Research Article

# Comparison Of Intrathecal Morphine and Buprenorphine With Ropivacaine To Attenuate Pressure Response To Carboperitoneum in Total Laparoscopic Hysterectomy Under General Anaesthesia

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**Abstract**

Background: Total laparoscopic hysterectomy (TLH) is associated with pneumoperitoneum-induced sympathetic stimulation and postoperative pain that can compromise haemodynamic stability. Intrathecal opioids combined with ropivacaine may attenuate this stress response and enhance analgesia, but direct comparative data on buprenorphine versus morphine in this setting are limited.

Objective: To compare intrathecal buprenorphine and intrathecal morphine, each combined with 0.75% hyperbaric ropivacaine, for attenuation of the pressor response to carboperitoneum, postoperative analgesic profile, and opioid-related adverse effects during TLH under general anaesthesia.

Methods: In this randomized controlled trial, 80 ASA I–II women aged 30–60 years undergoing elective TLH were allocated equally to Group B (intrathecal buprenorphine 60 mcg with 1 ml 0.75% hyperbaric ropivacaine) or Group M (intrathecal morphine 100 mcg with 1 ml 0.75% hyperbaric ropivacaine), followed by standardized general anaesthesia. Heart rate and mean arterial pressure (MAP) were recorded at baseline, during spinal anaesthesia, at intubation, and serially through carboperitoneum. Postoperative pain (VAS) was assessed for 24 hours along with time to first rescue analgesia, total rescue doses, and adverse effects.

Results: Baseline characteristics were comparable between groups. MAP rose more during spinal anaesthesia in Group B than Group M (4.35 ± 4.83 vs 0.88 ± 5.15 mmHg, $p = 0.001$) and remained consistently higher in Group B throughout carboperitoneum (all $p \leq 0.002$ on repeated-measures ANOVA). VAS scores over 24 hours were significantly lower in Group M ($p = 0.001$), while time to first rescue analgesia was longer in Group B (18.16 ± 3.59 vs 16.05 ± 3.38 hours, $p = 0.015$); total 24-hour rescue analgesic requirement did not differ significantly. Nausea was more frequent in Group M (37.5% vs 10%, $p = 0.004$); vomiting, pruritus, urinary retention and respiratory depression were low and comparable, with no respiratory depression in either group.

Conclusion: Intrathecal morphine 100 mcg with ropivacaine provides superior attenuation of carboperitoneum-induced MAP elevation and lower postoperative pain scores than intrathecal buprenorphine 60 mcg, at the cost of more postoperative nausea; buprenorphine offers a modestly longer interval to first rescue analgesia with a more favourable nausea profile. Opioid choice can therefore be individualized based on hemodynamic priorities and tolerability.

**Keywords:** Intrathecal morphine, Intrathecal buprenorphine, Ropivacaine, Laparoscopic hysterectomy, Carboperitoneum, Postoperative analgesia.

## INTRODUCTION

Total laparoscopic hysterectomy (TLH) is increasingly preferred for benign and early malignant gynaecological disease owing to reduced pain, faster mobilization and shorter hospital stay compared with open surgery. However, $CO_2$ pneumoperitoneum and steep Trendelenburg positioning raise intra-abdominal pressure and provoke sympathetic activation—tachycardia, hypertension and increased systemic vascular resistance—that conventional general anaesthesia often fails to fully blunt, particularly in patients with limited cardiovascular reserve. High-dose systemic opioids or deep inhalational anaesthesia used to control this response can delay recovery and cause respiratory depression and postoperative nausea and vomiting (PONV).

Intrathecal opioids combined with a local anaesthetic offer pre-emptive spinal analgesia that blunts nociceptive transmission from the peritoneum and abdominal viscera, thereby reducing the sympathetic component of the stress response without the drawbacks of high systemic opioid dosing. Morphine, a hydrophilic pure μ-agonist, provides prolonged analgesia via slow cerebrospinal fluid clearance but carries a higher risk of delayed respiratory depression, pruritus and nausea. Buprenorphine, a highly lipophilic partial μ-agonist/κ-antagonist with high receptor affinity and slow dissociation, has rapid onset and durable analgesia with reportedly more stable haemodynamics and fewer respiratory events. Ropivacaine, a long-acting amide with a favourable safety margin over bupivacaine, is

commonly combined with these opioids for spinal anaesthesia in laparoscopic surgery.

Although both morphine and buprenorphine have been separately studied for postoperative analgesia, direct comparative evidence on their ability to attenuate the intraoperative pressor response to carboperitoneum during TLH under general anaesthesia is limited. This study was therefore undertaken to compare intrathecal morphine and buprenorphine, each combined with hyperbaric ropivacaine, with respect to intraoperative haemodynamic stability, postoperative analgesia, and safety during TLH.

**Aim of the Study**

To compare intrathecal morphine and buprenorphine with ropivacaine in attenuating the pressure response to carboperitoneum in total laparoscopic hysterectomy under general anaesthesia.

## MATERIALS AND METHODS

**Study Design and Population**

This randomized controlled trial was conducted at Adichunchanagiri Institute of Medical Sciences & Hospital following Institutional Ethics Committee approval and written informed consent from all participants. Eighty adult female patients (ASA I–II, aged 30–60 years) scheduled for elective TLH of duration < 2 hours under general anaesthesia were enrolled by computer-generated simple random allocation into two equal groups of 40: Group B received intrathecal buprenorphine 60 mcg with 1 ml 0.75% hyperbaric ropivacaine, and Group M received intrathecal morphine 100 mcg with 1 ml 0.75% hyperbaric ropivacaine.

