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Effectiveness of Epidural Morphine For Post-Cesarean Analgesia

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ABSTRACT

Objective: To assess the efficacy and safety of epidural morphine in controlling postoperative pain after cesarean section.
Study Design: Quasi-experimental study.
Place and Duration of Study: Operation Theatre Complex Combined Military Hospital Bannu, Pakistan, from Nov 2022 to Aug 2023.
Methodology: One hundred full-term gravid patients planned for elective caesarean section were selected. Their ages ranged from 18 to 40 years, all in the ASA II category. They were divided into Group-A and Group-B alternatively. Group-A patients received Epidural Morphine 3 mg in 17 ml Injection Bupivacaine 0.5% while Group-B patients received 17 ml of 0.5% injection Bupivacaine in Epidural. All patients were monitored for pain, pruritus, nausea and vomiting, and respiratory depression.
Results: Mean analgesia duration in Group-A 1801.20±111.20 was (30 hours and 01 minute), and 236.6±31.19 minutes (3 hours 56 minutes) in Group-B. In Group-B, only 3 patients developed pruritus, significantly less than in Group-A, where 22 had pruritus. Twelve patients in Group-A complained of nausea and vomiting as compared to 6 in Group-B. No patient in either group developed respiratory depression.
Conclusion: We found that 3mg epidural morphine provided analgesia for a prolonged duration. It is safe in terms of respiratory risks. However, the incidence of pruritus, nausea and vomiting increased with epidural morphine.

Keywords: Cesarean Section, Epidural, Morphine, Postoperative Analgesia

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INTRODUCTION

Caesarean section is the most common surgery usually performed under spinal or epidural anaesthesia.[1] Postoperative pain is a major concern for patients.[2] Pain causes delayed recovery and raises the risk of thromboembolic events and postpartum depression.[3] Several modalities are in use for postoperative pain control, including intravenous (IV) paracetamol, NSAIDs and opioids like nalbuphine and tramadol.[4] The use of NSAIDs, however, is avoided in the presence of pregnancy-induced hypertension (PIH) due to the increased risk of renal failure and bleeding diathesis.[5] Bernstein et al. concluded that IV paracetamol offers no benefit in acute post caesarean pain.[6]

Choosing epidural anaesthesia in cesarean sections has the advantage of the epidural catheter that can be used for postoperative analgesia. However, epidural postoperative analgesia with local anaesthetic agents may cause lower limb numbness and weakness along with a risk of hypotension in a time-dependent and dose-dependent manner.[7,8] Opioids are often added to the solution. This decreases the concentration of local anaesthetic solutions and improves the quality and duration of the block. Unfortunately, epidural opioids are also associated with complications including postoperative nausea and vomiting (PONV), pruritus, respiratory depression, etc.[9,10]

We conducted the study to assess the value of epidural morphine in managing post-cesarean pain during the first 24 hours for quality and duration of analgesia and common side effects of sedation, nausea and vomiting, pruritus and respiratory depression. We aimed to compare the efficacy and safety of epidural morphine to routine epidural local anaesthetic solutions. This study could help in improving postpartum care in this patient population.

METHODOLOGY

This quasi-experimental study was conducted at Combined Military Hospital Bannu from November 2022 to August 2023, after approval was obtained from the Hospital Ethical Review Committee (Serial No. 6 dated 1 Nov 2022).

Inclusion Criteria: Female ASA II full-term (37-40 weeks) multiparous parturient, aged between 18-40

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years, scheduled for elective Lower Segment Cesarean Section (LSCS) were included.

Exclusion Criteria: Patients who refused spinal or epidural anaesthesia, known or suspected dural puncture, body mass index > 30 kg/m2, twin pregnancy, patients with a medical history of hypertension, diabetes, PIH/ eclampsia, suffering from major pulmonary or cardiovascular disease, thrombocytopenia, allergic to local anaesthetic/ morphine, and patients with a history of obstructive sleep apnea were excluded.

Sample size calculation was done using WHO sample size calculator, with duration of analgesia 19.6±10.3 hours in morphine group.[9,10] This came to 100. After obtaining written informed consent, demographic characteristics were recorded, including maternal age, height and weight and length of surgery. Patients were recruited using non-probability convenience sampling.

All patients received a preoperative medication with intravenous Injection metoclopramide 10mg and injection Ondansetron 4mg. They were preloaded with 10 ml/kg Ringers Lactate solution before the block.

