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Review Article

Perioperative steroids for lumbar disc surgery: A meta-analysis of randomized controlled trials

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Abstract

Background: Our review question was “Does perioperative steroids administration, in comparison with other treatments or placebo, improve either postoperative pain control, length of hospital stay, or return to work in patients undergoing lumbar disc surgery?”

Methods: We searched PubMed, CINAHL PLUS, and Cochrane databases for randomized control trials (RCTs) studying the role of steroids for lumbar disc surgery. Studies that compared perioperative steroids with other treatments or placebo were included. Study outcomes included postoperative back pain, leg pain, length of hospital stay, and return to work. Data was extracted through a proforma. Means and mean differences were calculated for continuous data, whereas odds ratios were calculated for dichotomous data. Data were analyzed with the help of Rev Man 5.

Results: Twenty RCTs were included in the review. Quantitative analysis could be performed on 19 RCTs. Intraoperative steroids improve control of back pain at 24–48 hours. Although there was some benefit of steroid administration in controlling postoperative leg pain, it disappeared at 1 year and in the overall pooled analysis. The length of hospital stay was much shorter in the steroid group. The frequency of adverse events and complications also favored steroid administration.

Conclusion: Intraoperative epidural steroid administration offers some benefit in pain control with a significant reduction in the length of hospital stay. However, there is insufficient evidence to support the routine use of oral and intravenous steroids in the perioperative period.

Key Words: Lumbar surgery, lumbar surgery outcomes, microdiscectomy, perioperative steroids, randomized control trials

INTRODUCTION

The incidence of lumbosacral radiculopathy is estimated to be approximately 3–5%, and therefore, lumbar disc surgery is one of the most common procedures performed by spine surgeons in United States[17,18]. Because radicular pain may be partially attributed to inflammatory mediators, some surgeons have utilized
perioperative steroids\textsuperscript{(8)} (e.g., strong anti-inflammatory effect, modulation of pain receptors).\textsuperscript{(8)} Here, we reviewed the current randomized controlled trial (RCT) literature regarding the use of perioperative steroids in lumbar disc surgery.

**MATERIALS AND METHODS**

The study included an analysis of RCT studies for adult patients undergoing surgery for lumbar disc herniation who received preoperative, intraoperative, or postoperative steroids, administered through any route, i.e., oral, intravenous, or epidural. We searched PubMed, CINAHL PLUS, and Cochrane databases for randomized control trials (RCTs) studying the role of steroids for lumbar disc surgery. A detailed search strategy is given in Appendix 1. We identified the differences in the mean pain scores [e.g., visual analog scale (VAS) at 24 hours, 48 hours, 72 hours, 1 week, 1 month, and 1 year], mean length of hospital stay (LOS), mean number of days to return to work, and the percentage of adverse events (AE) in patients receiving perioperative steroids vs. control patients (who received no steroids).

**Data extraction**

Two reviewers separately and independently extracted the data, which was then recorded in Microsoft Excel. In cases where desired data was not reported by authors, the corresponding authors were contacted for more details or missing data.

**Risk of bias assessment**

Risk of bias was assessed for each of the selected RCT on six quality parameters, i.e., comparability of treatment groups, standardization of care protocol, blinding of care, adequacy of outcomes, blinding of outcomes, and completeness of follow-up. Each parameter was given a score of 1-point if it was adequately described in the article. No score was given for absence of quality parameter or inadequate description of the same. Study quality level was obtained by adding the scores of each parameter to grade the studies from a total of 6 points.

**RESULTS**

Twenty RCTs were included in this systematic review, and quantitative analysis was performed on 19 studies [Table 1]. The process of study selection is shown in Figure 1.

Two RCTs by Ludin \textit{et al}.\textsuperscript{(12)} and Hurlbert \textit{et al}.\textsuperscript{(10)} had maximum quality level of 6, whereas RCT by Debi \textit{et al}.\textsuperscript{(5)} showed the lowest quality score of 1. Most studies had quality level of 3 or 4. Summary of study characteristics is presented in Table 2.

