

Effects of Varying Baricity of Bupivacaine on its Sequential Administration in Spinal Anesthesia

Kazi Rafsan*^{ORCID}, Shyama Prosad Mitra^{ORCID}, Lutful Aziz^{ORCID}

Department of Anesthesia & Pain Medicine, Evercare Hospital, Dhaka, Bangladesh.

*Address for correspondence: Dr. Kazi Rafsan, Department of Anesthesia & Pain Medicine, Evercare Hospital, Dhaka, Bangladesh. E-mail: kzrafsan@gmail.com

Abstract

Background: Baricity, defined as the density of a local anesthetic relative to cerebrospinal fluid (CSF), plays a crucial role in determining intrathecal drug spread and block characteristics. Bupivacaine, commonly used in spinal anesthesia, is available in hyperbaric and isobaric formulations. Although their individual effects are well studied, the impact of sequential administration of hyperbaric and isobaric bupivacaine remains unclear.

Aim of the Study: The study aimed to compare the clinical efficacy of sequential administration of hyperbaric and isobaric bupivacaine in spinal anesthesia.

Methods: This prospective randomized observational trial was conducted in the Department of Anesthesia and Pain Medicine, Evercare Hospital Dhaka, Bangladesh, over a one-year study period from January 2024 to December 2024. A total of 120 ASA I-II patients scheduled for surgery below umbilicus were divided into four groups ($n = 30$ each). Group H received 3 ml of 0.5% hyperbaric bupivacaine, Group I received 3 ml of isobaric bupivacaine, Group H+I received 1.5 ml hyperbaric followed by 1.5 ml isobaric, and Group I+H received the reverse sequence. Spinal anesthesia was performed at L4-5 with a 25-G Quincke needle in the sitting position. Outcomes included sensory and motor block characteristics, hemodynamic changes, analgesia duration, and complications.

Results: Baseline hemodynamics were comparable. Heart rate reduction at 30 minutes post-spinal block was significant ($P = 0.043$), with the greatest decline in Group I+H. Systolic and diastolic pressures decreased consistently across groups without significant differences. Sensory and motor onset times were similar, although Group H+I showed the fastest sensory onset (1.4 ± 0.75 min). Block duration varied significantly: Group I+H had the longest sensory (194.1 ± 27.8 min) and motor block (178.4 ± 24.3 min), while Group H had the shortest.

Conclusion: Ephedrine use and hypotension were lower in the combined groups, though differences were not statistically significant. Other adverse events were infrequent and evenly distributed. Sequential hyperbaric-isobaric administration enhances block duration with stable hemodynamics. The I+H sequence provided the longest anesthesia, while H+I offered the most rapid onset, suggesting combination strategies may optimize spinal anesthesia for surgery below umbilicus.

Keywords: Baricity, bupivacaine, spinal anesthesia, hyperbaric, isobaric, hemodynamics

Introduction

Spinal anesthesia (SA), delivered as a subarachnoid block (SAB), remains a cornerstone technique for infraumbilical surgery because it

is efficient, inexpensive, and provides reliable surgical anesthesia with rapid onset and good muscle relaxation, advantages that are particularly important in high-throughput operating theatres and in resource-constrained systems common

