

## A Prospective Observational Hospital-Based Assessment of the Epidural or Intrathecal Morphine for Post-Operative Analgesia Following Laparoscopic Endometriosis Surgery

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### Abstract

**Aim:** The aim of the present study was to assess epidural or intrathecal morphine for post-operative analgesia following laparoscopic endometriosis surgery.

**Methods:** The present study was department of Anesthesia, Anugrah Narayan Magadh Medical College and Hospital, Gaya, India for 15 months and 100 patients were included in the study.

**Results:** Majority of the patients (26%) were belonged to overweight (25.00–29.99) category followed by 24% Obesity class III ( $\geq 40$ ). 78% cases completed  $\leq 12$  years of school and 68% were married. 66% had no analgesia followed by 32% non-opioid analgesia. Mean pain scores were significantly higher at one week (1.62,  $P < 0.0001$ ), four weeks (0.63,  $P = 0.02$ ), and six months (0.27,  $P = 0.04$ ), but not at three months following surgery. During the first two postoperative days, opioid analgesia (98%,  $P = 0.09$ ) and NSAIDS (60%,  $P = 0.7$ ), a significantly higher proportion of patients required Paracetamol (95%,  $P = 0.03$ ). At 3–5 days after surgery. Analgesic use was comparable between groups after 60 days after surgery.

**Conclusion:** The results of this study showed that laparoscopic surgery for endometrial cancer is associated with less need for epidural and postoperative analgesic prescription compared with open surgery, saving on costs of analgesia and highlighting a further significant benefit to patients and the healthcare system of laparoscopic treatment over traditional open abdominal surgery.

**Keywords:** Epidural, intrathecal morphine, analgesia, laparoscopy, endometriosis

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### Introduction

Regional analgesia with epidural analgesia (EDA) in abdominal surgery is recommended in most enhanced recovery after surgery (ERAS) protocols for use both during surgery and postoperatively. [1,2] Single-dose intrathecal morphine provides

good analgesia during the first postoperative days after abdominal cancer surgery, [3–6] and improves the recovery after hysterectomy for benign conditions. [7,8] Pain is an important component in the assessment of health-related quality of life

(QoL). Besides the human suffering, insufficiently treated postoperative pain complicates mobilisation, increases the risk for complications and might prolong hospitalisation.

A critical element of ERAS programs is perioperative and postoperative analgesia. Not only does effectively administered analgesia enable greater patient satisfaction by minimising acute postoperative pain, but through alleviating the acute physiological stress response to surgery it facilitates enhanced recovery outcomes including early mobilisation and return to normal activity, reduced length of hospital stay, and reduced cardiac, respiratory and gastrointestinal postoperative complications leading to improved long-term patient survival rates. [9] The optimal analgesic regime for surgical procedures is a critical clinical question that remains under ceaseless debate as the field of anaesthesia evolves. A multimodal approach combining regional anaesthesia, centrally-acting analgesics such as paracetamol, and drugs with a peripheral nonsteroidal anti-inflammatory effect is recommended to minimise the opioid-related side effects while maintaining an effective level of pain control. [10] Epidural analgesia has been considered the cornerstone analgesic modality for major surgeries due to its ability to provide superior postoperative pain control (as measured by visual analogue pain scores at rest and on movement) compared to intravenous opioid administration. [11] This is regardless of the type of surgery, type and time of pain assessment, analgesic agent, and epidural regimen. [12,13]

Additionally, intra-operative and post-operative opioid requirements were found to be significantly reduced up to 48 hours after surgery. The primary concern with intrathecal morphine is the increased risk of postoperative respiratory depression. [14] Consequently, patients who have been managed with intrathecal opioid analgesia require close monitoring in an post-

anaesthetic care unit (PACU) or intensive care unit (ICU) post-operation, and naloxone is administered to reverse opioid-induced respiratory depression.

The aim of the present study was to assess epidural or intrathecal morphine for post-operative analgesia following laparoscopic endometriosis surgery.

### Materials and Methods

The present study was department of Anesthesia, Anugrah Narayan Magadh Medical College and Hospital, Gaya, India for 15 months and 100 patients were included in the study.

Women were eligible if they were 18 years or older and had a histologically confirmed endometrioid adenocarcinoma of the endometrium of any grade, an Eastern Cooperative Oncology Group (ECOG) score of less than two, and imaging studies (computed tomography (CT) of the abdomen and pelvis and chest radiograph or chest CT) suggesting the absence of extra uterine disease.

Patients were excluded if they had histological cell type other than endometrioid on curettage, clinically advanced disease (stage II–IV) or bulky lymph nodes on imaging, uterine size greater than 10 weeks of gestation, estimated life expectancy of less than 6 months, medically unfit for surgery, or patient compliance or geographic proximity preventing adequate follow-up or if they are unfit to complete quality of life questionnaires.

