

## Incidence of hypotension between Intrathecal Hyperbaric Bupivacaine with and without Fentanyl in Geriatric Patients Undergoing Urological Surgeries

Thavat Chanchayanon, M.D.<sup>1</sup>, Mareeya Chearong, M.D.<sup>2</sup>, Piyaporn Vasinanukorn, M.D.<sup>1</sup>,  
Natsana Withayanuphakorn, B.S.<sup>1</sup>, Tidarat Sangkaew, B.S.<sup>1</sup>

<sup>1</sup>Department of Anesthesiology, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.

<sup>2</sup>Pattani Hospital, Mueang, Pattani 94000, Thailand.

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### Abstract:

**Objective:** We aimed to assess the efficacy, the incidence of hypotension and adverse consequences of using intrathecal hyperbaric bupivacaine in comparison to a combination of low dose hyperbaric bupivacaine and fentanyl, in geriatric patients undergoing urological surgeries.

**Material and Methods:** Our study was a prospective, triple-blinded and randomized controlled. One hundred and forty-eight geriatric participants scheduled for urological surgeries were randomly assigned into two groups: Group B (n=74) received intrathecal injection with 0.5% hyperbaric bupivacaine 1.5 milliliters (ml) alone (7.5 milligrams; mg), while Group F (n=74) received 0.5% hyperbaric bupivacaine 1 ml (5 mg) plus 0.5 ml of fentanyl (25 micrograms; mcg) making up to a total volume of 1.5 ml.

**Results:** One hundred and forty-eight patients were included however, six patients were excluded from statistical analysis, due to an inadequate level of anesthesia; hence, 142 patients were analyzed. The incidence of hypotension in group B was: 9.7%, and in group F the percentage was 12.9%, respectively (p-value=0.74). There was no significant difference in regards to the highest sensory level in both groups. The anesthesia level in group B was Thoracic level 11 (T10–T12), and in group F it was 11 (T10–T12) (p-value=0.68), while the analgesia level in group B was Thoracic level 7 (T6–T8) with group F being a Thoracic level 6 (T6–T8) (p-value=0.16). The occurrence of bradycardia, and respiratory depression did not differ between the 2 groups.

**Contact:** Assoc. Prof. Thavat Chanchayanon, M.D.  
Department of Anesthesiology, Faculty of Medicine, Prince of Songkla  
University, Hat Yai, Songkhla 90110, Thailand.  
E-mail: cardiacpsu@gmail.com

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**Conclusion:** Intrathecal administration of 5 mg of 0.5% hyperbaric bupivacaine, plus 25 mcg of fentanyl provided an adequate level of sensory blockade, but did not decrease the frequency of hypotension.

**Keywords:** geriatric, hyperbaric bupivacaine, hypotension, spinal anesthesia, urological surgeries

## Introduction

We commonly use spinal anesthesia as an anesthetic modality for geriatric urological patients scheduled for surgeries,<sup>1</sup> as it is thought that spinal anesthesia is able to maintain cerebral function.<sup>2</sup> Spinal anesthesia for urological surgeries offers rapid onset of action, relaxation of muscle as well as pain relief.<sup>3</sup> However, intraoperative hypotension is a frequent, and somewhat serious consequence within the geriatric population.<sup>4,5</sup>

As well as this, many of them have underlying medical conditions, thus it is quite crucial to reduce the level of spinal blockade in order to avoid cardiopulmonary adverse effects.<sup>6</sup> Utilization of low-dose bupivacaine is suggested, but it may not provide a sufficient block for surgery.<sup>7,8</sup>

Adding opioids, with local anesthetic, leads to a better quality of intraoperative analgesia.<sup>9</sup> It was shown that a combination of intrathecal opioids, and local anesthetic provides an analgesic effect in a synergistic way.<sup>10,11</sup>

