

Comparison of Two Different Doses of Hyperbaric Bupivacaine with Fentanyl for Spinal Anaesthesia in Elderly Patients Undergoing Routine Endoscopic Urological Surgery: A Randomized Controlled Study

Original
Article

Neha Atwal¹, Jyoti Pathania² and Aparna Sharma³

¹Anaesthetist Civil Hospital Nadaun, Himachal Pradesh, ^{2,3}Indira Gandhi Medical College, Shimla, Himachal Pradesh, India.

ABSTRACT

Background: The major drawback of spinal anesthesia in elderly patients is the per operative hypotension and its sequel. We compared two doses (7.5 mg or 10 mg) of hyperbaric bupivacaine 0.5% with 25µg fentanyl in 150 elderly patients undergoing routine urological surgery with respect to hemodynamic profile.

Results: The time to onset of sensory block (min) was comparable amongst the two groups (2.41±0.86 and 2.25±0.79) in group A and B respectively. The mean time to regression of block to S2 level was at 3.56±0.53 hrs. in group A and 4.01±0.71 hrs in group B ($p<0.0001$). The maximum mean height of sensory block was at T8 level in 73.3% patients and T10 level in 18.6% patients of group A. In group B patients 58.6% had the sensory level at T6 level in 33% patients it was at T8 and in 8% it was at T4 level ($p<0.0001$). Onset of motor block was earlier in group B and was at 3.89±0.8 min over 4.23±1.01 in group A. ($p=0.026$). The time to regression of motor block was earlier in group A (4.07±0.54 hrs over 4.69±0.58 hrs in group B). ($p<0.0001$). The decrease in MAP from baseline values was more in group B over group A (0% vs. 4.7%, $p<0.05$) but the incidence of hypotension and bradycardia were statistically comparable amongst the groups ($p>0.05$).

Conclusion: The use of 7.5mg bupivacaine with 25 µg fentanyl intrathecally results in adequate anaesthesia and analgesia coupled with stable hemodynamic as required for transurethral surgery of around 2 hrs. duration.

Key Words: Anaesthesia, hypotension, transurethral resection of prostate (TURP).

Received: 24 November 2023, **Accepted:** 22 January 2024

Corresponding Author: Aparna Sharma, MD, Indira Gandhi Medical College, Shimla, Himachal Pradesh, India.
Tel.: +91-8219712580, **E-mail:** aparnasharmarina@gmail.com

ISSN: 2090-925X, 2024, Vol.16, No. 1

INTRODUCTION

Although single shot spinal anaesthesia is the commonest technique used for endoscopic urological surgery, but it is reported to have around 15%-41% incidence of hypotension in elderly patients during peri operative period.^[1,2] Thus advantage of better control of pain, reduced airway interventions, decreased incidence of DVT and prompt recognition of TURP syndrome with regional techniques are masked by increased incidence of hypotension that ensues after this block and may delay the early discharge of patients from the hospital.^[3] Thus the onus of the research for reducing this morbidity is on adding adjuvant and thereby decreasing the dose of the local anaesthetics for such routine surgery. The addition of adjuvant generally decrease the baricity of the local anaesthetic there by changing the distribution pattern of the local anaesthetic adjuvant drug (LA-A) in the spinal cord. This may result in higher peak level of the drug that is achieved.^[4,5] Researchers have used as low as 4mg LA-A drug with fentanyl but the maximum

reported height reached is low and the duration of action is around 40 min to 60 min in such scenario hence analgesic supplementation is required intraoperatively in some patients.^[6] There is still no agreement on the ideal dose to be used, but conventionally 12.5-15 mg dose of heavy bupivacaine with or without fentanyl is used in practice. Thus we hypothesized to use low than conventionally used doses of local anaesthetic (7.5 or 10 mg) with adjuvant fentanyl, as in experimental studies the LA-A combination thus obtained is still found to be hyperbaric with respect to CSF.^[5] We compared the hemodynamic parameters, adequacy, onset and duration of blockade achieved in the study groups.

PATIENTS AND METHODS

This prospective randomized single blind controlled study was conducted over a period of one year from 1 Jan 2022 to 31 Dec 2022 in a tertiary care hospital after taking institutional ethical clearance and the study was registered with.

The study was carried out in accordance with the CONSORT guidelines, the principles of the Declaration of Helsinki, 2013 and written informed consent was obtained from the patients.

