



Received on 21 May 2024; received in revised form, 25 June 2024; accepted, 17 July 2024; published 01 October 2024

A COMPARATIVE STUDY BETWEEN USE OF LOW DOSE BUPIVACAINE AND BUPIVACAINE PLUS FENTANYL IN SPINAL ANAESTHESIA IN TRANSURETHRAL RESECTION OF PROSTATE

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Keywords:

Bupivacaine, Fentanyl, Prostate

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ABSTRACT: Spinal anaesthesia is most frequently used for transurethral prostatectomy (TURP), because it permits early recognition of TURP syndrome. However, many elderly patients can have coexisting cardiac or pulmonary disease so, it is important to limit the distribution of spinal block in such patients. **Aim and Objectives:** To evaluate the efficacy and effect of addition of fentanyl 25 µg (0.5 ml) intrathecally to bupivacaine 5mg (0.5%) (1ml) and low dose bupivacaine 7.5mg (0.5%) (1.5 ml) alone for TURP. **Methodology:** It was a comparative prospective study under which 60 subjects were enrolled and divided into 2 groups of 30 patients each. Group A will receive Low dose bupivacaine 7.5mg (0.5%) (1.5 ml) Group B will receive bupivacaine 5mg (0.5%) (1ml) and fentanyl 25 µg (0.5). **Results:** Sensory block duration is higher in group B patients while time of onset of sensory block is low in Group B patients (1.18 ± 0.31) in compare to Group A (1.59 ± 0.34), similar findings were observed for motor block. In Group A complications of Hypotension (in 3 patients), Shivering (in 3 patients), Bradycardia (in 1 patient) and Vomiting (in 1 patient) were reported, while in Group B only pruritus (in 3 patients) was noted which is peculiar of fentanyl. **Conclusion:** Addition of intrathecal Fentanyl to Bupivacaine leads to early motor recovery with good haemodynamic stability. It also reduces the need for post-operative analgesics without any significant adverse effects.

INTRODUCTION: Transurethral resection of the prostate (TURP) interventions is primarily transient, and due to the fact that a large number of elderly patients undergo these interventions; reducing complications, early hospital discharge, and reducing the cost of treatment are desirable ^{1,2}.

Spinal anaesthesia is most frequently used for transurethral prostatectomy (TURP), because it permits early recognition of TURP syndrome which includes the signs and symptoms of water intoxication, fluid overload as well as bladder perforation because patient is awake ³.

In addition, short-acting spinal anaesthesia may help to prevent complications associated with delayed immobilization. However, many patients undergoing anaesthesia for TURP are elderly and have coexisting cardiac or pulmonary disease. It is important to limit the distribution of spinal block to

<p>QUICK RESPONSE CODE</p> 	<p>DOI: 10.13040/IJPSR.0975-8232.15(11).3204-09</p> <hr/> <p>This article can be accessed online on www.ijpsr.com</p> <hr/> <p>DOI link: https://doi.org/10.13040/IJPSR.0975-8232.15(11).3204-09</p>
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reduce adverse haemodynamic and pulmonary effects in such patients. Lipophilic opioids (e.g. fentanyl and sufentanil) are increasingly being administered intrathecally as adjuncts to local anaesthetics. They enhance spinal anaesthesia without prolonging motor recovery and discharge time⁴⁻⁶.

The present study hypothesized that if by using very small doses of local anaesthetic, one can limit the distribution of spinal block, but low dose bupivacaine cannot provide an adequate level of sensory block. Intrathecal opioids enhance analgesia from subtherapeutic dose of local anaesthetic and make it possible to achieve successful spinal anaesthesia using otherwise inadequate doses of local anaesthetic.

METHODOLOGY: Study was conducted after approval from institutional ethical committee with reference no: 29/2020. It was a comparative prospective study conducted at tertiary care hospital during January 2021 to June 2021 under which 60 subjects were enrolled and divided into 2 groups of 30 patients each⁷.

Group A will receive Low dose bupivacaine 7.5mg (0.5%) (1.5 ml). Group B will receive bupivacaine 5mg (0.5%) (1ml) and fentanyl 25 µg (0.5).

