



# Comparison of Fractionated Dose Versus Bolus Dose Injection in Spinal Anaesthesia for Patients Undergoing Elective Caesarean Section – A Randomised Double Blinded Study

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## KEYWORDS

Bolus injection;  
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Fractionated dosing;  
Hemodynamic stability;  
Hypotension;  
Levobupivacaine;  
Intrathecal block;  
Postoperative analgesia;  
Randomized controlled trial.Spinal anesthesia.

## ABSTRACT:

**Background:** Spinal anesthesia is widely used for infraumbilical surgeries due to its rapid onset and effective blockade. Levobupivacaine, a safer alternative to bupivacaine, provides reliable spinal anesthesia. However, the method of administration—bolus vs. fractionated—can significantly impact block quality and patient safety. This study investigates the clinical effects of fractionated versus bolus intrathecal dosing of levobupivacaine with buprenorphine in patients undergoing elective lower abdominal and lower limb surgeries.

**Methods:** A prospective, randomized, double-blinded trial was conducted with 50 ASA I–II patients divided into two groups: Group B (Bolus) received a single intrathecal injection, while Group F (Fractionated) received the same dose in two aliquots with a 90-second interval. Outcomes measured included onset and duration of sensory and motor block, duration of postoperative analgesia, hemodynamic stability, vasopressor requirement, and incidence of side effects.

**Results:** Both groups had comparable onset times for sensory and motor block. However, Group F showed significantly prolonged sensory and motor block durations and longer postoperative analgesia (349.46 vs. 285.15 min). Hemodynamic parameters were better maintained in the fractionated group, with reduced incidence of hypotension (12% vs. 36%) and lower vasopressor use. Nausea and vomiting were also less frequent in Group F.

**Conclusion:** Fractionated intrathecal administration of levobupivacaine with buprenorphine provides superior hemodynamic stability, longer-lasting analgesia, and fewer side effects compared to bolus dosing. This technique is recommended for safer and more effective spinal anesthesia, particularly in patients at risk of cardiovascular instability.

## INTRODUCTION

Spinal anesthesia is a widely accepted and routinely practiced technique for caesarean surgeries , particularly because of its rapid onset, predictable effect, cost-effectiveness, and reduced risk of systemic complications compared to general anesthesia.<sup>1</sup> Among the local anesthetic agents used for subarachnoid block,

*levobupivacaine*—a pure S-enantiomer of bupivacaine—has emerged as a safer alternative due to its lower cardiotoxic and neurotoxic potential while maintaining an excellent anesthetic profile.<sup>2</sup> Its reduced affinity for myocardial sodium channels compared to racemic bupivacaine provides it with enhanced cardiovascular



safety, making it especially suitable for patients with cardiovascular vulnerabilities.<sup>3</sup>

However, the technique of intrathecal administration—particularly the *dosing strategy*—plays a crucial role in determining the efficacy and safety of spinal anesthesia.<sup>4</sup> Traditionally, a single **bolus dose** of local anesthetic is administered into the subarachnoid space, which often leads to an abrupt and extensive sympathetic blockade. This sudden sympathetic outflow suppression can precipitate *significant hypotension*, bradycardia, and other cardiovascular disturbances, especially in elderly or high-risk patients. Moreover, large bolus doses may be associated with variable spread of the anesthetic agent, resulting in unpredictable block height and duration.<sup>5</sup>

In recent years, **fractionated dosing**—in which the total intrathecal anesthetic dose is split into two aliquots administered with a brief interval—has gained clinical interest.<sup>6</sup> This technique is hypothesized to provide more controlled drug dispersion within the cerebrospinal fluid (CSF), leading to a more gradual sympathetic blockade.<sup>7</sup> The benefits potentially include reduced incidence and severity of hypotension, greater hemodynamic stability, and prolonged sensory and motor blockade.<sup>8</sup> Fractionated administration also allows anesthesiologists a short window to assess early block characteristics and potentially halt injection if early signs of a high spinal block emerge.<sup>9,10</sup>

Despite these theoretical advantages, limited clinical data exist comparing fractionated versus bolus dosing of **levobupivacaine** specifically in spinal anesthesia for infraumbilical procedures. Furthermore, the inclusion of **buprenorphine**, a potent lipophilic opioid adjunct with intrinsic local anesthetic-like effects, introduces a layer of complexity. While it enhances postoperative analgesia, it can also contribute to opioid-related side effects such as nausea, vomiting, pruritus, and respiratory depression, although these effects are dose-dependent and often self-limiting.<sup>11</sup>