Morphine is the first opioid used intrathecally, but comes with a wide variety of clinically relevant side-effects, especially respiratory depression. This has limited its utility.<sup>12</sup> Favorable pharmacokinetic and pharmacodynamics profiles of lipophilic opioids, for example; fentanyl, makes them better alternatives, because of a rapid uptake, faster onset and shorter duration of action. This minimizes the rostral spread of the lipophilic drugs to reach the respiratory center avoiding delayed respiratory depression.<sup>13</sup>

Adding fentanyl to low doses of local anesthetic increases the quality of the spinal blockage as well as

the duration of the sensory block.<sup>14,15</sup> Kuusniemi et al.<sup>16</sup> demonstrated that mixing 25 micrograms (mcg) of fentanyl to 5 mg of bupivacaine provided an effective level of anesthesia and motor block. Gupta et al.,<sup>17</sup> revealed that intrathecal administration with 7.5 milligrams (mg) of bupivacaine contributed to 13.3% of hypotension, whereas, a decreased dose of bupivacaine to 5 mg, in combination with fentanyl 25 mcg resulted in no event of hypotension.

We intended to assess the effects of giving 7.5 mg of bupivacaine intrathecally in comparison to 5 mg of bupivacaine, plus 25 mcg of fentanyl in elderly patients undergoing urological surgeries.

## Material and Methods

This trial was approved by the Ethics Committee of the Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand, on the 5<sup>th</sup> of September 2016 (EC 59-182-08-1). Its registered number is TCTR 2017012001.

### Participants

We included 148 American Society of Anesthesiologists Physical Status (ASA) classes II–III participants. Their age had to be at least 65 years old. All of them were scheduled for elective urological surgeries, under spinal anesthesia, between; October 2016 and July 2017.

We excluded those with abnormalities of the spine, skin infections on the targeted area, a known allergy to amide local anesthetics, abnormal bleeding tendency, did not want to proceed with spinal anesthesia, or had received inadequate anesthesia.

### Standard operating procedures

All participants gave written informed consent. Before performing spinal anesthesia, crystalloid 500 ml was given to each patient.

Patients were randomly assigned to either of the 2 groups (B or F) by using a randomized computer-generated sequence. The sequenced numbers were kept in a separate, opaque envelope.

Patients in group B (n=74) received intrathecal administration of 7.5 mg of 0.5% bupivacaine, while those in group F (n=74) received intrathecal injection of 5 mg of 0.5% bupivacaine, plus 25 mcg of fentanyl.

A 1.5 ml identical solution was prepared for all subjects. The syringes had no identity to indicate group allocation.

Spinal anesthesia was done by an attending anesthesiologist, who was blinded to the subject assignment. All spinal anesthesia was performed at L3–L4 level, using a 27G Quincke needle in either lateral decubitus or sitting position.

After the procedure, each patient was frequently measured for systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial blood pressure (MAP). All parameters were recorded every minute, for the first 15 minutes and then every 5 minutes until the surgery finished.

Levels of spinal block was examined by a pinprick test every 2 minutes, until the maximum and fixed level had been established. The highest levels of both anesthesia and analgesia were recorded. The levels of motor block were measured by using the Bromage score: 0=no motor blockage, 1=hip blocked, 2=hip and knee blocked, 3=hip, knee and foot blocked, consequently. Follow-up was carried out every 10 minutes during post-anesthesia care, until the patients were discharged.

### Outcome of the study

The incidence of hypotension was the primary outcome of this study.

Secondary endpoints were: levels of anesthesia, analgesia and motor blockade. Adverse events were also considered as secondary endpoints.

Hypotension was clarified as: SBP<20.0% of pre-operative value, or MAP<60 mmHg. Hypotension was managed using 6 mg of ephedrine or 10 mcg of norepinephrine, given intravenously.

Bradycardia was clarified as: a heart rate <45 beats/minute, with this being managed by intravenous administration of 0.6 mg of atropine.

Respiratory depression was clarified as: a respiratory rate<10 beats/minute or oxygen saturation<90.0%, with room air. All patients were given supplemental oxygen via face mask at 6 liters/minute.