Exclusion criteria included refusal of consent, known allergy or hypersensitivity to the study drugs, ASA III–IV status, local infection at the injection site, contraindications to spinal anaesthesia, and ongoing treatment with anticoagulants/antiplatelets, MAO inhibitors, phenothiazines, or tricyclic antidepressants. Sample size (n = 29/group, rounded to 40 to allow for attrition) was calculated from the mean and standard deviation of systolic blood pressure reported in prior literature, with $\alpha = 0.05$ and power = 80%.

**Procedure**

After overnight fasting and premedication (oral ranitidine 150 mg and alprazolam 0.5 mg), patients received standard ASA monitoring and a wide-bore intravenous line. Under aseptic precautions, a 26G Quincke needle was used to administer the assigned intrathecal drug at the L3–L4 interspace at 0.2 ml/sec without barbotage, after which patients were positioned supine. General anaesthesia was induced with fentanyl, midazolam, glycopyrrolate, propofol and vecuronium, and maintained with oxygen, nitrous oxide and isoflurane. $CO_2$ pneumoperitoneum was created 5 minutes after intrathecal injection and intra-abdominal pressure maintained at 12–14 mmHg with 15° Trendelenburg tilt; $ETCO_2$ was kept between 35–40 mmHg. Neuromuscular blockade was reversed with neostigmine and glycopyrrolate at the end of surgery.

**Data Collection and Analysis**

Heart rate, blood pressure, MAP, $SpO_2$ and $ETCO_2$ were recorded at baseline, during spinal anaesthesia, at intubation, and every 5 minutes for the first 30 minutes and every 15 minutes thereafter through carboperitoneum. Postoperatively, pain was assessed on a 0–10 Visual Analogue Scale (VAS) up to 24 hours, along with time to first rescue analgesia (IV paracetamol 1 g), total rescue doses, and adverse effects (nausea, vomiting,

pruritus, urinary retention, respiratory depression). Parametric data were compared using Student's t-test and categorical data using the chi-square test; repeated-measures ANOVA was used for serial haemodynamic and VAS data. A p-value < 0.05 was considered statistically significant.