across South Asia, including Bangladesh.^[1,2] Yet, SAB is also physiologically “unforgiving”, sympathetic blockade can produce clinically relevant hypotension, bradycardia, nausea, and reduced organ perfusion, with reported hypotension rates varying widely depending on population risk, block height, dose, and definitions.^[1,3] Large reviews and mechanistic work continue to highlight that preventing hemodynamic instability after SAB is a persistent global priority because it directly affects intraoperative safety, vasopressor exposure, and recovery trajectories.^[3] Bupivacaine is among the most frequently used intrathecal local anesthetics worldwide, and its baricity, whether hyperbaric (typically dextrose containing) or isobaric (plain), is a key determinant of intrathecal spread, dermatomal level, and the extent of sympathetic blockade.^[1,4] Contemporary evidence shows ongoing uncertainty around “best” bupivacaine formulation across diverse adult surgical populations, with systematic reviews and randomized studies reporting broadly comparable anesthesia success but clinically meaningful differences in spread characteristics, sensory and motor block duration, and vasopressor needs in specific contexts.^[5-7] Predicting block height remains imperfect, even in large datasets, reinforcing the need for protocolized approaches that can improve consistency and safety across routine cases.^[8] A pragmatic strategy that has reemerged is manipulating baricity through combined or sequential intrathecal administration, aiming to achieve adequate surgical anesthesia while reducing abrupt sympathectomy and hypotension. Recent randomized work in lower abdominal surgery suggests that mixing hyperbaric with isobaric bupivacaine can improve hemodynamic stability, while also altering sensory and motor block duration, a tradeoff that may be clinically relevant for short to moderate duration infraumbilical procedures.^[1] Similarly, sequential injection approaches have been evaluated in high-risk surgical populations, including orthogeriatric lower limb surgery, with a focus on reducing hypotension and vasopressor exposure.^[9] However, most available evidence

is context-specific, often obstetric or elderly-focused, and generalizability to routine adult infraumbilical surgery in South Asian tertiary hospitals is uncertain, especially where patient profiles, perioperative pathways, and case mix differ from high-income settings.^[2,4,10] Against this backdrop, local evidence is needed to clarify whether varying bupivacaine baricity and its sequential administration meaningfully improve hemodynamic stability and block performance in everyday elective infraumbilical surgery. Therefore, this study aims to compare the effects of different baricity strategies, including sequential hyperbaric and isobaric bupivacaine administration, on heart rate and blood pressure profiles, onset and duration of sensory and motor block, vasopressor requirements, and intraoperative adverse events among ASA I–II adults undergoing elective surgery below the umbilicus.

Methods

This prospective, randomized, controlled clinical study was conducted over a 12-month period, from January 2024 to December 2024, in the operating theatres under the supervision of the Department of Anesthesia and Pain Medicine, Evercare Hospital, Dhaka, Bangladesh. A total of 120 adult patients were enrolled and allocated into four equal groups of 30 patients each according to the baricity and sequence of intrathecal bupivacaine administration. Randomization was performed using a computer-generated random sequence, and group allocation was concealed in sealed opaque envelopes opened immediately prior to spinal anesthesia.

- **Group H (Hyperbaric group, $n = 30$):** Received spinal anesthesia using hyperbaric bupivacaine only, administered intrathecally as the sole local anesthetic formulation.
- **Group I (Isobaric group, $n = 30$):** Received spinal anesthesia using isobaric bupivacaine only, administered intrathecally as the sole formulation.

- **Group H+I (Sequential hyperbaric then isobaric, $n = 30$):** Received spinal anesthesia by sequential intrathecal administration, with hyperbaric bupivacaine first, followed by isobaric bupivacaine.
- **Group I+H (Sequential isobaric then hyperbaric, $n = 30$):** Received spinal anesthesia by sequential intrathecal administration, with isobaric bupivacaine first, followed by hyperbaric bupivacaine.

Adult patients aged 18 to 60 years, of either sex, classified as American Society of Anesthesiologists (ASA) physical status I or II, and scheduled for elective surgery below the level of the umbilicus with an expected duration of ≤ 120 minutes were included after obtaining written informed consent. Patients were excluded if they had ASA physical status $\geq III$, coagulopathy or were receiving anticoagulant therapy, local or systemic infection, untreated hypovolemia, severe cardiomyopathy, renal failure requiring hemodialysis, bronchial asthma, peripheral neuropathy, autonomic dysfunction, prior lumbar spine surgery or vertebral deformity, increased intra-abdominal girth, pregnancy, or known allergy to local anesthetic agents.

Baseline demographic variables included age, sex, and ASA classification. Intraoperative hemodynamic variables monitored were systolic blood pressure, diastolic blood pressure, heart rate, and peripheral oxygen saturation. Measurements were recorded at baseline and at predefined intervals following subarachnoid block. Primary outcome variables included onset time of sensory block, onset time of motor block, duration of sensory block, and duration of motor block. Secondary outcomes included time to achieve maximum sensory level, intraoperative vasopressor requirement, particularly ephedrine, and incidence of adverse events such as hypotension, bradycardia, tachycardia, shivering, and nausea or vomiting. Hypotension and bradycardia were defined according to standard institutional criteria and managed as per protocol.

