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Randomized Clinical Comparison of Three Different Doses of Bupivacaine with Fentanyl for TURP-Search for Optimal Dose to Be Used in Day Care Urological Procedures.

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ABSTRACT

Background: Patients who are candidates for TURP are elderly with cardiovascular and respiratory diseases with anticipated problems during spinal anesthesia. **Aim:** To compare three different doses (5mg, 7.5mg and 10mg) of Bupivacaine after adding 25 mcg of fentanyl during spinal anesthesia in transurethral resection of prostate surgeries. **Methods:** Single blinded Randomized clinical study conducted in 75 patients. The subjects were allocated in to three groups. Group A - received Inj. 0.5% Bupivacaine 5 mg, Group B- received Inj. 0.5% Bupivacaine 7.5 mg, Group C - received Inj.0.5% Bupivacaine 10 mg added with 25 mcg of Fentanyl. Baseline and intraoperative vital parameters, time to sensory block at t10, maximum sensory height, time to two segment sensory regression, total duration of sensory blockade, grading of motor blockade and total duration of motor blockade were recorded. **Results:** Maximum sensory level achieved in Group A was T9, Group B T7 and in Group C it was T5. Time to T10 level in Group A was 7.88 ±0.80 minutes, Group B 5.41 ±0.50 minutes and Group C 3.33 ±0.65 minutes. Two segment sensory regression times in Group A was 56.8±13.61 minutes, Group B 79.58 ±25.32 minutes, and Group C was 116.25 ±9.35 minutes. Total duration of pain free interval in Group A was 84.6 ±20.41 minutes, Group B 104.12 ±45.89 minutes. Group C was 194.20 ±41.53 minutes. **Conclusion:** Low dose of Bupivacaine (5mg) with addition of Fentanyl 25µg can be used for painless TURP surgeries when compared to higher doses (7.5mg and 10 mg) without any major side effects and facilitates early discharge.

Keywords: TURP, Urology, Spinal anesthesia, Bupivacaine, Fentanyl, elderly, Day care.

INTRODUCTION

Elderly males are frequent candidates for Trans Urethral resection of Prostate and have preexisting multiple comorbid illnesses making the choice of anesthesia difficult .Subarachnoid block was usually performed in TURP (transurethral resection of the prostate) surgeries as it helps in early recognition of symptoms arising out of TURP Syndrome or bladder perforation.

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Bupivacaine is the most commonly used local anesthetic. Use of Bupivacaine, a long acting local anesthetic agent prevents early discharge from the hospital due to residual motor blockade along with bladder distension necessitating continuous bladder drainage. The level of blockade necessary for the surgical procedure is around T10 and procedure rarely exceeds an hour i.e. sixty minutes. Longer duration of the procedure results in higher incidences of TURP syndrome and excessive blood loss. When used alone, Bupivacaine in higher doses produces significant motor blockade for a prolonged duration.[1] Lipophilic opioids such as Fentanyl when added to LA agents for intrathecal administration enhances sensory effects of spinal anesthesia without prolonging motor blockade and provides postoperative pain relief.[2] This facilitates early recovery from spinal anesthesia and discharge

allowing the procedure to be done as a day care procedure.[3]

The aim of this study to compare three doses of Hyperbaric Bupivacaine 5, 7.5 and 10 mg added to 25 mcg of Fentanyl to be administered intrathecally in patients posted for transurethral resection of Prostate.