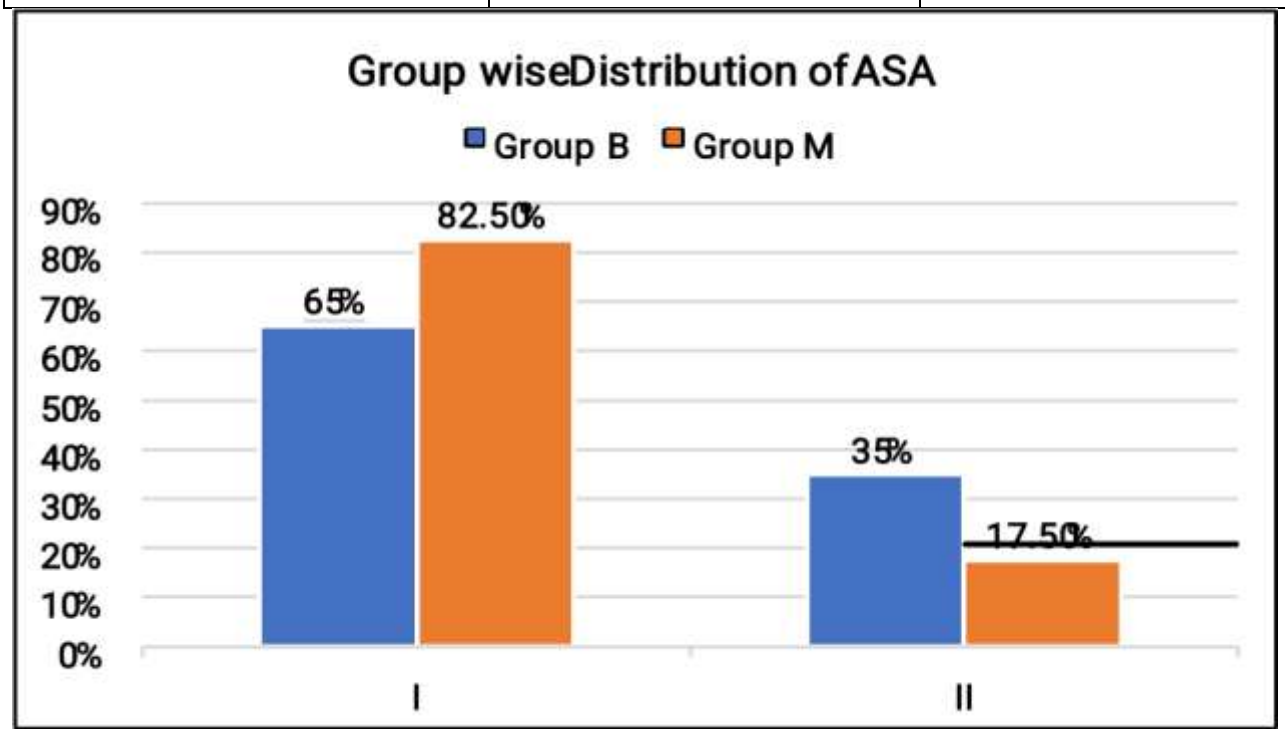
## RESULTS

**Baseline Demographic and Clinical Characteristics**

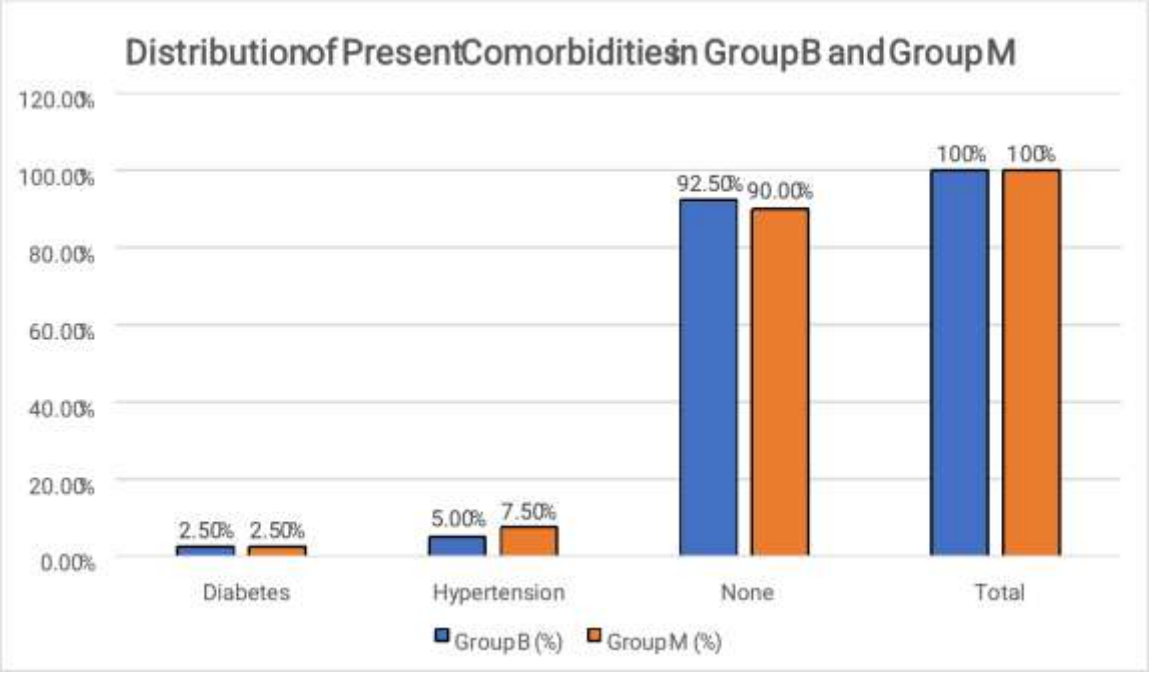
Baseline demographics, ASA status, comorbidities, prior surgical history, vital signs, and laboratory parameters were comparable between groups, minimizing confounding of subsequent hemodynamic and analgesic comparisons.

**Table 1. Baseline demographic, clinical and laboratory characteristics**

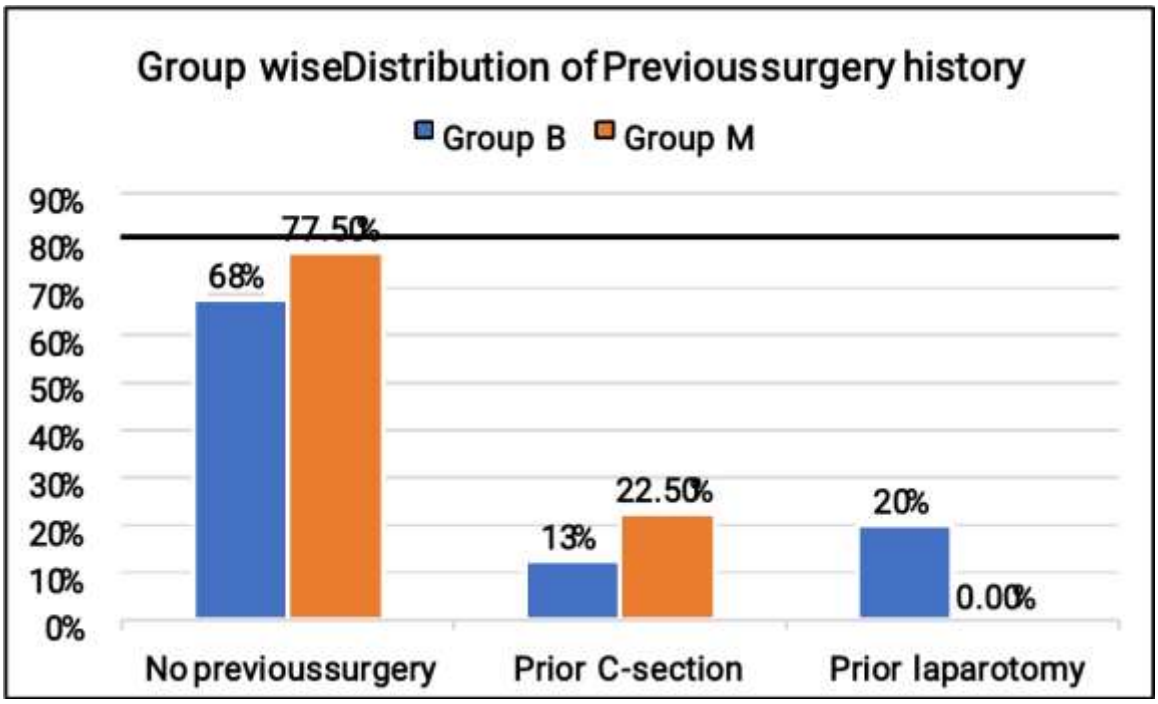
| Parameter | Group B (Mean ± SD) | Group M (Mean ± SD) |
|---|---|---|
| Age (years) | 47.30 ± 8.54 | 44.80 ± 9.11 |
| Weight (kg) | 72.96 ± 15.33 | 70.48 ± 12.09 |
| ASA I / II (%) | 65% / 35% | 82.5% / 17.5% |
| No comorbidity (%) | 92.5% | 90.0% |
| No previous surgery (%) | 68% | 77.5% |
| Hemoglobin (g/dL) | 12.99 ± 1.08 | 12.83 ± 0.86 |
| Platelets (per µL) | 249,543.5 ± 30,725.6 | 246,525.5 ± 32,030.8 |