This study aims to fill a critical gap in the literature by comparing the **clinical efficacy, safety profile, and side effects** of fractionated versus bolus dosing of intrathecal levobupivacaine combined with buprenorphine. The primary focus is on the **onset and duration** of sensory and motor blockade, **hemodynamic stability** (especially incidence of hypotension and vasopressor requirement), and **postoperative adverse effects** such as nausea,

vomiting, and shivering. By identifying the optimal dosing strategy, this research seeks to guide anesthesia practice towards safer and more effective techniques—especially in populations susceptible to cardiovascular complications or requiring prolonged postoperative analgesia.

## AIM

To evaluate and compare the clinical efficacy and safety of fractionated versus bolus dosing of intrathecal levobupivacaine in spinal anaesthesia for patients undergoing elective caesarean section, with a focus on hemodynamic stability, sensory and motor block characteristics, and postoperative analgesia.

## OBJECTIVES

### Primary Objective:

- To compare **hemodynamic stability** between fractionated and bolus dose administration of intrathecal levobupivacaine in patients undergoing elective lower segment caesarean section (LSCS).

### Secondary Objectives:

- To compare the **onset, level, and duration of sensory block** between the two dosing techniques.
- To evaluate the **onset, intensity, and duration of motor block** using the modified Bromage scale.
- To assess the **duration of postoperative analgesia** and time to first rescue analgesic.
- To record and compare the **incidence of adverse effects**, including hypotension, bradycardia, nausea, vomiting, shivering, and other opioid-related side effects.

## MATERIALS AND METHODS

### Materials and Methods

This randomized, double-blinded, prospective interventional study was conducted in the Department of Anaesthesiology at Chettinad Hospital and Research Institute, following approval from the Institutional Human Ethics Committee (Proposal ID: IHEC-I/3192/24). The study was carried out over a three-month period and aimed to compare the efficacy and safety of fractionated versus bolus dosing of intrathecal



levobupivacaine in patients undergoing elective caesarean section.

A total of 50 parturients scheduled for elective lower segment caesarean section (LSCS) under spinal anesthesia were recruited. Eligible participants were aged between 18 and 40 years, with American Society of Anesthesiologists (ASA) physical status I or II, and met the height requirements for dosing based on a standardized protocol of 0.07 mg/cm. Exclusion criteria included refusal to participate, contraindications to spinal anesthesia, history of significant cardiovascular, hepatic, or neurological disease, known hypersensitivity to amide-type local anesthetics or opioids, and cases requiring emergency surgery.

All participants provided written informed consent after the study was explained in both English and their local language. Patients were randomly divided into two groups using a computer-generated random number table. Group A (Bolus Group) received the full calculated dose of 0.5% heavy levobupivacaine as a single intrathecal bolus injection over 10 seconds. Group B (Fractionated Group) received the same total dose in two stages: two-thirds of the dose was administered initially, followed by the remaining one-third after a 90-second interval, both at a rate of 0.2 mL/s. To maintain blinding and avoid observer bias, patients in the bolus group were also kept in the sitting position for 90 seconds after the injection to match the administration protocol of the fractionated group.

All patients were preloaded with 10–15 mL/kg of Ringer's lactate over 10 minutes before spinal anesthesia. Under aseptic precautions, spinal anesthesia was administered in the sitting position at the L3–L4 or L4–L5 interspace using a 25-gauge Quincke spinal needle. After confirming cerebrospinal fluid flow, the calculated dose of 0.5% heavy levobupivacaine (with buprenorphine as an adjuvant) was administered according to the assigned group.

Post-procedure, patients were placed in the supine position with a left lateral wedge to avoid aortocaval compression. Oxygen supplementation at 3 L/min was provided via nasal cannula. Standard intraoperative monitoring included non-invasive blood pressure, pulse oximetry, and electrocardiography. Hemodynamic parameters such as heart rate, systolic and diastolic blood pressure, mean arterial pressure (MAP), and oxygen

saturation (SpO<sub>2</sub>) were recorded at baseline and at regular intervals up to 60 minutes after administration.

