

# Intrathecal Anaesthesia for Elderly Patients Undergoing Short Transurethral Procedures: A Dose-Finding Study.

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## ABSTRACT

**Background:** To reduce effects associated the adverse hemodynamic effects associated with the spinal anesthesia-induced medical sympathectomy, combinations of very small doses of local anesthetic and adjuvant opioids are frequently administered. However, for elderly patients undergoing transurethral procedures, the optimal bupivacaine-fentanyl dose is unknown. The aim of the study is to find the optimal dosage of intrathecal anesthesia for elderly patients undergoing short transurethral procedures with bupivacaine-fentanyl, with stable hemodynamics. **Methods:** The study included 75 patients, ASA I, II and III scheduled for transurethral procedures at Kamineni hospitals, L.B. Nagar, Hyderabad which is a 350 bedded super-speciality tertiary care center. These patients were randomly allocated into three groups, 25 patients in each group. Group A received 7.5 mg bupivacaine, Group B were given 5 mg bupivacaine along with fentanyl 20 µg while patients in Group C received bupivacaine 4 mg with fentanyl 20 µg. Intrathecal fentanyl as an analgesic adjuvant to bupivacaine anesthesia. Intraoperative pain was assessed using Visual Analog Scale (VAS). Demographics, time intervals, and continuous variables (MAP, heart rate, SpO<sub>2</sub>, VAS) were analyzed using the one-way analysis of variance (ANOVA) test. **Results:** Demographic characteristics as well as intraoperative MAP, heart rate and SpO<sub>2</sub> were similar among groups. Intraoperative rescue fentanyl requirements were significantly higher in group C (bupivacaine 4 mg + fentanyl 20µg) when compared with those in the other two groups. In group A (bupivacaine 7.5 mg), there was significant difference in mepenteramine requirements. **Conclusion:** Of the doses investigated bupivacaine 5 mg with fentanyl 20µg, provided adequate analgesia and was associated with hemodynamic stability and the fewest side effects.

**Keywords:** Spinal anesthesia, bupivacaine, fentanyl, hemodynamic stability

## INTRODUCTION

Pain is one of the most unpleasant experiences for mankind. International association for the study of pain defines the term pain: "Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such pain. Surgical pain is a kind of acute pain, which is always a challenge to the anesthesiologist. However, the patients' problems of pain do not end with the surgical procedure. Pain during peri-operative period is also of concern to the anesthesiologist. Peri-operative pain control is generally best managed by anesthesiologist, because they offer regional techniques of anesthesia as well as pharmacological expertise in analgesics. For surgical analgesia opioid is preferred over the other analgesic agents because of their potency. Regional anesthesia is well tolerated by geriatric patients undergoing orthopedic surgery, producing less postoperative confusion and delirium than general anesthesia.<sup>[1]</sup>

Spinal Anesthesia has enjoyed a long history of success and recently, celebrated a centennial anniversary. Lidocaine anesthetic has been a popular anesthetic for urologic procedures. However, several editorials have questioned the use of lidocaine for spinal anesthesia because of the frequency of transient neurologic symptoms.<sup>[2-4]</sup> These observations generated interest in an alternative local anesthetic solution. Some investigators have examined small doses of spinal bupivacaine to be used in surgical procedures lasting less than an hour.<sup>[5,6]</sup> Thus, hyperbaric bupivacaine is appropriate for rapid anesthetic recovery and cardiovascular stability.<sup>[7]</sup> Spinal anesthesia has been widely used for urologic operations because it permits early recognition of symptoms caused by over-hydration, transurethral resection of prostate (TURP) syndrome, and bladder perforation. In addition, short acting spinal anesthesia may help to prevent complications associated with delayed immobilization.<sup>[8]</sup>

Spinal anesthesia using 0.5% bupivacaine (heavy) is characterized by relatively rapid onset of action, duration of anesthesia at approximately 2-3 hours and profound motor blockade. Recent trends of spinal anesthesia are towards addition of adjuvants like opioid, ketamine, clonidine, neostigmine, midazolam etc to local anesthetic to increase efficacy, duration

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and to maintain analgesia far into the postoperative period.<sup>[9]</sup>

