



Original Research Article

LOW-DOSE SPINAL ANESTHESIA WITH ADJUVANTS VS STANDARD DOSE SPINAL ANESTHESIA FOR DAY-CARE SURGERIES

Brijesh GC¹, Achyutha J², Sruthi Reddy MK³

¹Professor, Sri Siddhartha Medical College and Research Centre, B.H. Road, Agalkote, Tumkur, Karnataka, India.

²Consultant Anaesthesiologist, Motherhood Hospital, Ambalipura, Sarjapur Road, Bengaluru, Karnataka, India.

³Consultant, Apollo cradle maternity and children's hospital, AECS layout, Brooke field, ITPL main road, Bengaluru, Karnataka, India.

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Corresponding Author:

Dr. Brijesh GC,
Professor, Sri Siddhartha Medical
College and Research Centre, B.H.
Road, Agalkote, Tumkur, Karnataka,
India.
Email: brijudoc@gmail.com

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ABSTRACT

Background: Day-care surgeries require anesthetic techniques that facilitate rapid recovery, early ambulation, and timely discharge. Although standard-dose spinal anesthesia provides reliable surgical conditions, it may prolong motor blockade and delay discharge. Low-dose spinal anesthesia combined with intrathecal opioid adjuvants has been proposed to maintain adequate anesthesia while enhancing recovery. This study compared low-dose hyperbaric bupivacaine with fentanyl versus standard-dose hyperbaric bupivacaine in patients undergoing infra-umbilical day-care surgeries.

Materials and Methods: This prospective randomized single-center study was conducted from 1 December 2024 to 30 November 2025. Ninety adult patients (ASA I–II) scheduled for elective infra-umbilical day-care surgeries were randomized into two groups (45 each). Group A received 7.5 mg of 0.5% hyperbaric bupivacaine with fentanyl 25 µg, while Group B received 12.5 mg of 0.5% hyperbaric bupivacaine. The primary outcome was time to discharge readiness (modified PADSS ≥ 9). Secondary outcomes included sensory block characteristics, motor recovery, ambulation time, duration of postoperative analgesia, hemodynamic changes, adverse effects, and satisfaction scores. Statistical analysis was performed using independent t-test and Chi-square test, with $p < 0.05$ considered significant.

Results: Eighty-eight patients were analyzed (44 per group). Demographic characteristics were comparable ($p > 0.05$). Time to discharge readiness was significantly shorter in Group A (182.4 ± 28.6 minutes) compared to Group B (261.7 ± 36.9 minutes, $p < 0.001$). Motor recovery and ambulation were significantly faster in Group A ($p < 0.001$). Hypotension and urinary retention were significantly lower in Group A ($p = 0.03$ and $p = 0.02$, respectively). Pruritus was more frequent in Group A but mild. Surgical adequacy and satisfaction were comparable.

Conclusion:

Low-dose spinal anesthesia with intrathecal fentanyl provides effective anesthesia with faster recovery and improved hemodynamic stability, making it suitable for ambulatory infra-umbilical procedures.

Keywords: Low-dose spinal anesthesia; fentanyl; ambulatory surgery; discharge readiness; bupivacaine; day-care surgery.

INTRODUCTION

The growing demand for ambulatory and day-care surgeries has significantly influenced anesthetic practice.^[1,2] An ideal anesthetic technique for day-care procedures should provide rapid onset, adequate

surgical anesthesia, minimal hemodynamic disturbance, early ambulation, effective postoperative analgesia, and timely discharge.^[2,3] Spinal anesthesia remains one of the most commonly employed techniques for infra-umbilical surgeries because of its reliability, simplicity, cost-

effectiveness, and favorable patient acceptance.^[3,4] However, the use of conventional or standard doses of intrathecal local anesthetics may prolong motor blockade, delay ambulation, increase urinary retention, and contribute to hypotension, thereby delaying discharge in ambulatory settings.^[4,5]

