

STUDY OF EFFECTS OF INTRATHECAL CLONIDINE AS AN ADJUVANT WITH 0.5 % HYPERBARIC BUPIVACAINE IN VAGINAL HYSTERECTOMY UNDER SPINAL ANAESTHESIA AT A TERTIARY HOSPITAL

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Abstract

Background: Subarachnoid blockade with local anaesthetics provide intense analgesia by segmental blockade of central neural axis but the duration is short lasting. Various drugs are administered intrathecally along with local anaesthetics to prolong the duration of action. Present study was aimed to study effects of intrathecal clonidine as an adjuvant with 0.5 % hyperbaric bupivacaine in vaginal hysterectomy under spinal anaesthesia at a tertiary hospital. **Material and Methods:** Present study was prospective, randomized double-blind, controlled, single center study, conducted in patients of age 45 – 65 years, normotensive, ASA grade I and II, scheduled for vaginal hysterectomy under spinal anaesthesia. **Results:** In this study 40 patients were enrolled. Hemodynamic variables (Pulse rate, systolic blood pressure & diastolic blood pressure) were studied. In present study, we noted that duration of onset to peak sensory block was 5.45 ± 0.50 min, duration of onset to motor block was 7.05 ± 0.22 min, duration of sensory block was 189.80 ± 6.49 min, duration of motor block was 247.28 ± 8.42 min & mean duration of post-operative analgesia was 495.93 ± 22.43 min. Number of analgesic injections required were 3 in majority patients. Visual analogue scale score was 0 at 1 hr., 2 hr., 3 hr. & 4 hr. while at 6 hr., 8 hr., 10 hr., 12 hr., 18 hr. & 24 hrs. median VAS was < 5. Bradycardia was noted in one patient and hypotension occurred in two patients, which were managed effectively. Overall incidence of side effects was low. **Conclusion:** Clonidine is a good adjuvant drug and its use intrathecally as an additive to bupivacaine extends the duration of spinal anaesthesia significantly, lowering the need to administer general anaesthesia if duration of surgery is prolonged.

Keywords: Clonidine, adjuvant drugs, intrathecally, bupivacaine, spinal anaesthesia

Introduction

Effective pain relief after surgery is essential for optimal care of surgical patients. Inadequate pain control, apart from being inhuman may result in increased morbidity and mortality.¹ The advantage of post operative pain management include patient comfort and therefore satisfaction, earlier mobilization, fewer pulmonary and cardiac complications, reduced risk of deep vein thrombosis, fast recovery with less likelihood of the development of neuropathic pain and reduced cost of care. Regional anaesthesia avoids the complications of general anaesthesia and also intubation while providing adequate analgesia and muscle relaxation in the operative area. It thus is a good alternative to general anaesthesia. It also provides postoperative pain relief.²

Subarachnoid blockade with local anaesthetics provide intense analgesia by segmental blockade of central neural axis but the duration is short lasting. Various drugs are administered intrathecally along with local anaesthetics to prolong the duration of action e.g. adrenaline, neostigmine, opioids, clonidine. Various drugs intrathecally and epidurally have been tried for post-operative analgesia. These include morphine, pethidine, pentazocine, methadone, tramadol, fentanyl, sufentanil, neostigmine, midazolam, adenosine, clonidine and dexmedetomidine.³

These spinal adjuncts are used not only to reduce side effects of local anaesthetics, but also to prolong analgesia.⁴ Clonidine is said to prolong the duration of intrathecally administered local anaesthetic and has potent antinociceptive properties.⁵ Present study was aimed to study intrathecal clonidine as an adjuvant with 0.5 % hyperbaric bupivacaine in vaginal hysterectomy under spinal anaesthesia at a tertiary hospital.

Aims And Objective

Aim of our study was to evaluate the effectiveness of clonidine with 0.5% bupivacaine for spinal anaesthesia in terms of

- 1.Changes in hemodynamic parameters
- 2.Onset and duration of sensory and motor blockade
- 3.Duration of postoperative analgesia and postoperative sedation.
- 4.Complications, if any

Material And Methods

Present study was prospective, randomized double-blind, controlled, single center study, conducted in department of Anaesthesia, at XXX medical college & hospital, XXX, India. Study duration was of 2 years. Study approval was obtained from institutional ethical committee.

