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ORIGINAL RESEARCH **OBSTETRIC ANESTHESIA**

Comparative study on analgesia duration with bupivacaine-buprenorphine combination vs. bupivacaine alone for cesarean delivery

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ABSTRACT

BACKGROUND: Spinal anesthesia has been the preferred type of anesthesia for cesarean sections and other obstetric operations. Bupivacaine has been used for this purpose being long acting. Lately various narcotic analgesics have been added to prolong the analgesia and reduce the expected toxicity of bupivacaine alone. We evaluated the duration of analgesia achieved with the combination of bupivacaine-buprenorphine versus bupivacaine alone in cesarean delivery under spinal anesthesia.

Methods: A comparative study was conducted at a tertiary care teaching healthcare center in Karachi, Pakistan. One hundred patients scheduled for elective cesarean section were enrolled and divided into two groups. Group A received 10 mg of hyperbaric bupivacaine 0.5% along with normal saline, while Group B received the same dose of bupivacaine along with buprenorphine 75 µg. Preoperative assessment, intraoperative procedures, and postoperative management were performed following standard protocols of our institution. Statistical analysis was conducted using independent t-tests and chi-square tests.

Results: The findings revealed significantly longer mean time to request for analgesia in Group B compared to Group A (825.33 min vs. 166.78 min; P = 0.182), Only 14 patients in Group B (28%) required analgesia within 24 h, while all patients in Group A requested analgesia within that time frame (P = 0.0001). Moreover, an insignificantly lower incidence of hypotension and reduced need for phenylephrine administration was observed in Group B compared to Group A (P = 0.585). Group B also demonstrated a lower incidence of nausea (P = 0.380) and vomiting (P = 0.370) compared to Group A, but the difference was statistically not significant.

Conclusion: This study suggests that the addition of buprenorphine to bupivacaine in spinal anesthesia for cesarean delivery provides prolonged analgesia, reduces the incidence of nausea and vomiting, and decreases the need for vasopressor administration. These findings support the potential benefits of using the bupivacaine-buprenorphine combination in cesarean deliveries.

Key words: Cesarean Delivery; Opioids, Intrathecal; Anesthesia, Spinal; Bupivacaine; Buprenorphine; Analgesia, Duration

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1. INTRODUCTION

Pain management is essential in ensuring the well-being of patients undergoing cesarean delivery.[1] Studies have highlighted the significant concern among young obstetric patients regarding pain during and after the procedure.[2] Acute postoperative pain can have long-term adverse effects on the human body, including chronic pain, postpartum depression, and negative impact on mother-neonate bonding and breastfeeding.[3] Additionally, pain management plays a crucial role in preventing stress-related complications, neuroendocrine responses to surgery, and thromboembolism.[4] Unfortunately, surgical pain is often underestimated and undermanaged, with many patients experiencing moderate to severe pain during the postoperative recovery period.[5]

To address the cesarean delivery pain, an optimal anesthesia technique is required. It should provide effective intra-operative and postoperative pain control without sedation, allowing parturient to remain active, pain-free, and mobile to care for themselves and their newborns. One approach involves using adjuvants to spinal anesthesia to enhance the quality and duration of analgesia. Opioid analgesics such as buprenorphine, have been widely utilized in spinal anesthesia for enhanced pain control since the discovery of spinal cord opioid receptors.[6]

Buprenorphine, a thebaine derivative, has emerged as a promising intrathecal analgesic.[7] Previous studies have reported positive outcomes with the intrathecal use of buprenorphine, demonstrating its ability to prolong postoperative analgesia without significant adverse effects.[8]

Given the benefits associated with buprenorphine, it is crucial to conduct a comparative study to evaluate the analgesic duration achieved with the bupivacaine-buprenorphine combination versus bupivacaine alone for cesarean delivery. Such a study would contribute to optimizing pain management strategies in cesarean delivery, improving patient experiences, and facilitating successful mother-neonate bonding.

The rationale for this study is rooted in the need for an optimized analgesic approach that effectively relieves postoperative pain while minimizing adverse effects.[9] Current analgesic methods, including NSAIDs and opioids, often provide inadequate pain relief for cesarean delivery patients.[10] By comparing the analgesic duration of the bupivacaine-buprenorphine combination and bupivacaine alone, this study aimed to identify the optimal approach that prolongs postoperative analgesia without compromising the well-being of mothers or the breastfeeding newborn. The objectives of this study were to assess the duration of analgesia achieved with the bupivacaine-buprenorphine combination compared to bupivacaine alone in cesarean delivery.

2. METHODOLOGY

This comparative study was conducted after obtaining approval from the institutional ethical review board at the Department of Anesthesiology, Jinnah Postgraduate Medical Centre, Karachi, Pakistan, from March to June 2023. A total of 100 patients scheduled for elective cesarean section under spinal anesthesia were enrolled and divided into two groups, with 50 parturient in each group. Group A received spinal injection of hyperbaric bupivacaine 0.5% 10 mg along with one ml of normal saline, while Group B received hyperbaric bupivacaine 0.5% 10 mg along with 75 µg of buprenorphine in one ml intrathecally.