Reducing the dose of intrathecal local anesthetic has been proposed as a strategy to shorten motor blockade and enhance recovery.^[6] Nevertheless, low-dose spinal anesthesia alone may risk inadequate sensory block, intraoperative discomfort, or need for supplemental analgesia.^[6,7] The addition of intrathecal opioid adjuvants such as fentanyl enhances sensory block by synergistic action at the spinal cord level without significantly prolonging motor blockade.^[7,8] This combination potentially allows reduction of local anesthetic dose while maintaining adequate surgical conditions.^[8]

Fentanyl, a lipophilic opioid, has a rapid onset and short duration of action when administered intrathecally.^[8,9] It improves intraoperative analgesia and prolongs postoperative pain relief without significantly increasing motor block duration.^[7,9] However, it may be associated with side effects such as pruritus, nausea, and vomiting, which must be evaluated in ambulatory practice.^[5,9]

Although several studies have examined low-dose spinal anesthesia techniques, evidence remains variable regarding optimal dosing strategies and their impact on discharge readiness in day-care surgeries.^[6,8,10] Furthermore, institutional discharge protocols and patient populations may influence outcomes. Therefore, this prospective randomized single-center study was conducted to compare low-dose hyperbaric bupivacaine combined with intrathecal fentanyl versus standard-dose hyperbaric bupivacaine in patients undergoing infra-umbilical day-care surgeries over a 12-month period (1 December 2024 to 30 November 2025).

The primary objective was to compare time to discharge readiness between the two techniques. Secondary objectives included comparison of block characteristics, ambulation time, duration of postoperative analgesia, hemodynamic changes, adverse effects, and patient and surgeon satisfaction.

MATERIALS AND METHODS

Study Design and Duration

This prospective, randomized, comparative clinical study was conducted in the Department of Anesthesiology at a tertiary care teaching hospital from **1 December 2024 to 30 November 2025**

Sample Size

Based on previous literature and assuming a minimum clinically significant difference of 45 minutes in discharge readiness time between groups, with $\alpha = 0.05$ and power = 80%, the calculated sample size was 40 patients per group. To compensate for potential dropouts, **45 patients were**

enrolled in each group, making a total of **90 patients**.

Study Population

A total of 90 patients who met the eligibility criteria were enrolled in the study after obtaining written informed consent. All patients were evaluated preoperatively with detailed history, physical examination, and routine laboratory investigations as per institutional protocol.

Inclusion Criteria

1. Age between **18 and 65 years**.
2. American Society of Anesthesiologists (ASA) physical status **I or II**.
3. Scheduled for **elective infra-umbilical day-care surgery** under spinal anesthesia.
4. Expected duration of surgery **less than 90 minutes**.
5. Ability to understand the study protocol and provide **written informed consent**.

Exclusion Criteria

1. Refusal to participate or inability to provide informed consent.
2. Contraindications to spinal anesthesia, including:
 - Coagulopathy or ongoing anticoagulant therapy
 - Infection at the site of spinal puncture
 - Severe hypovolemia
3. Known hypersensitivity or allergy to local anesthetics or opioids (fentanyl).
4. Severe cardiovascular disease (e.g., significant valvular disease, uncontrolled hypertension, ischemic heart disease).
5. Severe respiratory, hepatic, or renal dysfunction.
6. Neurological disorders affecting sensory or motor function assessment.
7. Body Mass Index (BMI) > 35 kg/m².
8. Pregnant patients.
9. Patients requiring conversion to general anesthesia for reasons unrelated to spinal block efficacy (excluded from final analysis).

Randomization

After confirming eligibility and obtaining written informed consent, patients were randomly allocated into two equal groups (45 patients in each group) using a **computer-generated randomization sequence**.

Allocation concealment was ensured using **sequentially numbered, sealed opaque envelopes**. Each envelope contained the group assignment and was opened immediately before administration of spinal anesthesia by an anesthesiologist not involved in data collection.

This method ensured unbiased group allocation and minimized selection bias.