Inclusion Criteria:

- Age: 60-80 years
- ASA I, II, III
- With informed valid consent

Exclusion Criteria: Patients with a history of spine surgery, mental retardation, infection at injection sites, coagulopathy, a history of opioid and chronic analgesic use, hypersensitivity to local anaesthetics or opioids, peripheral neuropathy, coronary artery disease, advanced cardiac valve disease or an ejection fraction <50% were excluded from the study.

Procedure: All the patients were kept nil by mouth overnight. No patient received any sedative or narcotic premedication before arrival in the operation theatre. All patients had received Inj. Ondansetron 4 mg i.v 30 min. before surgery. Patients were taken to the O.T. and heart rate,

blood pressure, ECG, SpO₂, respiratory rate, temperature were noted intravenous line was secured with 18 G intra cath. A standard subarachnoid block was performed in L2-L3 / L3-L4 Space in sitting / lateral position with 22G/23G BD spinal needle (Quinky needle type, 3.5-inch-long) under all aseptic and antiseptic precautions after local infiltration of skin and subcutaneous tissue with 2 cc 2 % lignocaine. Drugs were injected after confirming free flow of CSF and according to group selected. Immediately after completion of block, patients remained in supine position until adequate sensory and motor blockade reached to required level of surgery. After that all the patients were placed in the supine lithotomy position and then surgery was started.

Data Analysis: Data will be entered in Microsoft excel and analysed using Epi-info. Continuous variables will be expressed as mean standard deviation. Appropriate statistical tests will be applied accordingly. Unpaired t test will be done for comparative analysis. P-value less than 0.05 will be taken for significance level.

RESULTS: Total 60 male subjects were enrolled in study with division in 2 groups of 30 subjects each. Group A subjects received Low dose bupivacaine 7.5mg (0.5%) (1.5 ml) and Group B subjects received bupivacaine 5mg (0.5%) (1ml) and fentanyl 25 µg (0.5). **Fig. 1** Comparison of Anthropometric Parameters.

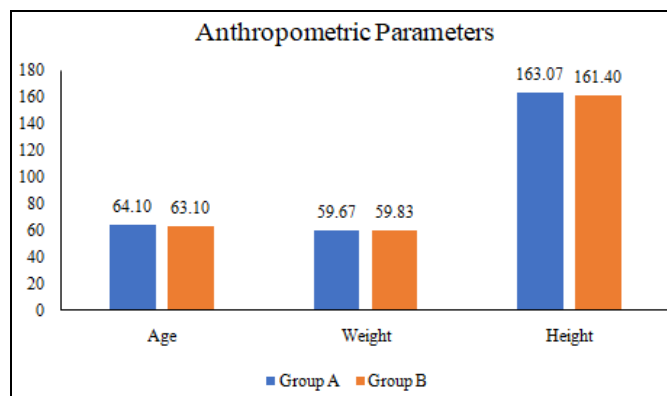


FIG. 1: SHOWS ANTHROPOMETRIC PARAMETERS FOR BOTH THE GROUPS. Group A patients has mean Age of 64.10 ± 2.06 years while Group B patients has mean age of 63.13 ± 2.54 years. Mean weight for Group A patients was 59.67 ± 7.11 kg and for Group B patients was 59.83 ± 9.20 kg. Mean height for Group A patients was 163.07 ± 3.39 cm and for Group B patients it was 161.40 ± 5.06 cm. There is no any statistically significant difference observed between both the groups.

