal hernia repair and orthpaedic surgeries were the most common surgeries undertaken.

**Table 5:** Showing Onset of Sensory Analgesia

| Onset of sensory analgesia (sec) | Number of patients | |
|---|---|---|
| | Clonidine group | Buprenorphine group |
| 0 – 30 sec | 39(78%) | 29(58%) |
| 31 – 60 sec | 9(18%) | 19(38%) |
| 61-90sec | 1(2%) | 2(4%) |
| >91 sec. | 1(2%) | 0(0%) |
| Total | 50(100%) | 50(100%) |
| Mean ± SD | 24.22±19.70 Sec | 32.78±15.65 Sec |
| z-value | 2.40 | |
| p-value | 0.018,S,p<0.05 | |

The onset of sensory analgesia was assessed subjectively when patient had a sensation of tingling or numbness or warmth in lower limbs, and confirmed objectively using non-traumatic pin-prick method tested immediately after making the patient supine and thereafter at 30 sec intervals from the time of intrathecal drug injection (t=0).
Maximum number of patients in both the group's i.e.78% in Clonidine group and 58% in Buprenorphine group had onset of sensory analgesia within 30 seconds. However, 96% patients depicted an onset within 1 minute (60 sec.) in either of groups.

**Table 6:** Showing Time of $T_{10}$ Sensory Block

| Time of sensory block to $t_{10}$ in min | Number of patients | |
|---|---|---|
| | Clonidine group | Buprenorphine group |
| 0 - 2 | 09 | - |
| 3 – 4 | 35 | 08 |
| 5– 6 | 06 | 11 |
| 7 -8 | - | 12 |
| 9-10 | - | 12 |
| >10 min | - | 07 |
| Total | 50 | 50 |
| Mean ± SD | 3.66 ±1.11 Min | 7.69±2.9 Min |
| z-value | 5.99 | |
| p-value | 0.000,S,p<0.05 | |

9 (18%) patients in Clonidine group attained $T_{10}$ sensory level in 2 minutes which we found in none patient of Buprenorphine group. 35 patients (70%) in Clonidine group and 08 (16%) in Buprenorphine group had attained cephalic sensory level of $T_{10}$ in 3-4 minutes.
In Clonidine group all patients achieved $T_{10}$ sensory level within 5 minutes whereas, maximum number 31 patients (62%) in Buprenorphine group took >7 minutes to achieve this. The mean time to attain the cephalic sensory level of $T_{10}$ was 3.66 ±1.11 min in Clonidine group, and 7.69 ± 2.9 min and Buprenorphine groups respectively and found to be statistically significant (p=<0.001).

**Table 7:** Showing Time of Maximum Sensory Block

| Time of maximum sensory block (min) | Number of patients | |
|---|---|---|
| | Clonidine group | Buprenorphine group |
| 0 - 2 | 1(2%) | 0(0%) |
| 3 - 4 | 4(8%) | 1(2%) |
| 5 - 6 | 14(28%) | 5(10%) |
| 7 - 8 | 8(16%) | 3(6%) |
| 9 - 10 | 14(28%) | 17(34%) |
| 11 - 15 | 7(14%) | 16(32%) |
| 16 - 20 | 2(4%) | 7(14%) |
| >20 | 0(0%) | 1(2%) |
| Total | 50(100%) | 50(100%) |
| Mean ± SD | 8.70 ± 3.69 Min | 11.96 ± 4.78 Min |
| z-value | 3.81 | |
| p-value | 0.000,S,p<0.05 | |

41 (82%) patients in Clonidine group achieved the maximum sensory level within 10 minutes, while only 26 (52%) patients in Buprenorphine group could achieve this in 10 minutes. 24 patients (48%) in

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Buprenorphine group took more than 10 minutes to achieve the maximum sensory level, as against only 9 patients (18%) in Clonidine group.