Preoperative assessments, including history taking, physical and general examinations, and routine investigations were conducted in the pre-anesthesia clinic. Patients were categorized according to the physical status classification of the American Society of Anesthesiologists. Detailed explanations of the technique, along with its benefits, risks, and alternatives, were provided to the patients, and informed written consent was obtained. Patients were encouraged to inform the attending anesthetist if they experienced any pain or discomfort during the intrathecal injection placement and postoperatively.

Inclusion criteria for the study were written informed consent, physical status ASA I or II, elective cesarean delivery, age between 20 and 35 y, a BMI between 20 and 30 kg/m^2. Patient refusal, serious medical problems, ASA III and above, coagulopathy, history of motion sickness or hyperemesis gravidarum, abnormal anatomy of the spine, infection at the site of lumbar puncture, and partial or failed block were excluded from study.

During the intraoperative procedure, patients were pre-medicated with inj. metoclopramide 10 mg as prophylaxis for aspiration. The operating room was prepared for both spinal anesthesia and general anesthesia, with all necessary equipment for emergency airway management and emergency drugs available. Baseline readings were recorded after applying essential monitors, including non-invasive blood pressure monitor, continuous ECG monitor, oximeter, and temperature probe.

Spinal anesthesia was established under a sterile technique in the L3-L4 interspinous space with a 25G pencil point spinal needle with patient in sitting position. After the injection, the patient lied supine, and the time was noted. Oxygen supplementation at 3-4 L/min was provided via a facemask, and blood pressure was

monitored at 3-min intervals throughout the procedure. Motor efficacy of the block was assessed using the Bromage scale, and sensory efficacy was assessed using a cold sponge. Once the efficacy of the block was confirmed, the surgeons were allowed to proceed with the surgery.

Any side effects of spinal anesthesia, such as hypotension (fall in BP > 20% of the baseline) or bradycardia (heart rate < 50/min), were treated with appropriate interventions, including co-loading, phenylephrine, or atropine. Other side effects of intrathecal opioids, such as nausea/vomiting, respiratory depression, and pruritus, were managed with ondansetron, naloxone, and antihistamines, respectively. Any additional complaints, such as shivering or ECG changes, were also noted. Newborns were received by neonatology team and assessed for the APGAR score.

In cases of breakthrough intolerable pain, rescue analgesia was provided in the form of Nalbuphine 0.1 mg/kg. Postoperative anesthesia instructions included no sedation and no analgesics unless requested by the patient. Patients were monitored hourly for blood pressure, pulse rate, and respiratory rate for a duration of 24 h. Objective pain assessment was conducted periodically using the Wong Baker faces pain rating scale. The total duration of analgesia was measured from the time of spinal injection to the first request for analgesia. Paracetamol infusion was administered after the request for analgesia.

The data was collected on a predesigned proforma. An independent t-test was used to assess the association between continuous variables, while the Chi-Square test or Fisher's exact test were employed to determine the association between categorical variables. The independent t-test and Fisher's exact test were applied to compare the mean request for analgesia and the number of patients who did not request analgesia within 24 h between Group A and Group B, respectively.

Table 1: Comparative demographic data in both the groups

Description		Group A (n=50)	Group B (n=50)	P value
Age (y)		24.24 ± 2.78	26.24 ± 2.05	0.0001
BMI (kg/m^2)		25.14 ± 1.83	24.92 ± 1.88	0.555
Parity		1.18 ± 0.38	1.32 ± 0.47	0.108
ASA	I	31 (62%)	26 (52%)	0.313
	II	19 (38%)	24 (48%)	

Applied Independent t-test & Chi-Square test; Data presented as mean ± SD or n (%)

Table 2: Parameters assessed

Description	Group A (n=50)	Group B (n=50)	P value
Request for analgesia (Mean time in min)	166.78 ± 9.69	825.33 ± 44.27	0.182
Number of patients who requested for analgesia in 24 h	50 (100.0%)	14 (28.0%)	0.0001*

*Applied Fisher's Exact & Independent t-test; Data presented as mean ± SD or n (%); *P < 0.05 significant*

Table 3: Side effects encountered in both the groups

Description	Group A (n=50)	Group B (n=50)	P value
Hypotension	9 (18.0%)	7 (14.0%)	0.585
Bradycardia	1 (2.0%)	1 (0.0%)	1.000
Nausea	7 (18.0%)	5 (10.0%)	0.380
Vomiting	6 (12.0%)	4 (8.0%)	0.370

Applied Chi-Square &Fisher's Exact test; Data presented as n (%)

3. RESULTS

All the 100 participants included in the study, were divided in control group and research group.