**Graph 1:** Bar graph on group-wise distribution of ASA physical status.




**Graph 2:** Bar graph on distribution of present comorbidities in Group B and Group M.



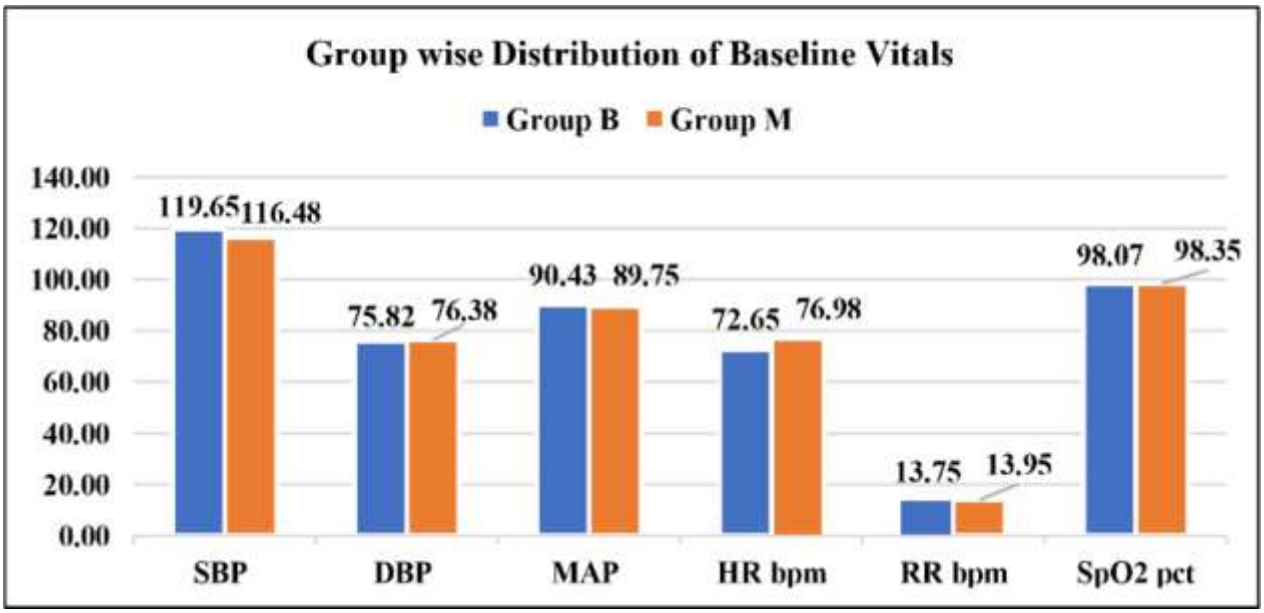

**Graph 3**: Bar graph on group-wise distribution of previous surgery history.

**Baseline Vital Parameters**

**Table 2. Baseline vital parameters**

| Parameter | Group B | Group M |
|---|---|---|
| SBP (mmHg) | 119.65 ± 10.04 | 116.48 ± 10.89 |

| Parameter | Group B | Group M |
|---|---|---|
| DBP (mmHg) | 75.82 ± 6.35 | 76.38 ± 6.06 |
| MAP (mmHg) | 90.43 ± 5.46 | 89.75 ± 5.50 |
| Heart rate (bpm) | 72.65 ± 7.05 | 76.98 ± 7.60 |
| Respiratory rate (bpm) | 13.75 ± 1.19 | 13.95 ± 1.15 |
| $SpO_2$ (%) | 98.07 ± 1.05 | 98.35 ± 1.00 |



Graph 4: Bar graph on group-wise distribution of baseline vital parameters.

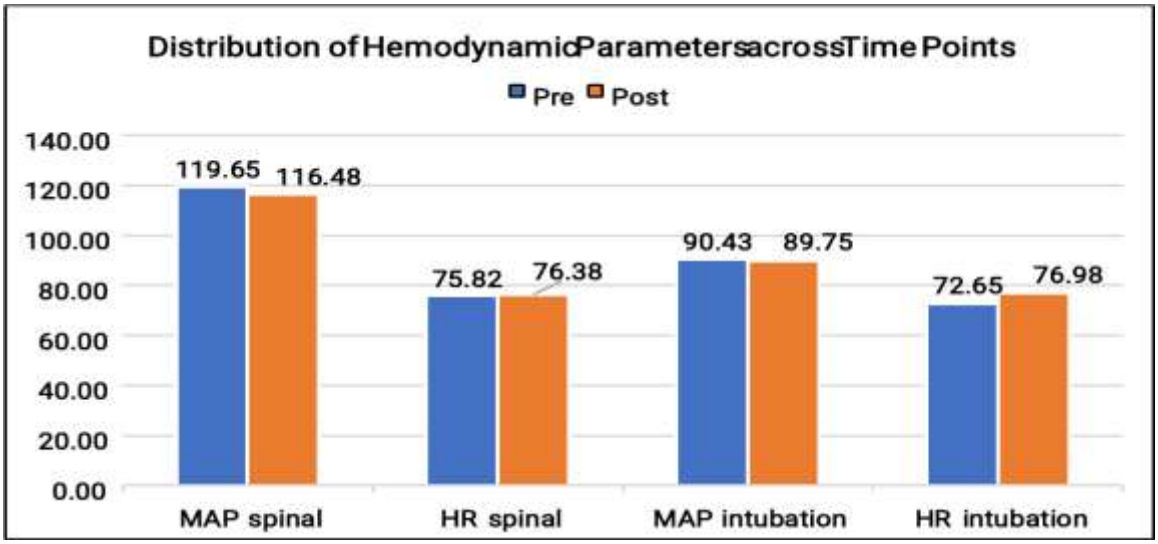
**Hemodynamic Changes During Spinal Anaesthesia and Intubation**