TABLE 1: SENSORY BLOCKADE PARAMETER COMPARISON BETWEEN TWO GROUPS

Sensory Blockade	Group-A	Group-B	pValue
Time of onset sensory block (min) (Mean± SD)	1.59 ± 0.34	1.18 ± 0.31	0.00
Peak sensory block level	T10	T8	
Time to reach peak sensory block level (min) (Mean±SD)	5.54 ± 0.35	3.50 ± 0.57	0.00
Duration of sensory block (min) (Mean±SD)	159.60 ± 8.14	164.33 ± 6.09	0.01

Table 1 shows comparison for parameters of sensory block between both the groups. Mean onset of sensory block in Group A was 1.59 ± 0.34 minutes while in Group B it was 1.18 ± 0.31 . Peak Sensory level for Group B patients was T8 level and Group A it was T10 level. Regarding mean time taken to reach peak sensory level, in Group B patients it was 3.50 ± 0.57 minutes while in Group

A patients it was 5.54 ± 0.35 minutes. Duration of sensory block was reported longer in Group B patients (164.33 ± 6.09 minutes) in compare to 159.60 ± 8.14 minutes in Group A.

All of above findings shows statistical significant difference between both the groups (p value <0.05) for sensory block parameters.

TABLE 2: MOTOR BLOCKADE PARAMETER COMPARISON BETWEEN TWO GROUPS

Motor Blockade	Group-A	Group-B	pValue
Time of onset motor block (min) (Mean±SD)	2.74 ± 0.16	1.72 ± 0.69	0.00
Duration of motor block (min) (Mean±SD)	139.60 ± 8.14	121.33 ± 9.45	0.00

Table 2 shows comparison for parameters of motor block between both the groups. Mean onset of motor block in Group A was 2.74 ± 0.16 minutes while in Group B it was 1.72 ± 0.69 minute. Regarding duration of motor block Group B patients has mean duration of motor block of

121.33 ± 9.45 minutes which is less in comparison of Group A (139.60 ± 8.14 minutes).

Statistical significant difference was found between both the groups (p value <0.05) related to parameters of Motor block.

TABLE 3: COMPARISON OF HEART RATE BETWEEN TWO DRUGS

Time	Group A	Group B	p value
Pre-operative	85.87 ± 9.60	87.27 ± 10.55	0.59
5min	81.53 ± 8.25	83.63 ± 9.52	0.36
10min	80.67 ± 7.39	81.80 ± 8.44	0.58
15min	80.77 ± 8.59	81.50 ± 7.08	0.72
20min	79.53 ± 8.03	80.57 ± 6.85	0.59
30min	77.77 ± 8.46	82.10 ± 7.52	0.04
40min	76.53 ± 8.01	82.37 ± 7.36	0.00
50min	76.13 ± 7.42	82.87 ± 7.08	0.00
60min	75.30 ± 7.24	81.60 ± 6.88	0.00
90 min	76.17 ± 7.34	82.73 ± 7.02	0.00

Table 3 shows comparison of heart rate between Group A and Group B patients. Observations were noted during Pre-operative time, 5 min, 10 min, 15 min, 20 min, 30 min, 40 min, 50 min, 60 min and 90 min. In Group A patients mean heart rate ranges from 85.87 ± 9.60 from pre-operative time to 76.17 ± 7.34 after 90 min of observation which shows decreasing trend in heart rate after induction. similarly, in Group B Patients Heart rate ranges from 87.27 ± 10.55 to 82.73 ± 7.02 at the end of 90 min of observation. Statistically significant difference was noted at 30 min, 40 min, 50 min, 60 min and at 90 min between Group A and Group B patients (p<0.05). **Fig. 2** Comparison of Mean Arterial Pressure.

Statistically significant difference was observed in Mean arterial pressure between both the groups at 30 min, 40 min, 50 min, 60 mins and 90 min time interval (p value <0.05).

TABLE 4: COMPARISON OF INTRA-OP COMPLICATION BETWEEN TWO GROUPS

Intra-operative complication	Group A	Group B
Hypotension	3	0
Bradycardia	1	0
Pruritus	0	3
Nausea	0	0
Vomiting	1	0
Shivering	3	0
Respiratory depression	0	0