Study Groups

A total of 90 patients were randomly allocated into two equal groups of 45 patients each:

1. **Group A (Low-Dose + Adjuvant Group)**
Patients in Group A received:
 - **0.5% hyperbaric bupivacaine 7.5 mg (1.5 mL)**
 - **Fentanyl 25 µg (0.5 mL)**

The total intrathecal volume administered was **2.0 mL**

2. Group B (Standard-Dose Group)

Patients in Group B received:

- **0.5% hyperbaric bupivacaine 12.5 mg (2.5 mL)**

The total intrathecal volume administered was **2.5 mL**.

Anesthetic Technique

All patients were kept nil per oral as per institutional fasting guidelines. A thorough pre-anesthetic evaluation was performed one day prior to surgery. On arrival in the operating room, standard monitoring including electrocardiography (ECG), non-invasive blood pressure (NIBP), and pulse oximetry (SpO₂) was applied. Baseline heart rate, systolic and diastolic blood pressure, mean arterial pressure, and oxygen saturation were recorded.

An 18G intravenous cannula was secured, and patients were preloaded with **Ringer's lactate 10 mL/kg** over 15–20 minutes prior to administration of spinal anesthesia.

Under strict aseptic precautions, spinal anesthesia was administered in the sitting position at the **L3–L4 intervertebral space** using a **25G Quincke spinal needle** via the midline approach. After confirming free flow of cerebrospinal fluid, the assigned study drug was injected intrathecally over 10–15 seconds without barbotage.

Patients were immediately positioned supine after injection. Oxygen supplementation at 3–4 L/min via face mask was provided when required.

Intraoperative monitoring of heart rate, blood pressure, and oxygen saturation was carried out at regular intervals:

- Every 2 minutes for the first 10 minutes
- Every 5 minutes thereafter until completion of surgery

Management of Hemodynamic Changes

- **Hypotension** (defined as a decrease in systolic blood pressure >20% from baseline or SBP <90 mmHg) was treated with intravenous fluids and **mephentermine 6 mg IV bolus** as required.
- **Bradycardia** (heart rate <50 beats/min) was treated with **atropine 0.6 mg IV**.

Sedation was not routinely administered but was provided if required using intravenous midazolam in titrated doses.

All intraoperative events and interventions were recorded.

Intraoperative Monitoring and Management

All patients were monitored intraoperatively using standard monitoring modalities, including:

- Continuous electrocardiography (ECG)
- Non-invasive blood pressure (NIBP)
- Pulse oximetry (SpO₂)

Baseline heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and oxygen saturation were recorded prior to spinal anesthesia.

After administration of spinal anesthesia, hemodynamic parameters were recorded at the following intervals:

- Every 2 minutes for the first 10 minutes
- Every 5 minutes thereafter until completion of surgery

Oxygen supplementation at 3–4 L/min via face mask was provided when necessary.

Definitions and Management of Hemodynamic Changes

- **Hypotension** was defined as a decrease in systolic blood pressure greater than 20% from baseline or systolic blood pressure less than 90 mmHg.
 - Managed with rapid intravenous fluid administration and **mephentermine 6 mg IV bolus**, repeated as required.
- **Bradycardia** was defined as heart rate less than 50 beats per minute.
 - Treated with **atropine 0.6 mg IV**.
- Persistent hypotension despite initial management was treated with additional vasopressor support as per institutional protocol.

Assessment of Block Adequacy

- Sensory block level was assessed using pinprick method at regular intervals.
- Motor block was assessed using the Modified Bromage Scale.
- In case of inadequate block or patient discomfort, supplemental intravenous analgesics or sedation were administered.
- Conversion to general anesthesia, if required, was documented and such cases were excluded from final analysis.

All intraoperative events, interventions, drug requirements, and complications were recorded systematically.

Assessment of Block Characteristics

Block characteristics were assessed systematically following administration of spinal anesthesia.

Sensory Block Assessment

Sensory block was evaluated using the **pinprick method** with a sterile blunt needle along the midclavicular line bilaterally.

The following parameters were recorded:

1. **Time to onset of sensory block:** Time from intrathecal injection to loss of pinprick sensation at the T10 dermatome.
2. **Maximum sensory level achieved:** Highest dermatome level attained after spinal injection.
3. **Time to achieve maximum sensory level.**
4. **Two-segment regression time:** Time from attainment of maximum sensory level to regression of two dermatomal segments.