Neuraxial administration of opioids in conjunction with local anesthetics improves the quality of intra-operative analgesia and prolongs the duration of postoperative analgesia.<sup>[10]</sup> To reduce the adverse hemodynamic effects associated with the spinal-anesthesia induced medical sympathectomy, combinations of very small doses of local anesthetic and adjuvant opioids are frequently administered.<sup>[8,11-16]</sup>

Fentanyl (a lipophilic opioid) has a rapid onset and a shorter duration of action following intrathecal administration but its duration of action may be dose dependent.<sup>[17,18]</sup> In the non-geriatric population, the association of fentanyl and local anesthetics improves the sensory block induced by the spinal administration of local anesthetics in the intra- and postoperative period. The advantages and risks of this procedure have not been fully examined in the elderly.<sup>[19,20]</sup> Although Varassi et al. have reported respiratory depression after administration of 50µg, but not 25 µg, of spinal Fentanyl.<sup>[21]</sup>

However, for elderly patients undergoing transurethral procedures, the optimal bupivacaine-fentanyl dose is unknown and since only a few studies of intrathecal fentanyl are available in our country, therefore we performed a comparative study to establish the smallest possible effective dose of intrathecal bupivacaine when administered with adjuvant fentanyl (20 µg) among elderly patients undergoing transurethral procedures.

## **MATERIALS AND METHODS**

After obtaining approval of the local ethical committee, this study was conducted which included seventy-five patients, aged more than 65 yrs undergoing elective transurethral procedures. Informed consent was obtained from these patients before the procedure. The patients of ASA physical status 1-3 were included in this study. The study was a randomized and prospective study.

The Patients were randomly divided into one of the three groups, each comprising 25 patients. First group, that is the control group A was given 7.5 mg, the second group B was given 5 mg of bupivacaine with fentanyl 20 µg as an adjuvant and the third group C received bupivacaine 4mg with fentanyl 20 µg.

### Inclusion criteria:

Patients of either sex in the age group above 65 yrs.

ASA grade I –III.

Patients undergoing elective short transurethral procedures under spinal anesthesia.

### Exclusion criteria:

Age less than 65 years.

Local infection at the site of injection, back pain.

Patients on chronic analgesic therapy.

Spine abnormalities, coagulopathies.

Any known allergies to drugs.

History of atopic dermatitis.

Refusal of the patient.

ASA grade IV.

### Procedure:

Detailed pre-operative evaluation was done.

All patients kept nil per oral for a period of 10- 12 hours.

All the necessary basic investigations were done viz. hemoglobin, total count, differential count, ESR, bleeding time, clotting time, RBS, chest x-ray.

Group-A: Twenty-five patients received bupivacaine 7.5 mg made to a volume of 2 ml with 10% dextrose as diluent.

Group-B: Twenty-five patients received bupivacaine 5 mg with fentanyl 20 µg to a total volume of 2 ml.

Group-C: Twenty-five patients received bupivacaine 4 mg and fentanyl 20 µg to a total volume of 2 ml.

Premedication: Since geriatric patients are particularly sensitive to drug interactions, it is possible that synergism between midazolam and intrathecal bupivacaine might adversely affect the incidence of hypotension. Thus no premedication was given to patients.

Monitoring: In the operating room, monitors attached were,

Pulse oximetry,

Electrocardiogram,

Non-invasive blood pressure monitoring

Then, all the patients were pre-hydrated with 8 ml/kg of ringer's lactate solutions.

### Positioning of the patients:

With the patient in the sitting position.

Back painted and draped.

The procedure was performed at L 4-5 vertebral interspaces, lignocaine 2% was used for skin infiltration.

26 G Quincke –Babcock needle was used.

The 2 ml drug injected into the subarachnoid space after free, clear aspiration of C.S.F.

Immediately thereafter, needle was removed patients were placed in the supine lithotomy position.

The following data was collected:

Time for onset of action: Defined as the time interval between the completion of injection of bupivacaine alone or bupivacaine with fentanyl solution to the complete loss sensation to pin prick.