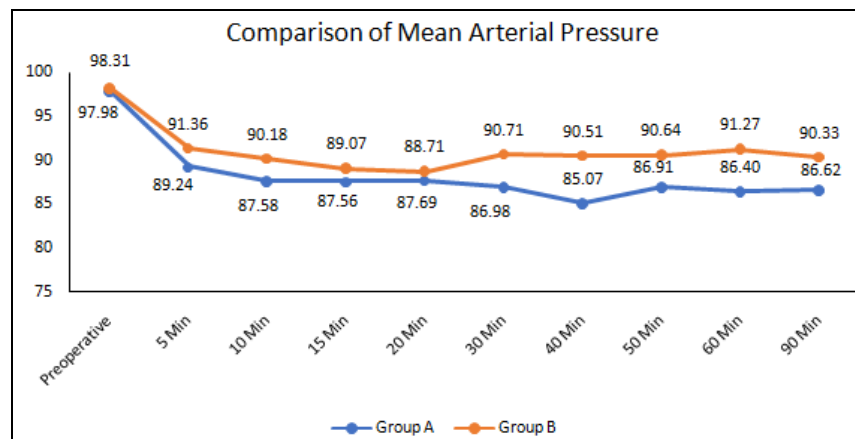


FIG. 2: SHOWS COMPARISON OF MEAN ARTERIAL PRESSURE BETWEEN BOTH GROUPS. Mean arterial pressure is obtained by $DP + 1/3(SP - DP)$ or $MAP = DP + 1/3(PP)$ Where DP is the diastolic blood pressure, SP is the systolic blood pressure, and PP is the pulse pressure. In group A patients Mean Arterial Pressure ranges from 97.98 ± 8.11 mm of Hg at pre-operative time to 85.07 ± 4.14 mm of Hg at 40 min and 86.62 ± 3.83 mm of Hg at 90 min which shows decline in MAP. Similarly, in Group B patients it ranges from 98.31 ± 8.15 mm of Hg at preoperative period to 88.71 ± 6.14 mm of Hg at 20 min and at the end of 90 min it was 90.33 ± 6.01 mm of Hg.

Table 4 shows intra operative complications of both the group. In Group A complications of Hypotension (in 3 patients), Shivering (in 3 patients), Bradycardia (in 1 patient) and Vomiting (in 1 patient) were reported, while in Group B in which Fentanyl was utilized with low dose Bupivacaine only pruritus (in 3 patients) was noted which is peculiar of fentanyl. No patients have suffered from respiratory depression or nausea in any group.

DISCUSSION: With increase knowledge of potential safety, benefits, increased experience with the technique and moreover early diagnosis of TURP syndrome in awake state, spinal anaesthesia is becoming more popular and preferred technique in TURP. Intra thecal opioids are synergistic with local anaesthetics as it intensify the sensory block without increase in the sympathetic block. The addition of fentanyl to hyperbaric bupivacaine increases the intra-operative quality of subarachnoid block and synergistic antinociceptive effects with local anaesthetics. Lipophilic opioids are increasingly being administered intrathecally as adjuvant to local anaesthetics. They enhance spinal anaesthesia without prolonging motor recovery and discharge time. The spread of sensory block was assessed by pin prick and motor block by Bromage score. In present study, the onset time for a maximum sensory block was lower in group B as compared to group A and total duration of sensory block was longer in group B as compared to group A. Onset of motor blockade was delayed in group

A as compared to Group B and duration of motor blockade was longer in group A. Number of studies have used $25\mu\text{g}$ of intra thecal fentanyl as adjunct to the anesthetic agent with good results. $25\mu\text{g}$ of fentanyl provides maximum duration of post-operative analgesia with minimal side effects like respiratory depression and pruritus as studied by Biswas, *et al.*,⁸ As studied by Dehlgren, *et al.*,⁹ and Liu, *et al.*,⁵ found that fentanyl $20\mu\text{g}$ in combination with spinal lidocaine prolongs sensory anaesthesia without prolonging recovery of motor function or time to micturition. Kuusneimi, *et al.*,¹⁰ concluded that the addition of $25\mu\text{g}$ of fentanyl to 5mg bupivacaine resulted in shorter lasting motor block but maintained the same level of sensory analgesia as with larger doses of bupivacaine ($7.5, 10\text{mg}$) with or without fentanyl.