**Postoperative back pain**

Six studies assessed postoperative back pain at 24 hours. The analysis favored the use of steroids, with a mean difference of −0.16 [95% confidence interval (CI) = −0.26, −0.05]. This difference was

| Study author and year | Comparable | Standardization of care protocol | Blinding of care | Adequate outcomes | Blinding of outcome | Completeness of Follow up | Study quality level |
|-----------------------|------------|----------------------------------|------------------|-------------------|---------------------|----------------------------|---------------------|
| Abrishamkar \textit{et al}. (2011) | Y | Y | Can’t tell | N | Y | Y | 4 |
| Aljabi \textit{et al}. (2015) | Y | Y | N | N | Y | Can’t tell | 3 |
| Aminmansour \textit{et al}. (2006) | Y | Y | Y | N | Y | Can’t tell | 4 |
| Bahari \textit{et al}. (2010) | Y | Y | Y | N | Can’t tell | Can’t tell | 3 |
| Debi \textit{et al}. (2002) | Can’t tell | Y | N | N | Can’t tell | N | 1 |
| Diaz \textit{et al}. (2012) | Y | Y | Y | Y | Y | Y | 6 |
| Dikmen \textit{et al}. (2005) | Y | Y | Can’t tell | N | Can’t tell | Y | 3 |
| Glasser \textit{et al}. (1993) | Y | Y | N | N | Y | N | 3 |
| Hurlbert \textit{et al}. (1999) | Y | Y | Y | Y | Y | Y | 6 |
| Jirarattanaphochai \textit{et al}. (2007) | Y | Y | Y | N | Y | N | 4 |
| Langmary \textit{et al}. (1995) | Y | Y | Y | N | Y | N | 4 |
| Lotfinia \textit{et al}. (2007) | Y | Y | Y | N | Y | Y | 5 |
| Lundin \textit{et al}. (2003) | Y | Y | Y | Y | Y | Y | 6 |
| Manniche \textit{et al}. (1994) | Y | Y | Y | N | Y | N | 4 |
| McNeill \textit{et al}. (2005) | Can’t tell | Y | N | N | Y | N | 3 |
| Mirzai \textit{et al}. (2002) | Y | Y | N | N | Y | Y | 4 |
| Modi \textit{et al}. (2009) | Y | Y | Y | N | N | N | 3 |
| Poberoskin \textit{et al}. (1999) | Y | Y | Y | N | Y | Can’t tell | 4 |
| Rasmussen \textit{et al}. (2008) | Y | Y | N | Y | Y | Y | 5 |
| Watters \textit{et al}. (1989) | Y | N | Y | N | Y | Y | 4 |
Table 2: Summary of methods and clinical characteristic of studies include in the review