Sensory block was assessed every 2 minutes for the first 10 minutes and then every 5 minutes until stabilization of the maximum level.

Motor Block Assessment

Motor block was assessed using the Modified Bromage Scale:

- 0 – Full movement of hip, knee, and ankle
- 1 – Inability to raise extended leg (hip blocked)
- 2 – Inability to flex knee
- 3 – Inability to flex ankle (complete motor block)

The following parameters were recorded:

1. **Time to onset of motor block** (time to reach Bromage score ≥ 1).
2. **Maximum motor block achieved.**
3. **Time to complete motor recovery**, defined as return to Bromage score 0.

Motor block was assessed at 5-minute intervals intraoperatively and periodically in the postoperative period until complete recovery.

Postoperative Assessment

After completion of surgery, patients were shifted to the **Post-Anesthesia Care Unit (PACU)** for monitoring and recovery assessment.

Vital parameters including heart rate, blood pressure, respiratory rate, and oxygen saturation were monitored at regular intervals until discharge criteria were met.

Primary Outcome

The primary outcome was time to discharge readiness, defined as the time from intrathecal injection to achievement of a **modified Post-Anesthetic Discharge Scoring System (PADSS) score ≥ 9** .

The modified PADSS assessed:

- Vital signs stability
- Ambulation status
- Nausea and vomiting
- Pain control
- Surgical bleeding

Patients were considered fit for discharge when PADSS ≥ 9 was achieved and no medical concerns were present.

Secondary Outcomes

1. **Time to ambulation:**
Time from spinal injection to the ability to walk with minimal or no assistance.
2. **Duration of postoperative analgesia:**
Time from spinal injection to first request for rescue analgesic (VAS ≥ 4).
3. **Pain Assessment:**
Postoperative pain was evaluated using the **Visual Analog Scale (VAS)** (0 = no pain, 10 = worst imaginable pain) at 0, 1, 2, 4, and 6 hours postoperatively.
4. **Adverse Effects Monitoring:**
Patients were monitored for:
 - Hypotension
 - Bradycardia
 - Postoperative nausea and vomiting (PONV)
 - Pruritus
 - Urinary retention (inability to void within 6 hours requiring catheterization)
 - Respiratory depression (respiratory rate < 10 /min or SpO₂ $< 92\%$)
5. **Patient and Surgeon Satisfaction:**
Satisfaction was assessed using a 5-point Likert scale (1 = very dissatisfied, 5 = very satisfied).

All postoperative events, interventions, and time parameters were recorded systematically for statistical analysis.

Ethical Approval

The study was conducted after obtaining approval from the Institutional Ethics Committee. The research was carried out in accordance with the ethical principles of the Declaration of Helsinki. Written informed consent was obtained from all participants prior to inclusion in the study after explaining the nature and purpose of the research. Confidentiality of patient information was strictly maintained, and data were anonymized during analysis.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using **Statistical Package for the Social Sciences (SPSS) version 25.0** (IBM Corp., Armonk, NY, USA).

Continuous variables were expressed as **mean \pm standard deviation (SD)**, and categorical variables were presented as **frequency and percentage**.

Normality of data distribution was assessed using the **Shapiro–Wilk test**. For normally distributed continuous variables, comparisons between the two groups were performed using the **independent Student’s t-test**. For non-normally distributed data, the **Mann–Whitney U test** was applied.

Categorical variables were analyzed using the **Chi-square test** or **Fisher’s exact test** when appropriate. Time-related outcomes such as discharge readiness and ambulation time were compared using independent t-test.

A **p-value < 0.05** was considered statistically significant.

RESULTS

A total of 90 patients were enrolled in the study during the period from December 2024 to November 2025. Two patients (one from each group) were excluded due to protocol deviations. Therefore, **88 patients (44 in Group A and 44 in Group B)** were included in the final analysis.