Boucher, *et al.*¹¹ suggested that fentanyl did not change the characteristics of spinal block with spinal procaine. Various studies have indicated the synergism between intra thecal opioids and local anaesthetics may allow a reduction in the dose of local anaesthetics and reduce hypotension, while still maintaining adequate anaesthesia⁶. In present study, fentanyl increases dermatomal spread without affecting motor function. These results are consistent with the studies done by Beers, *et al.*,¹² and Cheng Wang, *et al.*,¹³. A. Karmaz, *et al.*¹⁴ evaluated the effects of intra thecal administration of low dose bupivacaine 4mg with fentanyl $25\mu\text{g}$ (Group B) and compared it with plain bupivacaine 7.5mg (Group A) for TURP and reported that

median sensory height of T10 in both the groups. The addition of fentanyl provides adequate analgesia for TURP. The mean level of motor block was higher, and duration of motor block was longer in Group A. There was not any significant difference in mean heart rate and Blood pressure up to 20 min in Group A and Group B. Similar kind of findings were observed by Prajapati J *et al.*,⁷ regarding all the hemodynamic parameters. Fluid loading has not always been effective since the reduced physiological reserve of the elderly makes them less able to increase their cardiac output in response to fluid loading. A. Kararmaz, *et al.*,¹⁴ studied that intra thecal bupivacaine 4 mg combined with fentanyl 25 µg provides adequate anaesthesia for TURP in elderly patients and is associated with a lower incidence of hypotension than a conventional dose of bupivacaine (7.5 mg). Critchley, *et al.* suggested that in order to avoid hypotension a preloading of 500 ml of inj. Ringer lactate solution was administered, followed by continuous infusion of 8 ml/kg/hr throughout the operation.

Regarding intra and post-operative complications, Pruritus was the most common adverse effect in patients who received intra thecal fentanyl as previously reported by investigators. Liu, *et al.*⁵ found that the addition of 20 µg of fentanyl intrathecally leads to pruritus. Some authors studied intra thecal fentanyl at doses of 7.5 µg, 10 µg, 12.5 µg. They found that incidence of pruritus (in 5 patients) and nausea, vomiting was same at all doses. In our study, 3 patients of group B had complaining of itching (pruritus) but none of the patient's needed treatment. No patient of both groups suffered from nausea. Shivering during spinal anaesthesia is complication in elderly patient undergoing TURP. Shivering is known to increase oxygen consumption, ventilation and cardiac output which can result in morbidity in patients with limited cardiopulmonary reserve. In present study, no patient of group B had shivering while 3 patients of group A had shivering. Which is in Line with A. Kararmaz *et al.*,¹⁴ studies. This confirms that the addition of fentanyl to low dose bupivacaine decreases incidence of shivering in spinal anaesthesia in elderly patients.

CONCLUSION: In this study 25µg of Fentanyl was used as an adjuvant to 1ml (5mg) of hyperbaric

Bupivacaine and compared the effects with 1.5ml (7.5mg) of hyperbaric Bupivacaine. Our observations revealed that addition of Fentanyl was found to be advantageous in the following ways:

1. Quickens onset of sensory and motor block.
2. Provided excellent surgical anaesthesia and good muscle relaxation to facilitate the positioning.
3. Provides haemodynamic stability.
4. Earlier motor recovery.
5. No respiratory depression and no intravenous supplementation.
6. Reduces the incidence of shivering.
7. Can produce mild pruritus which does not require any treatment.
8. No post-operative complications like TNS.

This study shows that intrathecal Fentanyl 25µg acts synergistically to potentiate Bupivacaine induced sensory block, with early motor recovery good haemodynamic stability, reduces the need for post-operative analgesics, without any significant adverse effects.

ACKNOWLEDGEMENT: Nill

CONFLICTS OF INTEREST: Nill

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How to cite this article:

Patel UV, Kothari A and Dave BB: A comparative study between use of low dose bupivacaine and bupivacaine plus fentanyl in spinal anaesthesia in transurethral resection of prostate. *Int J Pharm Sci & Res* 2024; 15(11): 3204-09. doi: 10.13040/IJPSR.0975-8232.15(11).3204-09.

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