Patients of age group 60 – 85 years, of either gender or American Society of Anaesthetists (ASA) physical status I-III scheduled for routine urological surgery (TURP/TURBT) were included in the study. Patients in whom spinal anaesthesia was contraindicated due to refusal for consenting to participate in the study, infection at the site, coagulopathy, anatomical deformity of spinal cord, moderate to severe stenotic valvular heart disease, history of acute coronary syndrome in last 6 months, hypertension with diastolic blood pressure more than 100mmhg or hypotension with systolic blood pressure less than 90 mmhg and known allergy to local anaesthetic were excluded from the study.

The sample size was calculated using openepi software in accordance with the study by Sendil MM^[1] where the difference in hypotension was 13% (15% and 28% hypotension incidence where 7.5 mg or 10 mg bupivacaine was used with adjuvant respectively). Thus at 80 % power, 95% CI with 1:1 allocation the sample size calculated was 146 patients. since we expected some loss of patients during the study so 155 patients were include for the recruitment. Randomization was done by a computer generated random number table. The numbers were kept in 150 sealed envelopes and one envelope was opened just after shifting the patient inside the operation theater and the drug was given by another anesthetist not involved in recording the parameters. Thus the patient, surgeon and observer were privy to the allocated group. The observer entered the operation theatre once the drug had been given and evaluated the block parameters in the patients there after.

Group A (n=75) received hyperbaric Bupivacaine (0.5%) 7.5mg with Fentanyl 25µg, Group B (n=75) received hyperbaric Bupivacaine (0.5%) 10 mg with Fentanyl 25µg. Baseline vitals of the patient as heart rate, MAP (mean arterial pressure), SpO₂ (saturation of peripheral oxygen) were recorded and intravenous line was secured with 18G cannula. Under aseptic precautions, lumbar puncture was performed at L3-L4 inter space and the study drug was injected intrathecally. The onset of sensory block level was checked along the midclavicular line using 20 G disposable hypodermic needle every 2 minutes from injection of drug till T10 level was achieved and the surgery was started. The time to peak level of sensory block was calculated from time of drug injection intrathecally to time at which sensory blockade reached highest dermatome level and stabilized for 2 consecutive test. Time to sensory regression was observed as sensation of pin prick perceived at sacral dermatome S2 level.

Motor blockade was assessed using the Bromage scale, where Grade 1 score corresponded to ability to lift legs against gravity, Grade II with ability to flex knee but unable to flex legs, grade III with unable to flex knee but free movement of feet and grade IV with inability to move any joint. Onset of motor blockade was taken as time to achieve grade \geq III and regression of motor blockade was taken as time for complete recovery of motor block to Bromage grade I.

Heart Rate, SpO₂, MAP were recorded at every 2 minutes intervals for 20 minutes. Thereafter parameters were recorded every 5min interval till the duration of surgery. Rescue analgesia was to be supplemented if required in the form of fentanyl 50 µg intravenously. Patients having inadequate block height 15 min post lumbar puncture, abdominal pain during the surgery, received general anesthesia and were excluded from the study as failure of block. Duration of surgery was recorded and any adverse effects of opioids as pruritis, nausea and vomiting were to be noted.

Decrease in 20% MAP from baseline or systolic pressure less than 90mmhg was taken as an episode of hypotension and intravenous mephenteramine in 3 mg increments was used and recorded. Bradycardia was defined as heart rate less than 50 beats/min and was treated by injection atropine 0.6mg intravenously.

The data entry was done in the Microsoft excel spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, ver. 25.0. For statistical significance, *p value* of less than 0.05 was considered statistically significant. The quantitative data were presented as the means \pm SD and as median with 25th and 75th percentiles (inter quartile range). The following statistical tests were applied for the results. The comparison of the variables which were quantitative in nature was analyzed using Independent t test. The comparison of the variables which were qualitative in nature were analyzed using Chi-Square test. If any cell had an expected value of less than 5 then Fisher's exact test was used.

RESULTS

The study was conducted on 155 patients undergoing routine endoscopic urological surgery (TURP and TURBT) under spinal anaesthesia. Five patients were excluded and finally data from 150 patients was analysed (Fig. 1).

The demographic profile of Age, BMI, height, ASA physical status, duration of surgery and intravenous fluid used peri-operatively was comparable amongst the groups. The mean duration of surgery was 1.93 \pm 0.7 hrs. in both the groups. (Table 1)