All data were recorded prospectively on structured case record forms. Data were entered and analyzed using SPSS version 26. Continuous variables were expressed as mean \pm standard deviation after assessment of normality. Categorical variables were presented as frequencies and percentages. Intergroup comparisons of continuous variables were performed using one way analysis of variance, and post hoc testing was applied where appropriate. Categorical variables were analyzed using the Chi square test or Fisher's exact test as applicable. A P value of <0.05 was considered statistically significant.

Ethical approval was obtained from the institutional review committee before commencement of the study. All participants received detailed information regarding the purpose, procedures, potential risks, and benefits of the study in understandable language. Written informed consent was obtained from each patient prior to enrollment, and confidentiality of patient data was strictly maintained throughout the study.

Results

Across all patients, mean age was 37.23 ± 14.28 years (range 15–74), and the four groups had comparable ages, 34.63 ± 9.83 in Group H vs 39.47 ± 17.24 in Group I, H+I, and I+H, with no significant difference ($P = 0.131$). Males predominated overall (72/120, 60%) vs females (48/120, 40%), and sex distribution was similar across groups (male counts: 20, 13, 20, 19), not significant ($P = 0.193$). ASA status was also comparable: Class I 80/120 (66.7%) vs Class II 40/120 (33.3%), with no between-group difference ($P = 0.44$) [Table 1].

Baseline HR was similar across groups, roughly 82–91 bpm (Group H 88.4 ± 16.3 , Group I 91.4 ± 14.2 , H+I 89.6 ± 15.8 , I+H 81.9 ± 17.4), and HR gradually decreased over 30 minutes in all groups. By 30 minutes, HR was lowest in I+H (68.8 ± 14.5) and H+I (70.6 ± 14.5) compared

with *H* (77.3 ± 14.5) and *I* (76.9 ± 13.6), and this was the only timepoint reaching statistical significance ($P = 0.043$); earlier timepoints were not significant [Table 2].

Baseline SBP was broadly comparable (about 132–139 mmHg), highest in H+I (139.3 ± 9.7). SBP fell at 2–10 minutes post-SAB in all groups, then stabilized around 107–111 mmHg by 25–30 minutes. None of the SBP comparisons were statistically significant at any timepoint, although 10 minutes was borderline ($P = 0.051$) [Table 3].

Baseline DBP was essentially identical across groups (about 81–82 mmHg, $P = 0.976$). DBP

decreased after SAB to the mid-60s to low-70s across timepoints, with similar patterns in all groups. There were no significant between-group differences at any timepoint (all P -values >0.05) [Table 4].

Onset times were similar across groups: sensory onset ranged from 1.4 ± 0.75 min (H+I) to 2.1 ± 1.3 min (I), not significant ($P = 0.125$), and motor onset ranged from 2.9 ± 1.5 min (H+I) to 3.5 ± 2.2 min (H), also not significant ($P = 0.632$). In contrast, block durations differed clearly: sensory duration increased from 163.2 ± 36.0 min (H) to 194.1 ± 27.8 min (I+H), showing a significant difference ($P = 0.003$). Motor duration showed

Table 1: Demographic characteristics of patients

Variables	All (<i>n</i> = 120)	Group H (<i>n</i> = 30)	Group I (<i>n</i> = 30)	Group H+I (<i>n</i> = 30)	Group I+H (<i>n</i> = 30)	<i>P</i> -value
	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	
Age						
Mean \pm SD	37.23 ± 14.28	34.63 ± 9.83	39.47 ± 17.24	39.47 ± 17.24	39.47 ± 17.24	0.131
Range	15–74	17–63	17–64	16–74	16–74	
Gender						
Male	72	20	13	20	19	0.193
Female	48	10	17	10	11	0.199
ASA classification						
Class I	80	23	17	20	20	0.44
Class II	40	7	13	10	10	0.435