Table 1 illustrates the demographic data in both groups i.e. Group A and Group B. The mean age in Group A and Group B was 24.24 ± 2.78 y and 26.24 ± 2.05 y, respectively (Table 1). BMI in Group A and Group B was 25.14 ± 1.83 kg/m^2 and 24.92 ± 1.88 kg/m^2, respectively.

The findings indicate that in Group A, the mean time to request for analgesia was 166.78 ± 9.69 min. In contrast, in Group B, the mean time to request for analgesia was significantly longer at 825.33 ± 44.27 min. Furthermore, all patients in Group A (100%) requested analgesia within 24 h after the procedure, while only fourteen patients in Group B (28%) required analgesia within the same time frame.

The findings in Table 3 show the incidence of side effects encountered in both Group A and Group B. Group B had a lower incidence of hypotension compared to Group A. There was also a reduced need for phenylephrine administration in Group B. However, there were no significant differences in the incidence of bradycardia or the use of atropine between the two groups.

In Group A, 18.0% experienced nausea compared to 10.0% in Group B (P = 0.380). Similarly, 12.0% experienced vomiting in Group A compared to 8.0% in Group B (P = 0.370). These findings suggest that buprenorphine as an adjuvant in spinal anesthesia may reduce the incidence of nausea and vomiting compared to the control group (Table 4).

4. DISCUSSION

The present study aimed to compare the analgesic duration and side effects between the bupivacaine-buprenorphine combination (Group B) and bupivacaine alone (Group A) in patients undergoing cesarean delivery. Our findings demonstrated several significant differences between the two groups.

In terms of analgesic duration, our study revealed a significantly longer mean time to request for analgesia in Group B compared to Group A. This finding indicates that the bupivacaine-buprenorphine combination provides extended postoperative analgesia, which is consistent with the studies conducted by Ravindran et al.[11] and Deshmukh et al.,[12] who also reported prolonged analgesic duration with buprenorphine as an adjuvant.

Furthermore, all patients in Group A requested analgesia within 24 h after the procedure, while only fourteen patients in Group B required analgesia within the same time frame. This significant difference supports the superior analgesic efficacy of the bupivacaine-buprenorphine combination, as noted in previous studies.[12, 13]

Regarding the incidence of side effects, Group B showed a lower incidence of hypotension compared to Group A, which aligns with the findings of Arora et al.[14] and Haribabu et al.[15] These studies also reported a reduced need for vasopressor administration with the addition of buprenorphine. However, the incidence of bradycardia and the use of atropine were similar between the two groups, consistent with our findings.

Current study also revealed a difference in the incidence of nausea and vomiting between the two groups. In Group A, 18% of the patients experienced nausea, while only 10%of the patients in Group B reported nausea. Similar findings were observed for vomiting, with 12% of patients in Group A experiencing vomiting compared to 4% in Group B. These results highlight the potential antiemetic properties of buprenorphine, which is consistent with the studies conducted by Ravindran et al.[11] and Jejani et al.[16]

Comparing our findings with the mentioned studies, Arora et al.[14] and Haribabu et al.[15] reported similar results regarding the reduction in hypotension incidence with the addition of buprenorphine. Ravindran et al[11] and Deshmukh et al[12] demonstrated prolonged analgesic duration with buprenorphine-bupivacaine combination, supporting our findings. Shrinivas et al[13] also observed a lower incidence of nausea and vomiting with buprenorphine, which aligns with our results. Dhawale et al[17] investigated the use of intrathecal fentanyl instead of buprenorphine and reported similar outcomes in terms of analgesic duration. However, no studies directly comparing bupivacaine-buprenorphine combination with bupivacaine alone for cesarean delivery were found.

5. LIMITATIONS

The limitations of this study include a small sample size, as well as the restriction to a single center, which may limit the generalizability of the findings. The short-term nature of the study focused on immediate postoperative outcomes, while long-term effects and durability of analgesia were not evaluated.

6. CONCLUSION

In conclusion, our study demonstrates that the addition of buprenorphine to spinal anesthesia with bupivacaine provides prolonged analgesia, reduces the incidence of nausea and vomiting, and decreases the need for vasopressor administration in cesarean deliveries. Further studies with larger sample sizes and longer follow-up periods are warranted to validate these findings and explore the optimal dosage and safety profile of this combination.

7. Data availability

The numerical data generated during this research is available with the authors.

8. Acknowledgement

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9. Conflict of interest

The study utilized the hospital resources only, and no external or industry funding was involved.

10. Authors' contribution

MS: Primary investigator, pain assessor, patient monitoring and follow up, data collection, data analysis and manuscript writing.

SM: Direct supervision, proof reading, manuscript editing.

GNM: Concept, conduction of the study, proof reading, manuscript editing.

MR: Investigator and surgeon involved in evaluation and assessment of the participants.

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