Table 2: Sensory and motor block characteristics between the two groups

	Group A	Group B	Total	<i>P value</i>
Onset of sensory block(min)				
Mean ± SD	2.41±0.86	2.25±0.79	2.33±0.82	
Median(25 th -75 th percentile)	2(2-3)	2(2-3)	2(2-3)	0.216 [‡]
Range	1-5	1-5	1-5	
Sensory regression (hrs.)				
Mean ± SD	3.56±0.53	4.01±0.71	3.79±0.67	
Median(25 th -75 th percentile)	3.5(3.25-3.83)	3.58(3.58-4.54)	3.58(3.5-4)	<0.0001 [‡]
Range	2.5-4.83	2.25-5.67	2.25-5.67	
Onset of motor block (min)				
Mean ± SD	4.23±1.01	3.89±0.8	4.06±0.92	
Median(25 th -75 th percentile)	4(4-5)	4(3-4)	4(3-5)	0.026 [‡]
Range	2-7	3-6	2-7	
Duration of motor blockade (Hrs.)				
Mean ± SD	4.07±0.54	4.69±0.58	4.38±0.64	
Median(25 th -75 th percentile)	4(4-4.17)	4.5(4.33-5)	4.25(4-4.958)	<0.0001 [‡]
Range	3-5.5	3.25-6	3-6	
Highest level of sensory block achieved				
T4	0(0%)	6(4%)	6(4%)	
T6	6(8%)	44(58.67%)	50(33.33%)	
T8	55(73.33%)	25(33.33%)	80(53.33%)	<0.0001 [*]
T10	14(18.67%)	0(0%)	14(9.33%)	

‡ independent t test, *Fisher's exact test

Table 3: Comparison of percentage decreases in mean arterial pressure (mmHg) between group I and II.

Percentage decrease in mean arterial pressure(mmHg)	Group A(n=75)	Group B(n=75)	Total	<i>P value</i>
At 2 minutes				
Mean ± SD	3.16 ± 8.5	3.34 ± 10.47	3.25 ± 9.5	
Median(25 th -75 th percentile)	4.35(-3.177-9.63)	6.12(-4.082-9.525)	4.76(-4.082-9.57)	0.735 [§]
Range	-20-20	-31.43-30.19	-31.43-30.19	
At 4 minutes				
Mean ± SD	2.45 ± 11.12	3.86 ± 12.83	3.16 ± 11.99	
Median(25 th -75 th percentile)	2.22(-4.35-9.175)	4.26(-2.418-14.286)	2.22(-4.082-11.765)	0.371 [§]
Range	-24.44-25.53	-30.77-24.53	-30.77-25.53	
At 6 minutes				
Mean ± SD	3.68 ± 10.55	4.34 ± 12.91	4.01 ± 11.75	
Median(25 th -75 th percentile)	4.26(0-10.909)	7.14(-4.168-13.037)	5.44(-2.273-11.189)	0.836 [§]
Range	-30-26.79	-31.43-30.77	-31.43-30.77	
At 8 minutes				
Mean ± SD	5.18 ± 13.21	2.52 ± 11.38	3.85 ± 12.36	
Median(25 th -75 th percentile)	7.69(-5.234-14.286)	4.08(-4.495-9.091)	4.84(-4.52-12.436)	0.152 [§]
Range	-24.44-32.2	-38.89-20.41	-38.89-32.2	
At 10 minutes				