Sensory blockade was assessed using pinprick testing, and motor blockade was evaluated using the modified Bromage scale. Time to onset, maximum level achieved, duration of block, and regression times were noted. Intraoperative hypotension, defined as a fall in MAP  $\geq 20\%$  from baseline, was treated with 6 mg IV ephedrine as required. Bradycardia (heart rate  $< 60$  bpm) was managed with IV atropine 0.6 mg.

Postoperative pain was assessed using a visual analogue scale (VAS) at 30-minute intervals for the first 2 hours, then hourly up to 6 hours. Duration of analgesia was defined as the time from spinal injection to the first request for rescue analgesia (VAS  $\geq 4$ ), which was managed with IV tramadol 50 mg. Adverse events including nausea, vomiting, shivering, respiratory distress, pruritus, and urinary retention were recorded for up to 24 hours postoperatively.

This study was designed to determine whether fractionated dosing of intrathecal levobupivacaine provides improved hemodynamic stability and prolonged analgesia compared to the traditional bolus technique, while also monitoring the incidence of opioid-related side effects such as nausea and vomiting.

## RESULTS:

**Table 1 : DEMOGRAPHIC CHARACTERISTICS OF STUDY POPULATION**

Parameter	Group B (Bolus)	Group F (Fractionated)
Mean Age (years)	37.24	39.36
Mean BMI (kg/m <sup>2</sup> )	25.07	24.45
ASA Grade I (%)	68.0	76.0
ASA Grade II (%)	32.0	24.0

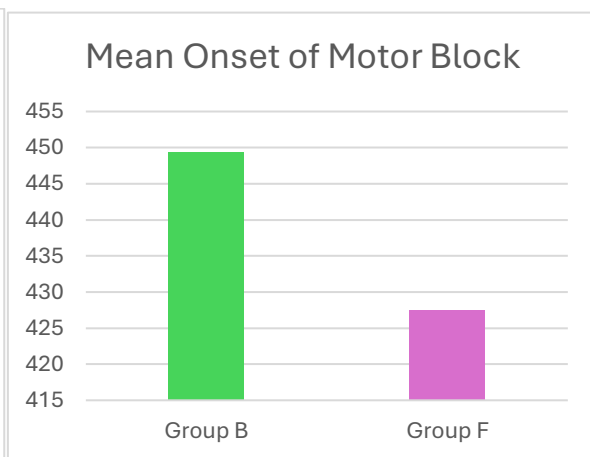
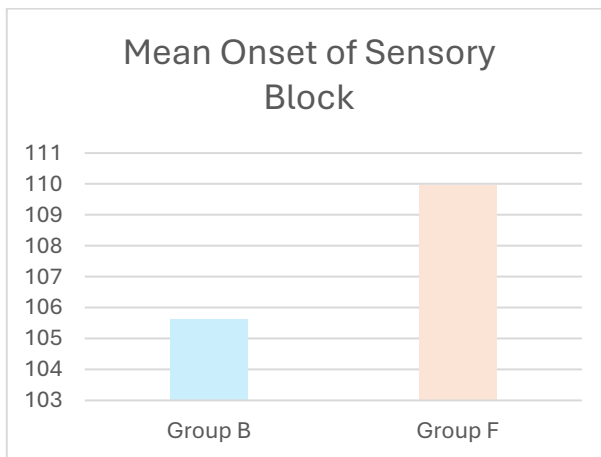


The demographic data presented indicate that both Group B (Bolus) and Group F (Fractionated) were comparable in terms of baseline characteristics, ensuring uniformity in population distribution. The mean age of participants was similar in both groups (37.24 years vs. 39.36 years). The mean body mass index (BMI) was also closely matched, with Group B at 25.07 kg/m<sup>2</sup> and Group F at 24.45 kg/m<sup>2</sup>, indicating a similar nutritional and physiological status. In terms of ASA classification, which assesses preoperative physical health, both groups had a balanced distribution with a marginally higher proportion of ASA Grade I patients in Group F (76%) compared to Group B (68%). This demographic parity supports the internal validity of the study and reduces the likelihood that outcomes were influenced by baseline patient differences.