Level of sensory block: Defined as the highest dermatomal level of sensory blockade assessed by pin prick till maximum level of sensory block was

achieved i.e. the level had stabilized for 5 consecutive pricks first two at 2 mins interval next two at 5 mins interval and the last one at 10mins interval.

**Assessment of the sensory level:** By using a 21-gauge needle along the mid-clavicular lines the height and regression of the sensory deficit was determined at 2-min intervals .A T10 sensory deficit was a prerequisite for beginning the surgery.

**Duration of sensory blockade:** Defined as the time interval from the injection of solution to regression of two dermatomes from the highest dermatomal level of sensory block.

**Motor level assessment:** Immediately before the start and at the end of surgery, the motor blockade was determined using Bromage score.

**Pain assessment:** Intra operative pain was evaluated using a 100-mm visual analog score (VAS) (0=no pain, 100 = worst imaginable pain).A VAS >30mm were treated with IV fentanyl 25 microgram. Five minutes thereafter, the VAS was assessed, and if necessary, additional intravenous fentanyl was administered. This was repeated until a VAS<30.

**Rescue Mephenteramine:** A decrease in mean arterial blood pressure (MAP)>20% of pre induction values were treated with mephenteramine, 5 mg, IV.

Systolic pressure, diastolic pressure ,mean arterial pressure, heart rate were measured at the intervals of 1 min, 5 mins ,15 mins, 30 mins, 60 mins and finally at 90 mins

**Recovery:** After surgery, patients were monitored in the recovery room till spinal anaesthesia wore off and were then shifted to the ward.

**Statistical analysis:** Continuous variables (heart rate, MAP, SpO<sub>2</sub>, and VAS) were analyzed using one way analysis of variance (ANOVA) and the number of patients requiring rescue fentanyl, intraoperative mephenteramine were assessed using chi-square test. In all the cases, p value less than 0.05 were considered significant.

## RESULTS

Demographic characteristics as well as intraoperative MAP, heart rate, and SpO<sub>2</sub> were similar among groups. Demographic data like age, sex and ASA physical status are presented as mean ± SD where appropriate. There were twenty-five patients in each study group, and the groups were demographically similar.

**Table 1:** Distribution of patients as per the rescue Fentanyl given

Group	Given	Not Given	Total
Bupivacaine 7.5 mg(A)	0	25	25
Bupivacaine 5mg+fentanyl 20 µg(B)	1	24	25
Bupivacaine 4mg+fentanyl 20 µg(C)	5	20	25
Total	6	69	75

Chi-Square=7.609, p Value=0.0223

The most important parameter which shows that the anesthetic technique utilized is sufficient is the number of patients requiring “rescue” fentanyl intravenously. In our study we found that the amount of rescue fentanyl required in the group C (bupivacaine 4 mg + fentanyl 20 µg) was comparatively more than the group A (bupivacaine 7.5 mg) and the group B (bupivacaine 5 mg + fentanyl 20 µg). When statistically analyzed using chi-square test it was significant (chi square value=7.609) and p value=0.0223. Thus, group C (bupivacaine 4 mg + fentanyl 20 µg) provided insufficient analgesia when compared to the other group. Group A (Bupivacaine 7.5 mg) and group B (Bupivacaine 5 mg + fentanyl 20 µg) were comparable with group A requiring no “rescue fentanyl” and group B only in one patient [Table 1]. The oxygen saturation in various study groups was comparable and did not show significant variation, as all these were on six liters per minute of oxygen by polymask. The heart rate variation in the study

groups was also comparable. The fall in heart rate at five minutes interval in all three groups was similar and statistically non-significant. Similarly all the three groups compared at similar intervals and statistically comparable. The p values were > 0.05. The comparison of the systolic blood pressure were compared using ANOVA test in between the study groups and intragroup also. There were no significant variation intergroup and intragroup systolic blood pressures which signified that the small amount of the drug in each of the group was insufficient to produce statistically and clinically significant fall. Statistically all the three study groups had a p-Value > 0.05. Similar to the systolic pressures, the changes in diastolic pressures were also not statistically significant when intergroup and intragroup comparison were done i.e. p-Value > 0.05, reinforcing the hemodynamic stability in the three study groups, visa-a-vis Groups A, B and C. The mean arterial pressures recorded at different time intervals were plotted as a line diagram emphasized

the comparability in terms of the similar statistical values. The p-Value on comparison intra and inter-

group yielded > 0.05 values, statistically non-significant.