Mean ± SD	2.33 ± 12.77	4.04 ± 13.79	3.19 ± 13.27	
Median(25 th -75 th percentile)	2.86(-4.444-12.005)	6(-4.444-15.239)	4.08(-4.444-12.927)	0.374 [§]
Range	-27.78-28.57	-27.5-28.3	-27.78-28.57	
At 12 minutes				
Mean ± SD	4.7 ± 12.23	-0.44 ± 12.75	2.13 ± 12.72	
Median(25 th -75 th percentile)	6(-1.02-12.075)	0(-7.94-8.163)	2.22(-4.913-10.153)	0.008 [§]
Range	-22.5-33.33	-41.67-28.57	-41.67-33.33	
At 14 minutes				
Mean ± SD	0.12 ± 13.06	3.75 ± 13.28	1.94 ± 13.25	
Median(25 th -75 th percentile)	0(-7.827-9.01)	4.44(-4.444-12.712)	0(-6.487-10.905)	0.093 [§]
Range	-30.56-28.57	-28.57-32.71	-30.56-32.71	
At 16 minutes				
Mean ± SD	1.98 ± 13.48	-0.4 ± 11.67	0.79 ± 12.62	
Median(25 th -75 th percentile)	4.67(-9.096-10.574)	0(-8.511-8.003)	0(-8.841-9.259)	0.271 [§]
Range	-25.71-32.74	-38.89-20.35	-38.89-32.74	
At 18 minutes				
Mean ± SD	2.81 ± 13.25	-0.51 ± 12.29	1.15 ± 12.84	
Median(25 th -75 th percentile)	5.56(-4.444-11.216)	0(-8.792-9.01)	2.04(-7.062-10.695)	0.061 [§]
Range	-31.43-26.53	-44.44-22.12	-44.44-26.53	
At 20 minutes				
Mean ± SD	-0.42 ± 12.62	0.85 ± 13.24	0.22 ± 12.9	
Median(25 th -75 th percentile)	0(-7.827-7.34)	2.86(-10.126-10.548)	0(-8.889-9.773)	0.406 [§]
Range	-33.33-21.43	-27.5-23.73	-33.33-23.73	
At 25 minutes				
Mean ± SD	0.85 ± 12.11	1.06 ± 13.41	0.96 ± 12.73	
Median(25 th -75 th percentile)	0(-4.957-9.091)	2.86(-1-8.491)	0(-4.444-8.665)	0.369 [§]
Range	-27.5-35.71	-42.86-32.2	-42.86-35.71	
At 30 minutes				
Mean ± SD	-1.21 ± 14.01	2.04 ± 13.08	0.41 ± 13.61	
Median(25 th -75 th percentile)	-2.22(-8.889-8.163)	3.7(-3.177-8.553)	0.5(-6.667-8.349)	0.096 [§]
Range	-36.11-28.57	-35-33.33	-36.11-33.33	
At 35 minutes				
Mean ± SD	1.22 ± 12.18	0.12 ± 12.73	0.67 ± 12.42	
Median(25 th -75 th percentile)	0.99(-7.919-8.867)	0(-7.919-8.082)	0(-8.307-8.163)	0.519 [§]
Range	-28.57-25.93	-41.67-28.57	-41.67-28.57	
At 40 minutes				
Mean ± SD	1.02 ± 13.27	-0.03 ± 13.42	0.49 ± 13.31	
Median(25 th -75 th percentile)	0(-9.11-9.01)	0(-8.889-10.128)	0(-8.889-9.091)	0.785 [§]
Range	-30.56-28.57	-41.67-25.93	-41.67-28.57	
At 45 minutes				
Mean ± SD	-0.37 ± 14.83	-0.57 ± 14.18	-0.47 ± 14.46	
Median(25 th -75 th percentile)	-2.04(-8.792-10.221)	2(-8.673-8.163)	0(-8.841-9.05)	0.897 [§]
Range	-45.71-28.57	-42.86-25.23	-45.71-28.57	
At 50 minutes				
Mean ± SD	-0.55 ± 13.87	-1.28 ± 12.85	-0.92 ± 13.33	
Median(25 th -75 th percentile)	0(-10.102-9.01)	0(-7.626-8.163)	0(-8.889-8.531)	0.838 [§]
Range	-34.29-29.2	-42.86-27.78	-42.86-29.2	

Till resolution				
Mean \pm SD	-0.36 \pm 13.85	-1 \pm 12.04	-0.68 \pm 12.93	
Median(25th-75th percentile)	0(-8.99-9.01)	0(-8.661-8.163)	0(-8.889-8.163)	0.949 [§]
Range	-41.67-29.2	-42.86-23.73	-42.86-29.2	

§ Mann Whitney test

Table 4: Adverse effects (hypotension and bradycardia) in the two groups

	Group A	Group B	Total	<i>P</i> value
Hypotension absent	57 (76%)	46 (61.33%)	103 (68.67%)	0.053 [†]
Hypotension present	18 (24%)	29 (38.67%)	47 (31.33%)	
Bradycardia present	0 (0%)	1 (1.33%)	1 (0.67%)	<i>I</i> *
Mephenteramine single dose	16 (21.33%)	19 (25.3%)	35 (23.3%)	0.0952*
Mephenteramine \geq 2 dose	2 (2.6%)	10 (13.3%)	12 (8%)	