**Table 2 : COMPARISON OF KEY OUTCOMES**

Parameter	Group B (Bolus)	Group F (Fractionated)
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<b>Onset of Sensory Block (sec)</b>	105.63	109.98
<b>Onset of Motor Block (sec)</b>	449.43	427.53
<b>Duration of Sensory Block (min)</b>	173.08	195.83
<b>Duration of Motor Block (min)</b>	134.58	148.73
<b>Duration of Analgesia (min)</b>	285.15	349.46
<b>Patients Requiring Vasopressors (%)</b>	36.0	12.0
<b>Incidence of Hypotension (%)</b>	36.0	12.0
<b>Incidence of Nausea/Vomiting (%)</b>	12.0	4.0



**Figure 1 Mean Onset of Sensory Block    Figure 2 Mean Onset of Motor Block**

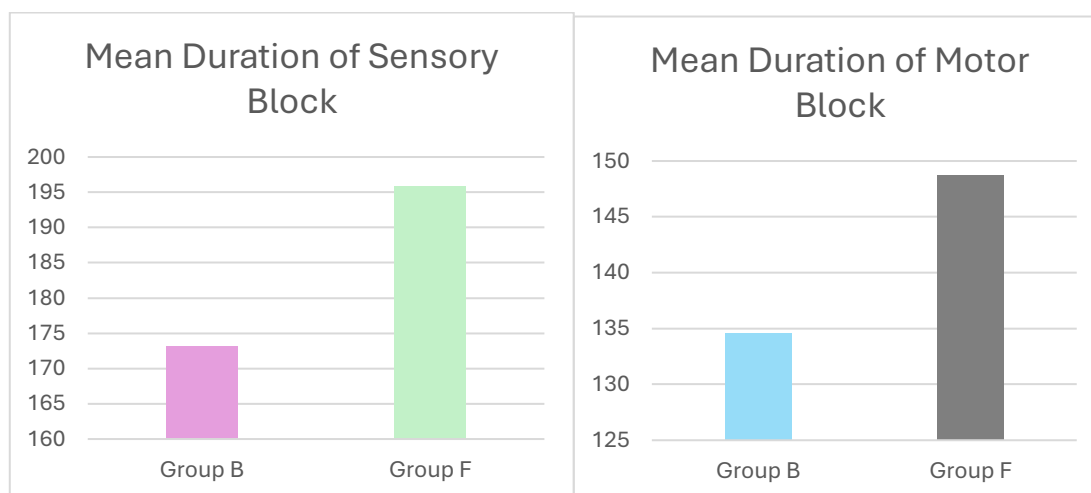


Figure 3 : Mean Duration of Sensory Block Figure 4 : Mean Duration of Motor Block

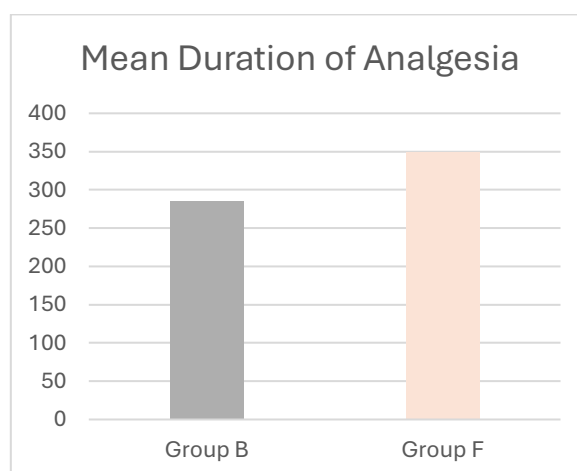


Figure 5 : Mean Duration of Analgesia

The comparison of clinical outcomes clearly highlights the advantages of fractionated dosing of levobupivacaine in spinal anesthesia. The onset times for both sensory and motor blocks were comparable between the two groups, suggesting that fractionation did not delay the effectiveness of the block. Notably, the duration of both sensory (195.83 min vs. 173.08 min) and motor block (148.73 min vs. 134.58 min) was significantly longer in the fractionated group, indicating prolonged anesthetic action. Furthermore, the duration of postoperative analgesia was markedly extended in Group F (349.46 min) compared to Group B (285.15 min), which is clinically beneficial for enhancing patient comfort and reducing the need for early rescue analgesics. Most importantly, Group F demonstrated superior

hemodynamic stability, with lower percentages of patients requiring vasopressors (12% vs. 36%) and experiencing hypotension (12% vs. 36%). The incidence of nausea and vomiting was also reduced in Group F (4%) compared to Group B (12%), suggesting a more favorable side-effect profile. These findings collectively underscore the clinical superiority of fractionated dosing in terms of block quality, safety, and patient outcomes.

