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Epidural or intrathecal morphine for post-operative analgesia following laparoscopic endometriosis surgery

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Abstract

Background: Endometriosis is the development of endometrial glands or stroma outside the uterine cavity, in the pelvis, ovaries, and fallopian tubes. Laparoscopy is the most common method used in management of endometriosis and it also eliminates endometriosis-related scar tissue, implants, and cysts. Epidural or intrathecal morphine is an effective way to alleviate post-operative pain after laparoscopic endometriosis surgery.

Methods: Literature search was conducted in three electronic databases-Google Scholar, Cochrane (Controlled Trials Register), and PubMed (MEDLINE/Index Medicus). Postoperative pain, epidural and intrathecal morphine, laparoscopy surgery, patient-controlled analgesia (PCA), opioids, and morphine were the search criteria used.

Results: After removing duplicate studies, the search yielded 106 results. Out of which 50 full-text publications that matched the inclusion criterion were retrieved.

Conclusion: Single intrathecal morphine injection is safe and effective in managing post-operative pain, however continuous epidural analgesia is risky and difficult to manage after laparoscopic endometriosis surgery.

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

1. Introduction

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^[1]. 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^[2].

Laparoscopy is the most common method used in management of endometriosis and it also eliminates endometriosis-related scar tissue, implants, and cysts. 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^[4].

The most common symptom in women suffering from endometriosis is pain. The types of symptoms experienced by the women are depicted in Fig. 1. 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^[5].

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^[6].

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^[7].

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^[8]. IT morphine is one of the simplest, cheapest, and most reliable post-operative pain relief agent. But has several adverse effects of its own^[9].

2. Methods

This paper provides clinicians managing acute post-operative pain with a narrative review of epidural and intrathecal morphine. Literature search was conducted in three electronic databases-Google Scholar, Cochrane (Controlled Trials Register), and PubMed (MEDLINE/Index Medicus). Animal studies were also considered in the search. Postoperative pain, epidural and intrathecal morphine, laparoscopy surgery, patient-controlled analgesia, opioids, and morphine were among the search criteria. In some cases, earlier studies were cited in place of newly updated material. The procedure, benefits, complications, side effects and length of stay in hospital was examined and analysed among the collected research papers.

3. Results

After removing duplicate studies, the search yielded 106 results. Out of which 50 full-text publications that matched the inclusion criterion were retrieved. After thorough manuscript examination, 20 studies were eliminated and 15 studies were selected as they best described laparoscopic surgery, 8 were selected as they best described epidural morphine injection and 7 were selected as they best described intrathecal morphine injection.

3.1 Procedure used for epidural and intrathecal morphine

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,^[10] 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. Orthostatic hypotension and syncope may be linked to the sitting position in some patients. This makes it crucial for an assistant to support the patient continuously throughout the process^[11].

The procedure for IT morphine is a bit similar to epidural. The injections of morphine is given in the subarachnoid space between two lumbar vertebrae, typically L2-L3 or L3-L4. Because of its hydrophilic properties, morphine gradually spreads in the cerebrospinal fluid (CSF) after

administration. IT morphine provides analgesia more quickly than alternative methods of delivery via binding to spinal opioid receptors and the analgesic effect lasts for 18 to 24 hours. IT morphine is a desirable addition to postoperative pain control regimes following laparoscopic endometriosis surgery because it has the capacity to deliver sufficient analgesia at lower dosages^[12].

3.2 Comparison between epidural and intrathecal morphine

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.^[13] According to the literature by Hassan *et al.*^[14] and one retrospective investigation by Coppes *et al.*^[15], epidural morphine is probably less effective for post-operative analgesia than intrathecal morphine. However, nothing is known about the effectiveness of combining epidural analgesia with intrathecal morphine. In contrast to intrathecal morphine used alone, it was predicted that the combination of patient-controlled epidural analgesia (PCEA) and intrathecal morphine may be more effective for post-operative analgesia^[14].

3.3 Predictors of Post-operative Pain

A number of researches have evaluated the predictors of postoperative pain and drug usage. Postoperative pain is diverse and complex in severity. Pre-existing pain, anxiety, age, type of surgery, demand for information, genetic variables, and smoking history are a few of these issues. The primary predictors of postoperative analgesic use include kind of operation, age, and psychological distress. In addition, evaluating the pain score on venous cannulation before surgery is said to be a beneficial practical strategy.^[15-17]

3.4 Indication and benefits of epidural and 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.^[18] The likelihood of postoperative cardiac, pulmonary, and thromboembolic complications is also reduced with epidural analgesia. Epidural analgesia can escalate patient recovery and life quality after major surgery as a part of multimodal analgesia which is superior to intravenous drugs alone for pain management^[19].

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^[20].