Within-group analysis showed that MAP and heart rate rose significantly from pre- to post-spinal values in both groups combined (MAP 87.81 ± 5.92 to 89.54 ± 1.65 mmHg, $p = 0.007$; HR 72.89 ± 7.16 to 82.36 ± 1.37 bpm, $p < 0.001$), and similarly during intubation (MAP $p < 0.001$; HR $p < 0.001$). Between-group comparison showed a significantly greater MAP rise during spinal anaesthesia in Group B than Group M (4.35 ± 4.83 vs 0.88 ± 5.15 mmHg, $p < 0.001$); heart rate change during spinal anaesthesia and both MAP and HR changes at intubation did not differ significantly between groups.

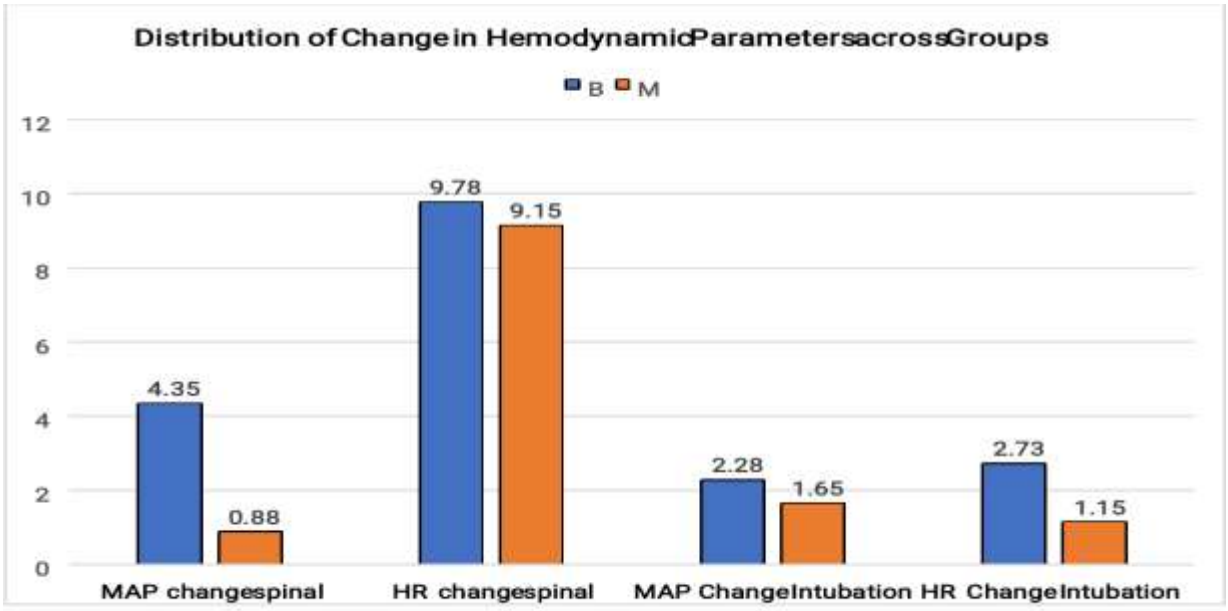
**Table 3. Between-group hemodynamic changes during spinal anaesthesia and intubation**

| Parameter (change) | Group B | Group M | p-value |
|---|---|---|---|
| MAP change – spinal | 4.35 ± 4.83 | 0.88 ± 5.15 | <0.001* |
| HR change – spinal | 9.78 ± 7.12 | 9.15 ± 7.32 | 0.765 |

| Parameter (change) | Group B | Group M | p-value |
|---|---|---|---|
| MAP change – intubation | 2.28 ± 3.07 | 1.65 ± 2.67 | 0.419 |
| HR change – intubation | 2.73 ± 4.66 | 1.15 ± 3.77 | 0.057 |




**Graph 5**: Distribution of hemodynamic parameters (MAP and HR) across time points during spinal anaesthesia and intubation.