If a patient had nausea or vomiting, ondansetron 0.1 mg/kg was given intravenously.

Any patient who complained of itching was given a single dose of 10 mg of chlorpheniramine intravenously.

### Sample size calculation

Based on previous research<sup>17</sup> a statistical power analysis was performed for sample size estimation. To detect a 13.0% difference in complication rates, with a significance level set to 0.05 and a power set to 0.8, 70 samples per group were required. Based on a drop-out rate of 10.0%, total sample size of 156 was needed (78 patients per each group).

### Statistical analysis

Continuous variables were shown as median and interquartile range (IQR) for non-normally distributed data, or mean and standard deviation (S.D.) for normally distributed data.

Categorical variables were demonstrated as frequency and percentage, whilst the comparison of continuous variables were acquired by using two-way analysis of Student's t-test. Categorical variables were compared by using Fisher's exact test, with any changes in SBP, DBP, and MAP being compared by using generalized estimating equation.

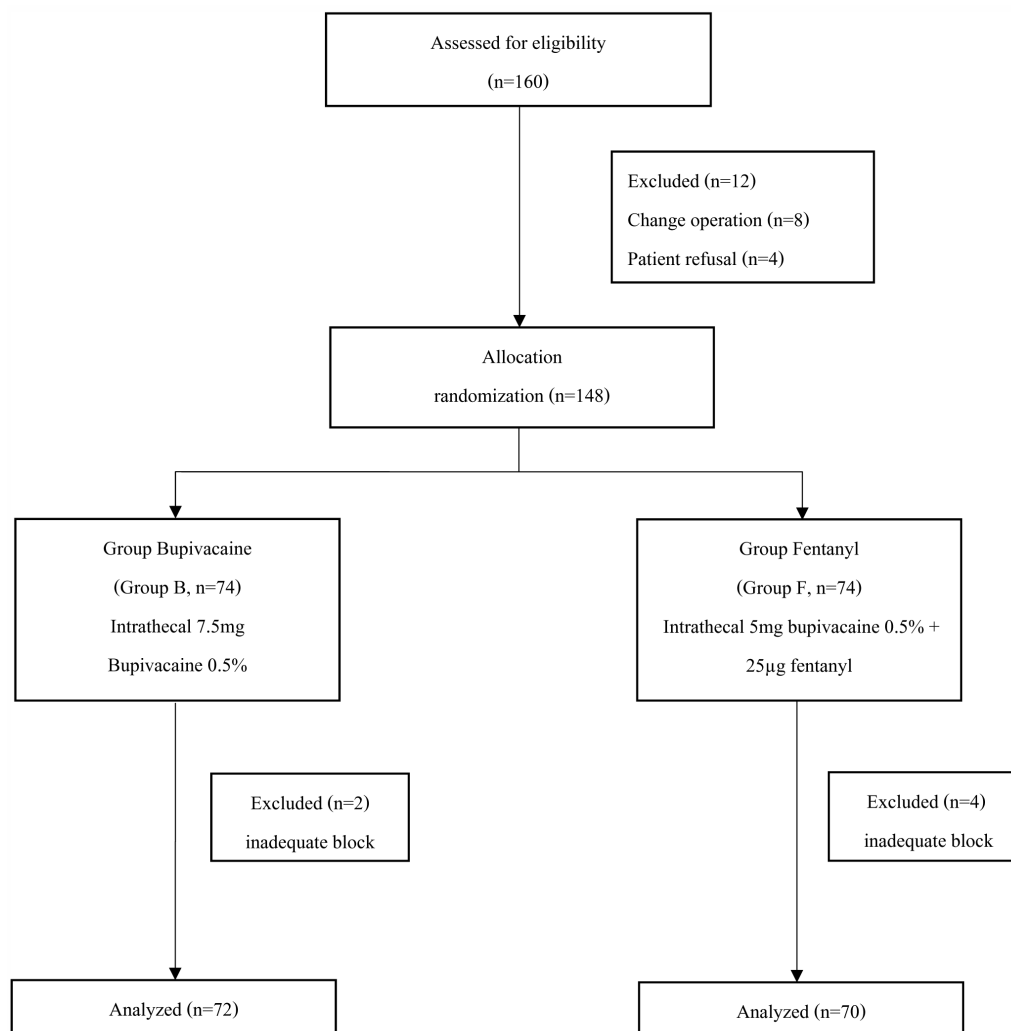
A p-value value of less than 0.05 was regarded as statistically significant. The per-protocol analysis was applied in this study.

