Efficacy of epidural local anesthetic and dexamethasone in providing postoperative analgesia: A meta-analysis

ABSTRACT

**Background:** Dexamethasone is a potent anti-inflammatory, analgesic, and antiemetic drug. Individual randomized controlled trials found a possible benefit of epidural dexamethasone. The purpose of this meta-analysis is to estimate the benefit of epidural dexamethasone on postoperative pain and opioid consumption and to formulate a recommendation for evidence-based practice.

**Materials and Methods:** Prospective, randomized controlled trials comparing the analgesic efficacy of epidural local anesthetic and dexamethasone combination, with local anesthetic alone for postoperative pain management after abdominal surgery, were planned to be included in this meta-analysis. PubMed, PubMed Central, Scopus, and Central Register of Clinical Trials of the Cochrane Collaboration (CENTRAL) databases were searched for eligible controlled trials using the following search words: “Epidural,” “dexamethasone,” and “postoperative pain,” until February 20, 2015.

**Results:** Data from five randomized control trials have been included in this meta-analysis. Epidural dexamethasone significantly decreased postoperative morphine consumption (mean difference −7.89 mg; 95% confidence interval [CI]: −11.66 to −3.71) and number of patients required postoperative rescue analgesic boluses (risk ratio: 0.51; 95% CI: 0.41–0.63).

**Conclusion:** The present data shows that the addition of dexamethasone to local anesthetic in epidural is beneficial for postoperative pain management.

**Key words:** Dexamethasone; epidural; opioid consumption; postoperative pain

Introduction

Since its discovery in the 1940s, dexamethasone, a selective glucocorticoid agonist with strong anti-inflammatory properties, has been used in the treatment of variety of conditions such as rheumatoid arthritis, allergic disorders, bronchial asthma, inflammatory bowel disease, autoimmune disorders, and certain malignancies. Its role as a drug for postoperative nausea and vomiting (PONV) prophylaxis is well-established in literature. Apart from PONV prophylaxis, dexamethasone is being used in the perioperative settings to reduce the cerebral and airway edema. Recently, the analgesic efficacy of this drug has been the topic of intense scientific research. Epidural injection of steroids remains one of the most effective treatments for chronic pain conditions such as lumbosacral radiculopathy, sciatic, and femoral neuralgias. Administration of dexamethasone preoperatively by oral or intravenous route has been shown to provide postoperative analgesia. Several studies have analyzed the analgesic efficacy of epidural...
dexamethasone. However, randomized control trials (RCTs) are not unanimous in reporting the postoperative analgesic efficacy of epidural dexamethasone. This meta-analysis was done to assess whether epidural dexamethasone is a good adjunct to local anesthetic for postoperative analgesia.

**Materials and Methods**

The reporting of this systematic review and meta-analysis follows the PRISMA recommendations.[13]

**Protocol and registration**

A protocol for this systematic review and meta-analysis has not been registered.

**Eligibility criteria**

Prospective, randomized controlled trials comparing the analgesic efficacy of epidural local anesthetic and dexamethasone combination, with local anesthetic alone for postoperative pain management after abdominal surgery, were planned to be included in this meta-analysis. RCTs reporting at least postoperative opioid consumption was included in this analysis. We did not impose any language restriction and seek for unpublished trials or data those are not reported in published studies.

**Information sources and search method**

Two authors (BJS and SM) independently searched PubMed, PubMed Central, Scopus, Central Register of Clinical Trials of the Cochrane Collaboration (CENTRAL), and Google Scholar for eligible controlled trials using following search words: “Epidural,” “dexamethasone,” and “postoperative pain,” until February 20, 2015. The detailed search strategy in PubMed is described in Appendix 1. No non-English database was searched. A manual search was done in the reference lists of the resulting list of publications for any relevant trials.

**Study selection**

Two authors (BJS and PK) independently searched for the potentially eligible trials and selected the trials to be included. It was decided that, if any disagreement arises between these two authors, would be settled by a third author (DKB).

**Exclusion criteria**

Prospective observational studies, retrospective analysis, trials conducted in pediatric populations, case reports, case series, animal studies, and studies not reporting on any one of the predefined outcome were excluded from the analysis. However, in any study that fulfills our inclusion criteria, if any possibilities of biases are found, a sensitivity analysis was planned to be done for each outcome excluding that study.

**Data collection**

We collected the required data from the full-text of the trials. Initially, all data were tabulated in Microsoft Excel™ spreadsheet. One author (BJS) initially extracted data from the eligible trials, and these data were cross-checked independently by another author (PK). Statistical analyses were done by two authors (SM and BJS) independently and cross-validated.

**Data items**

The following data were collected from each of their studies: Name of the first author, year of publication, patient population, surgical procedure done, details of epidural anesthesia, postoperative epidural analgesic protocol, anesthetic technique and use of rescue analgesic postoperative opioid consumption, postoperative pain scores at different time points, postoperative opioid-related adverse effects, and any other reported complications. All opioid usage was converted into the equianalgesic doses of intravenous morphine for making the comparison easier.[13] If two or more studies reported the endpoint of interest, meta-analysis was done.