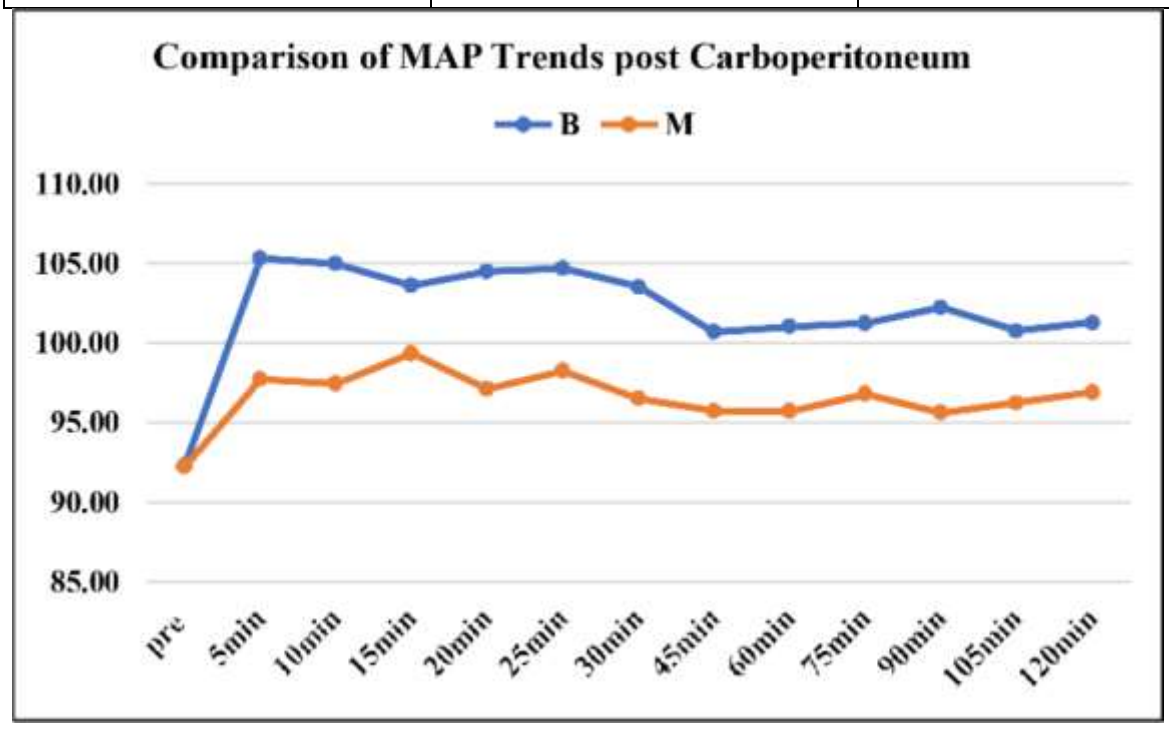

**Graph 6**: Distribution of change in hemodynamic parameters across groups.

**Mean Arterial Pressure Trends Post Carboperitoneum**

Pre-carboperitoneum MAP was comparable between groups (92.27 ± 1.54 vs 92.20 ± 1.86 mmHg). Following pneumoperitoneum, MAP rose in both groups but remained consistently higher in Group B at every recorded interval through 120 minutes, indicating superior attenuation of the pressor response with intrathecal morphine. Repeated-measures ANOVA confirmed significant effects of time ($p < 0.001$), time × group interaction ($p = 0.002$), and overall group ($p = 0.001$).

**Table 4. MAP trends post carboperitoneum (Time: p<0.001; Time×Group: p=0.002; Group: p=0.001)**

| Time | Group B (mmHg) | Group M (mmHg) |
|---|---|---|
| Pre-carboperitoneum | 92.27 ± 1.54 | 92.20 ± 1.86 |
| 5 min | 105.32 ± 8.64 | 97.73 ± 8.31 |
| 10 min | 104.98 ± 8.57 | 97.43 ± 7.18 |
| 15 min | 103.62 ± 7.42 | 99.35 ± 8.84 |
| 20 min | 104.48 ± 8.83 | 97.12 ± 9.37 |
| 25 min | 104.70 ± 6.42 | 98.23 ± 8.40 |
| 30 min | 103.55 ± 10.15 | 96.50 ± 9.00 |
| 45 min | 100.70 ± 7.83 | 95.72 ± 8.88 |
| 60 min | 101.02 ± 8.91 | 95.70 ± 8.22 |
| 75 min | 101.23 ± 7.56 | 96.78 ± 9.52 |
| 90 min | 102.23 ± 8.10 | 95.60 ± 7.46 |
| 105 min | 100.75 ± 7.78 | 96.23 ± 9.22 |
| 120 min | 101.27 ± 7.79 | 96.90 ± 8.33 |



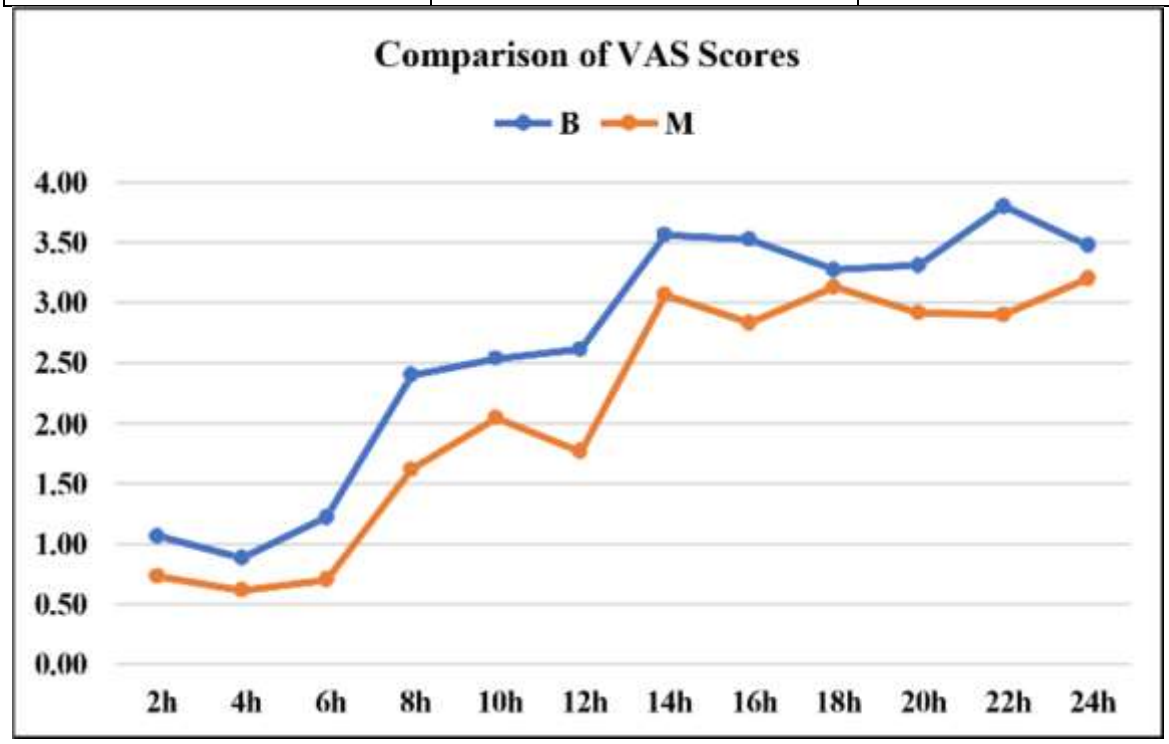
**Graph 7:** Line graph comparing MAP trends post carboperitoneum between groups.

