International Journal of Research and Review
www.ijrrjournal.com E-ISSN: 2349-9788; P-ISSN: 2454-2237

Original Research Article

Comparison of Clonidine and Fentanyl as Adjuvants to Hyperbaric Bupivacaine for Spinal Anaesthesia in Patients Undergoing Transurethral Resection of Prostate: A Prospective Study

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ABSTRACT

Background: Spinal anaesthesia is widely used for urological operations particularly in transurethral surgical procedures as it permits early recognition of symptoms caused by over hydration (TURP syndrome) and bladder perforation.
Methods: This study was done over a period of sixteen months in 60 patients (two groups of 30 each) in age group of 50years and above who underwent transurethral resection of prostate (TURP) under spinal anaesthesia. Group A: Patients received intrathecal Bupivacaine 2.2ml with Clonidine 30µg. Group B: Patients received intrathecal Bupivacaine 2.2ml with Fentanyl 20µg. The outcomes for sensory block were observed as time to achieve T10 level, highest level of sensory block and time to achieve it, time to two segment regression of sensory block and regression to T12 level. The outcomes for motor block were observed as time to achieve maximum motor block and time to motor block regression to bromage grade 0. The results was tabulated and statistically analysed using SPSS (Statistical Package for Social Sciences) Software version 15.0, Chi-square test was used for qualitative data (sex, ASA grade), HR, Mean blood pressure, was compared within the group against baseline values using paired *t*-test.
Results: Time to sensory regression to T12 level was found to be significantly (p=0.0001) higher in Group A (120.33±9.46) than Group B (104.33±8.78). The total time of regression to bromage 0 was significantly (p=0.0001) higher in Group A (200.83±17.71) compared to Group B (156.50±13.78). The time of request of analgesia was significantly (p=0.01) higher in Group A than Group B.
Conclusion: As an adjuvant to hyperbaric bupivacaine, clonidine (30 mcg) showed longer duration of sensory block and longer post operative analgesia when compared to fentanyl (20mcg) in subarachnoid block for trans-urethral resection of prostate.
Keywords: spinal anaesthesia; clonidine; fentanyl; hyperbaric bupivacaine; TURP

INTRODUCTION

Spinal anaesthesia is widely used for urological operations particularly in transurethral surgical procedures as it permits early recognition of symptoms caused by over hydration (TURP syndrome) and bladder perforation. Transurethral resection of prostate (TURP) is largely restricted to geriatric population.

Bupivacaine, the most commonly used drug for subarachnoid block, may produce hypotension and bradycardia. [1]

High doses of bupivacaine may lead to myocardial depression, heart blocks and dysrhythmias in patients who already have a high incidence of anesthesia-related complications, especially hypotension increasing the risk of ischemia to various vital organs. [2] The addition of certain adjuvants can reduce some of these side effects by reducing the dose of bupivacaine.

Spinal anaesthesia and post operative analgesia can be prolonged by adding certain adjuvants like adrenaline, midazolam, opioids, neostigmine and clonidine to local anaesthetics. [3] Administration of opioids as adjuvants to local anaesthetics intrathecally results in both synergistic and multimodal analgesia. [4] Morphine, fentanyl, sufentanil and many more agonist opioids have proven their safety and efficacy in decreasing the dose of local anaesthetics and providing effective postoperative analgesia. [5]

Fentanyl is preferred as an adjuvant in spinal anaesthesia because of its rapid onset and short duration of action with lesser incidence of respiratory depression. [3,6] However pruritus, nausea, vomiting, activation of herpes labialis, urine retention and late and especially unpredictable respiratory depression of other opioids have directed research towards non opioids. [7]

Alpha 2 agonist medications are increasingly used as adjuvants in anaesthesia and analgesia. They can be prescribed orally, transdermally, intravenously, perineuraly, or through the neuraxial route. Besides analgesia and sedation they decrease sympathetic tone and attenuate the stress response to anaesthesia and surgery.

Clonidine is the most commonly used alpha 2 agonist for neuraxial anaesthesia. [8] Clonidine stimulates alpha 2 adreno receptors in the brain and spinal cord, resulting in reduction of sympathetic outflow from the central nervous system and in decrease in peripheral resistance, renal vascular resistance, plasma rennin activity, heart rate, cardiac output, and blood pressure.

It is suggested that intrathecal clonidine prolongs sensory and motor block of spinal anaesthesia. It decreases local anaesthetic requirement and prolongs postoperative analgesia. [9,10] Other beneficial effects include antiemesis, reduced post spinal shivering, anxiolysis and sedation. Unlike spinal opioids clonidine does not produce pruritus or respiratory depression.