Baseline Characteristics

There were no statistically significant differences between Group A (low-dose bupivacaine + fentanyl) and Group B (standard-dose bupivacaine) in terms of age, gender distribution, body mass index (BMI), ASA physical status, or duration of surgery ($p > 0.05$). The groups were comparable at baseline.

Block Characteristics

The onset of sensory block to T10 dermatome was comparable between the groups ($p = 0.08$). However, the maximum sensory level achieved was significantly higher in Group B (median T6) compared to Group A (median T8) ($p = 0.01$).

Two-segment regression time was significantly shorter in Group A (74.5 ± 15.2 minutes) compared to Group B (101.3 ± 19.4 minutes) ($p < 0.001$). Similarly, motor recovery time (time to Bromage 0)

was significantly shorter in Group A (92.6 ± 18.4 minutes) than in Group B (158.9 ± 25.7 minutes) ($p < 0.001$).

Primary Outcome: Time to Discharge Readiness

The time to achieve modified PADSS ≥ 9 was significantly shorter in Group A (182.4 ± 28.6 minutes) compared to Group B (261.7 ± 36.9 minutes), with a mean difference of 79.3 minutes ($p < 0.001$).

Recovery Profile

Time to ambulation was significantly shorter in Group A (118.5 ± 22.4 minutes) compared to Group B (196.3 ± 30.7 minutes) ($p < 0.001$).

The duration of postoperative analgesia (time to first analgesic request) was significantly longer in Group A (214.8 ± 34.2 minutes) than in Group B (168.5 ± 31.6 minutes) ($p < 0.001$).

Hemodynamic Events

The incidence of hypotension was significantly lower in Group A (9.1%) compared to Group B (27.3%) (p

$= 0.03$). Vasopressor requirement was also significantly higher in Group B ($p = 0.04$). Although bradycardia was more frequent in Group B (15.9%) than Group A (6.8%), this difference was not statistically significant ($p = 0.18$).

Postoperative Adverse Effects

Pruritus occurred more frequently in Group A (13.6%) compared to Group B (2.3%) ($p = 0.05$). Urinary retention was significantly higher in Group B (20.5%) compared to Group A (4.5%) ($p = 0.02$). There was no significant difference in postoperative nausea and vomiting between groups ($p = 0.75$). No respiratory depression was observed in either group.

Satisfaction Scores

Patient satisfaction was significantly higher in Group A (4.6 ± 0.4) compared to Group B (4.3 ± 0.5) ($p = 0.01$). Surgeon satisfaction scores were comparable between the groups ($p = 0.39$).

Table 1: Demographic and Baseline Characteristics

Variable	Group A (n=44)	Group B (n=44)	p-value
Age (years)	40.9 \pm 9.8	42.1 \pm 10.2	0.56
BMI (kg/m ²)	25.1 \pm 3.0	25.6 \pm 3.4	0.47
ASA I/II (n)	30/14	28/16	0.64
Duration of surgery (min)	51.6 \pm 12.5	53.8 \pm 13.1	0.42

Table Notes: Values are expressed as mean \pm standard deviation (SD) or number of patients. There were no statistically significant differences between Group A and Group B in demographic or baseline surgical characteristics ($p > 0.05$).

Table 2: Block Characteristics

Parameter	Group A	Group B	p-value
Onset to T10 (min)	4.7 \pm 1.1	4.3 \pm 1.0	0.08
Maximum sensory level	T8	T6	0.01*
Two-segment regression (min)	74.5 \pm 15.2	101.3 \pm 19.4	<0.001*
Time to Bromage 0 (min)	92.6 \pm 18.4	158.9 \pm 25.7	<0.001*

Table Notes: Values are expressed as mean \pm standard deviation (SD) unless otherwise stated. Maximum sensory level is presented as median dermatome level achieved. $p < 0.05$ was considered statistically significant. Bromage 0 indicates complete motor recovery.