| Author and year          | Location         | Follow-up | No. of patients | Age in years (Mean±std or median/range) | Males (%) | Operative procedure | Steroid formulation | Route of administration |
|--------------------------|------------------|-----------|-----------------|----------------------------------------|-----------|---------------------|---------------------|-----------------------|
| Abrishamkar et al. (2011)| Iran             | 2 weeks   | 66              | 45.4±10.33                             | 47        | MD                  | 40 mg MP acetate     | EPI                   |
| Aljabi et al. (2014)     | United Arab Emirates | 1 month  | 150             | 45.1±13.7                              | 43.33     | MD                  | 80 mg MP Acetate     | EPI                   |
| Aminmansour et al. (2006)| Iran             | 2 months  | 61              | 38.5±10.39                             | 57.4      | MD                  | DMZ 40 mg in 20 cc syringe | IV                     |
| Bahari et al. (2010)     | Ireland          | 8 weeks   | 100             | 39.3 (group 1); 42.7 (group 2); 41.8 (Group 3); 39.2 (Group 4) | 0.40    | MD                  | 10 mg of TAC acetone or 10 mg of TAC acetone | EPI        |
| Debi et al. (2002)       | Israel           | 1 year    | 61              | 40.9±12.14                             | 70.5      | MD, LM              | MP 80 mg acetate in 2 ml | EPI                   |
| Diaz et al. (2012)       | Canada           | 3 years   | 201             | 51                                     | 59.70     | MD, LM              | MP 80 mg acetate in 2 ml | EPI                   |
| Dikmen et al. (2005)     | Turkey           | NR        | 31              | 42.5                                   | 52        | MD, LM              | DMZ 8 mg            | EPI                   |
| Glasser et al. (1993)    | USA              | 1 month   | 32              | 46.1±4.2                               | NR        | MD, LM              | 250mg IV MP + 160mg IM MP + 30 ml of 0.25% bupivacaine with 1:200,000,80 mg MP | IV, IM, EPI |
| Hurlbert et al. (1999)   | USA              | 3 months  | 60              | 51±3.3                                 | 61.67     | MD, LM              | MP 80 mg, 1 mg morphine | EPI                   |
| Jirratannaphochai et al. (2007) | Thailand      | 3 months  | 103             | 52.0±11.6                              | 46.60     | MD, LM, PSF         | MP 80 mg, 0.375% bupivacaine infiltrated | EPI                   |
| Langmayr et al. (1995)   | Austria          | 6 months  | 26              | 43                                     | 76.92     | MD                  | Betamethasone 2 ml of IT | IT                     |
| Lotfinia et al. (2007)   | Iran             | 96 hours  | 150             | 38.09±0.86                             | 44.67     | MD                  | MP 40 mg            | EPI                   |
| Lundin et al. (2003)     | Sweden           | 2 years   | 80              | 41.15                                  | 55        | MD                  | MP 160 mg IM and 250 mg IV MP sodium succinate + 80 mg MP | IV, IM, EPI |
| Manniche et al. (1994)   | Denmark          | 156 weeks | 93              | 40.47                                  | 68.82     | MD                  | PD 50 mg daily for fourteen days of surgery, then 25 mg daily for the following fourteen days | PO                     |
| McNeill et al. (2005)    | USA              | 48 hours  | 166             | NR                                     | 60.20     | MD, LM              | MP 40 mg or 40 mg MP acetate + 5 mg morphine | EPI                   |
| Mirzai et al. (2002)     | Turkey           | 12 hours  | 44              | 39.3±8.26                              | 56.81     | MD                  | 40 mg of MP          | EPI                   |
| Modi et al. (2009)       | Korea            | Variable  | 57              | 29.82±7.16 intervention; 30.14±8.15 (control) | 80.70     | MD                  | 40 mg of MP          | EPI                   |
| Pobereskin et al. (2000) | United Kingdom   | 24 hours  | 93              | 44.5 (Control); 44.8 (Group 1); 46.3 (Group 2 ) | 50.53     | MD                  | TAC 40 mg/ml or 20 mg/ml OR 40 mg MP acetate + 5 mg Morphine | EPI                   |
| Rasmussen et al. (2008)  | Denmark          | 2 years   | 200             | 42.5±7.02                              | 61        | MD                  | 40 mg MP acetate     | EPI                   |
| Watters et al. (1989)    | USA              | 1d        | 20              | NR                                     | 80        | MD                  | 6 mg of DMZ IV just before surgery and every 6 hours postop for four doses, followed by 4 mg orally every 6 hours for four doses, and finally 2 mg orally every 6 hours for four doses | IV, PO                 |

Abbreviations: MD, Microdiscectomy; PSF, pedicle screw fixation; EPI, epidural; IV, Intravenous; IT, Intrathecal; IM, intramuscular; PO, oral; MP, methylprednisolone; DMZ, Dexamethasone; Tramcinolone, TAC; prednisolone, PD; N/M, not mentioned; USA, United States of America

Statistically significant with a P value of 0.003 [Figure 2]. Analysis showed similar trend at 1 month and for overall analysis.

Postoperative leg pain
The overall analysis favored the use of epidural steroids for reduction of leg pain. The analysis
showed significant pain reduction with epidural steroids at 1 week and 1 year. The overall effect favored steroid group with mean difference of $-0.18$ ($-0.29$, $-0.07$). Test for effect Z was 3.32 ($P$ value $= 0.001$).

**Length of hospital stay**
The overall mean difference on LOS favored steroid group with a value of $-0.93$ ($-1.31$, $-0.55$), with a $P$ value of 0.00001.

**Return to work**
The mean number of days for return to work favored the steroid group with a mean difference of $-2.90$ ($95\%$ CI: $-3.94$, $-1.86$).

**Adverse events**
Fifteen RCTs reported AEs and an odds ratio of 0.71 ($95\%$ CI: 0.41, 1.26) favored steroid group [Figure 3].