## Results

Figure 1 revealed the details of the 148 patients included in this study. Patient characteristics are demonstrated in Table 1. There was no difference of demographic data between the 2 groups.

No difference in the incidence of hypotension (SBP, DBP and MAP) was found between the 2 groups (Table 2, Figure 2).

The incidences of unwanted consequences between the 2 groups are displayed in Table 3. No significant differences were demonstrated.



**Figure 1** Consort flow diagram

**Table 1** Demographic data and anesthesia related information

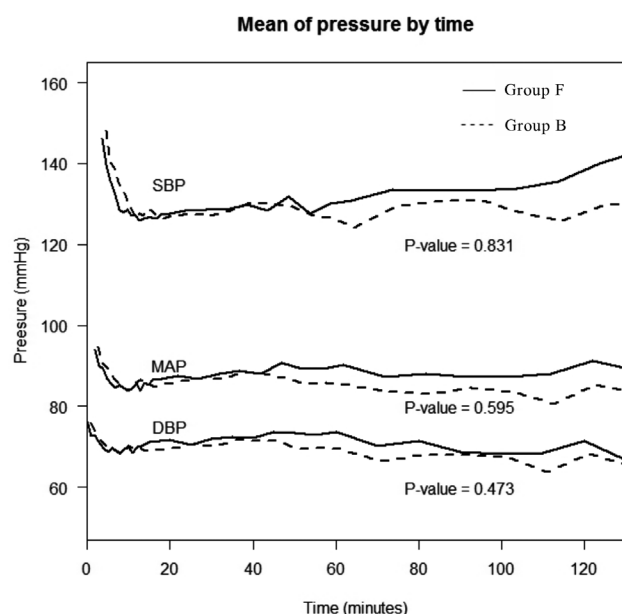
Parameter	Group B (n=72)	Group F (n=70)	P-value
Age (years), median (IQR)	71 (67, 79)	72 (67, 78)	0.79
Body mass index (kg/m <sup>2</sup> ), mean (S.D.)	24 (3.8)	25 (4)	0.11
ASA, number (%)			
II	53 (73.6)	55 (78.6)	0.66
III	19 (26.4)	15 (21.4)	
Number of spinal attempt (%)			
1 attempt	43 (59.7)	43 (61.4)	0.97
>1 attempt	29 (40.3)	27 (38.6)	
Position of patients during spinal block (%)			
Lateral decubitus	72 (100.0)	69 (98.6)	0.49
Sitting	0 (0.0)	1 (1.4)	
Adjustment of position of operating table (%)			
No adjustment	41 (56.9)	44 (62.9)	0.58
With adjustment	31 (43.1)	26 (37.1)	
Duration (mins), median (IQR)	40 (30, 55)	40 (30, 60)	0.55
Use of ephedrine (mg), median (IQR)	12 (8, 12)	6 (6, 11)	0.45
Use of norepinephrine (mcg), median (IQR)	20 (15, 25)	10 (10, 10)	1.00
Use of atropine (mg), median (IQR)	0 (0, 0)	0.6 (0.6, 0.6)	1.00
Estimate blood loss (ml), median (IQR)	50 (20, 158)	50 (10, 155)	0.41