Patients were assigned to groups A or B. Group-A patients received Morphine 3 mg in 17 ml injection Bupivacaine 0.5% while Group-B patients received 17 ml of 0.5% Bupivacaine via epidural. Preoperative Non-Invasive Blood Pressure (NIBP), pulse, and SpO2 were recorded and monitored throughout surgery at 5-minute intervals. In all patients, epidural space was identified by loss of resistance to air and a test dose of 3ml of 2% lignocaine with adrenaline was given. They were observed for increased heart rate or signs of local anaesthetic toxicity. An epidural catheter was passed and was advanced 4-5cm cephalad in all patients at the L2/3 level. After the epidural injection, patients were put in the supine position with 15° to 20° Left Uterine Displacement. Oxygen was given to all patients with a facemask at 6L/min. After 10-20 minutes, sensory level was checked with a pinprick. Surgery was allowed after a sensory level T6 was achieved. Hypotension was treated with injection normal saline or IV Phenyl-epinephrine (50ug bolus) and bradycardia was managed with IV Atropine 1.0 mg. After delivery of the baby, all patients received IV 10 IU Syntocinon bolus and 20 IU Syntocinon in IV infusion given over 4 hours. Tablet Misoprostol was placed in the uterus before closure or per rectal after surgery. All patients were kept in Post Anesthesia Care Unit (PACU) for 30 min after surgery and then shifted to High Dependency Unit (HDU). All patients were observed for the next 24 hours for pain, postoperative nausea and vomiting (PONV), pruritus and respiratory depression. Pain intensity was measured at 2 hourly intervals after discharge to PACU. Pain intensity was measured with a Visual Analogue Score (VAS)2,3 with "0" as no pain and "10" as worst pain experienced. In our study we defined postoperative pain when VAS ≥ 4 or patient demanded for analgesia. Duration of analgesia was the time from epidural dose to the time onset of pain.

Adverse effects of nausea and vomiting (PONV), pruritus, and respiratory depression were recorded. A fall in SpO2<92% or respiratory rate < 8 was taken as respiratory depression. For our study we classified pruritus and PONV on basis of therapy. Pruritus 0 = no, 1 =mild no medication required, 2 = received medication. For PONV 0= no, 1= mild – patient received a single dose of antiemetic, 2 = Severe – more than one dose of antiemetic administered to the patient in 24 hours.

IV Naloxone was made available to manage any patients suffering from respiratory depression (Respiratory Rate <8), and SpO2<91%.

Nausea and vomiting were treated with IV Dimenhydrinate/Dexamethasone/Ondansetron 4mg/Metoclopramide. The itching was initially treated with pheniramine maleate and, if not settled, then IV Naloxone.

Statistical Package for the Social Sciences (SPSS) version 26 was used for data analysis. Quantitative variables are given as Mean±Sd Deviation (SD) and t-test was applied. Side effects were presented as frequencies and percentages and Chi-square test was used to compare the groups. A *p*-value < 0.05 was considered statistically significant.

RESULTS

One hundred patients enrolled in the study were divided into two equal groups. No significant difference was found in the demographic data and surgical time duration of the two groups. (Table-I). The mean duration of analgesia in Group-B was 236.6±31.19 minutes and 1801.20±111.20 minutes in Group-A. The frequency of adverse events was calculated for both groups. (Table III). Forty-four percent patients in Group-A developed pruritus as compared to only 3% in Group-B. However, eighteen patients reported it on direct questioning only and did not require any treatment. Only four patients required

drug therapy for pruritus. PONV was also significantly higher in Group-A patients. None of the patients in both groups developed respiratory depression.