**Table 8:** Showing Maximum Cephalic Sensory Level Achieved (Dermatome)

| Maximum cephalic sensory level (dermatome) | Number of patients | |
|---|---|---|
| | Clonidine group | Buprenorphine group |
| $<T_2$ | - | - |
| $T_3$ - $T_4$ | 04 | - |
| $T_5 – T_6$ | 13 | 11 |
| $T_7 – T_8$ | 26 | 22 |
| $T_9$-$T_{10}$ | 07 | 18 |
| Total | 50(100%) | 50(100%) |
| Median cephalic level | $T_7$ | $T_8$ |
| Mean ± SD | 7.12 ± 1.5 | 7.8 ± 1.37 |
| z-value | 1.78 | |
| p-value | 0.05,NS,p>0.05 | |

The highest sensory level achieved was $T_{7-8}$ in maximum number of patients in both the groups i.e. 26 and 22 patients in Clonidine group and Buprenorphine groups respectively.11 patients (22%) in Buprenorphine group and 13 patients in Clonidine group had a sensory level of $T_{5-6.}$
The median sensory level was $T_7$ in Clonidine group and $T_8$ in Buprenorphine group, with a comparable mean and amongst both the groups.

**Table 9:** Showing Onset of Motor Blockade

| Onset of motor blockade (sec) | Number of patients | |
|---|---|---|
| | Clonidine group | Buprenorphine group |
| 0 – 30 | 23(46%) | 16(32%) |
| 31 – 60 | 21(42%) | 23(46%) |
| 61 – 90 | 2(4%) | 11(22%) |
| 91 – 120 | 4(8%) | 0(0%) |
| >120 | 0(0%) | 0(0%) |
| Total | 50(100%) | 50(100%) |
| Mean ± SD | 34.10 ± 25.66 sec | 42.74 ± 20.14 Sec |
| z-value | 1.87 | |
| p-value | 0.06,NS,p>0.05 | |

The onset of motor blockade was taken from the time of drug injection into the intrathecal space to the time of appearance of numbness in patient's legs.
23 patients (46%) in Clonidine and 16 patients (32%) in Buprenorphine group had onset of motor block within 30 seconds. 11 patients (22%) in Buprenorphine group and 2 (4%) in Clonidine group showed onset within 60 seconds. Only 4 patients (8%) in Clonidine group had motor onset in between 91-120 seconds. Thus the mean time of onset of motor block was 34.10±25.66 seconds in Clonidine group and 42.74 ± 20.14 seconds in Buprenorphine group and was statistically insignificant.

**Table 10:** Showing Time of Maximum Motor Blockade

| Time of maximum motor blockade (min) | Number of patients | |
|---|---|---|
| | Clonidine group | Buprenorphine group |
| 0 – 2 | 11(22%) | 0(0%) |
| 3 – 4 | 22(44%) | 2(4%) |
| 5 – 6 | 8(16%) | 9(18%) |
| 7 – 8 | 3(6%) | 23(46%) |
| 9 – 10 | 3(6%) | 13(26%) |
| 10 -15 | 2(4%) | 1(2%) |
| 16 - 20 | 1(2%) | 2(4%) |
| Total | 50(100%) | 50(100%) |
| Mean ±SD | 5.10 ± 3.39 min | 8.32 ± 2.78 min |
| z-value | 5.18 | |
| p-value | 0.000,S,p<0.05 | |

All the patients in both the groups achieved grade III motor blockade, only the difference was time required to achieve this.
Almost 82% (41 patients) in Clonidine group attained a grade III motor blockade within 6 minutes of commencement of motor blockade, compared to only 11 patients (22%) in Buprenorphine group.

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The difference in mean time from onset of motor blockade to maximum block was 5.10±3.39 min in Clonidine group and 8.32+_2.78 min in Buprenorphine which was statistically significant (p value <0.05).

**Table 11:** Showing Distribution of Patients According to Duration of Surgery

| Duration of surgery (min) | Number of patients | |
|---|---|---|
| | Clonidine group | Buprenorphine group |
| 30 - 60 | 9(18%) | 14(28%) |
| 61 - 90 | 31(62%) | 28(56%) |
| 91 - 120 | 9(18%) | 8(16%) |
| 121 - 150 | 1(2%) | 0(0%) |
| TOTAL | 50(100%) | 50(100%) |
| Mean + SD | 81.12 ± 19.57 min | 76.02 + 19.62 min |
| z-value | 1.30 | |
| p-value | 0.19,NS,p>0.05 | |

Maximum number of surgeries in both groups lasted between 61-90 minutes i.e.in 40 (80%) patients in Clonidine group and 42 (84)% patients in Buprenorphine group.
Mean duration of surgery was 81.12±19.57 min. in Clonidine group and 76.02+ 19.62 min Buprenorphine group, which was insignificant statistically