**Postoperative Visual Analogue Scale (VAS) Scores**

VAS scores rose progressively over 24 hours in both groups but were consistently lower in Group M at most time points. Repeated-measures ANOVA showed significant effects of time ($p < 0.001$) and group ($p < 0.001$).

**Table 5. Postoperative VAS scores over 24 hours (Time: p<0.001; Group: p<0.001)**

| Time | Group B | Group M |
|---|---|---|
| 2h | 1.07 ± 0.88 | 0.73 ± 0.61 |
| 4h | 0.88 ± 0.73 | 0.61 ± 0.62 |
| 6h | 1.22 ± 1.05 | 0.70 ± 0.78 |
| 8h | 2.40 ± 1.12 | 1.62 ± 0.90 |
| 10h | 2.54 ± 0.88 | 2.05 ± 1.23 |
| 12h | 2.62 ± 1.45 | 1.77 ± 0.91 |
| 14h | 3.56 ± 1.57 | 3.07 ± 1.33 |
| 16h | 3.53 ± 1.25 | 2.83 ± 1.28 |
| 18h | 3.28 ± 1.63 | 3.13 ± 1.36 |
| 20h | 3.31 ± 1.32 | 2.92 ± 1.19 |
| 22h | 3.81 ± 1.24 | 2.90 ± 1.11 |
| 24h | 3.48 ± 1.50 | 3.20 ± 1.09 |




**Graph 8:** Line graph comparing postoperative VAS scores between groups.

**Rescue Analgesia**

Mean time to first rescue analgesia was significantly longer in Group B (18.16 ± 3.59 hours) than Group M (16.05 ± 3.38 hours, p = 0.015). Total 24-hour rescue analgesic doses were comparable between groups (Group B 1.53 ± 0.78 vs Group M 1.30 ± 0.99, p = 0.264).

**Table 6. Rescue analgesia requirements**

| Parameter | Group B | Group M | p-value |
|---|---|---|---|
| Time to first rescue (hours) | 18.16 ± 3.59 | 16.05 ± 3.38 | 0.015* |
| Total rescue doses (24h) | 1.53 ± 0.78 | 1.30 ± 0.99 | 0.264 |

**Adverse Effects**

Nausea was significantly more frequent in Group M than Group B (37.5% vs 10%, p = 0.004). Vomiting occurred equally in both groups (15% each, p = 1.000). Pruritus (17.5% vs 10%, p = 0.33) and urinary retention (5% vs 0%, p = 0.152) were numerically higher in Group M but not statistically significant. No patient in either group developed respiratory depression.

**Table 7. Incidence of opioid-related adverse effects**

| Adverse Effect | Group B, n (%) | Group M, n (%) | p-value |
|---|---|---|---|
| Nausea | 4 (10%) | 15 (37.5%) | 0.004* |
| Vomiting | 6 (15%) | 6 (15%) | 1.000 |
| Pruritus | 4 (10%) | 7 (17.5%) | 0.33 |
| Urinary retention | 0 (0%) | 2 (5%) | 0.152 |
| Respiratory depression | 0 (0%) | 0 (0%) | — |

## DISCUSSION

This study compared intrathecal buprenorphine and morphine, each combined with ropivacaine, for attenuating the haemodynamic pressor response to carboperitoneum and for postoperative analgesic efficacy and safety during TLH under general anaesthesia. Comparable baseline age, weight, ASA status, comorbidities, prior surgical history, vital parameters and laboratory values between groups—consistent with similar hysterectomy cohorts in the literature (Borkotoky et al.; Warta et al.; Engström et al.)—support attribution of the observed intraoperative and postoperative differences to the pharmacological properties of the two opioids rather than to demographic imbalance.

Intrathecal morphine produced significantly better attenuation of the MAP rise during spinal anaesthesia and throughout carboperitoneum, an effect sustained across the entire pneumoperitoneum period on repeated-measures ANOVA. This is consistent with reports by Qin et al. and Yang et al., who found reduced intraoperative opioid requirement and improved recovery scores with morphine–ropivacaine neuraxial techniques, suggesting that morphine's pure μ-agonism provides more consistent modulation of spinal sympathetic outflow during sustained nociceptive stimulation than buprenorphine's partial agonism. Heart rate and intubation-related changes, however, did not differ significantly between groups, indicating the differentiating effect of the two opioids was concentrated in the neuraxial and pneumoperitoneum phases rather than during airway manipulation.

Morphine was also associated with significantly lower VAS pain scores across the 24-hour postoperative period, in agreement with Warta et al., Engström et al. and Qin et al., who reported reduced pain scores and opioid consumption with intrathecal morphine after laparoscopic or robotic hysterectomy. This is attributable to morphine's hydrophilicity, which permits rostral cerebrospinal fluid spread and broader spinal and supraspinal

nociceptive suppression. Conversely, buprenorphine conferred a significantly longer interval to first rescue analgesia, consistent with its high receptor affinity and slow dissociation kinetics reported by Borkotoky et al., even though total 24-hour rescue analgesic consumption was similar between groups—indicating that both agents ultimately achieve comparable overall analgesic adequacy, achieved through different temporal profiles (morphine via lower peak intensity, buprenorphine via delayed onset of breakthrough pain).