Table-I: Comparison of Demographic Data in Study Group (n = 100)

	Group-A n = 50 Mean±SD	Group-B n = 50 Mean±SD	*p*-value
Age (years)	29.46±4.26	28.68±4.44	0.65
Weight (kg)	63.54±3.22	63.06±2.66	0.21
Height (cm)	162.00±44.00	162.00±34.00	0.05
Duration of surgery (minutes)	55.54±6.59	55.88±6.91	0.58

Table-II: Comparison of Postoperative Analgesia in Study Groups (n= 100)

	Group-A n = 50 Mean±SD	Group-B n = 50 Mean±SD	*p*-value
Duration of Analgesia (minutes)	1801.20±111.20	236.60±31.19	<0.01

Table-III: Frequency of Side Effects in Study Groups (n=100)

		Group-A n = 50	Group-B n = 50	*p*-Value
Pruritus	Mild	18(36%)	3(6%)	<0.01
	Severe	4(8%)	0	
Postoperative Nausea and Vomiting	Mild	14(28%)	6(12%)	0.02
	Severe	3(6%)	0	

DISCUSSION

Opioids have been in use for the control of pain for centuries. They are most widely used to control postoperative pain.[3] Opioids are administered via various routes.[9] Increased use of neuraxial anaesthesia for cesarean sections not only increased the safety but also provided an alternative route for the administration of analgesics. It is now established that highly specific opioid receptors are present on the substantia gelatinosa and direct application of opioids to these receptors results in analgesia.[11] This discovery increased the use of opioids in neuraxial anaesthesia. The opioids administered via the epidural route diffuse through the dura into the intrathecal space. Morphine is widely distributed in CSF and binds to these receptors on the dorsal horn of the spinal cord. Thus, it reliably prevents nociceptive input from multiple dermatomes and produces analgesia.[12] Bernards et al. showed a much greater bioavailability of morphine, which is hydrophilic, as compared to lipophilic opioids after epidural administration.[13] In previous experimental studies, it is observed that after peri-spinal administration lipid solubility is inversely proportional to spinal selectivity, so it is higher for hydrophilic drugs.[11]

Palmer et al. reported that epidural morphine has a ceiling effect at 3.75mg.[14] It is established in previous studies that the incidence of adverse effects increases with the increase in the epidural dose of morphine. Usually, it is lesser when the epidural dose is less than 5mg. Yurashevich *et al.*, stated that 3mg epidural morphine is an adequate balance between analgesia and adverse effects.[15]

As in the previous studies, patients of Group-A who received epidural morphine remained pain-free for 24 hours.[3,7,9,10] We found that a single dose of 3mg epidural morphine easily meets the first 24-hour analgesic requirement of a patient.

Pruritus was observed in 44% of patients receiving epidural morphine in our study. The incidence of pruritus was comparable with previous studies.[9,10,15,16] It is established in previous studies that the incidence of pruritus is not related to the dose of morphine. However, it is worth mentioning that pruritus did not bother most of the patients. It was noted only on direct questioning. Only in four patients it was severe enough that they required therapy, where IV Promethazine 15mg was given. None of the patients required a second drug. Although the mechanism of pruritus is complex it is considered that the interaction of morphine with 5-HT3 receptors plays some role in its genesis.[16] All our patients received Ondansetron 8mg preoperatively which may also be a factor in reducing the severity of symptoms.

PONV was present in both groups, significantly more in patients who received morphine. Only 3 patients in that group required therapy more than once. All previous investigations have shown morphine increased PONV even at very low doses.[9,10,15,17]

The major safety concern in using epidural morphine is delayed respiratory depression.[10,15,17] It is the main reason for its reluctant use in our clinical practice. In our study, none of the patients developed hypopnea, a fall in SpO2 or respiratory depression. The obstetric patients are usually anxious and additionally, progesterone improves ventilation by increasing respiratory centre sensitivity to CO2.[18] Also in previous studies it was found that respiratory depression occurs at an epidural dose of 4mg or

more.[10,11] However, more studies with a larger sample size may be required to find the exact danger.

LIMITATION OF STUDY

We noted that the present study has a few limitations. A smaller sample size was the main limitation in identifying the danger of delayed respiratory depression. A study with a larger sample size preferably multicentre can do this more accurately. We used oxygen saturation (Spo2) measured by pulse oximetry and respiratory rate for the inadequacy of ventilation is less reliable and sensitive. Studies with more sensitive measuring tools like end-tidal CO2 can detect respiratory depression early and reliably detect minor changes in ventilation. Moreover, Visual Analogue Scale was used for pain assessment which is entirely subjective and largely depends on pain threshold and perception that vary from individual to individual. A large sample size can overcome this.

CONCLUSION

We found that 3mg epidural morphine provided analgesia for a prolonged duration. It is safe in terms of respiratory risks. However, the incidence of pruritus, nausea and vomiting increased with epidural morphine.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

IUH & SSU: Data acquisition, data analysis, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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