**Table 12:** Showing Time of 2-Segment Regression of Sensory Block

| Time of 2-segment regression (min) | Number of patents | |
|---|---|---|
| | Clonidine group | Buprenorphine group |
| 60-90 | 0(0%) | 42(84%) |
| 90 – 120 | 36(72%) | 8(16%) |
| 121 – 150 | 11(22%) | 0(0%) |
| 151 – 180 | 3(6%) | 0(0%) |
| 181 – 210 | 0(0%) | 0(0%) |
| Total | 50(100%) | 50(100%) |
| Mean + SD | 119.28 ± 24.56 min | 79.40 ± 15.67 min |
| z-value | 9.67 | |
| p-value | 0.000,S,p<0.05 | |

36 (72%) patients in Clonidine group had two segment regression time of sensory level in 90-120 minutes. It was found that 42 (84%) patients in Buprenorphine group depicted a 2 segment regression time within 90 minutes, and all patients depicted the same within 120 minutes (2 hours).
Almost 14 (28%) patients in Clonidine group had a 2 segment regression time of >120 minutes.
The mean of two segment regression time in Clonidine group was 119.28±24.56min as compared to 79.40+15.67 min in Buprenorphine group and found to highly significant statistically (p<0.000)

**Table 13:** Showing Total Duration of Motor Blockade

| Total duration of motor blockade (min) | Number of patients | |
|---|---|---|
| | Clonidine group | Buprenorphine group |
| 120 – 180 | 0(0%) | 22(44%) |
| 181 – 240 | 16(32%) | 24(48%) |
| 241 – 300 | 29(58%) | 4(8%) |
| 301 – 360 | 5(10%) | 0(0%) |
| Total | 50(100%) | 50(100%) |
| Mean + SD | 277.90+ 37.56 | 198.80 + 42.21 |
| z-value | 9.90 | |
| p-value | 0.000,S,p<0.05 | |

Motor blockade was maintained for 241-300 minutes by maximum number of patients, 29 (58%) in Clonidine group as compared to only 4 patients (8%) in Buprenorphine group, where duration of motor blockade lasted for < 240 min in 46 (92%) of patients.
Mean duration of motor blockade in Clonidine group was 277.90+ 37.56 min as compared to 198.80+42.21 min in Buprenorphine group, and was statistically significant.

**Table 14:** Showing Duration of Analgesia

| Total duration of analgesia (min) | Number of patients | |
|---|---|---|
| | Clonidine group | Buprenorphine group |
| 180 – 240 | 2(4%) | 14(28%) |
| 241 – 300 | 16(32%) | 25(50%) |

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| | | |
|---|---|---|
| 301 – 360 | 19(38%) | 11(22%) |
| 361 – 420 | 8(16%) | 0(0%) |
| 421 – 480 | 5(10%) | 0(0%) |
| Total | 50(100%) | 50(100%) |
| Mean ±SD | 355.80 ± 63.85 min | 283.20 ± 51.84 min |
| z-value | 6.24 | |
| p-value | 0.000,S,p<0.05 | |

25 patients (50%) in Buprenorphine group and 16 (32%) in Clonidine group had duration of analgesia in between 241-300 min. 19 (38%) of patients in Clonidine group had analgesia for 301-360 min, which was observed in only in 11 (22%) patients in Buprenorphine group.
A duration of 361-480 min analgesia was observed in 13 (26%) patients in Clonidine group while none in Buprenorphine group had analgesia more than 360 min. Mean duration of analgesia in Clonidine group was 355.80+ 63.85 min which was 283.20+ 51.83 min in Buprenorphine group. This was highly significant statistically (p-value <0.001).

**Table 15:** Showing Mean Pain Score at Various Time Interval from Time of Drug Injection Up to Time Of Patient's First Request For Analgesia

| Time | Clonidine | Buprenorphine | z-value | p-value |
|---|---|---|---|---|
| 0 min | 0.86±1.56 | 0.78±1.51 | 0.26 | 0.796,NS,p>0.05 |
| 60 min | 0±0 | 0±0 | - | - |
| 120 min | 0±0 | 0.50±0.81 | 4.34 | 0.000,S,p<0.05 |
| 180 min | 0.32±0.68 | 1.42±1.12 | 5.90 | 0.000,S,p<0.05 |
| 240 min | 0.66±0.91 | 2.15±1.46 | 5.93 | 0.000,S,p<0.05 |
| 300 min | 2.25±1.81 | 3.04±1.58 | 1.82 | 0.074,NS,p>0.05 |
| 360 min | 3.50±1.88 | 4.36±0.67 | 2.21 | 0.032,S,p<0.05 |
| 420 min | 3.38±1.60 | 0±0 | - | - |
| 480 min | 4±0 | 0±0 | - | - |

Scoring of pain was done on Visual Analogue Scale preoperatively and then from the time of drug injection up to the time of patients first request for analgesia. The mean pain score at 240 min was 0.66±0.90 cm in Clonidine group as compared to 2.17 ±1.46 cm in Buprenorphine group.
The VAS remained below 4 cm till 360 min Buprenorphine group and till 420 min. in Clonidine group depicting good quality of analgesia with both the drugs.