Table 2: Comparison of mean heart rate (HR) among all groups

Parameters	Group H (<i>n</i> = 30)	Group I (<i>n</i> = 30)	Group H+I (<i>n</i> = 30)	Group I+H (<i>n</i> = 30)	<i>P</i> -value
	Mean \pm SD				
Baseline	88.4 ± 16.3	91.4 ± 14.2	89.6 ± 15.8	81.9 ± 17.4	0.115
2 minutes after SAB	88.2 ± 16.1	90.2 ± 15.0	87.7 ± 15.2	81.8 ± 16.6	0.197
5 minutes after SAB	87.1 ± 14.7	87.6 ± 16.6	82.1 ± 14.3	78.7 ± 15.5	0.101
10 minutes after SAB	83.7 ± 14.7	85.7 ± 16.7	78.7 ± 15.0	76.2 ± 15.4	0.079
15 minutes after SAB	81.6 ± 14.3	82.1 ± 14.0	76.7 ± 15.6	74.1 ± 14.4	0.069
20 minutes after SAB	80.2 ± 15.8	79.7 ± 12.8	74.3 ± 15.0	72.6 ± 14.2	0.108
25 minutes after SAB	77.8 ± 14.8	78.5 ± 13.0	71.2 ± 14.5	71.3 ± 13.8	0.072
30 minutes after SAB	77.3 ± 14.5	76.9 ± 13.6	70.6 ± 14.5	68.8 ± 14.5	0.043

Table 3: Comparison of systolic blood pressure (SBP) among all groups

Parameters	Group H (n = 30)	Group I (n = 30)	Group H+I (n = 30)	Group I+H (n = 30)	P-value
	Mean ± SD				
Baseline	132.5 ± 9.5	135.8 ± 15.7	139.3 ± 9.7	132.3 ± 11.8	0.087
2 minutes after SAB	115.3 ± 19.6	123.1 ± 18.1	126.7 ± 14.0	119.4 ± 16.8	0.068
5 minutes after SAB	111.0 ± 16.3	108.8 ± 19.8	116.7 ± 16.6	115.1 ± 16.1	0.268
10 minutes after SAB	105.4 ± 15.1	102.7 ± 16.0	112.5 ± 13.8	110.6 ± 15.8	0.051
15 minutes after SAB	105.7 ± 13.2	104.6 ± 14.0	108.0 ± 12.5	109.3 ± 11.8	0.479
20 minutes after SAB	109.7 ± 11.0	105.5 ± 15.3	106.8 ± 11.7	109.8 ± 10.8	0.542
25 minutes after SAB	110.9 ± 11.2	106.3 ± 14.7	106.8 ± 9.0	108.3 ± 8.8	0.372
30 minutes after SAB	110.8 ± 11.3	111.0 ± 13.3	108.3 ± 9.6	107.5 ± 9.1	0.512

Table 4: Comparison of diastolic blood pressure (DBP) among all groups

Parameters	Group H (n = 30)	Group I (n = 30)	Group H+I (n = 30)	Group I+H (n = 30)	P-value
	Mean ± SD				
Baseline	81.0 ± 7.1	81.5 ± 8.6	81.8 ± 8.9	81.9 ± 8.4	0.976
2 minutes after SAB	70.0 ± 14.4	74.1 ± 10.3	74.2 ± 11.2	72.3 ± 11.1	0.458
5 minutes after SAB	68.4 ± 11.1	66.4 ± 11.0	69.1 ± 10.6	68.5 ± 9.4	0.766
10 minutes after SAB	64.6 ± 9.3	62.2 ± 10.0	67.3 ± 8.5	65.7 ± 8.1	0.17
15 minutes after SAB	63.6 ± 9.2	62.3 ± 8.7	63.1 ± 8.7	64.6 ± 8.7	0.796
20 minutes after SAB	65.4 ± 9.7	62.8 ± 10.3	61.5 ± 7.0	63.8 ± 6.9	0.372
25 minutes after SAB	65.6 ± 8.5	62.6 ± 10.4	61.8 ± 6.2	62.0 ± 5.8	0.224
30 minutes after SAB	65.3 ± 10.5	65.2 ± 10.3	64.9 ± 10.2	61.6 ± 5.9	0.377

the same pattern, from 153.7 ± 32.6 min (H) up to 178.4 ± 24.3 min (I+H), also significant ($P = 0.001$) [Table 5].