MATERIALS AND METHODS

Single blinded Randomized control clinical study was conducted in Rajiv Gandhi Government General Hospital, Chennai. Institutional ethical committee approval and written informed consent were obtained. 75 male patients aged above 60 years undergoing TURP surgery were recruited for the study. After getting consent and explaining details of the procedure, the anesthetic technique using Bupivacaine in different doses along with Fentanyl was performed in elective elderly male surgical patients posted for TURP surgery belonging to ASA 2. Patients who have coagulation problems, cardiac or renal disease, neurological illness, mental illness, spinal deformity, allergy to local anesthetics were excluded from the study. Patients were randomly allocated to one of three groups I, II and III in 1:1:1 ratio. Group I (n = 25) received Hyperbaric Bupivacaine 5 mg with Fentanyl 25 µg. Group II (n = 25) received Hyperbaric Bupivacaine 7.5 mg with Fentanyl 25 µg. Group III (n = 25) received Hyperbaric Bupivacaine 10 mg with Fentanyl 25 µg. On the day of surgery, pulse rate, blood pressure and respiratory rate were recorded prior to the procedure. IV line was started with 18 gauge intravenous cannula and infused with 5 ml/kg crystalloid. Emergency drugs and equipments were kept ready before anaesthetic intervention. Patients were put in right lateral position and with strict aseptic precaution, lumbar puncture was done with 25 Gauge Quinke spinal needles in L3—L4 interspace. After ensuing free flow of CSF, drug was injected as per the dose and group assigned. After injecting the drug patients were put in supine position. All patients were monitored using electrocardiography, heart rate and NIBP and pulse oximetry. Parameters recorded were time to reach sensory block T 10, maximal sensory block height, motor blockade, time to two segment sensory regression, time to complete sensory regression, time to complete motor regression, Heart Rate, BP, SPO2 were recorded every five minutes till the end of surgery. Patient was observed for pruritus, nausea, vomiting, pain, bradycardia, hypotension and respiratory depression. The level of sensory block was assessed using pinprick method. Motor block was assessed using the Modified Bromage Scale (0 = no motor block, 1 = inability to raise extended legs, 2 = inability to flex knees, 3 = inability to flex ankle joints). After attaining T 10 level of sensory block and Modified Bromage Grade 2 or 3 motor blocks, the patient was put up in lithotomy position and surgery was started. Hypotension was defined as a systolic blood pressure (SBP) < 90 mm Hg or a decrease in SBP by 30% or more from baseline values, and was initially treated by Normal saline solution; when needed Inj Ephedrine 3 mg was given in increments until the correction of SBP. Bradycardia was defined as a heart rate <50 bpm or a decrease of more than 20% from the baseline value and was treated by Atropine 0.5 mg. Respiratory depression was defined as a respiratory rate less than 8 breaths / min and / or oxygen saturation less than 85% in room air. Other adverse effects, including pruritus, nausea and vomiting were recorded. Analgesia was noted by the Visual Analog Scale. When the Pain score was more than 6, supplementary analgesia was given. Duration of the procedure was recorded. Sensory level at the end of the surgery was noted. All patients were followed up in the postoperative period for any complications like postoperative nausea, vomiting, pruritus, hypotension and respiratory depression. The information collected regarding all the cases were documented in a Master Chart. Analysis of the collected data was done using Epidemiological Information Package (EPI 2002). Using this software, range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. ANOVA and Kruskul Wallis chi-square test was used to test the significance of difference between quantitative variables.

RESULTS

In this randomized study conducted in 75 patients, the subjects were allocated into three groups (A, B, C). Group A - Received Inj. 0.5% Bupivacaine 5 mg, Group B - Received Inj. 0.5% Bupivacaine 7.5 mg, Group C - Received Inj.0.5% Bupivacaine 10 mg. All the three groups received 25 mcg of Inj Fentanyl. Patients in all three groups were comparable with respect to age, sex, height, weight, nature of surgery and the duration of the procedure.

Table 1: Comparison of demographic parameters and duration of the TURP surgery.

Variables	Group A	Group B	Group C	P Value
Age	66.76 ±4.88	66.20 ±4.12	64.44 ±3.39	0.131
Height	163 ±3.10	164 ±2.81	164 ±3.38	0.852
Weight	60.64 ±5.6	60.52 ±5.21	59.64 ±5.1	0.774
Duration of the Procedure	60 ±8.66	52.20 ±21.46	54.4. ±3.49	1.691

Decreased Systolic blood pressure more than 30% from the baseline value or less than 90 mm hg was considered hypotension. Systolic blood pressure changes observed at 5,10,15,20 mins were statistically significant among the three groups (P < 0.001). There was no hypotension in Group A. Five

in Group B had hypotension. All the patients in Group C had hypotension.