There are a number of studies on the use of intrathecal clonidine with bupivacaine in various lower abdominal surgeries, however only a few studies have been conducted to evaluate its efficacy in urological surgeries like transurethral resection of prostate. Hence, this study has been planned to compare the efficacy of intrathecal clonidine and fentanyl as adjuvants to hyperbaric bupivacaine spinal anaesthesia in patients undergoing transurethral resection of prostate.

MATERIALS AND METHODS

Prospective, randomized comparative study was conducted on 60 patients, who underwent TURP under spinal anaesthesia, in the age group of 50 years and above over a period of 16 months. The patients were randomly allocated into two groups by using ‘computer generated random numbers’. Group A: Patients received intrathecal Bupivacaine 2.2 ml with Clonidine 30µg. Group B: Patients received intrathecal Bupivacaine 2.2 ml with Fentanyl 20 µg. Sample size was calculated using MedCalc Software version 11.5.0.0. Patients who had, contraindications for spinal anesthesia, ASA ≥ III, BMI ≥ 30, cardiac dysrhythmias, allergy to the study drugs, sedative drugs consumption, taking α adrenergic receptor antagonist, ACE inhibitors, angiotensin receptor blockers, failure of spinal block and the need for general anesthesia were excluded from the study.

Preoperatively, after taking detailed history and clinical examination, routine investigations were done and consent was taken. The entire anesthetic procedure

including the drugs used was explained to the patient. As patients were studied for sedative effect of adjuvants, other sedatives as premedication were avoided.

Intra-operatively, after connecting monitors to patient, base line parameters were recorded. An intravenous line was established and patients were co-loaded with crystalloids. Under all aseptic precautions lumbar puncture was performed at the L3-4 or L4-5 level by using a 25 gauge Quincke's spinal needle in sitting position. Group A patient received 2.2 ml of 0.5% heavy bupivacaine with 30 µg (0.2ml) of clonidine and total volume was made to 2.6 ml with normal saline. Group B patient received 2.2 ml of 0.5% heavy bupivacaine with 20 µg of fentanyl (total volume 2.6 ml). The surgical position was made after complete establishment of sensory & motor blockade and oxygen 4 l/min was given by face mask. Sensory block was assessed bilaterally by using analgesia to pin-prick with a short hypodermic needle in the midclavicular line and motor block by modified bromage scale. Sensory and motor block were assessed every 2 minutes until the level established and thereafter every 15 minutes. After performing spinal block, heart rate, MAP, SPO_2, sedation score were recorded every 2 minutes for first 10 minutes and then every 5 min for the first 30 min, every 15 min for the next hour and thereafter, half hourly till the request for supplemental analgesia.

The outcomes for sensory block were observed as time to achieve T10 level, highest level of sensory block and time to achieve it, time to two segment regression of sensory block and regression to T12 level. The outcomes for motor block were observed as time to achieve maximum motor block and time to motor block regression to bromage grade 0. The side effects as hypotension, bradycardia, sedation, nausea, vomiting and any other were noted. The results was tabulated and statistically analysed using SPSS (Statistical Package for Social Sciences) Software version 15.0, Chi-square test was used for qualitative data (sex, ASA grade), HR, Mean blood pressure, was compared within the group against baseline values using paired *t*-test.

RESULTS

Total of 60 patients, 30 in each group were evaluated prospectively.

There was no significant (p>0.05) difference in age, weight, height and BMI between the groups showing comparability of the groups in terms of basic characteristics (table 1).

Table-1: Basic characteristics of patients between the groups

Basic characteristics	Group A (n=30)	Group B (n=30)	p-value1
Age in years	67.03±6.01	66.33±6.46	0.66
Weight in kg	68.03±7.76	69.57±9.17	0.48
Height in cms	169.53±5.31	168.67±5.07	0.52
BMI in kg/mtr^2	23.61±1.88	24.37±2.26	0.16

[1]Unpaired t-test

There was no significant (p>0.05) difference in ASA grade between the groups showing comparability of the groups in terms of ASA grade (table 2).

Table-2: Comparison of ASA grade between the groups

ASA grade	Group A (n=30)		Group B (n=30)		p-value1
	No.	%	No.	%	
I	12	40.0	14	46.7	0.60
II	18	60.0	16	53.3	

[1]Chi-square test

Time to reach T10 level was insignificantly (p>0.05) lower in Group A (5.50±1.01) compared to Group B (5.70±0.79) (fig 1).

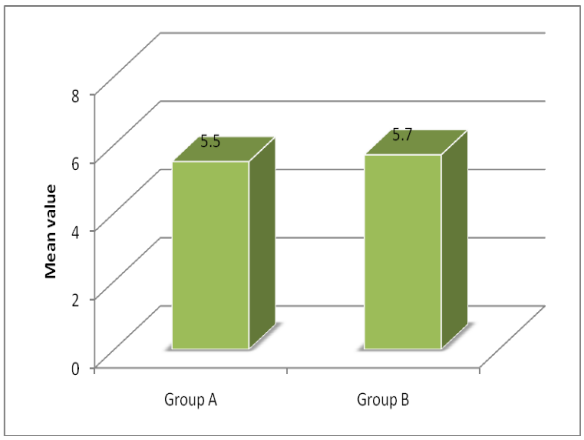

Fig. 1: Comparison of time to reach T10 level between the groups

T10 sensory level was in 50% patients of Group A and 40% of Group B.

