

A Hospital Based Study Assessing Epidural or Intrathecal Morphine for Post-Operative Analgesia Following Laparoscopic Endometriosis Surgery: An Observational Study

Soumya Singh¹, Amit Kumar Singh², Uma Shanker Singh³

¹Senior Resident, Department of Anesthesiology, AIIMS, Patna, Bihar, India

²Senior Resident, Department of General Medicine, AIIMS, Patna, Bihar, India

³Associate Professor, Department of Pathology, Mahatma Gandhi Medical College, Jamshedpur, Jharkhand, India

Received: 03-01-2023 / Revised: 01-03-2023 / Accepted: 20-03-2023

Corresponding author: Dr. Amit Kumar Singh

Conflict of interest: Nil

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 conducted at department of Anesthesiology, AIIMS, Patna, Bihar, India for 10 months and 100 patients were included in the study.

Results: Majority of the patients (28%) were belonged to overweight (25.00–29.99) category followed by 22% Obesity class III (≥ 40). 75% cases completed ≤ 12 years of school and 65% were married. 65% 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.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

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. 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]

Endometriosis is the development of endometrial glands or stroma outside the uterine cavity, in the pelvis, ovaries, and fallopian tubes. Induction, in situ development, and transplantation are potential mechanisms of its growth at ectopic sites. [9] Endometrial cells can move from the uterus to other part of the body via lymphatic or blood circulation, as well as along the fallopian tubes. According to the induction theory, a combination of hormonal, immune, and genetic variables can cause undifferentiated cells to develop into endometrial tissue. [10]

Laparoscopy is the most common method used in management of endometriosis and it also eliminates endometriosis-related scar tissue, implants, and cysts. [11] Laparoscopy is a low-risk, minimally invasive procedure to treat endometriosis and it is routinely performed under general anaesthesia as a day care surgery. The majority of patients are discharged from the hospital on the same day. However, some patients may need overnight observation. [12]

The most common symptom in women suffering from endometriosis is pain. Women can feel a variety of pains, such as dyspareunia, dysmenorrhoea, and pelvic pain. High numbers of sensory and autonomic nerve fibres are present in endometriotic lesions, providing a pathway for painful sensations. A variety of immunological and inflammatory cells are stimulated by endometriosis, which exhibits an inflammatory condition. These immune cells release immune modulators that intensify pain perception. The post-operative pain following laparoscopic endometriosis surgery can be alleviated by using epidural and intrathecal morphine. [13]

Although epidural analgesia may decrease the risk of cardiovascular and pulmonary complications in high-risk patients undergoing major surgery, it is invasive, costly, time consuming, and labour

intensive. There is developing evidence that other forms of regional analgesia may be more cost effective without sacrificing efficacy. [14,15] Minimally invasive procedures have been found to be associated with smaller postoperative analgesia requirements compared with open surgery in patients treated for gynaecological cancers [16,17] and in ovarian metastasectomy from gastric cancer. [18]

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 conducted at department of Anesthesiology, AIIMS, Patna, Bihar, India for 10 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 extrauterine 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

Variables	N=100
Age in years, mean (SD)	55 (10)
BMI category N (%)	
Normal (18.50–24.99)	12 (12)
Overweight (25.00–29.99)	28 (28)
Obesity class I (30.00–34.99)	20 (20)
Obesity class II (35.00–39.99)	18 (18)
Obesity class III (≥ 40)	22 (22)
Education	
Completed ≤ 12 years of school	75 (75)
Completed > 12 years of school	25 (25)
Marital status	
Married or living together	65 (65)
Other	35 (35)
Employment	
Retired	45 (45)
Employed full time	15 (15)
Employed part time or casual	10 (10)
Other	30 (30)
Baseline analgesic use	
No analgesia	65 (65)
Non-opioid analgesia	32 (32)
Opioid analgesia	3 (3)

Majority of the patients (28%) were belonged to overweight (25.00–29.99) category followed by 22% Obesity class III (≥ 40). 75% cases completed ≤ 12 years of school and 65% were married. 65% 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
Analgesic classes 0–2 days after surgery		
Opioid	98 (98)	0.09
NSAID	60 (60)	0.65
Paracetamol	95 (95)	0.03
No analgesia	-	-
Analgesic classes 3–5 days after surgery		
Opioid	22 (22)	<0.0001
NSAID	20 (20)	<0.0001
Paracetamol	60 (60)	<0.0001
No analgesia	30 (30)	-
Analgesic classes 6–14 days after surgery		
Opioid	15 (15)	<0.0001
NSAID	15 (15)	0.0032
Paracetamol	45 (45)	<0.0001
No analgesia	48 (48)	-
Analgesic classes 15–60 days after surgery		
Opioid	10 (10)	0.015
NSAID	10 (10)	0.24
Paracetamol	30 (30)	0.0002
No analgesia	60 (60)	-
Analgesic classes 61–150 days after surgery		
Opioid	6 (6)	0.98
NSAID	5 (5)	0.63
Paracetamol	10 (10)	0.16
No analgesia	82 (82)	-
Analgesic classes 151–310 days after surgery		
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. [19] 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 prolong immobility and hospitalization. [20] 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. [21]

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 [22] 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. [23] According to the literature by Hassan et al. [24] and one retrospective investigation by Coppes et al [25], 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. [26] 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. [27]

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. [28] Based on pain scores, postoperative analgesia was evaluated in five randomized controlled trials. [29-32] 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. [29] Therefore, our chosen studies suggest that intrathecal morphine offers superior analgesia to epidural analgesic modalities for up to 24 hours following surgery. [32]

Camann et al. [33] 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. [34] 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 [35], 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.