**DISCUSSION**
Perioperative steroids better control back and leg pain. The administration of perioperative steroids resulted in improved postoperative back pain and postoperative leg pain. The overall mean difference in postoperative back pain between the two groups was small and not statistically significant, i.e., $-0.11$ ($CI = 0.25$, $0.02$), with a $P$ value of 0.1. RCTs by Pobereskin et al.,[14] Bahari et al.,[4] and Aminmansour et al.[3] had two intervention groups assessing different regimens of steroids in comparison to controls. Each of the regimens by these three trials were analyzed separately [Figure 2]. Only one study by Lutfina et al.[11] assessed postoperative back pain at 48 and 72 hours, with a mean difference of $+0.06$ and $+0.19$ favoring control groups. One RCT by Glasser et al. assessed postoperative back pain at one week with a mean difference of $-0.43$ ($CI = -3.03$, $2.17$).
The overall effect Z was 0.32 (P value = 0.75). Two RCTs by Glasser et al.[7] and Modi et al.[13] assessed postoperative back pain at 1 month, with a mean difference of −0.49 (CI = −0.58, −0.39) favoring steroid group. Two RCTs by Rasmussen et al.[16] and Modi et al.[13] assessed postoperative back pain at 1 year, with a mean difference 0.07 (CI = −0.03, 0.16).

Analysis favored the steroid group for better postoperative leg pain control at 1 week and 1 year postoperatively [Figure 4].

RCT by Aminmansour et al.[1] studied two steroid regimens, which we analyzed separately. Mean difference was −0.19 (CI = −0.42, 0.04). Overall effect Z was 1.59 (P value = 0.11). Three RCTs assessed postoperative leg pain at 48 hours. Mean difference between steroid and control group was 0.07 (CI = −0.30, 0.45). The effect Z was 0.59 (P value = 0.70). Three RCTs assessed postoperative leg pain at 1 week, with a mean difference of −0.05 (−0.07, −0.03). Test for overall effect Z was 4.25 with a significant P value of <0.001. Mean differences for postoperative leg pain at 72 hours and 1 month were not statistically significant between the groups. Rasmussen et al. assessed postoperative leg pain at 1 year, with a mean difference of −2.33 (CI = −2.58, −2.08).

Perioperative steroids reduce length of stay

Patients receiving perioperative steroids exhibited shorter LOS. Eight of the nine RCTs included in analysis showed shorter hospital stay in steroid group with mean difference of −0.95 (−1.31, −0.55) [Figure 5].

Perioperative steroids reduced time to return to work

Only one RCT by Aljabi et al.[2] evaluated time for return to activity and favored steroid group [Figure 6]. Fifteen RCTs did not show an increase in adverse
### Figure 3: Forest plot – meta-analysis of adverse effects

| Study or Subgroup | Steroid | Control | Mean Difference | Mean Difference IV, Random, 95% CI |
|-------------------|---------|---------|-----------------|----------------------------------|
| **24-hour post-op** | | | | |
| Glasser et al     | 1.67   | 3.54   | -1.54 [-4.56, 1.48] | |
| Langmore et al    | 0.15   | 0.04    | -0.14 [-0.18, -0.10] | |
| Aminmansour et al (40mg) | 1.15 | 1.14 | 0.36 [0.28, 0.44] | |
| Aminmansour et al (80mg) | 2.88 | 2.22 | 6.5%  | |
| Loftinia et al    | 0.51   | 0.51    | -0.03 [0.15, 0.10] | |
| Jirrattanaphochal et al | 2.05 | 2.05 | 0.69 [0.30, 0.97] | |
| Abushamkal et al  | 0.63   | 0.78    | -0.21 [-0.95, 0.23] | |
| **Subtotal (95% CI)** | | | | |
| | 184    | 267    | -0.19 [-0.45, 0.07] | |

Heterogeneity: Tau² = 0.05; Chi² = 66.19, df = 6 (p < 0.000001); I² = 91%
Test for overall effect: Z = 1.59 (p = 0.11)