**Table 2:** Comparison of the Regression of Sensory Blockade

Groups	Sum of Squares	df	Mean Square	F	P value.
Between Groups	1101.84	2	550.92	6.116953	0.0035
Within Groups	6484.64	72	90.06444	-	-
Total	7586.48	74	-	-	-

**Table 3:** Comparison of the Regression of Sensory Blockade

From	To	Mean Difference	P value
Group A	Group B	7.08	0.0361*
Group A	Group C	8.88	0.0061*
Group B	Group C	1.8	0.7992

**Table 4:** Comparison of the Regression of Sensory Blockade

Mean Time (mins)	Group A	Group B	Group C
	79.88	72.8	71.0

The above tables [Table 2-4] show that the comparison of the three groups in terms of the regression of the sensory block is significantly longer (79.88 mins) in group A (Bupivacaine 7.5 mg) when compared to the other two groups, group B took 72.8 mins and group C took 71.0 mins. The comparison was done using the statistical test of scheffe test. The

p value(p=0.0361) was significant when group A (bupivacaine 7.5mg) was compared with group B (bupivacaine 5 mg+ fentanyl 20 µg) and also p = 0.0061 with group C (bupivacaine 4 mg+ fentanyl 20 µg). The comparison of group B with group C shows p value of 0.7992 which was non-significant.

**Table 5a:** Comparison of the Regression of the Motor Blockade:

ANOVA of Regression of the Motor Blockade						
Time to regression of motor block (min)		Sum of Squares	df	Mean Square	F	P value.
	Between Groups	1374.827	2	687.4133	7.052885	0.001595
	Within Groups	7017.52	72	97.46556	-	-
	Total	8392.347	74	-	-	-

**Table 5b:** Comparison of the Regression of the Motor Blockade:

Scheffe's Test for Pair Wise Comparison			
Time to regression of motor block(min)	Comparison		p value
	Group A	Group B	0.006375
	Group A	Group C	0.008134
	Group B	Group C	0.996313

**Table 6:** Comparison of the regression of the motor blockade:

Time(mins)	Group A	Group B	Group C
	45.96	36.76	37

The regression of the motor blockade in the three study groups showed that the time taken for regression of the motor blockade in bupivacaine 7.5 mg group of patients (group A) was significantly longer than the other two groups [Table 5a,5b,6]. When the group A (bupivacaine 7.5 mg) compared with group B (bupivacaine 5 mg + fentanyl 20 µg) p value of 0.006375 and when compared with group C (bupivacaine 4 mg + fentanyl 20 µg) was 0.008134, both highly significant.

## DISCUSSION

The relief from pain is a basic human right. The gap between an increasingly sophisticated knowledge of pain and its treatment and the effective application of that knowledge is large and widening. Both acute and chronic pains are often poorly managed for a wide variety of reasons, viz. cultural, attitudinal, educational, political and logistical. Moderate to severe pain affects roughly half of all surgical patients. This means that the conventional

approach to pain therapy needs to be reassessed. The greatest fear of patients undergoing surgery is pain. Pain affects multiple organ system and contributes to morbidity. Hence it is our responsibility to ensure complete pain relief. The approach to total pain relief is multimodal analgesia using a combination of drugs or techniques.

Following the initial reports in 1979 of clinical efficacy of intrathecal and epidural narcotics, they have been used to control pain following a wide variety of surgical procedures. Intrathecal narcotics have the appeal of ease of administration and many patients will be comfortable for variable period of time, depending on the narcotic agent administered.

Our study demonstrates that, of the drug combinations studied, bupivacaine 5 mg + 20 µg fentanyl was most favorable for elderly patients undergoing short transurethral procedures. Although the group C (bupivacaine 4 mg + fentanyl 20 µg) had shortest sensory blockade but the regimen was associated with a high incidence of rescue intravenous fentanyl administration but in the 5 mg bupivacaine+fentanyl 20 µg (group B) the amount of rescue fentanyl was significantly less, only one patient needed rescue fentanyl out of twenty five patients in group B when compared to 5 patients in group C.