## DISCUSSION

This randomized, double-blinded study compared the clinical efficacy, hemodynamic effects, and side-effect profile of fractionated versus bolus intrathecal dosing of levobupivacaine in patients undergoing elective lower abdominal and lower limb surgeries.<sup>12</sup> The results



demonstrate a clear clinical advantage of **fractionated dosing** in terms of block characteristics, postoperative analgesia, and cardiovascular stability.<sup>13</sup>

In this study, although the **onset times** for both sensory and motor blocks were statistically similar between the two groups, the **duration of sensory and motor blockade** was notably prolonged in the fractionated group.<sup>14,15</sup> These findings are consistent with the theory that fractionated dosing allows for better control of drug spread in the cerebrospinal fluid (CSF), resulting in a denser and more sustained neural blockade.<sup>16,17</sup> The controlled deposition of the local anesthetic may reduce the variability of cephalad spread and promote a more uniform block level, leading to prolonged analgesia and motor block without compromising onset.<sup>18</sup>

One of the most significant clinical benefits observed was the **prolonged duration of postoperative analgesia** in Group F (349.46 minutes) compared to Group B (285.15 minutes).<sup>19</sup> This extended pain relief can contribute to improved patient satisfaction and reduced reliance on systemic analgesics in the immediate postoperative period.<sup>20</sup> The addition of buprenorphine, a long-acting lipophilic opioid, may have contributed to the analgesic duration in both groups, but its effect was likely more pronounced in the fractionated group due to optimized spread and absorption within the spinal cord.<sup>21</sup>

A key observation was the **superior hemodynamic stability** in the fractionated group, evidenced by a lower incidence of hypotension (12% vs. 36%) and reduced requirement for vasopressors.<sup>22</sup> These results highlight the importance of sympathetic blockade dynamics in spinal anesthesia. Bolus administration can lead to rapid onset of sympathectomy and abrupt cardiovascular compromise, particularly in obstetric and high-risk surgical patients. In contrast, fractionated administration appears to modulate this response by achieving a more gradual sympathetic block, thereby preserving hemodynamic parameters within safer limits.

The **side-effect profile** was also more favorable in Group F, with fewer patients experiencing nausea and vomiting (4% vs. 12%). These symptoms are commonly associated with intrathecal opioids like buprenorphine but may also be aggravated by hypotension. Thus, the lower incidence in the fractionated group may reflect both better cardiovascular stability and reduced central opioid concentration fluctuations.<sup>23</sup>

From a practical standpoint, fractionated dosing remains a simple and feasible technique that requires minimal additional effort but offers substantial clinical benefits. It may be especially valuable in high-risk patient populations where cardiovascular compromise could lead to significant morbidity.<sup>24,25</sup>

While the findings of this study are promising, there are limitations to consider. The sample size, although adequate for preliminary conclusions, may limit the generalizability of the results. Further multicenter studies with larger populations and stratification by surgical type, comorbidities, and opioid dosing could provide more robust evidence. Additionally, long-term follow-up to assess neurological outcomes or late-onset complications was not within the scope of this study.

## CONCLUSION

This randomized controlled study demonstrates that **fractionated dosing of intrathecal levobupivacaine**, when compared to the conventional bolus technique, offers several clinical advantages in patients undergoing elective lower abdominal and lower limb surgeries. Fractionated administration significantly prolongs the duration of both sensory and motor blockade, enhances postoperative analgesia, and, most importantly, provides **superior hemodynamic stability with a lower incidence of hypotension and vasopressor requirement**.

While both dosing methods achieved adequate anesthesia, fractionated dosing was associated with **reduced incidence of adverse effects**, including nausea and vomiting, likely due to a more gradual sympathetic blockade and steadier distribution of intrathecal buprenorphine. These findings suggest that fractionated intrathecal administration is a safe, effective, and practical alternative to bolus dosing, especially in patients at risk for cardiovascular instability.

Incorporating this technique into routine clinical practice may improve patient outcomes, reduce the need for intraoperative interventions, and enhance overall perioperative care. Further studies with larger cohorts are warranted to confirm these findings and explore the potential benefits in other surgical populations and dosing regimens.



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