However, T8 sensory level was in 23.3% patients of Group A and 26.7% of Group B. There was no significant (p>0.05) association of maximum sensory level between the groups (fig 2).

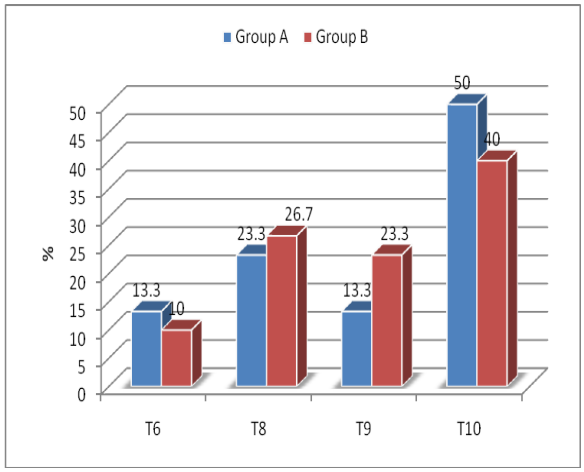

Fig. 2: Comparison of maximum sensory level between the groups

Time to reach highest sensory blockade level was found to be insignificantly (p>0.05) lower in Group A (6.93±1.50) than Group B (7.23±1.19). Time to sensory regression to T12 level (table 3) was found to be significantly (p=0.0001) higher in Group A (120.33±9.46) than Group B (104.33±8.78).

Table-3: Comparison of time to sensory regression to T12 level between the groups

Groups	Time in minutes (Mean±SD)
Group A	120.33±9.46
Group B	104.33±8.78
p-value1	0.0001*

*Significant

Time to reach bromage 3 was found to be insignificantly (p>0.05) higher in Group A (7.47±2.16) than Group B (7.43±2.02). However, total time of regression to bromage 0 was significantly (p=0.0001) higher in Group A (200.83±17.71) compared to Group B (156.50±13.78) (table 4).

Table-4: Comparison of time to reach bromage 3 and time of regression to bromage 0 between the groups

Groups	Time in minutes (Mean±SD)	
	Time to reach bromage 3	Time of regression to bromage 0
Group A	7.47±2.16	200.83±17.71
Group B	7.43±2.02	156.50±13.78
p-value1	0.95	0.0001*

*Significant

There was no significant (p>0.05) difference in heart rate, mean arterial pressure (MAP), SPO_2, respiratory rate (RR) and sedation scores at all the time periods between the groups. Time of request of analgesia (fig 3) was significantly (p=0.01) higher in Group A (317.67±41.99) than Group B (294.67±30.22).

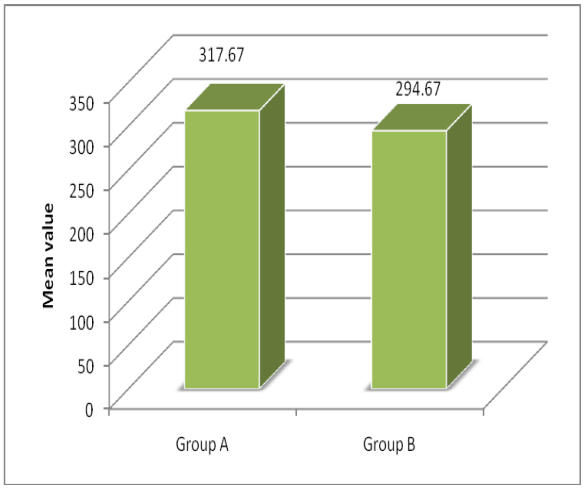

Fig. 3: Comparison of time of request for analgesia between the groups

Duration of surgery was insignificantly (p>0.05) higher in Group A (62.57±4.35) than Group B (62.67±5.10). Pruritus was found in 10% of Group B. Hypotension was in 6.7% in both the groups.

The results were presented in frequencies, percentages and mean±SD. Chi-square test was used to compare categorical variables between the groups. Unpaired t-test was used to compare continuous variables between two groups. The p-value<0.05 was considered significant. All the analysis was carried out on SPSS 16.0 version.