Bradycardia is defined as heart rate less than 50 or less than 20% from the baseline value. There was no bradycardia observed in Groups A and B. Six patients had bradycardia in Group C which can be directly attributed to the high sensory level in this group. The difference in heart rate between the three groups was not statistically significant.

Table 2: Comparison of baseline vital parameters among three groups.

Variables	Group-A		Group-B		Group-C		P value
	Mean	SD	Mean	SD	Mean	SD	
SBP	121.60	27.97	118.35	27.46	124.08	9.56	0.705
DBP	70.96	16.01	70.61	16.36	73.17	4.64	0.787
MAP	88.20	19.67	86.17	19.74	89.25	5.88	0.816
HR	66.64	16.02	71.20	6.73	68.80	6.58	0.335
RR	12.96	2.98	13.52	1.39	13.40	1.26	0.594
SPO2	98.92	19.80	98.92	1.04	98.92	0.95	0.372

Table 3: Depiction of statistically significant difference with respect to Systolic blood pressure among three groups.

SBP	Group-A	Group-B	Group-C	P value
	Mean (SD)	Mean (SD)	Mean(SD)	
At Base Minutes	121.60 (27.97)	118.35 (27.46)	124.08 (09.56)	0.846
At 5 Minutes	123.33 (10.90)	110.64 (11.72)	90.88 (18.32)	<0.0001
At 10 Minutes	120.00 (9.64)	105.28 (11.41)	89.83 (3.06)	<0.0001
At 15 Minutes	118.92 (9.87)	103.73 (10.52)	93.33 (3.42)	<0.0001
At 20 Minutes	112.88 (25.25)	100.26 (24.23)	97.58 (06.21)	0.032

Onset of sensory blockade was earlier in Group C. T10 sensory level was achieved much earlier in group C when compared with groups A and B and the difference was statistically significant (P< 0.001). Maximum sensory level achieved in Group A was T 9, Group B was T 7 and in Group C it was T 5. Most of the patients in Group A had T9 level (76%), Group B T9 (56%) and equal number of patients had T6 or T7 (36%) in Group C. All the patients in Group B and C had a motor block of Grade 3. Two patients in group A had a motor block of Grade 3. All others in group A had a motor block of Grade 2 which was sufficient enough to put the patient in lithotomy. Duration of analgesia was measured by two segment sensory regression time. There was delay in the two segment sensory regression in sensory level in Group B and C when compared to Group A, but the mean duration of analgesia before the onset of two segment sensory regression was sufficient for the surgery to be over. There was significant statistical difference observed between the three groups (P<0.0001). Total duration of pain free interval was longer in Group C when compared to Groups A and B. The postoperative analgesia was significantly prolonged in Groups B and C and the difference was statistically significant (P<0.0001). Pain perceived by patients in the postoperative period in Group A was manageable with Inj Tramadol 50 mg slow IV with the average VAS score of 4. Total duration of motor blockade measured as time for complete motor regression in Group C was prolonged when compared to Group A and B and the difference was statistically significant (P<0.001).

Table 4: Statistical analysis with respect to heart rate among three groups.

Heart Rate	Group-A	Group-B	Group-C	P value
	Mean (SD)	Mean (SD)	Mean(SD)	
At Base Minutes	**66.64 (16.02)**	**71.20 (6.73)**	**68.80 (6.58)**	**NS**
At 05 Minutes	**65.04 (15.35)**	**66.56 (6.62)**	**64.56 (5.58)**	**NS**
At 10 Minutes	**64.56 (15.36)**	**63.76 (5.73)**	**60.96 (5.17)**	**NS**
At 15 Minutes	**64.16 (15.22)**	**62.64 (5.99)**	**57.92 (5.73)**	**NS**
At 20 Minutes	**63.76 (15.00)**	**61.55 (5.66)**	**57.17 (6.57)**	**NS**
At 25 Minutes	**63.84 (15.24)**	**61.64 (5.88)**	**57.75 (8.86)**	**NS**

Table 5: Statistical analysis of sensory and motor regression among three groups.