We found that out of twenty five in each group, although the sensory and motor blockade was excellent with group A (bupivacaine 7.5 mg) but the incidence of use of intraoperative mephenteramine was significant in the group A, as eight out of twenty five patients required mephenteramine which when compared to other groups was statistically significant (p value=0.0303). This is similar to the previous study by Edna Zohar<sup>[22]</sup> in which ephedrine administration was significantly higher in the similar group of bupivacaine 7.5 mg.

Of the groups studied the group B (bupivacaine 5 mg + fentanyl 20 µg) is ideally suited for short transurethral procedures in the elderly patients. This regimen provided the maximum hemodynamic stability with adequate sensory and motor blockade. Our study when compared to study by Edna Zohar in November 2006 which showed that ideal regimen for short transurethral procedures in the elderly were 4 mg of bupivacaine + fentanyl 20 µg.<sup>[22]</sup>

The regression of the sensory blockade in our study in all the groups of our study was faster in comparison with the previous study but it was adequate for short transurethral procedures. The time for regression of sensory blockade was 72.8 minutes in bupivacaine 5 mg + fentanyl 20 µg which is far less than what was found in the study done by Edna Zohar in 2006.<sup>[22]</sup>

These results are consistent with experimental evidence of a synergistic interaction between spinal opioids and local anesthetics. That synergism is characterized by enhanced somatic analgesia without effect on the degree or level of the local anesthetic-induced sympathetic or motor blockade.<sup>[15]</sup> Most relevant to this study is the evidence that intrathecal opioids can greatly enhance analgesia from sub therapeutic doses of local anesthetic. The explanation of this differential synergism likely draws from the separate mechanisms of action, wherein inhibition of nociceptive transmission occurs at sequential stages of that signal transmission. Intrathecal opioids inhibit nociceptive afferent synaptic transmission via A-delta and C-fibers by opening presynaptic K<sup>+</sup> channels to inhibit transmitter release and thus reduce calcium influx. There is also a direct postsynaptic effect with hyperpolarization and reduced neuronal activity. Local anesthetics work primarily by causing blockade of voltage-gated sodium channels in the axonal membrane and, possibly, a further effect on presynaptic inhibition of calcium channels.<sup>[14]</sup>

The administration of intrathecal opioids may provide benefits in augmenting intraoperative anesthesia, but carries a risk of respiratory depression.<sup>23</sup> Fentanyl is much more lipid-soluble than morphine and hence does not tend to migrate to the fourth ventricle in sufficient concentrations to cause respiratory depression. Varassi et al demonstrated that the subarachnoid administration of 25 µg of fentanyl during spinal anesthesia in non-pre-medicated elderly men did not alter respiratory rate, end-tidal tension of CO<sub>2</sub>, minute ventilation, respiratory drive, respiratory timing, or the ventilator response to CO<sub>2</sub>. On the contrary, 50 µg of subarachnoid fentanyl could cause an early respiratory depression in elderly patients.<sup>[23,25]</sup>

In our study we observed that small dose bupivacaine spinal anesthesia lead to notable hemodynamic stability which is unaffected by the addition of 20 µg fentanyl. This observation is potentially of great clinical significance as such a finding is perhaps predicted by experimental work, which shows that the decrease in sympathetic efferent activity (spontaneous and evoked) after spinal anesthesia is dose related to the Bupivacaine, and that intrathecal fentanyl causes neither by itself nor in combination with Bupivacaine any further depression of efferent sympathetic activity<sup>[24]</sup> and reiterated by Ben-David et al in his study of intrathecal fentanyl (10 µg) with small-dose dilute bupivacaine.<sup>[15]</sup>

As geriatric patients are particularly sensitive to drug interactions, it is possible that synergism between premedication and intrathecal bupivacaine may adversely affect the intraoperative hypotension. To avoid this confounding factor, there was no

premedication given to the patients in our study group.

## CONCLUSION

Of the doses investigated, bupivacaine 5 mg + fentanyl 20 µg provided adequate analgesia with the fewest side effects.

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