Inclusion criteria

- Patients of age 45 – 65 years,
- Normotensive patients,
- ASA grade I and II, scheduled for vaginal hysterectomy under spinal anaesthesia, willing to participate in present study.

Exclusion criteria

- ASA grade III and IV patients
- Patients with significant cardiovascular, renal, hepatic dysfunction.
- Patients having allergy to either clonidine or bupivacaine.
- Morbidly obese patients
- Having contraindications to spinal anaesthesia.

In this study 40 patients who undergoing vaginal hysterectomy under spinal anaesthesia were enrolled(Clonidine group)

Study was explained to patients in local language & written consent was taken for participation & study. Patients were examined one day prior to surgery and baseline recordings of pulse; blood pressure and other vitals were recorded.

Preoperative investigations such as Haemoglobin, Platelet count, bleeding time, clotting time, Blood sugar level, Renal function tests, Liver function tests, Serum electrolytes, Serum proteins, Urine routine and microscopy, ECG, Chest X ray & PT/INR were done in all patients.

All patients received subarachnoid block with 0.5% Hyperbaric bupivacaine 3 ml (15 mg) + 30 mcg Clonidine (as an adjuvant) to achieve blockade of T6-T8 dermatome. After intrathecal drug injection, intraoperatively data for Pulse rate, Blood pressure, O₂ saturation & ECG was recorded during 1st 2 hours at 5,15, 30, 45, 60,90,120 minutes. During surgery, patient did not receive any sedation.

Assessment of postoperative sedation done by using Ramsay sedation scale. Assessment of postoperative analgesia done by using Visual analogue scale. Postoperatively data was recorded for first 4 hour every hourly, for next 8 hours every 2 hourly, for next 12 hours every 6 hourly interval up to 24 hours.

Duration of Anaesthesia was measured as time interval from intrathecal injection to regression of sensory block below L1. Assessment of pain was done using " Visual Analogue Scale" between 0-10. Patients were supplemented with analgesic if VAS > 4 and monitored for the time to first analgesic usage and total 24-hour consumption of analgesic. Inj. Diclofenac 75mg intramuscular was given here. Motor block was assessed according to "Modified Bromage Scale"

Bromage 0	Patient is able to move hip, knee and ankle
Bromage 1	Patient unable to move hip but able to move knee and ankle
Bromage2	Patient unable to move hip and knee but able to move ankle
Bromage3	Patient unable to move hip, knee and ankle

Sedation score was assessed by "Ramsay Sedation Scale"

Score	Level of sedation
1	Anxious or agitated or restless or both
2	Co-operative, oriented and tranquil
3	Responding to commands only
4	Brisk response to light glabellar tap
5	Sluggish response to light glabellar tap
6	No response to light glabellar tap

Statistical evaluation was done 2 independent Sample t-test and Mann-Whitney U test. The detailed data was entered into well tabulated Microsoft Excel sheet and subsequently analysed statistically.

Results

In this study 40 patients who underwent vaginal hysterectomy under spinal anaesthesia were enrolled. In present study, mean age was 54.23 ± 6.175 years, mean weight was 56.63 ± 4.63 kg, mean Height was 154.48 ± 6.50 cm & mean duration of surgery was 96.30 ± 4.08 minutes.

Table 1: General characteristics

Characteristics	Mean \pm SD
Mean age (years)	54.23 \pm 6.175
Mean Weight (kg)	56.63 \pm 4.63
Mean Height (cm)	154.48 \pm 6.50
Mean duration of surgery	96.30 \pm 4.08

Hemodynamic variables (Pulse rate, systolic blood pressure & diastolic blood pressure) were studied. Mean pulse rate at various points as pre operative, after spinal block at 5 min, 15 min, 30 min, 45 min, 60 min, 90 min & 120 min was stable with subarachnoid block with 0.5% Hyperbaric bupivacaine 3ml (15 mg) + 30mcg Clonidine (as an adjuvant).