References

1. Nygren J, Thacker J, Carli F, Fearon KC, Norderval S, Lobo DN, Ljungqvist O, Soop M, Ramirez J. Guidelines for perioperative care in elective rectal/pelvic surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations. *Clinical nutrition*. 2012 Dec 1;31(6): 801-16.
2. Feldheiser A, Aziz O, Baldini G, Cox BP, Fearon KC, Feldman LS, Gan TJ, Kennedy RH, Ljungqvist O, Lobo DN, Miller T. Enhanced Recovery After Surgery (ERAS) for gastrointestinal surgery, part 2: consensus statement for anaesthesia practice. *Acta Anaesthesiologica Scandinavica*. 2016 Mar;60(3):289-334.
3. Devys JM, Mora A, Plaud B, Jayr C, Laplanche A, Raynard B, Lasser P, Debaene B. Intrathecal+ PCA morphine improves analgesia during the first 24 hr after major abdominal surgery compared to PCA alone. *Canadian Journal of Anesthesia*. 2003 Apr 1;50(4):355.
4. Andrieu G, Roth B, Ousmane L, Castaner M, Petillot P, Vallet B, Villers A, Lebuffe G. The efficacy of intrathecal morphine with or without clonidine for postoperative analgesia after radical prostatectomy. *Anesthesia & Analgesia*. 2009 Jun 1;108(6):1954-7.
5. Sakowska M, Docherty E, Linscott D, Connor S. A change in practice from epidural to intrathecal morphine analgesia for hepato-pancreato-biliary surgery. *World journal of surgery*. 2009 Sep; 33:1802-8.
6. Bujedo BM, Santos SG, Azpiazu AU. A review of epidural and intrathecal opioids used in the management of postoperative pain. *J Opioid Manag*. 2012 May 1;8(3):177-92.

7. Borendal Wodlin N, Nilsson L, Kjölhede P, GASPI Study Group. The impact of mode of anaesthesia on postoperative recovery from fast-track abdominal hysterectomy: a randomised clinical trial. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2011 Feb;118(3):299-308.
8. Kroon UB, Rådström M, Hjelthe C, Dahlin C, Kroon L. Fast-track hysterectomy: a randomised, controlled study. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 2010 Aug 1;151(2):203-7.
9. Jiang L, Yan Y, Liu Z, Wang Y. Inflammation and endometriosis. *Frontiers in Bioscience-Landmark*. 2016 Jun 1;21(5):941-8.
10. Signorile PG, Baldi F, Bussani R, Viceconte R, Bulzomi P, D'Armiento M, D'Avino A, Baldi A. Embryologic origin of endometriosis: analysis of 101 human female fetuses. *Journal of cellular physiology*. 2012 Apr;227(4):1653-6.
11. Jacobson TZ, Duffy JM, Barlow DH, Farquhar C, Koninckx PR, Olive D. Laparoscopic surgery for subfertility associated with endometriosis. *Cochrane Database of Systematic Reviews*; c2010, (1).
12. Duffy JM, Arambage K, Correa FJ, Olive D, Farquhar C, Garry R, Barlow DH, Jacobson TZ. Laparoscopic surgery for endometriosis. *Cochrane Database of Systematic Reviews*; c2014, (4).
13. Fauconnier A, Staraci S, Huchon C, Roman H, Panel P, Descamps P. Comparison of patient-and physician-based descriptions of symptoms of endometriosis: a qualitative study. *Human reproduction*. 2013 Oct 1;28(10):2686-94.
14. Rawal N. Epidural technique for postoperative pain: gold standard no more?. *Regional Anesthesia & Pain Medicine*. 2012 May 1;37(3):310-7.
15. Tilleul P, Aissou M, Bocquet F, Thiriart N, Le Grelle O, Burke MJ, Hutton J, Beaussier M. Cost-effectiveness analysis comparing epidural, patient-controlled intravenous morphine, and continuous wound infiltration for postoperative pain management after open abdominal surgery. *British journal of anaesthesia*. 2012 Jun 1;108(6):998-1005.
16. Martinek IE, Haldar K, Tozzi R. Laparoscopic surgery for gynaecological cancers in obese women. *Maturitas*. 2010 Apr 1;65(4):320-4.
17. Medeiros LR, Stein AT, Fachel J, Garry R, Furness S. Laparoscopy versus laparotomy for benign ovarian tumor: a systematic review and meta-analysis. *International Journal of Gynecologic Cancer*. 2008 May 1;18(3).
18. Lee M, Paek J, Lee SH, Yim GW, Kim SW, Kim S, Kim JH, Kim YT, Nam EJ. Feasibility and surgical outcomes of laparoscopic metastasectomy in the treatment of ovarian metastases from gastric cancer. *International Journal of Gynecologic Cancer*. 2011 Oct 1;21(7).
19. Simmons SW, Taghizadeh N, Dennis AT, Hughes D, Cyna AM. Combined spinal epidural versus epidural analgesia in labour. *Cochrane database of systematic reviews*; c2012, (10).
20. Bos EM, Hollmann MW, Lirk P. Safety and efficacy of epidural analgesia. *Current opinion in anaesthesiology*. 2017 Dec 1;30(6):736-42.
21. Gehling M, Tryba M. Risks and sideeffects of intrathecal morphine combined with spinal anaesthesia: a metaanalysis. *Anaesthesia*. 2009 Jun;64(6):643-51.
22. Silva M, Halpern SH. Epidural analgesia for labor: Current techniques. *Local and regional anesthesia*. 2010 ;3:143.
23. Kjölhede P, Bergdahl O, Wodlin NB, Nilsson L. Effect of intrathecal morphine and epidural analgesia on postoperative recovery after abdominal