† Chi square test, * Fisher's exact test

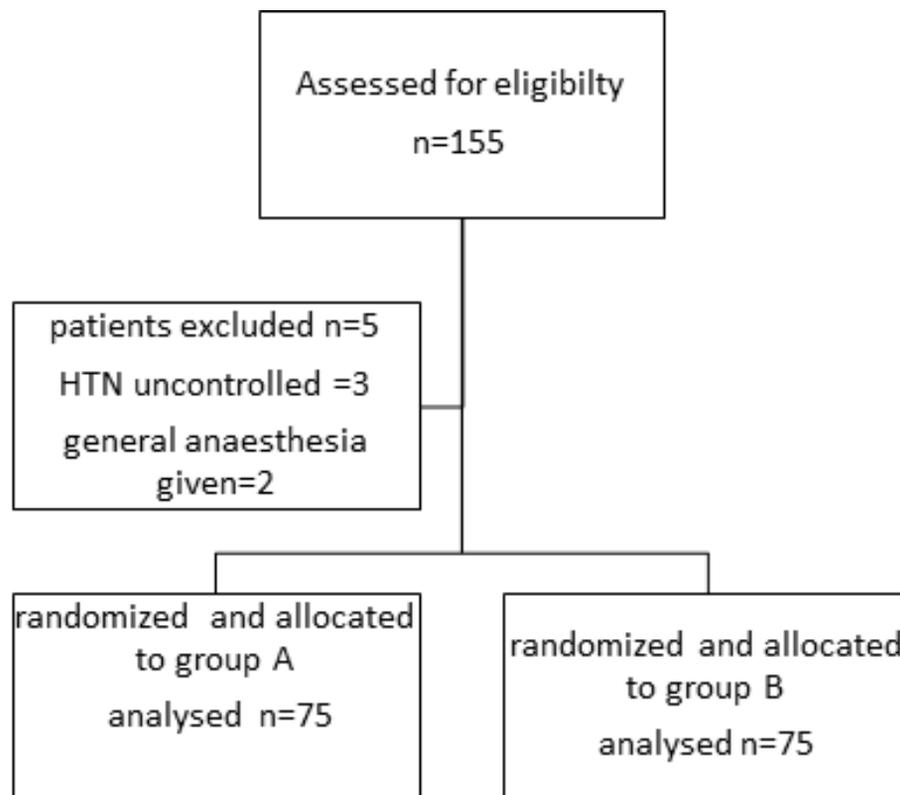


Fig. 1: Consort diagram

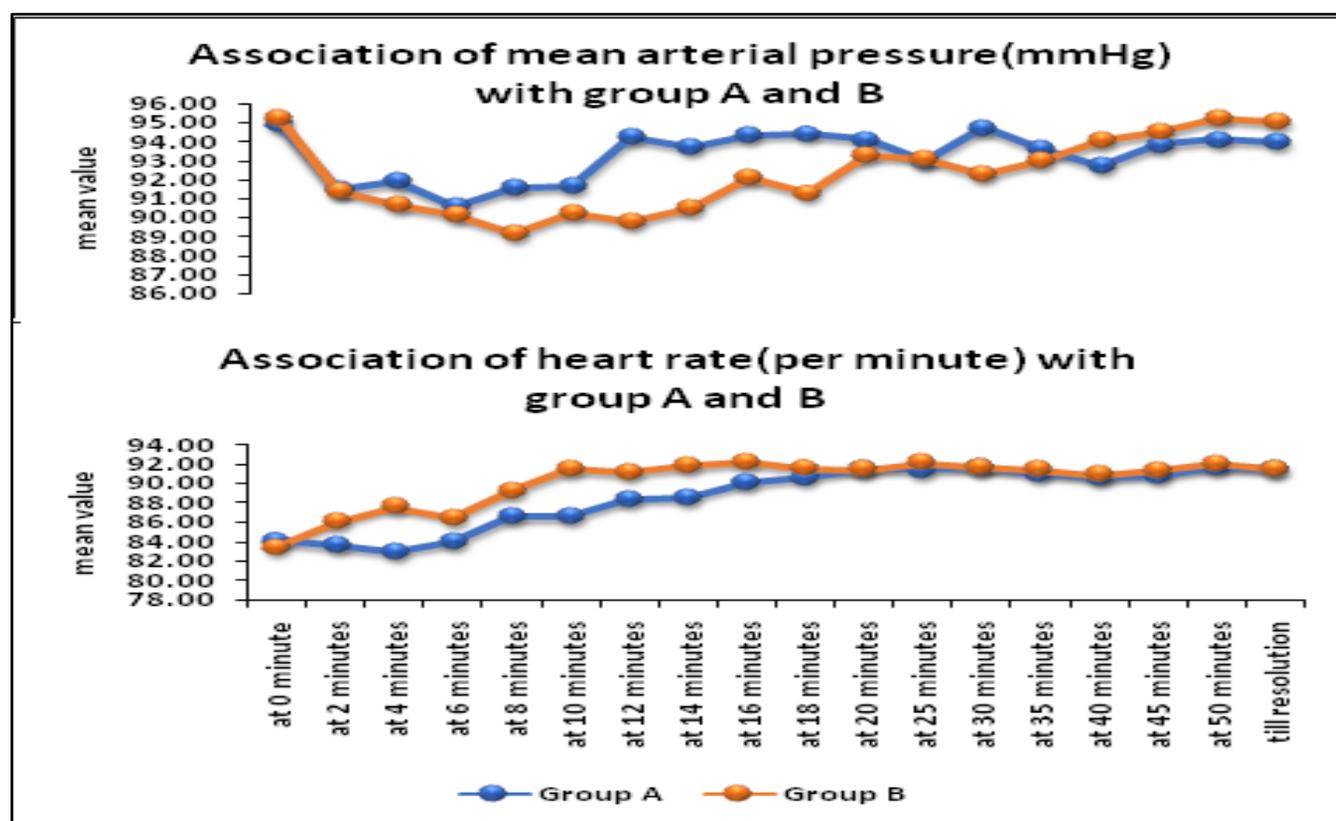


Fig. 2: Haemodynamic parameters in both the groups

DISCUSSION

Regional anaesthesia undoubtedly has more advantage in geriatric patients undergoing endoscopic urological surgery, but the quest to reduce the morbidity associated with spinal anaesthesia continues in such scenario. The main targets are controlling hemodynamic profile while optimizing the anaesthesia and analgesia during the above said period. In majority of the endoscopic surgery, T10 level of anaesthesia of 1-2 hrs. duration is required^[3]. Regional anaesthesia with single shot spinal block is the preferred choice due to ease, safety in giving the block and due to low cost involved. The incidence of hypotension and other side effects noted during these urological procedures are well documented and reported to be around 151%-412%.^[1,2] In routine practice 12.5 mg to 15 mg dose of plain heavy bupivacaine 0.5% is used for single shot spinal in such subset of patients.

The main approach to reduce the hypotension seen in perioperative period after spinal block is to reduce the dose of the local anaesthetics or add adjuvant without jeopardizing the baricity and physiological parameters of the drugs used. The reduction in baricity may change the distribution of the local anaesthetic mixture resulting in variable height of the spinal block achieved. The mean density (mean \pm SD gm/ml) of CSF is 1.0003 ± 0.0003 , of hyperbaric bupivacaine 0.5% is 1.02143 ± 0.00002 and of fentanyl is 0.99897 ± 0.00001 . Thus Fentanyl is the most commonly used adjuvant in anaesthesia practice is

hypobaric and there is decrease in baricity when it is added to the hyperbaric bupivacaine as an adjuvant. In literature the density (mean \pm SD gm/ml) for 7.5mg bupivacaine with 25 μ g fentanyl is 1.01513 ± 0.00053 [- 0.00630 change] and for 10 mg bupivacaine with 10 μ g fentanyl it is 1.0189 ± 0.00004 [-0.00099 change]. The reduction in density of around 0.0006 