Table 2: Preoperative to intraoperative pulse rate

Pulse rate at	Mean	SD
Pre operative	77.35	6.43
5 min	76.55	5.28
15 min	75.43	4.82
30 min	73.65	4.90
45 min	73.15	3.45
60 min	73.00	2.72
90 min	73.55	4.31
120 min	73.10	2.56

In present study, after subarachnoid block with 0.5% Hyperbaric bupivacaine 3ml (15 mg) + 30mcg Clonidine (as an adjuvant) mean systolic blood pressure at various points as pre operative, after spinal block at 5 min, 15 min, 30 min, 45 min, 60 min, 90 min & 120 min was stable & no major fluctuations were noted.

Table 3: Preoperative to intraoperative mean systolic blood pressure

Systolic blood pressure	Mean	SD
Pre operative	121.15	5.58
5 min	112.60	5.75
15 min	114.75	5.61
30 min	116.85	4.15
45 min	118.50	2.39
60 min	119.45	2.60
90 min	119.85	2.37
120 min	119.90	2.48

In present study, after subarachnoid block with 0.5% Hyperbaric bupivacaine 3ml (15 mg) + 30mcg Clonidine (as an adjuvant) mean diastolic blood pressure at various points as pre operative, after spinal block at 5 min, 15 min, 30 min, 45 min, 60 min, 90 min & 120 min was stable & no major fluctuations were noted.

Table 4: Preoperative to intraoperative mean diastolic blood pressure

Diastolic blood pressure	Mean	SD
Pre operative	78.70	3.96
5 min	76.40	4.06
15 min	76.05	4.16
30 min	77.20	3.62
45 min	78.70	2.42
60 min	78.75	2.38
90 min	79.35	1.72
120 min	79.50	2.11

In present study, we noted that duration of onset to peak sensory block was 5.45 ± 0.50 min, duration of onset to motor block was 7.05 ± 0.22 min, duration of sensory block was 189.80 ± 6.49 min, duration of motor block was 247.28 ± 8.42 min & mean duration of post-operative analgesia was 495.93 ± 22.43 min. Number of analgesic injections required were 3 in majority patients.

Table 5: Anaesthesia characteristics

Characteristic	In minutes (mean \pm SD)
Onset to peak sensory block	5.45 ± 0.50
Onset to motor block (grade IV)	7.05 ± 0.22
Duration of sensory block	189.80 ± 6.49
Duration of motor block	247.28 ± 8.42
Mean duration of post-operative analgesia	495.93 ± 22.43
Number of analgesic injections required	3

Visual analogue scale score was 0 at 1 hr., 2 hr., 3 hr. & 4 hr. while at 6 hr., 8 hr., 10 hr., 12 hr., 18 hr. & 24 hrs. median VAS was < 5 .

Table 6: Mean visual analogue scale

VAS at	Min	Max	Median
1 hr.	0	0	0
2 hr.	0	0	0
3 hr.	0	0	0
4 hr.	0	0	0
6 hr.	1	5	2
8 hr.	0	6	5
10 hr.	1	2	1
12 hr.	2	5	2
18 hr.	2	6	5
24 hr.	2	6	2

In present study, mean Ramsay sedation score of 2 was noted at at 1 hr., 2 hr., 3 hr., 4 hr., 6 hr., 8 hr., 10 hr., 12 hr., 18 hr. & 24 hrs.

Table 7: Mean Ramsay sedation score

RSS at	Min	Max	Median
1hr	2	2	2
2hr	2	2	2
3hr	2	2	2
4hr	2	2	2
6hr	2	2	2
8hr	2	2	2
10hr	2	2	2
12hr	2	2	2
18hr	2	2	2
24hr	2	2	2

Bradycardia was noted in one patient and hypotension occurred in two patients, which were managed effectively. Overall incidence of side effects was low.

Table 8: Side effects

Side effects	Number (%)
Bradycardia	1 (2.5 %)
Hypotension	2 (5 %)

Discussion

Spinal anaesthesia is the most commonly used technique for lower abdominal surgeries as it is very economical and easy to administer. Postoperative pain is a major concern after surgery and because spinal anaesthesia using only local anaesthetics is associated with relatively short duration of action, early analgesic intervention is needed in the postoperative period. A number of adjuvants such as clonidine, midazolam, fentanyl and others are studied to prolong the effect spinal anaesthesia and postoperative analgesia.