Variables	Group-A		Group-B		Group-C		P value
	Mean	SD	Mean	SD	Mean	SD	
Two Segment Sensory regression	56.80	13.61	79.58	25.32	116.25	9.35	<0.0001
Complete Sensory Regression	84.60	20.41	104.12	45.89	194.20	41.53	<0.0001
Complete Motor Regression	63.20	15.87	85.32	32.96	136.88	29.20	<0.0001

Nausea and vomiting was not found in any of the groups. Pruritus developed in 88% of patients in Group A, 76% in Group B and 80% of the patients in Group C, none of them needed any intervention. Pain was measured using VAS. There was mild pain in Group A at the end of surgery almost in all the patients managed with Inj Tramadol 50 mg IV. There was excellent pain relief in Group C and good pain relief in Group B.

DISCUSSION

The most determining factor for the success of regional anesthesia and time until recovery is the dose of local anesthetic drug. The increased availability of lipid soluble opioids with shorter latency and demonstration of synergistic effect of opioids when combine with local anesthetic drugs have led to the widespread use of neuraxial opioids. Use of opioid as an adjuvant in spinal anesthesia allows early ambulation and reduces the length of hospital stay.[4] Addition of Fentanyl in the dose of 25 mcg to Bupivacaine administered intrathecally provides maximum duration of postoperative analgesia with minimal side effects without affecting the motor blockade. The lumbar interspace chosen for injection of hyperbaric Bupivacaine may influence the level of the block. All patients in our study, had the anesthetic solution injected in the L3 - L4 interspace with the same velocity and the orifice of the spinal needle turned cephalad. If the motor block was less intense, there was faster recovery and mobilization of the patient. These findings were as per the findings of Vaghadia when comparing a small dose hypobaric Lidocaine – Fentanyl spinal anesthesia and conventional dose hyperbaric Lidocaine.[5] Yang et al studied the effect of intrathecal fentanyl on the onset and duration of hyperbaric Bupivacaine in patients undergoing TURP and concluded that Fentanyl 25 mcg prolongs the duration of sensory block and postoperative analgesia.[6] Ben David et al explored the synergism between intrathecal opioids and local anesthetics thereby concluding that reduced dose of bupivacaine when combined with fentanyl provides adequate surgical anesthesia, less hypotension and virtually eliminated the use of vasopressors to augment blood pressure.[7] Karamaz et al while studying the effect of low dose Bupivacaine and fentanyl in patients undergoing TURP concluded that the addition of Fentanyl 25 mcg to low dose Bupivacaine (4 mg) provides adequate analgesia for TURP (Median sensory height T10) with fewer side effects in elderly patients when compared with the conventional dose of Bupivacaine.[8] In our study median peak sensory height was T10 in Group A, T9 in Group B and T7 in Group C. Iheb Labbene et al suggested that the use of low dose of Bupivacaine (5 mg) added to Fentanyl (25 mcg) resulted in short acting sensory block without prolonged motor block and a lower incidence of major side effects as compared to conventional dose of Bupivacaine with fentanyl.[9] Kussineimi et al studied the effects of adding Fentanyl 25mcg to three different doses of Bupivacaine (5, 7.5 and 10 mg) and compared with 10 mg of Bupivacaine alone and concluded that the addition of 25 mcg of fentanyl to 5mg of Bupivacaine resulted in shorter lasting motor blockade but prolonged sensory blockade comparable with higher doses of Bupivacaine with or without fentanyl.[10] Our study, motor blockade in Group A was less profound and shorter in duration and sensory blockade was adequate for surgical procedure though short lasting when compared to 7.5 and 10 mg of Bupivacaine with fentanyl. Addition of intrathecal Fentanyl did not enhance the onset of sensory or motor blockade or prolong the duration of motor blockade. Hypotension is common during subarachnoid block and episodes of severe hypotension can be life threatening, especially for endoscopic urological surgery in the elderly. Hypotension is a dangerous side effect and may cause severe cardiovascular side effects especially when coronary heart disease is present. In our study the peak sensory level was higher and more intense motor blockade in Group B and C contributing to hypotension and bradycardia present in few participants (at 5, 10, 15, 20 minutes post spinal) necessitating intervention and longer stay in hospital though with lesser requirement of postoperative analgesics. In our study the time to two segment sensory regression, complete sensory regression and complete sensory regression was shorter and there was statistically significant difference between Group A and Groups B and C. But the sensory blockade prior to sensory regression in group A was adequate for the completion of the surgical procedure. Gupta et al observed similar findings in his study involving 40 patients for ambulatory inguinal herniorraphy. Postoperative analgesia was significantly prolonged in groups receiving higher dose of Bupivacaine. Pruritus is the commonest complication of intrathecal opioid use. In our study all the groups experienced pruritus (70-80%) but none of them needed treatment. Nausea or vomiting was not reported in any of the participants. Though intrathecal opioids can cause respiratory depression, addition of 25 mcg of fentanyl did not alter respiratory rate, end tidal carbon dioxide tension, minute ventilation, respiratory drive or the ventilator response to carbon dioxide as proved by Varrassi et al.[11,12]