g/dL changes the distribution pattern of drug in spinal cord, so LA-A dose lower than 7.5 mg bupivacaine was not taken in the study^[4,5]. In literature there are studies which have used 3mg to 5 mg bupivacaine with fentanyl for day care surgery of around 40-50 min duration. The peak median sensory level reached was variable and was reported to be at L I(SI-T6) level, with reported incidence of use of analgesics intraoperatively and less to no motor block seen at such low doses.^[6,7] Hence in the study, we took 7.5 mg and 10 mg dose of heavy bupivacaine 0.5% with 25 μ g fentanyl to see the feasibility of these doses for safe and effective anaesthesia for endoscopic urological surgery.

The mean duration of surgery (TURP and TURBT) was 110-120 min and all surgeries were successfully completed with these doses of local anaesthetic and adjuvant. The duration is longer than reported by majority of the studies where only patients undergoing TURP were included. The study was done in a teaching hospital where urologist with different years of experience operated upon patients and majority of patients were undergoing TURBT surgery so this could have resulted in longer duration of surgery in the study. Similar results were observed by Desai D

et al.^[8] who took patients ≥ 65 years age undergoing femur surgery of around 2 hrs duration, sandal *et al.* and labbane *et al.*^[1,9] who concluded on feasibility of surgery at such dose though the duration of surgery in their studies was of 45 to 60 min only.

The onset of anaesthesia was statistically similar in both the groups and was 2.25 to 2.41 min in the study. Desai D *et al.*, Dalvi NP *et al.* and Shidhaye *et al.*^[8,10,11] reported less time of onset of anaesthesia of 0.9 min to 1.3 min as either the study was done on parturient or the onset was checked at L1 level which is earlier than T10 level taken in our study. Kotwani M *et al.* checked the onset every 5min hence could have reported longer time of onset of anaesthesia of 9.8 min in patients receiving 7.5mg bupivacaine with 25 μ gm fentanyl.^[12]