The local anaesthetics act by blocking sodium channels and α_2 adreno receptor agonist acts by binding to presynaptic C fibers and post synaptic dorsal horn neurons. Intrathecal clonidine when combined with spinal bupivacaine prolongs the sensory block by depressing the release of C-fiber transmitters and by hyperpolarization of post-synaptic dorsal horn neurons. Motor block prolongation by α_2 -adrenoreceptor agonists may result from binding these agonists to motor neurons in the dorsal horn of the spinal cord. Intrathecal α_2 -receptor agonists have been found to have antinociceptive action for both somatic and visceral pain.

We found that the duration of sensory blockade was 189.80 ± 6.49 min and the duration of motor blockade was 247.28 ± 8.42 min in patient receiving clonidine with bupivacaine. Sethi BS *et al.*,⁶ has also shown the comparable results in which the duration of sensory blockade was 218 min (150-240 min) and duration of motor blockade was 205(90-300 min) in patient receiving clonidine (1 mcg/kg) with bupivacaine. Similarly, the duration of analgesia was 495.93 ± 22.43 min in patients receiving clonidine with bupivacaine.

Shah BB *et al.*,⁷ found the similar results where the duration of post operative analgesia in clonidine (30 mcg) group was 436.65 ± 149.84 min. Our results were comparable with the study conducted by Sanchan P *et al.*,⁸ in which they found that the time to reach peak sensory blockade was 4.43 ± 0.26 min and the duration of motor block was 189.50 ± 16.31 min with 75mcg of clonidine.

Besides, the duration of sensory block was 189.80 ± 6.49 min and time for first analgesic request was 495.93 ± 22.43 min in Clonidine group. Khezri MB *et al.*,⁹ found similar results where the mean duration of sensory block was 169.66 ± 25.69 min and time for first rescue analgesic was 519.44 ± 86.25 min in patients receiving clonidine (75 mcg) with bupivacaine

In our study the mean duration of motor block was 247.28 ± 8.42 min and the duration of postoperative analgesia was 495.93 ± 22.43 min in clonidine group. Singh RB *et al.*,¹⁰ found that the mean duration of motor block was 280.80 ± 66.88 min and the duration of postoperative analgesia was 510.6 ± 133.64 min in patients receiving clonidine (50mcg) with bupivacaine.

The duration of sensory block was 189.8 ± 6.49 min and the duration of motor block was 247.27 ± 8.42 min in clonidine group. Number of diclofenac injections used in Clonidine group was 2-3 (median 2). Chopra P *et al.*,¹¹ found the comparable results where the duration of sensory block was 177.8 ± 43.8 min in patients receiving clonidine (30mcg).

The duration of motor block in clonidine group was 206.6 ± 43.6 min. Number of diclofenac injections used in clonidine group was 1.16(1-2). We found that the mean time to reach peak sensory level was 5.45 ± 0.50 min in Clonidine group. Bhattacharjee A *et al.*,¹² found that the mean time to reach peak sensory level in clonidine (75mcg) group was 6.25 ± 2.13 min.

In our study the mean duration of sensory block was 189.8 ± 6.49 min and mean sedation score was 2 in our clonidine group. We observed hypotension in 1 patient and bradycardia in 2 patients. Baj B *et al.*,¹³ found the similar results where mean duration of sensory block was 192.50 ± 31.39 min and mean sedation score by using Ramsay sedation score was 2.03 ± 0.414 min with 25 mcg of clonidine. They also noted hypotension in 2 patients and bradycardia in 3 patients.

Thus, we can safely conclude, 30 mcg clonidine is an attractive alternative as an adjuvant to spinal bupivacaine in surgical procedures of prolonged duration with minimal side effects and excellent quality of spinal analgesia. Clonidine offers a better effect owing to earlier onset and prolonged duration of sensory and motor blockade as well as longer duration of postoperative analgesia.

Conclusion

Clonidine is a good adjuvant drug and Its use intrathecally as an additive to bupivacaine extends the duration of spinal anaesthesia significantly, lowering the need to administer general anaesthesia if duration of surgery is prolonged. Further clonidine also provides excellent postoperative analgesia.

Conflict of Interest: None to declare

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