Details of medication use including medication name, dose, frequency, unit, route of administration, start date, and end date of prescription were recorded for each patient. Information was collected in detail during the perioperative period and then during the patients' postoperative one-week, four-weeks, three month and six-month data clinical follow-up. Recorded start dates and end dates of analgesic prescription were used to categorise

analgesic use into more distinct periods of time, up to a maximum record postoperatively.

Free-text entries of all medication names were scanned and classified into drug classes by one medical professional. All drugs classified as analgesics were further categorised by one of the authors in consultation with anaesthetists, into opioid and non-opioid analgesia, and opioid analgesics further classified by route of administration (epidural, parenteral, or oral).

#### Statistical Analysis

Baseline demographic and clinical characteristics were compared between treatment arms using descriptive statistics. Descriptive statistics and chi-squared tests

of heterogeneity were used to compare epidural, parenteral, or oral opioid requirements within two days of surgery and postoperative opioid and non-opioid analgesic requirements up to 10 months following surgery between treatment arms, based on comparisons of prescription start and end dates to date of surgery. Perioperative opioid use within two days of surgery was categorized by the most invasive route of administration for each patient. Long-term use of analgesics was explored by counting each patient in more than one analgesic category if they were prescribed more than one type of analgesic class. *t*-tests were used to compare postoperative pain scores between treatment arms.

#### Results

**Table 1: Patient details**

<b>Variables</b>	<b>N=100</b>
Age in years, mean (SD)	56 (12)
<b>BMI category N (%)</b>	
Normal (18.50–24.99)	14 (14)
Overweight (25.00–29.99)	26 (26)
Obesity class I (30.00–34.99)	20 (20)
Obesity class II (35.00–39.99)	16 (16)
Obesity class III ( $\geq 40$ )	24 (24)
<b>Education</b>	
Completed $\leq 12$ years of school	78 (78)
Completed $> 12$ years of school	22 (22)
<b>Marital status</b>	
Married or living together	68 (68)
Other	32 (32)
<b>Employment</b>	
Retired	46 (46)
Employed full time	14 (14)
Employed part time or casual	10 (10)
Other	30 (30)
<b>Baseline analgesic use</b>	
No analgesia	66 (66)
Non-opioid analgesia	32 (32)
Opioid analgesia	2 (2)

Majority of the patients (26%) were belonged to overweight (25.00–29.99) category followed by 24% Obesity class III ( $\geq 40$ ). 78% cases completed  $\leq 12$  years of school and 68% were married. 66% had no analgesia followed by 32% non-opioid analgesia.

**Table 2: Pain score**

Pain score	N%	P Value
1 week	1.62 (2.01)	<0.0001
4 weeks	0.63 (1.34)	0.02
3 months	0.48 (1.39)	0.55
6 months	0.27 (0.98)	0.04

Mean pain scores were significantly higher at one week (1.62,  $P < 0.0001$ ), four weeks (0.63,  $P = 0.02$ ), and six months (0.27,  $P = 0.04$ ), but not at three months following surgery.

**Table 3: Postoperative analgesic use, excluding 7 pts without 6-week follow-up**

Pain score	N%	P Value
<b>Analgesic classes 0–2 days after surgery</b>		
Opioid	98 (98)	0.09
NSAID	60 (60)	0.65
Paracetamol	95 (95)	0.03
No analgesia	-	-
<b>Analgesic classes 3–5 days after surgery</b>		
Opioid	22 (22)	<0.0001
NSAID	20 (20)	<0.0001
Paracetamol	60 (60)	<0.0001
No analgesia	30 (30)	-
<b>Analgesic classes 6–14 days after surgery</b>		
Opioid	15 (15)	<0.0001
NSAID	15 (15)	0.0032
Paracetamol	45 (45)	<0.0001
No analgesia	48 (48)	-
<b>Analgesic classes 15–60 days after surgery</b>		
Opioid	10 (10)	0.015
NSAID	10 (10)	0.24
Paracetamol	30 (30)	0.0002
No analgesia	60 (60)	-
<b>Analgesic classes 61–150 days after surgery</b>		
Opioid	6 (6)	0.98
NSAID	5 (5)	0.63
Paracetamol	10 (10)	0.16
No analgesia	82 (82)	-
<b>Analgesic classes 151–310 days after surgery</b>		
Opioid	3 (3)	0.78
NSAID	3 (3)	0.89
Paracetamol	5 (5)	0.94
No analgesia	90 (90)	-

During the first two postoperative days, opioid analgesia (98%,  $P = 0.09$ ) and NSAIDs (60%,  $P = 0.7$ ), a significantly higher proportion of patients required Paracetamol (95%,  $P = 0.03$ ). At 3–5 days after surgery. Analgesic use was comparable between groups after 60 days after surgery.