**Table 16:** Showing Sedation Scoring (Ramsay score)

| Time | Clonidine | Buprenorphine | z-value | p-value |
|---|---|---|---|---|
| 0 min | 2.0±0 | 2.0±0 | NA | NA |
| 60 min | 2.56±0.57 (n=50) | 2.68±0.62 (n=50) | 1.001 | 0.319,NS,p>0.05 |
| 120 min | 2.48±0.57 (n=50) | 2.64±0.52 (n=50) | 1.446 | 0.151,NS,p>0.05 |
| 180 min | 2.40±0.49 (n=50) | 2.38±0.56 (n=50) | 0.188 | 0.851,NS,p>0.05 |
| 240 min | 2.24±0.43 | 2.13±0.49 (n=46) | 1.146 | 0.255,NS,p>0.05 |
| 300 min | 2.02±0.14 (n=45) | 2.04±0.36 (n=22) | 0.267 | 0.792,NS,p>0.05 |
| 360 min | 2±0 (n=32) | 1.90±0.30 (n=11) | 1.000 | 0.341,NS,p>0.05 |
| 400 min | 2±0 (n=13) | 0±0 | NA | NA |
| 480 min | 1.8±0.44 (n=5) | 0±0 | NA | NA |

(n=number of patients)
Scoring of sedation was done according to Ramsay Sedation score.

The mean sedation scores were found to be comparable at all-time intervals in both the groups. Thus, the patients remained cooperative, calm and tranquil at all-time intervals. Maximum number of patients in both the groups exhibited a score of 2-3 at all the time intervals, only a few patients having a score of 3-4 in either group at selected time interval of 60, 120 minutes in both the groups.

**Discussion**

Numerous studies since the first clinical use of intrathecal morphine in 1979 have confirmed the efficacy of spinally administered opioids for postoperative pain relief. However, opioids do not remain localized to the site of intrathecal injection after spinal injection, they undergo redistribution by rostral spread, which explains occurrence of nausea and vomiting in 15-35% patients, and respiratory depression. A lipid soluble non-ionized drug like Buprenorphine passes rapidly via the arachnoid granulations in to venous and lymphatic vessels, which allow a minimal increase of CSF concentration with minor risk of respiratory depression [15]. But, Buprenorphine is losing its popularity as an intrathecally administered agent due to its reported delayed respiratory depression and resistance to be reversed by Naloxone because of high receptor affinity and slow dissociation. However, low dose Buprenorphine intrathecally

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increases sensory block without affecting motor block and hemodynamic alterations, increases onset and duration of analgesia and minimal side effects [18].

Intrathecal Clonidine is being extensively evaluated as an alternative to neuraxial opioids for control of pain and has been proven to be a potent analgesic, free of at least some of the opioids related side effects [12]. Intrathecal Clonidine potentiates the effect of intrathecal local anesthetics and has been used as a sole agent as well as admixed with opioids and local anesthetics in labor analgesia and orthopedic surgeries [14]. Clonidine prolongs the duration of intrathecally administered local anaesthetics and has potent antinociceptive properties. But, the commonly administered doses of 60-75µg produce hypotension and bradycardia [19]. Doses of Clonidine >100 µm produces dose dependent hypotension and sedation [14]

Intrathecal Clonidine has been used in a wide range of 15-400 µg and has been administered either alone or in combination with local anesthetics or opioids. Until recently only a few studies have focused on small doses of intrathecal Clonidine in surgical patients [3].

**Conclusion**

Clonidine 37.5µg as an adjuvant to 15 mg 0.5% intrathecal Bupivacaine in infraumbilical surgeries shortened time to attain maximum sensory level and motor blockade along with significant increase in duration of sensory anesthesia and motor blockade as well as duration of analgesia as compared to 75 µg Buprenorphine used as an adjuvant to 15 mg 0.5% intrathecal Bupivacaine.

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