Table 3: Recovery Outcomes

Outcome	Group A	Group B	p-value
Time to ambulation (min)	118.5 \pm 22.4	196.3 \pm 30.7	<0.001*
Time to discharge readiness (min)	182.4 \pm 28.6	261.7 \pm 36.9	<0.001*
Time to first analgesic request (min)	214.8 \pm 34.2	168.5 \pm 31.6	<0.001*

Table Notes: Values are expressed as mean \pm standard deviation (SD). Time measurements were calculated from the time of intrathecal injection. Discharge readiness was defined as achievement of modified Post-Anesthetic Discharge Scoring System (PADSS) ≥ 9 . $p < 0.05$ was considered statistically significant.

Table 4: Hemodynamic Events and Complications

Variable	Group A	Group B	p-value
Hypotension	4 (9.1%)	12 (27.3%)	0.03*
Bradycardia	3 (6.8%)	7 (15.9%)	0.18
Vasopressor use	4 (9.1%)	11 (25.0%)	0.04*
Pruritus	6 (13.6%)	1 (2.3%)	0.05*
Urinary retention	2 (4.5%)	9 (20.5%)	0.02*
PONV	5 (11.4%)	6 (13.6%)	0.75

Table Notes: Values are expressed as number of patients with percentage in parentheses. Hypotension was defined as a decrease in systolic blood pressure $>20\%$ from baseline or SBP <90 mmHg; bradycardia was defined as heart rate <50 beats/min. $p < 0.05$ was considered statistically significant.

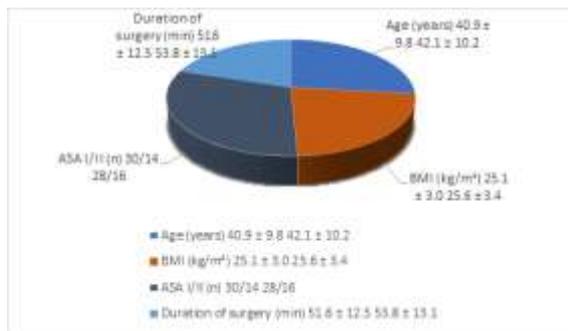


Figure 1: Comparison of Demographic and Baseline Characteristics Between Group A and Group B

Figure Notes: Data are presented as mean ± standard deviation (SD) or number of patients. There were no statistically significant differences between the two groups in age, BMI, ASA status, or duration of surgery ($p > 0.05$), indicating baseline comparability.

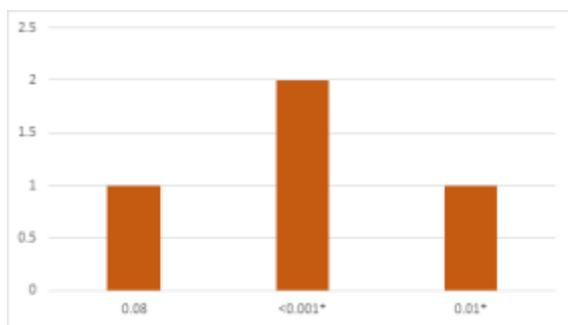


Figure 2: Comparison of Block Characteristics Between Group A and Group B

Figure Notes: Values are expressed as mean ± standard deviation (SD), except maximum sensory level which is presented as median dermatome level achieved. Group A demonstrated significantly shorter two-segment regression time and faster motor recovery (Bromage 0) compared to Group B ($p < 0.05$).

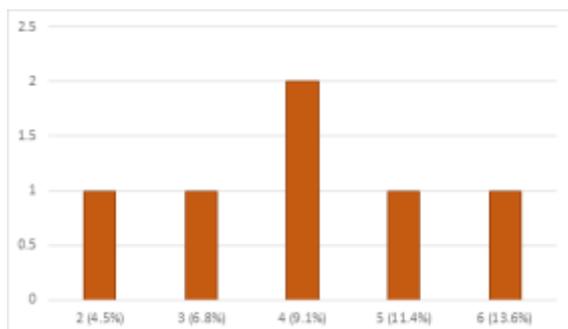


Figure 3: Comparison of Hemodynamic Events and Postoperative Complications Between Group A and Group B

Figure Notes: Data are presented as number of patients with percentage in parentheses. Group B demonstrated a significantly higher incidence of hypotension and urinary retention compared to Group A ($p < 0.05$), while pruritus was more frequent in Group A. Hypotension was defined as a decrease

in systolic blood pressure $>20\%$ from baseline or SBP <90 mmHg; bradycardia was defined as heart rate <50 beats/min.