3.5 Human related issues and side effects

Patient controlled analgesia (PCA) through unintentional/unauthorized administration of epidural morphine doses by family, friends, or medical staff, is a significant problem associated with negative effects. Out of 6069 PCA adverse events monitored via a database containing PCA error studies, it was reported that 460 caused patient injury or death. Out of 12 deaths, one patient died as a result of inadvertent PCA administration by a nurse^[21]. There was a case of dysfunctional cassette design in the PCA apparatus which caused variation of the morphine formulation, which resulted in inaccurate infusion dosage administration to the patients. At various levels, both human factors and equipment design are crucial in producing major adverse outcomes. The serious side effects are uncommon, but it can cause spinal injury, breathing issues, tachycardia, and numbness or tingling, according to the American College of Obstetricians and Gynaecologists (ACOG)^[22].

3.6 Need for rescue analgesia

Eight studies^[23-30] evaluated the need for rescue analgesia following surgery. It was demonstrated that patients treated with IT morphine needed less rescue analgesia than those treated with epidural analgesia. Contrary to this, in three out of the four trials^[24, 25, 27, 30] comparing IT analgesia to epidural analgesia, patients treated with IT morphine required more rescue analgesia than patients treated with epidural analgesia. Our literature review indicates that single-dose IT morphine requires larger levels of rescue analgesia. It cannot be inferred that IT morphine has the highest analgesic potency among all regimens studied, despite the fact that it produced the lowest pain scores in many researches^[29].

3.6.1 Effect of epidural and intrathecal morphine

3.6.1.1 In Children

A retrospective study conducted by Pieters *et al.*^[31] reported ten kids who were administered IT morphine. All patients received lumbar intrathecal injections of preservative-free morphine (Duramorph®) at a dose of 0.02 mg/kg prior to the start of surgery. In all 10 children, an adequate level of postoperative analgesia was reached. For the first 15 hours following surgery, no patient needed further analgesic medications. Laryngotracheoplasty, craniofacial reconstruction, and exploratory laparotomy were among the surgical procedures in which IT morphine was administered. IT morphine can produce respiratory depression and this depression may show 24 hours after the injection. As a result, it is recommended that postoperative respiratory status must be observed for 24 hours after the dose. With this exception, IT morphine administration offers safe and efficient postoperative analgesia^[32].

3.6.1.2 In elderly and frail patients

A significant and increasingly growing number of surgical patients are senior citizens. The goal of postoperative pain management should be to reduce side effects in this subgroup. The dose does not differ significantly in healthy elderly people; however, for frail elderly patients, a strategy employing 1-2 mg boluses of epidural or IT morphine with longer time intervals and a cap on the total dose is advised.^[33]

3.6.1.3 In obese patients

Obese patients with obstructive sleep apnea (OBA) 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^[34].

3.6.1.4 Recent modalities of epidural and intrathecal morphine

The investigation of new PCA administration methods is ongoing. In spinal fusion surgery, Motamed^[35], compared a baseline infusion rate plus demand with a variable infusion (feedback based) rate plus demand. The variable model required significantly less analgesic dose and had significantly less demand than the baseline infusion model, but there was no difference in the side effects.

In a recent study by Jung *et al.*^[36], the cumulative morphine requirements were much lower in the optimised background infusion mode in laparoscopic cholecystectomy patients, with no change in the need of antiemetic use. Before implementing the ways of opioids administration post operatively, more research on various types of surgery is required.

3.7 Length of stay in hospital

Five researches^[23, 25-28] evaluated duration of hospital stay of the patients. The trials found some difference in length of stay (LOS) between patients who received IT morphine and those who received epidural. However, all five studies comparing the length of stay (LOS) of patients treated with continuous epidural infusion with those treated with intrathecal morphine, indicated that patients treated with intrathecal morphine had a shorter length of stay. This can be explained by patients receiving intrathecal morphine needing less intravenous fluid therapy, allowing for an earlier removal of the urinary catheter and a quicker time to mobilize^[34].

3.8 Complications

Epidurals are quite safe because of substantial medical and technological advancements. Intravenous fluids are used to alleviate blood pressure drops. Spinal fluid leakage has the potential to cause headaches. Typically, oral painkillers, caffeine, and IV fluids are used as treatments. Patients occasionally experience soreness at the catheter insertion site for a few. Back pain does not persist long.^[37]

Comparing IT morphine to epidural analgesia, no evidence showed that it increased the risk of serious complications during or after surgery. Both the George *et al.*^[38] experiment and the Gehling *et al.*^[39] trial found that patients receiving intrathecal morphine had a higher incidence of pruritus and nausea. Peixoto *et al.*^[40] reported overall twenty-seven epidurals failure and one intrathecal failure during the period of chosen studies. There is strong evidence that intrathecal analgesia has a lower failure rate than epidural analgesia. The patients required more aggressive fluid resuscitation and consequently experienced a higher rate of respiratory and gastrointestinal problems as a result of the epidural blockade. High epidural failure rates were caused by inadequate analgesia and/or hemodynamic instability^[40].