### Figure 4: Forest plot – meta-analysis of postoperative leg pain

| Study or Subgroup | Steroid | Control | Mean Difference | Mean Difference IV, Random, 95% CI |
|-------------------|---------|---------|-----------------|----------------------------------|
| **24-hour post-op** | | | | |
| Glasser et al     | 1.67   | 2.5    | -1.19 [-3.76, 1.38] | |
| Langmore et al    | 0.05   | 0.013   | -0.05 [-0.07, -0.03] | |
| Jirrattanaphochal et al | 1.25 | 1.25 | 7.0%  | |
| **Subtotal (95% CI)** | | | | |
| | 114    | 165    | -0.04 [-0.38, 0.09] | |

Heterogeneity: Tau² = 0.01; Chi² = 18.70, df = 2 (p < 0.00001); I² = 89%
Test for overall effect: Z = 0.62 (p = 0.53)

### Additional Figures
- Figure 3: Forest plot – meta-analysis of adverse effects
- Figure 4: Forest plot – meta-analysis of postoperative leg pain
events for patients receiving steroid (e.g., indicating the safety of epidural steroids in surgery). However, there were considerable differences in what was defined as an adverse event by different RCTs.

Quality of randomized controlled trials
The quality of RCTs was assessed using a standardized 6-point scale specifically designed for systematic reviews. Only three RCTs conducted by investigators Diaz,[6] Hurlbert,[10] and Lundin et al.[12] had the maximum score. Another limitation of the RCTs was heterogeneity of outcomes. Most RCTs focused on short-term control of back and leg pain, and only two RCTs by Rasmussen et al.[16] and Modi et al.[13] assessed pain control at 1 year. Moreover, the method of reporting different variables also varied between different RCTs. For numerical data, some trials reported medians, which required conversion into means for analysis. This statistical problem was solved with the help of Cochrane Collaboration guidelines and article by Hozo.[9,18]

Previous systematic reviews on the topic had several limitations. The review by Ranguis et al. in 2010 missed several key trials,[13] and did not distinguish microdiscectomy from laminectomy, which are two different procedures. It also did not analyze steroids administered intravenously or in oral form.

Another review by Akinduro et al.[1] only examined the complications related to steroid use[1] addressing postoperative pain as a secondary outcome with no meta-analysis.

CONCLUSION
Intraoperative epidural steroid administration offers some benefit in pain control with a significant reduction in LOS. However, there is insufficient evidence to support the routine use of oral and intravenous steroids in the perioperative period.

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Conflicts of interest
There are no conflicts of interest.

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APPENDIX 1: SEARCH STRATEGY

- NLM PubMed:
  - ((“lumbar disc surgery”[All Fields] AND (“prednisolone”[MeSH Terms] OR “prednisolone”[All Fields]) OR (“methylprednisolone”[MeSH Terms] OR “methylprednisolone”[All Fields])) OR (“dexamethasone”[MeSH Terms] OR “dexamethasone”[All Fields]))) OR (“lumbar disc surgery”[All Fields] AND ((“postoperative period”[MeSH Terms] OR (“postoperative”[All Fields] AND “period”[All Fields]) OR “postoperative period”[All Fields] OR (“post”[All Fields] AND “operative”[All Fields]))) OR (“lumbar disc surgery”[All Fields] AND ((“postoperative period”[MeSH Terms] OR (“postoperative”[All Fields] AND “period”[All Fields]) OR “postoperative period”[All Fields] OR (“postoperative”[All Fields]))) OR (“lumbar disc surgery”[All Fields] AND ((“lumbosacral region”[MeSH Terms] OR (“lumbosacral”[All Fields] AND “region”[All Fields])) OR (“lumbosacral region”[All Fields] OR “lumbar”[All Fields]) AND disc[All Fields] AND (“surgery”[Subheading] OR “surgery”[All Fields] OR “surgical procedures, operative”[MeSH Terms] OR (“surgical”[All Fields] AND “procedures”[All Fields] AND “operative”[All Fields]) OR “operative surgical procedures”[All Fields] AND (“surgery”[All Fields] AND “general surgery”[MeSH Terms] OR (“general”[All Fields] AND “surgery”[All Fields]) OR (“general surgery”[All Fields]) AND (“steroids”[MeSH Terms] OR “steroids”[All Fields])) OR (“lumbar disc surgery”[All Fields] AND (“pain”[MeSH Terms] OR “pain”[All Fields]))

- CENTRAL (Cochrane)
  - Lumbar disc surgery AND steroid

- CINAHL PLUS (EBSCOHOST)
  - Lumbar disc surgery AND steroid