The height of anaesthesia required for such surgeries is generally at T10 level. we observed that. the maximum height of anaesthesia reached was T8 with 7.5 mg bupivacaine with fentanyl and at T6 with 10mg bupivacaine with fentanyl with 8% patients having T4 level of anaesthesia with this dose. Similar level of anaesthesia at T7 was observed by majority of researcher^[1,8,10] when they used lower concentration or volume of drug except by Verma V K *et al.*^[13] who observed T4 level in 92.5% patients with 7.5 mg and fentanyl dose, but they had taken patients undergoing LSCS hence could have achieved higher level of anaesthesia in their patients. The time of complete sensory regression to S2 level was significantly more with higher dose of local anaesthetic but was > 3 hrs with low dose also. Similar duration of sensory block of 3.46 hrs. to 4.5 hrs was observed by kuusniemi *et al.*^[7] and in a metaanalysis by Sirivanasandha *et al.*^[14] when they studied patients receiving 7.5 mg bupivacaine with fentanyl. Kotwani and Dalvi *et al.*^[12,10] though reported slightly less time of 2 hrs sensory block in their respective studies but the duration was assessed till the level of sensory block receded to L1 in their study as against S2 level studied in rest of the studies including ours.

The mean onset of motor block was earlier and duration of motor block was significantly prolonged in patients where 10 mg bupivacaine was used with adjuvant and it was over 4.69 hrs and around 4 hrs in 7.5 mg bupivacaine group. similar results were observed by various researchers like Bharathi *et al.*, Kuusniemi *et al.*, Dalvi *et al.* and labbane *et al.*^[15,7,10,9] albeit the time recorded due to variation in the end point of motor regression . few authors have taken end point of motor regression of Bromage <3) where as we took complete regression of motor blockade. (Bromage grade 1). Almost all studies have reported motor blockade of >1.5 hrs with the low dose anaesthetics. Thus the dose becomes suitable for most of the surgery of this much duration. The studies where 3-5 mg bupivacaine LA-A was used have reported less to no motor blockade.^[6,16,17]

The incidence of hypotension though was more in 10 mg group but was statistically insignificant (39% over 24% in low dose group). Majority of patients in low dose group required only single dose of. Vasopressor, over 13.3% requiring two doses in 10 mg group. Majority of researchers have reported incidence ranging from 0%-35% in low dose group and higher incidence of 41% in patients where higher dose of local anaesthetic use.^[1,2,9,12,13,18] The other side effects like pruritis, nausea and shivering were not observed in any of the patients unlike other studies where few side effects were reported with the use of opioid adjuvant.^[1,6,7,9,12,17]

Thus the study highlighted the adequacy of sensory and motor blockade of more than 2 hrs duration with lower incidence of hypotension and vasopressor use there by proving the efficacy of 7.5 mg bupivacaine with fentanyl for better patient outcomes. Hence the results can be extrapolated to other surgery of this duration in elderly (like inguinal surgery, fractures etc)

The limitation of the study was that the invasive MAP monitoring was not done and the baricity of the drug with adjuvant was not measured. The strength of the study was that all routinely performed endoscopic urological procedures were performed and the percentage decrease in MAP from baseline was also analysed in the study.

CONCLUSION

The use of 7.5mg bupivacaine with 25 μ gm fentanyl intrathecally results in adequate anaesthesia and analgesia coupled with stable hemodynamic as required for transurethral surgery of around 2 hrs. duration.

ABBREVIATIONS

TURP: Tran's urethral resection of prostate

TURBT: Trans urethral resection of bladder tumour

MAP: mean arterial pressure

ASA: American society of anaesthesiologist physical status classification

IV: Intravenous

μ g: Microgram

HR: Heart rate

Mg: milligram

CSF: Cerebral spinal fluid

LA-A: local anaesthetic adjuvant

BMI: Body mass Index

CONFLICT OF INTEREST

There are no conflicts of interest.