**Risk of bias assessment**

Quality of eligible trials was assessed using the tool of “risk of biases” according to Review Manager, version 5.2.3 software (RevMan; Cochrane Collaboration, Oxford, UK) and also by Jadad scoring system.[14] Random sequence generation, allocation concealment, blinding, incomplete data, and selective reporting were assessed independently by two authors (DKB and PK) based on the method of the trials, each was graded as “yes,” “no,” or “unclear,” which reflected a high risk of bias, low risk of bias, and uncertain bias, respectively, as per Cochrane methodology. Publication bias was assessed by visual inspection of funnel plot.

**Statistical analysis**

Meta-analyses were performed using RevMan (version 5.3.5).
Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). For continuous outcomes, a pooled mean difference (MD) was calculated using the inverse variance statistical method, as all studies have used the same unit. For dichotomous variables, pooled risk ratio (RR) was calculated using the Mantel-Haenszel method, as the number of included studies was small. The I² was used to evaluate heterogeneity of included studies. In case of significant heterogeneity (I² > 40%), random analysis model was used, and in other cases, fixed analysis model was used. All statistical variables were calculated with 95% confidence interval (95% CI). A two-sided P < 0.05 was considered significant.

**Results**

Five trials met the eligibility criteria after abstract perusal of 37 results obtained by the above-mentioned search strategy. Flow diagram of the study selection procedure has been depicted in Figure 1. Trial characteristics are shown in Table 1. Four out of five studies achieved a Jadad score of 5, and one study achieved a score of 4. All studies were done in patients undergoing abdominal surgery,\(^\text{[15-19]}\) and one study included thoracic surgery also.\(^\text{[18]}\) There was a significant variability in anesthetic regimens between trials.

Postoperative morphine consumption at 24 h was measured in all 5 trials, and it was found to be significantly lesser in epidural dexamethasone group (MD $-7.89$ mg; 95% CI: $-11.66$ to $-3.71$; $P = 0.0001$, Figure 2). Three trials\(^\text{[16,17,19]}\) reported the number of patients required rescue analgesia, and it was found; it is significantly less in patients received epidural dexamethasone (RR 0.51; 95% CI: 0.41-0.63; $P < 0.00001$, Figure 3). Analysis of two trials\(^\text{[16,17]}\) failed to show a statistically significant difference in the satisfaction score (MD 1.27; 95% CI: $-0.12$ to 2.66; $P = 0.07$).

![PRISMA flow diagram of study selection](image-url)
There was no difference in sedation score between epidural dexamethasone and placebo group (MD = 0.02; 95% CI: -0.15-0.19; \( P = 0.81 \)). No incidence of hypotension, bradycardia, and respiratory depression was reported in any of the trials.

**Discussion**

Principal finding of our meta-analysis is that the postoperative opioid consumption and the number of patients, who requested analgesia, were significantly lesser in patients who received epidural dexamethasone. Both oral and intravenous dexamethasone has been found to provide perioperative analgesia. However, no evidence suggest that epidural dexamethasone has any advantages over oral or intravenous dexamethasone, in terms of pain relief.

Controversy exists about the optimum epidural dose of dexamethasone. \( 4-8 \) mg does have been reported to provide significant opioid sparing effect. However, \( 8 \) mg dose provided superior analgesia than \( 4 \) mg dose. No incidence of hypotension, bradycardia or respiratory depression was reported after epidural dexamethasone administration. Pain relief was significantly higher in patients who received epidural dexamethasone than in those who did not.

Controversy exists about the optimum epidural dose of dexamethasone. The dose of dexamethasone required to provide significant opioid sparing effect seems to be around \( 4-8 \) mg. One study compared different doses of epidural dexamethasone. \( 4 \) mg dose provided significant analgesia than \( 6 \) mg dose. No incidence of hypotension, bradycardia or respiratory depression was reported after epidural dexamethasone administration. Pain relief was significantly higher in patients who received epidural dexamethasone than in those who did not.

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in neuraxial administration.\[24\] Further studies with better methods of assessing neurotoxic potential are needed before declaring the safety of neuraxial dexamethasone.

**Limitations**

Our meta-analysis is not free from limitations. First, the number of studies included in this analysis is small. Hence, a single study has a large influence in the ultimate outcome, which may lead to biases. Second, we have found significant heterogeneity in our primary outcome. Heterogeneity may be due to difference in the patient population, dose of epidural dexamethasone, type of surgery, volume of drug given, and dose of opioid added. However, as the number of included trials is small, a meta-regression analysis was not possible to identify source of heterogeneity. Third, there are inconsistencies in the data of acute pain-related endpoints. Because of all these reasons, we cannot apply and generalize the findings of this analysis to a general population.

**Conclusion**

The present data shows a potential role of dexamethasone as an adjuvant to local anesthetic for postoperative analgesia. However, these results should be interpreted with caution.

There is no clear assessment of neurological complications with epidural dexamethasone in most clinical trials. Additional studies are needed to support the findings of this meta-analysis, before adopting this technique in routine clinical practice.

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**Conflicts of interest**

There are no conflicts of interest.

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