- surgery for gynecologic malignancy: an open-label randomised trial. *BMJ open*. 2019 Mar 1;9(3):e024484.
24. Hassan WM, Nayan AM, Hassan AA, Zaini RH. Comparison of single-shot intrathecal morphine injection and continuous epidural bupivacaine for post-operative analgesia after elective abdominal hysterectomy. *The Malaysian journal of medical sciences: MJMS*. 2017 Dec;24(6):21.
25. Coppes OJ, Yong RJ, Kaye AD, Urman RD. Patient and surgery-related predictors of acute postoperative pain. *Current pain and headache reports*. 2020 Apr;24(4):1-8.
26. Breivik H, Norum H, Fenger-Eriksen C, Alahuhta S, Vigfusson G, Thomas O, et al. Reducing risk of spinal haematoma from spinal and epidural pain procedures. *Scandinavian Journal of Pain*. 2018 Apr 1;18(2):129-50.
27. Meylan N, Elia N, Lysakowski C, Tramer MR. Benefit and risk of intrathecal morphine without local anaesthetic in patients undergoing major surgery: meta-analysis of randomized trials. *British journal of anaesthesia*. 2009 Feb 1;102(2):156-67.
28. Sun K, Liu D, Chen J, Yu S, Bai Y, Chen C, et al. Moderate-severe post operative pain in patients undergoing video-assisted thoracoscopic surgery: Aretrospective study. *Scientific reports*. 2020 Jan 21;10(1): 1-8.
29. Forero M, Rajarathinam M, Adhikary S, Chin KJ. Continuous erector spinae plane block for rescue analgesia in thoracotomy after epidural failure: a case report. *A&A Practice*. 2017 May 15;8(10):254-6.
30. Yalamuri S, Klinger RY, Bullock WM, Glower DD, Bottiger BA, Gadsden JC. Pectoral fascial (PECS) I and II blocks as rescue analgesia in a patient undergoing minimally invasive cardiac surgery. *Regional Anesthesia & Pain Medicine*. 2017 Nov 1;42(6):764-6.
31. Wilson JM, Lohser J, Klaibert B. Erector spinae plane block for postoperative rescue analgesia in thoracoscopic surgery. *Journal of cardiothoracic and vascular anesthesia*. 2018 Dec 1;32(6): e5-7.
32. Svider PF, Nguyen B, Yuhan B, Zuliani G, Eloy JA, Folbe AJ. Perioperative analgesia for patients undergoing endoscopic sinus surgery: an evidencebased review. *International forum of allergy & rhinology* 2018 Jul (Vol. 8, No. 7, pp. 837-849).
33. Camann WR, Denney RA, Holby ED, Datta S. A comparison of intrathecal, epidural, and intravenous sufentanil for labor analgesia. *The Journal of the American Society of Anesthe siologists*. 1992 Nov 1;77(5):884-7.
34. De Oliveira GS, Agarwal D, Benzon HT. Perioperative single dose ketorolac to prevent postoperative pain: a meta-analysis of randomized trials. *Anesthesia & Analgesia*. 2012 Feb 1;114(2):424-33.
35. Jung KT, So KY, Kim SU, Kim SH. The optimizing background infusion mode decreases intravenous patient-controlled analgesic volume and opioid consumption compared to fixed-rate background infusion in patients undergoing laparoscopic cholecyst ectomy: A prospective, randomized, controlled, double-blind study. *Medicina*. 2021 Jan 6;57(1):42.