The higher incidence of nausea with intrathecal morphine mirrors findings by Kwon et al. and Shim et al., and reflects morphine's rostral spread to the area postrema and chemoreceptor trigger zone. Rates of vomiting, pruritus and urinary retention were low and statistically comparable between groups, and no respiratory depression occurred in either group, supporting the safety of both agents at the doses studied when administered with vigilant perioperative monitoring—consistent with safety data reported by Kwon et al. and Yang et al.

**Strengths and Limitations**

Strengths of this study include its prospective randomized design, standardized anaesthetic and surgical protocol, comparable baseline characteristics between groups, serial hemodynamic recording at clinically relevant intervals, and use of repeated-measures ANOVA to capture the temporal trajectory of MAP and pain. Limitations include the single-centre design, a sample size adequate for primary outcomes but underpowered for rare adverse events, restriction to only two intrathecal agents without dose-ranging, hemodynamic assessment limited to MAP and heart rate without cardiac output or systemic vascular resistance measurement, a 24-hour postoperative observation window, and the absence of patient-reported quality-of-recovery or satisfaction outcomes.

**Clinical Implications and Recommendations**

Intrathecal morphine may be preferable when intraoperative hemodynamic stability during carboperitoneum is the priority, particularly in patients at cardiovascular risk, provided antiemetic prophylaxis is used to offset its higher nausea incidence. Intrathecal buprenorphine may be favoured when a longer interval to first rescue analgesia is desired or in patients more sensitive to morphine-related side effects. Both agents were safe at the doses studied when combined with standardized monitoring, and opioid selection can be individualized to patient risk profile, surgical duration and recovery priorities. Future multicentre studies with larger samples, dose-ranging comparisons, multimodal analgesic combinations, extended follow-up, and patient-reported recovery outcomes would further refine intrathecal opioid selection for laparoscopic gynaecological surgery.

**SUMMARY**

This randomized controlled trial compared intrathecal buprenorphine (60 mcg) and intrathecal morphine (100 mcg), each combined with 0.75% hyperbaric ropivacaine, in 80 women (40 per group) undergoing total laparoscopic hysterectomy under general anaesthesia. Baseline demographic, clinical, and laboratory characteristics were comparable between groups, providing a sound basis for comparison. During spinal anaesthesia and throughout the carboperitoneum period, intrathecal morphine produced significantly better attenuation of the pressor response, with mean arterial pressure rising less and remaining consistently lower than in the buprenorphine group (all $p \leq 0.002$ on repeated-measures ANOVA). Postoperatively, morphine was associated with significantly lower Visual Analogue Scale pain scores over 24 hours ($p < 0.001$), whereas buprenorphine provided a modestly longer interval to first rescue analgesia ($18.16 \pm 3.59$ vs $16.05 \pm 3.38$ hours, $p = 0.015$); total 24-hour rescue analgesic requirements did not differ significantly between groups. Regarding safety, nausea was significantly more common with morphine (37.5% vs 10%, $p = 0.004$), while rates of vomiting, pruritus, and urinary retention were low and statistically similar between groups, and no patient in either group experienced respiratory depression. Taken together, these findings indicate that intrathecal morphine offers superior haemodynamic stability and postoperative analgesia at the cost of more nausea, while intrathecal buprenorphine offers a more favourable nausea profile with a longer duration to first rescue analgesia — allowing the choice of intrathecal opioid adjuvant to be individualized according to a patient's haemodynamic risk and tolerability profile.

## CONCLUSION

This randomized controlled trial compared intrathecal buprenorphine and morphine, each combined with hyperbaric ropivacaine, in patients undergoing total laparoscopic hysterectomy under general anaesthesia. Both agents were evaluated for their ability to attenuate the pneumoperitoneum-induced pressor response, provide postoperative analgesia, and maintain an acceptable safety profile, using comparable baseline cohorts to ensure that observed differences reflected the pharmacological properties of the drugs rather than confounding demographic factors.

Intrathecal morphine provided superior and sustained attenuation of the mean arterial pressure rise associated with carboperitoneum, together with significantly lower postoperative VAS pain scores over 24 hours — benefits attributable to its pure μ-opioid agonism and rostral cerebrospinal fluid spread, which allow broader and more consistent modulation of spinal sympathetic and nociceptive pathways. These findings suggest that intrathecal morphine may be particularly valuable when intraoperative hemodynamic stability is a priority, such as in patients with limited cardiovascular reserve.

Intrathecal buprenorphine, in contrast, offered a modestly longer duration to first rescue analgesia, reflecting its high receptor affinity and slow dissociation kinetics, along with a significantly lower incidence of postoperative nausea. Total 24-hour rescue analgesic consumption did not differ between the two agents, and rates of vomiting, pruritus and urinary retention were low and statistically similar; critically, no respiratory depression was observed with either drug, confirming the safety of both regimens at the studied doses

under vigilant perioperative monitoring.

Overall, the choice between intrathecal morphine and buprenorphine as adjuvants to ropivacaine in total laparoscopic hysterectomy can be individualized: morphine favours intraoperative hemodynamic control and superior early analgesia at the cost of more nausea, while buprenorphine favours a more favourable nausea profile with prolonged time to rescue analgesia. Both agents can be safely incorporated into standardized anaesthetic protocols, supporting evidence-based, patient-tailored selection of intrathecal opioid adjuvants in minimally invasive gynaecological surgery.

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