CONCLUSION

Addition of Fentanyl 25µg to 5 mg of Hyperbaric Bupivacaine provides reliable and satisfactory surgical anesthesia in elderly patients undergoing TURP surgeries, with an ideal peak sensory block height, stable haemodynamic status, reduced

duration of sensory and motor blockade and without any significant adverse effects when compared to the combination of 7.5 and10 mg Bupivacaine with Fentanyl , facilitating early discharge of patients and makes this technique suitable for day care endoscopic urological procedures.

REFERENCES

1. Goodman & Gilman, The pharmacological basis of therapeutics - 8th edition 1991.
2. Ben-David B, Solomon E, Levin H, and et al. Intrathecal Fentanyl with small dose dilute Bupivacaine; Better anesthesia without prolonging recovery. Anesth Analg 1997; 85; 560-565.
3. Patra P, Kapoor MC et al. Spinal anesthesia with Low dose Bupivacaine and Fentanyl for endoscopic urological procedures. Jour anesth clin pharmacol 2005;12(3):45-9.
4. Bromage PR et al. The price of intraspinal narcotic analgesia, basic constraints. Anesthesia Analgesia 2000, 60; 461-463.
5. Vaghadia McLeod DH, Mitchell GWE, and Merrick PM, Chilvers CR: Small-dose hypobaric Lidocaine-Fentanyl spinal anesthesia for short duration outpatient laparoscopy Anesth Analg 1997;84:59 – 64.
6. Yang J et al. Intrathecal fentanyl prolongs sensory bupivacaine spinal block. Canadian journal of anesthesia 1995; 42; 987-991.
7. Ben-David B, Frankel R, Arzumonov I, Marchevsky et al. Mini dose Bupivacaine – Fentanyl spinal anesthesia for surgical repair of Hip fracture in the aged. Anesthesiology 2000; 47; 6-10.
8. Karamaz et al. Low dose Bupivacaine with Fentanyl spinal anesthesia for transurethral prostatectomy. Anesthesia, volume 58, issue- 6. Page 526 - 530, 20 June – 2003.
9. Iheb Labbene et al. Spinal anesthesia for endoscopic urological surgery. Low dose versus varying doses of Bupivacaine. Military Hospital of Tunis. Department of Anesthesiology and Critical Care. M.E.J Anesthesia 19(2):2007
10. Kuusniemi KS, Pihlajamaki KK et al. The use of Bupivacaine& Fentanyl for spinal anesthesia for urologic surgery. Anaesth Analg 2000; 91; 1452-1456.
11. Varassi G, Celleno D, Capogna G, et al. Ventilatory effects of subarachnoid Fentanyl in the elderly. Anesthesia 47: 558 – 62, 1992.
12. Etches R, Sandler A, Daley M. Respiratory depression and spinal opioids. Can J Anesthesia 1989; 36; 165- 85.

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