3.9 Limitations

The analgesic regimes, healthcare facilities, and results differed significantly among the publications we chose. Each trial provided a different amount of intrathecal morphine and included a different additional analgesic. Contrary, trials evaluating epidural analgesia used comparable protocols, which entailed fentanyl 2 mg/mL mixed with 0.125% bupivacaine or 0.2% ropivacaine into the thoracic epidural space.^[41] Niu *et al.*^[42] trial was the only one to evaluate continuous intrathecal morphine infusion in the context of major endometriosis surgery, but nine of the other trials evaluated single-shot intrathecal morphine. Additionally, this study included endometriosis surgery and did not employ the proper statistical methods. In comparison to our other chosen studies, the results of Niu's study have a restricted potential to be generalised. The results that were recorded in each trial were heterogeneous. Studies that concentrated mainly on minor outcomes like pruritus, sedation, and nausea failed to collect data on pain scores or significant systemic consequences. Additionally, some outcomes could be monitored in a variety of ways. For example, the consumption of rescue analgesia could be determined by the percentage of patients who needed it or by the total amount of PCA morphine given within a specific postoperative period^[42].

4. Discussion

Surgery can cause moderate to severe pain, which can lead to complications in the days and weeks that follow the procedure. Despite decades of progress in postoperative pain management, a sizeable minority of patients still report high pain scores and inadequate pain relief. Pinto *et al.*^[23] reported numerous worldwide trials, over a span of 15 years

that compared epidural to intrathecal morphine.

Based on pain scores, postoperative analgesia was evaluated in five randomized controlled trials^[23, 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]. Some researchers reported that comparison between epidural and intrathecal, morphine yielded inconclusive results. In one prospective cohort and one retrospective cohort study, comparing intrathecal with epidural analgesic regimes, it was found that intrathecal morphine was superior for the first 72 hours following surgery.

Camann *et al.*^[43] 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 indicates that the best analgesic for immediate postoperative pain is single-dose IT morphine.

In endometriosis surgery, De Oliveira *et al.*^[44] 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.*^[36], 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.

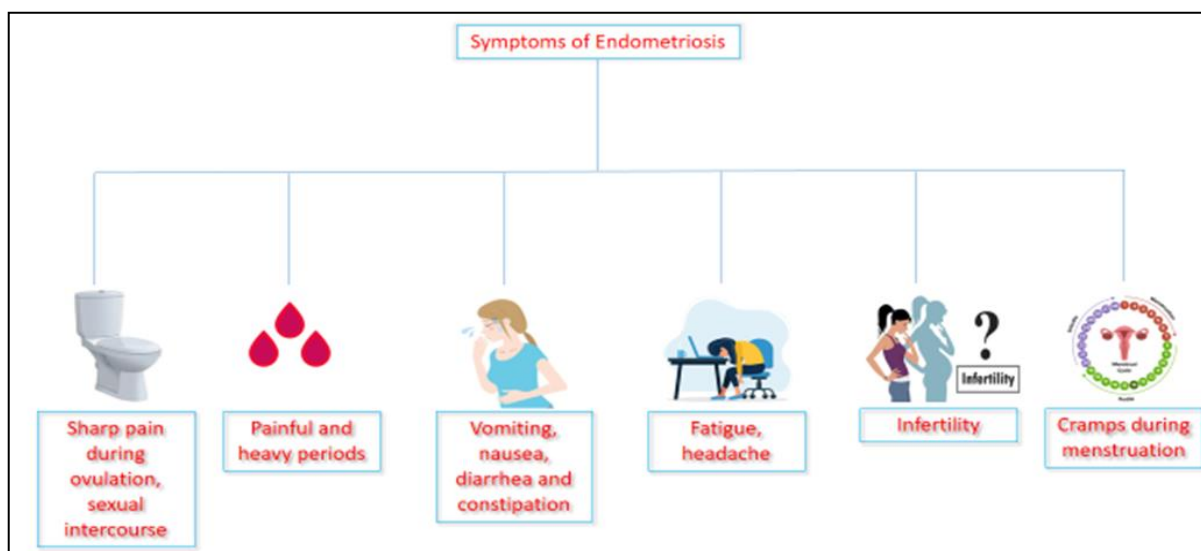


Fig 1: Symptoms of Endometriosis

5. Conclusion

This review suggests that single-shot IT morphine may be a better first-line analgesic approach for laparoscopic endometriosis surgery than epidural analgesia. Patients administered intrathecal morphine received a level of analgesia comparable to epidural analgesia, despite the fact that they need higher dosages of additional post-operative pain medication. Additionally, these individuals have a shorter LOS because they need less hydration therapy. Single intrathecal morphine is safer than its epidural

counterpart.

Conflict of Interest

Not available

Financial Support

Not available

6. References

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