## Discussion

Epidural analgesia involves injecting a variety of medications into the epidural space, for the purpose of pain relief whereas epidural anaesthesia connotes anaesthesia induced by injecting local anaesthetic agents in the epidural space and is instituted for conducting surgeries. Epidural analgesia is a desirable way to provide post-operative pain relief and reduce need for oral or injectable opioids, and simultaneously accelerating recovery from surgery. [15] Low-dose epidural local anaesthetic agents, in addition to producing analgesia, without overt sensory/motor blockade or systemic opioid-associated adverse effects, can have additional beneficial effects on bowel mobility. Epidural opioid doses are much smaller than those required systemically. Epidural analgesia quickens physiologic functions back to normal and thereby prevent prolonged immobility and hospitalization. [16] Post-operative pain relief can also be carried out through intrathecal (IT) route via usage of opioids. IT opioids have been recognised as a reliable method of post-operative pain management over a century. The first opioid used by the IT route was morphine and as an analgesic it regarded as the gold standard or benchmark in clinical practice. [17]

Epidural analgesia is provided by an epidural block given in a lateral or sitting position, which is typically driven by the anaesthesiologist and the patient's preferences. The sitting position is preferred when the spinous processes are difficult to palpate. Silva and Halpern [18] observed that neither the lateral nor the

sitting posture was obviously superior in terms of patient comfort, heavier individuals favoured the sitting position. To detect the midline, estimate the depth of the epidural space and the level of puncture ultrasound guided identification of the midline may be helpful. For the postoperative analgesia after laparoscopic endometriosis surgery, intrathecal or epidural morphine are typically employed. According to one study, epidural morphine alone was inferior to IT morphine for postoperative analgesia after laparoscopic endometriosis surgery. For post-operative analgesia, both intrathecal and epidural morphine are reportedly effective; however, it is unclear whether there is a significant difference between the two routes via which a single dosage of morphine is administered. [19] According to the literature by Hassan et al. [20] and one retrospective investigation by Coppes et al [21], epidural morphine is probably less effective for post-operative analgesia than intrathecal morphine.

Many people view epidural analgesia as an ideal postoperative analgesic approach for laparoscopic endometriosis surgery. The epidural has the potential to provide complete analgesia as long as it is in situ. To do this, typically an opioid and an epidural local anaesthetic are combined. Ambulatory epidural analgesia allows the patient to move around and undergo their daily activities pain-free. [22] There are many benefits of IT morphine after laparoscopic endometriosis surgery, IT morphine reduces pain intensity during ambulation and rest. Morphine-sparing is more noticeable following abdominal surgery as opposed to cardiac-thoracic surgery. To reduce postoperative pain after major surgery, intrathecal morphine without local anaesthetic agent is frequently administered with general anaesthesia. It is necessary to quantify risk-benefit and to evaluate dose-response. [23]

Obese patients with obstructive sleep apnea (OSA) are more likely to suffer upper

airway obstruction with opioids usage so need to be closely monitored. In fact, obese individuals may have altered tissue concentrations of morphine due to its lipophilic characteristics, as well as a marked reduction in the clearance of its glucuronide metabolites, putting them at an increased risk of respiratory depression. [24] Based on pain scores, postoperative analgesia was evaluated in five randomized controlled trials. [25-28] Patients receiving IT morphine showed significantly reduced pain scores during the first 24 hours following surgery, as compared to epidural. Patients receiving intrathecal morphine showed significantly reduced pain scores when compared to epidural for the whole 72-hour follow-up period. [25] Therefore, our chosen studies suggest that intrathecal morphine offers superior analgesia to epidural analgesic modalities for up to 24 hours following surgery. [28]

Camann et al. [29] reported that Intrathecal morphine provided analgesia as effective as epidural morphine. The results of each research proved variable, it is believed that single-shot intrathecal morphine provides analgesia comparable to continuous epidural analgesia. Overall, our findings also indicate that the best analgesic for immediate postoperative pain is single-dose IT morphine. In endometriosis surgery, De Oliveira et al. [30] compared the variable model that used significantly less analgesic dose and had significantly less demand than the base model, but there was no difference in the side effects. In a recent study by Jung et al [31], the cumulative morphine requirements were much lower in the optimised background infusion mode in laparoscopic endometriosis surgery patients, with no change in the requirements of antiemetic use.

### Conclusion

The results of this study showed that laparoscopic surgery for endometrial cancer is associated with less need for epidural and postoperative analgesic prescription compared with open surgery,

saving on costs of analgesia and highlighting a further significant benefit to patients and the healthcare system of laparoscopic treatment over traditional open abdominal surgery.

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