IQR=interquartile range, S.D.=standard deviation, mg=milligram, ml=milliliter, ASA=American Society of Anesthesiologist classification, mcg=microgram

**Table 2** Incidence of hypotension, maximum levels of anesthesia and analgesia and level of motor blockade

Parameter	Group B (n=72)	Group F (n=70)	P-value
Incidence, n (%)	7 (9.7)	9 (12.9)	0.74
Maximum level of anesthesia, median (IQR)	11 (10, 12)	11 (10, 12)	0.68
Maximum level of analgesia, median (IQR)	7 (6, 8)	6 (6, 8)	0.16
Motor block by Bromage score, n (%)			
0=no motor block	5 (6.9)	5 (7.1)	0.98
1=hip blocked	3 (4.2)	4 (5.7)	
2=hip and knee blocked	5 (6.9)	5 (7.1)	
3=hip, knee and ankle blocked	59 (81.9)	56 (80.0)	

IQR=interquartile range



**Figure 2** Comparison of changes in systolic blood pressure, diastolic blood pressure and mean arterial blood pressure between the 2 groups.

**Table 3** Adverse events, data were shown in number

Parameter	Group B (n=72)	Group F (n=70)	P-value
	Number (%)	Number (%)	
Bradycardia	0 (0.0)	2 (2.9)	0.24
Respiratory depression	2 (2.8)	1 (1.4)	1.00
Nausea	2 (2.8)	6 (8.6)	0.16
Vomiting	2 (2.8)	4 (5.7)	0.44
Itching	1 (1.4)	2 (2.9)	0.62
Shivering	4 (5.6)	3 (4.3)	1.00

## Discussion

The 2 groups showed the same efficacy of spinal block by measuring and comparing the levels of anesthesia, analgesia and motor blockade. Our results are compatible with those from the study done by Gupta et al.<sup>17</sup>

The Gupta et al.<sup>17</sup> study found 13.0% of hypotension in group B. However, there was no hypotension found in Group F. This was different from our study, as hypotension was found in 12.9% of patients in group F. The dose of fentanyl 25 mcg, administered intrathecally, may be too high for Thai people. Additionally, the average age of patients in our study was 71 years old. Elderly patients may be more susceptible to sustained hypotension in comparison to younger patients, in so saying, Gupta et al.'s<sup>17</sup> patients' age were 62.9 years of age on average.

Gupta et al.<sup>17</sup> found that group B had 3.3% of bradycardia. Group F had 3.3% of pruritus. No respiratory depression was found in both groups. Again, this result was different from our study, which found more side effects in group F than group B, however this was not statistically significance. Bradycardia was not evident in group B, but 2.9% of patients in group F had this finding. Group F had half the incidence of respiratory depression in comparison to group B.

This study demonstrated that spinal anesthesia, with a low dose of 0.5% bupivacaine (1 ml) in combination with 25 mcg of fentanyl provided adequate anesthesia, which was similar to using 0.5% bupivacaine (1.5 ml) alone in geriatric patients undergoing urological surgeries.

There were no significant differences in the occurrence of: bradycardia, respiratory depression, shivering, vomiting, nausea or itching between the 2 groups.

## Strengths and limitations

Our study was triple-blinded, with no bias of assessment.

We suggest to compare different doses of 0.5% hyperbaric bupivacaine (5, 7.5 and 10 mg), with and without fentanyl. Furthermore, we suggest further studies aiming to reduce the dose of intrathecal fentanyl (for example: 20

mcg), as this may be beneficial in terms of adverse event reduction.

One weakness of our study was the uncertainty and variety of anesthesiologists performing spinal anesthesia, which might have had an effect on the level of anesthesia and incidence of hypotension.

## Conclusion

Intrathecal bupivacaine 5 mg in combination with fentanyl 25 mcg gives adequate anesthesia for geriatrics patients undergoing urological surgeries, when compared to a usual dose of bupivacaine (7.5 mg). The overall incidence of adverse events did not differ in both groups.

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