DISCUSSION

The subarachnoid block has occupied an important place in the anaesthetic practice, since the time it is known. It provides efficient analgesia and adequate muscle relaxation and thus imparts optimal operating conditions in the patient. Subarachnoid block is a commonly used anaesthetic technique for lower abdominal

and lower limb surgery. There has been a practice and growing interest to increase the duration of spinal analgesia by adding the adjuvants like vasoconstrictors, opioids, neostigmine, ketamine, midazolam, magnesium etc. Vasoconstrictors (epinephrine, ephedrine and phenylephrine) prolong the duration of action of the local anesthetic by decreasing systemic absorption but have been found to induce neurological signs and symptoms due to reduced blood supply to the spinal cord. [11]

Fentanyl is preferred as an adjuvant in spinal anaesthesia because of its rapid onset and short duration of action with lesser incidence of respiratory depression. [3,6] However pruritus, nausea, vomiting, activation of herpes labialis, urine retention and late and especially unpredictable respiratory depression of other opioids have directed research towards non opioids. [7]

Alpha 2 agonist medications are increasingly used as adjuvants in anaesthesia and analgesia. They can be prescribed orally, transdermally, intravenously, perineuraly, or through the neuraxial route. Besides analgesia and sedation they decrease sympathetic tone and attenuate the stress response to anaesthesia and surgery.

Clonidine is the most commonly used alpha 2 agonist for neuraxial anaesthesia. [8] Clonidine stimulates alpha 2 adreno receptors in the brain and spinal cord, resulting in reduction of sympathetic outflow from the central nervous system and in decrease in peripheral resistance, renal vascular resistance, plasma rennin activity, heart rate, cardiac output, and blood pressure. It is suggested that intrathecal clonidine prolongs sensory and motor block of spinal anaesthesia. It decreases local anaesthetic requirement and prolongs postoperative analgesia. [9,10]

In our present study, time to reach T10 level was lower in Group A as compared to Group B and that was statistically insignificant which is similar to results of studies conducted by Srinivasagam K et al [12] and Mahendru et al. [13] Our study results are comparable with the studies conducted by Bhattacharjee et al [14] and Mahendru et al [13] showing that clonidine as an adjuvant to 0.50% hyperbaric bupivacaine does not prolong the time taken to achieve maximal sensory level when compared to fentanyl as an adjuvant. There was no significant association of maximum sensory level between the groups which is also comparable with the studies done by Chhabra et al [15] and Gupta et al. [16] Time to reach bromage 3 was higher in Group A than Group B however, was statistically insignificant, is comparable with Mahendru et al [13] and Chhabra et al. [15] The time of sensory regression to T12 is comparable with studies of Singh et al, [17] Chhabra et al, [15] Gupta et al [16] and Chopra et al [18] which was significantly (p=0.0001) higher in Group A than Group B. Gupta et al, [16] Chhabra et al [15] and Srinivasagam K et al [12] found that the time of regression to bromage 0 was significantly higher with clonidine in comparison to fentanyl which is similar to our study. Time of request of analgesia was significantly higher in Group A than Group B which is comparable with studies of Chhabra et al, [15] Srinivasagam K et al [12] and Gupta et al. [16] Heart Rate, Mean Blood Pressure, RR and SpO2 were found comparable between both the groups throughout the observation period in our study, similar findings were reported by Singh et al [17] and Mahendru et al. [13]

CONCLUSION

As an adjuvant to hyperbaric bupivacaine, clonidine (30 mcg) showed longer duration of sensory block and longer post operative analgesia when compared to fentanyl (20mcg) in subarachnoid block for trans-urethral resection of prostate. The onset of sensory and motor block was similar without significant haemodynamic changes. Thus, 30 mcg of clonidine dose provides maximum benefit and minimum side effects. Clonidine has the advantage of not having pruritus as a side effect. It is an attractive alternative to opioids and may provide a newer approach to pain therapy

with promising and favourable outcomes such as successful analgesia achieved with minimal side effects.

Abbreviations:
ASA – American Society of Anaesthesiologist
BW-Body Weight
BP-Blood Pressure
BMI-Body mass index
CSF – Cerebrospinal Spinal Fluid
CNS – Central Nervous System
CVS – Cardiovascular System
ECG-Electrocardiograph
F- Female
HR-Heart Rate
I.P. No.-In patient Number
IV - Intravenous
INJ-Injection
Kg – Kilogram
L – Liters
µg – Microgram
M-Male
Min - Minutes
ml - milliliter
mm of Hg - millimeter of mercury
MAP – Mean Arterial Pressure
NS-Normal Saline
RR – Respiratory Rate
SpO2 – Percentage saturation of Oxygen Saturation
S.D – Standard Deviation
S.No.-Serial Number
TURP -Trans Urethral Resection of Prostate
Yrs-Years

Conflict of Interests: No

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How to cite this article: Gahlawat PK, Sehrawat U, Makeen NWSA et.al. Comparison of clonidine and fentanyl as adjuvants to hyperbaric bupivacaine for spinal anaesthesia in patients undergoing transurethral resection of prostate: a prospective study. International Journal of Research and Review. 2019; 6(7):461-467.

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