REFERENCES

1. Sendil MM, Krishna KS, Nanthaprabu M, Anandan H. Randomized Clinical Comparison of Three Different Doses of Bupivacaine with Fentanyl for TURP-Search for Optimal Dose to Be Used in Day 105 Care Urological Procedures. *Annals of International Medical Dental Research*. 2016; 2(5):10-14.
 2. Mung'ayi V, Mbaya K, Sharif T, Kanya D. A randomized controlled trial comparing haemodynamic stability in elderly patients undergoing spinal anaesthesia at L5, S1 versus spinal anaesthesia at L3, 4 at a tertiary African hospital. *African Health Science*. 2015;15(2):466-79
 3. Brull Richard, Macfarlane JR and Chan Vincent WS Spinal epidural and caudal anaesthesia. In *Millers anesthesia*. 9th edition. Philadelphia(PA):Churchill Livingstone Elsevier;2020:1423
 4. Imbelloni L.E., Moreira A.D., Gaspar F.C., Gouveia M.A., Cordeiro J.A. Assessment of the densities of local anesthetics and their combination with adjuvants: An experimental study. *Rev. Bras. Anesthesiol*. 2009;59:154–165. doi: 10.1590/S0034-70942009000200003.
 5. Jasinski T, Migon D, Sporysz K, Kamysz W, Owczuk R. The Density of Different Local Anesthetic Solutions, Opioid Adjuvants and Their Clinically Used Combinations: An Experimental Study. *Pharmaceuticals (Basel)*. 2021 Aug 16;14(8):801. doi: 10.3390/ph14080801. PMID: 34451898; PMCID: PMC8401070.
 6. Kim S Y, Cho J E, Hong J Y, Koo B N, Kim J M and Kil H K. Comparison of intrathecal fentanyl and sufentanil in low-dose dilute bupivacaine spinal anaesthesia for transurethral prostatectomy *Br J Anaesth* 2009; 103: 750–4
 7. Kuusniemi KS, Pihlajamaki KK, Pitkanen MT *et al.* The use of 101 bupivacaine & fentanyl for spinal anaesthesia for urologic surgery. *Anaesthesia Analgesia* 2000; 91: 1452-1456
 8. Desai D. Spinal anaesthesia with low dose bupivacaine and fentanyl for femur surgeries in elderly patients. *Journal of Anesthesia & Critical care*. 2019;11(2): 60-64
 9. Labbene I, Lamine K, Gharsallah H, Jebali A, Adhoum A, Ghozzi S, Ben Rais N, Ferjani M. Spinal anaesthesia for endoscopic urological surgery-- low dose versus varying doses of hyperbaric bupivacaine. *Middle East Journal of Anaesthesiology*. 2007 Jun; 19(2):369-73
 10. Dalvi NP, Patil N. Comparison of Effect of Intrathecal Fentanylbupivacaine and Tramadol-bupivacaine Combination on Postoperative Analgesia in Lower Abdominal Surgeries. *Research Innovations in Anesthesia* 2016;1(2):35-40
 11. Shidhaye RV, Shah BB, Joshi SS, etc. Comparison of clonidine and fentanyl as adjuvant to intrathecal bupivacaine for spinal anaesthesia 104 and postoperative analgesia in patients undergoing caesarean section. *Sri Lankan Journal of Anaesthesiology*. 2013; 22:15-20
 12. Kotwani, M., Rupwate, K., Shivananda, P., & Magar, J. (2016). Comparison between high dose hyperbaric Bupivacaine (12.5 mg) alone versus low dose hyperbaric Bupivacaine (7.5 mg) with Fentanyl (25 µg) in spinal anaesthesia for inguinal hernia surgery. *International Journal Of Clinical Trials*, 3(3), 140-146
 13. Verma V K, Navaria R, Naithani U, Goyal A, Das S A, Low dose spinal anaesthesia for caesarean section in parturients having 106 pregnancy induced hypertension: Effect on haemodynamic response and vasopressor requirement: A prospective randomized double blind case control study. *Indian Journal of Clinical Anaesthesia* 2020;7(1):104-111
 14. Sirivanasandha B, Lennox PH, Vaghadia H. Transurethral resection of the prostate (TURP) with low dose spinal anaesthesia in outpatients: a 5 year review. *Canadian Journal of Urology*. 2011 Jun;18(3):5705-9.
 15. Bharathi N, Nagaraj Rao. Spinal Anaesthesia with Small-Dose Bupivacaine and Fentanyl in Elderly Patients undergoing TURP: Adverse Events and Patient Satisfaction. *Journal of Clinical and Biomedical Sciences* 2016; 6(4):134-138
 16. Kwak K, S Lee, Jeon H *et al.* Comparison of Clinical Effect of Low Dose Bupivacaine Added with Fentanyl and Conventional Dose Bupivacaine in Spinal Anesthesia for a Transurethral Resection of the Prostate. *Korean Journal of Anesthesiology*. 2002;43(4):418- 423.
 17. Kararmaz, A., Kaya, S., Turhanoglu, S. and Ozyilmaz, M.A. Low-dose bupivacaine-fentanyl spinal anaesthesia for transurethral prostatectomy. *Anaesthesia* .2003; 58: 526-530
 18. Venkata HG, Pasupuleti S, Pabba UG, Porika S, Talar G. A randomised controlled prospective study comparing a low dose bupivacaine and fentanyl mixture to a conventional dose of hyperbaric bupivacaine for caesarean section. *Saudi Journal of Anaesthesia* 2015;9(2):122-7.
-