DISCUSSION

The present prospective randomized study compared low-dose spinal anesthesia with intrathecal fentanyl to standard-dose spinal anesthesia in patients undergoing infra-umbilical day-care surgeries. The findings demonstrate that the low-dose technique significantly improves recovery parameters while maintaining adequate surgical anesthesia. Similar findings have been reported in previous studies evaluating reduced-dose spinal techniques in ambulatory settings.^[1-3]

The primary outcome of the study, time to discharge readiness, was significantly shorter in the low-dose group. Patients receiving 7.5 mg hyperbaric bupivacaine with fentanyl 25 μ g achieved discharge criteria approximately 80 minutes earlier than those receiving 12.5 mg bupivacaine alone. This reduction is clinically relevant in ambulatory settings where early discharge improves patient turnover and resource utilization.^[4,5]

Motor recovery was significantly faster in the low-dose group, as evidenced by shorter time to Bromage 0. The prolonged motor block observed in the standard-dose group likely contributed to delayed ambulation and discharge. Reduced local anesthetic dose results in less extensive sympathetic and motor blockade, thereby facilitating earlier functional recovery, as previously demonstrated in ambulatory anesthesia studies.^[2,6]

Time to ambulation was significantly shorter in the low-dose group, which is an essential determinant of safe discharge in day-care surgeries.^[4] Additionally, postoperative analgesia duration was longer in the fentanyl group, reflecting the synergistic effect of intrathecal opioid with local anesthetic.^[7,8] This provides the dual benefit of improved recovery without compromising analgesia.

Hemodynamic stability was superior in the low-dose group. The incidence of hypotension and vasopressor requirement were significantly lower compared to the standard-dose group. The greater sympathetic blockade associated with higher doses of bupivacaine likely explains the increased hypotension observed in Group B. These findings are consistent with earlier reports demonstrating improved cardiovascular stability with low-dose bupivacaine-opioid combinations.^[1,9]

Among adverse effects, pruritus was more common in the fentanyl group; however, it was mild and self-limiting. Similar observations have been reported with intrathecal fentanyl in various surgical populations.^[8,10] Urinary retention was significantly higher in the standard-dose group, likely due to prolonged sacral blockade, as described in previous literature.^[6,11] No respiratory depression was observed, supporting the safety profile of low-dose

intrathecal fentanyl when used in appropriate doses.^[7,12]

Overall, the low-dose spinal technique with fentanyl maintained adequate surgical conditions while significantly enhancing recovery profile. These findings support the use of reduced-dose spinal anesthesia with opioid adjuvants in ambulatory infra-umbilical procedures, in agreement with contemporary evidence and enhanced recovery principles.^[4,5]

Limitations

This was a single-center study with a relatively modest sample size. The findings may not be generalizable to high-risk patients (ASA III–IV) or surgeries of longer duration. Multicenter studies with larger sample sizes would strengthen the external validity of these results.

CONCLUSION

Low-dose spinal anesthesia using 7.5 mg hyperbaric bupivacaine combined with intrathecal fentanyl 25 µg provides effective and reliable surgical anesthesia for infra-umbilical day-care procedures. Compared to standard-dose spinal anesthesia, it significantly shortens time to ambulation and discharge readiness, enhances hemodynamic stability, and reduces the incidence of urinary retention, without compromising anesthetic adequacy.

Although a slightly higher incidence of mild pruritus was observed with fentanyl, no serious adverse effects such as respiratory depression occurred. Overall, low-dose spinal anesthesia with opioid adjuvant demonstrates a superior recovery profile and appears to be a safe and efficient technique for ambulatory surgeries.

Further multicenter studies with larger sample sizes are recommended to validate these findings and expand their applicability to broader patient populations.

Conflict of interest: The authors declare no conflicts of interest for this study.

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