The proportion requiring ephedrine was highest in Group H (14/30, 46.6%) and Group I (12/30, 40.0%), and lower in the sequential groups, H+I (7/30, 23.3%) and I+H (6/30, 20.0%). Mean dose among those requiring it ranged from 8.5 ± 2.4 (H+I) to 12.1 ± 7.8 (I). Overall, differences were not statistically significant ($P = 0.474$) [Table 6].

Hypotension was the most common event, again higher in single-technique groups, H 46.6% and I 40.0%, versus sequential groups H+I 23.3% and I+H 20.0%, but this difference was not significant ($P = 0.739$). Other events were

infrequent: bradycardia 3.3–6.6%, tachycardia only in Group H (6.6%), shivering 0–6.6%, and nausea/vomiting only in Group H (3.3%) [Table 7].

Discussion

Spinal anesthesia (SA) performance is shaped by technical factors, with local anesthetic baricity being one of the most important because it determines intrathecal distribution, spread, and regression of sensory and motor block in CSF.^[4,11] This study evaluated whether hyperbaric bupivacaine, isobaric bupivacaine, and sequential combinations of the two-influence block quality, hemodynamics, and adverse events during lower abdominal surgery, using a

Table 5: Distribution of patients according to onset of block and duration of block among all groups

Parameters	Group H (n = 30)	Group I (n = 30)	Group H+I (n = 30)	Group I+H (n = 30)	P-value
	Mean ± SD				
Onset of sensory block (minutes)	1.8 ± 1.1	2.1 ± 1.3	1.4 ± 0.75	1.9 ± 1.3	0.125
Duration of sensory block (minutes)	163.2 ± 36.0	180.5 ± 40.3	189.5 ± 28.2	194.1 ± 27.8	0.003
Onset of motor block (minutes)	3.5 ± 2.2	3.4 ± 2.0	2.9 ± 1.5	3.1 ± 2.0	0.632
Duration of motor block (minutes)	153.7 ± 32.6	173.8 ± 22.0	174.6 ± 22.8	178.4 ± 24.3	0.001

Table 6: Comparison of ephedrine requirement during intraoperative period

Group	n (%)	Mean ± SD	P-value
Group H (n = 30)	14 (46.6%)	10.0 ± 3.8	0.474
Group I (n = 30)	12 (40.0%)	12.1 ± 7.8	
Group (H+I) (n = 30)	7 (23.3%)	8.5 ± 2.4	
Group (I+H) (n = 30)	6 (20.0%)	9.2 ± 2.0	

Table 7: Comparison of adverse events during intraoperative period

Events	Group H (n = 30)	Group I (n = 30)	Group H+I (n = 30)	Group I+H (n = 30)	P-value
	n (%)	n (%)	n (%)	n (%)	
Hypotension	14 (46.6%)	12 (40.0%)	7 (23.3%)	6 (20.0%)	0.739
Bradycardia	1 (3.3%)	1 (3.3%)	1 (3.3%)	2 (6.6%)	
Tachycardia	2 (6.6%)	0	0	0	
Shivering	2 (6.6%)	0	2 (6.6%)	2 (6.6%)	
Nausea & vomiting	1 (3.3%)	0	0	0	

standardized intrathecal dose of 3 ml (15 mg) 0.5% bupivacaine across all groups.

Baseline characteristics were comparable among the four groups, including age, sex distribution, and ASA status ($P > 0.05$), supporting valid intergroup comparison. Similar demographic equivalence has been reported by Javed et al. and by Punshi and Afshan in studies comparing baricity-based spinal regimens.^[12,13]

Overall intraoperative hemodynamics were stable. Heart rate trends were similar initially ($P = 0.115$), although a statistically significant reduction at 30 minutes in the I+H group ($P = 0.043$) may reflect

an additive effect of sequential dosing. SpO₂ remained consistently high (98–100%) across time points, and systolic and diastolic blood pressures showed the expected post-SAB reductions without clinically meaningful intergroup separation. These findings align with Atashkhouei et al., who reported no significant differences in heart rate, blood pressure indices, or oxygen saturation between hyperbaric and isobaric bupivacaine regimens.^[4] In contrast, Solakovic observed greater decreases in systolic, mean, and diastolic blood pressure and pulse rate with hyperbaric solutions,^[14] and Hassan et al. (2024) similarly found more pronounced reductions in heart rate and mean arterial pressure with hyperbaric

bupivacaine compared with a hyperbaric–isobaric mixture.^[1] Taken together, prior evidence suggests hyperbaric solutions may exert stronger hemodynamic effects, while mixed or sequential strategies may blunt these changes, consistent with the stability observed here.

Vasopressor requirement showed numerical, but not statistical, differences. Ephedrine use was highest in the hyperbaric group (46.6%, 10.0 ± 3.8 mg) and also common in the isobaric group (40.0%, 12.1 ± 7.8 mg), whereas both combination groups had lower proportions and smaller mean doses (H+I: 23.3%, 8.5 ± 2.4 mg; I+H: 20.0%, 9.2 ± 2.0 mg; $P = 0.474$). This trend suggests potential clinical benefit of sequential approaches in reducing vasopressor exposure, although larger samples may be required to confirm significance. Prior studies remain mixed: Atashkhoei et al. reported higher vasopressor use with hyperbaric bupivacaine,^[4] while Yurtlu et al. and Javed et al. found no meaningful differences across hyperbaric, isobaric, and mixed regimens.^[12,15]

Block characteristics differed mainly in duration rather than onset. Sensory and motor onset times were comparable ($P > 0.05$), but sensory and motor block durations varied significantly (sensory $P = 0.003$; motor $P = 0.001$). The I+H sequence produced the longest sensory and motor durations, whereas the hyperbaric-only group showed the shortest, implying that delivering isobaric followed by hyperbaric may prolong anesthesia without delaying onset. This pattern is broadly consistent with published observations that hyperbaric solutions can provide faster, more predictable cephalad spread but may regress sooner, while isobaric solutions may yield longer-lasting anesthesia with more variable spread.^[6,15,16]

Adverse events were infrequent and broadly similar across groups. Hypotension was the most common event, occurring more often in the single-agent groups than in the combination groups, though without statistical significance ($P = 0.517$). Bradycardia, tachycardia, shivering, and nausea were rare. Comparable complication

profiles and lower hypotension rates with isobaric or mixed regimens have been described by Hassan et al. and Helmi et al.^[1,17], whereas Upadya et al. reported higher bradycardia, hypotension, and shivering with hyperbaric solutions.^[7] Yurtlu et al. similarly noted no major differences in adverse events between hyperbaric, isobaric, and mixed bupivacaine groups.^[18] Overall, all regimens appeared safe, with combination techniques showing favorable, although non-significant, trends toward reduced hypotension and vasopressor use, alongside a potentially longer block duration when isobaric was followed by hyperbaric.

Limitation of the Study

Limitations included a small sample size, single-center design, and prolonged operative times typical of a teaching hospital, which may have influenced block density and hemodynamic responses.

Conclusion

This study concludes hyperbaric, isobaric, and sequential hyperbaric–isobaric bupivacaine regimens provided effective spinal anesthesia with overall stable hemodynamics and low adverse-event rates. Although onset times were similar across groups, the isobaric followed by hyperbaric sequence (I+H) produced the longest sensory and motor block durations, with combination regimens showing a trend toward lower hypotension and reduced vasopressor requirement compared with single-agent techniques.

Recommendation

These results highlight the potential of combination strategies to optimize spinal anesthesia for lower abdominal surgeries by enhancing block duration while preserving hemodynamic stability. Future studies should focus on high-risk

populations such as elderly, obstetric, and comorbid patients to assess the safety benefits of baricity-specific regimens, and larger multicenter trials are recommended to confirm the hemodynamic advantages and extended block duration associated with combined hyperbaric-isobaric techniques.

Consent

Informed consent was obtained from all participants prior to enrolment in the study.

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