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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

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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

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perioperative steroids[8] (e.g., strong anti-inflammatory effect, modulation of pain receptors).[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 *et al.*[12] and Hurlbert *et al.*[10] had maximum quality level of 6, whereas RCT by Debi *et al.*[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

Table 1: Quality assessment of included studies

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 *et al*. (2011)	Y	Y	Can't tell	N	Y	Y	4
Aljabi *et al*. (2015)	Y	Y	N	N	Y	Can't tell	3
Aminmansour *et al*. (2006)	Y	Y	Y	N	Y	Can't tell	4
Bahari *et al*. (2010)	Y	Y	Y	N	Can't tell	Can't tell	3
Debi *et al*. (2002)	Can't tell	Y	N	N	Can't tell	N	1
Diaz *et al*. (2012)	Y	Y	Y	Y	Y	Y	6
Dikmen *et al*. (2005)	Y	Y	Can't tell	N	Can't tell	Y	3
Glasser *et al*. (1993)	Y	Y	N	N	Y	N	3
Hurlbert *et al*. (1999)	Y	Y	Y	Y	Y	Y	6
Jirarattanaphochai *et al*. (2007)	Y	Y	Y	N	Y	N	4
Langmayr *et al*. (1995)	Y	Y	Y	N	Y	N	4
Lotfinia *et al*. (2007)	Y	Y	Y	N	Y	Y	5
Lundin *et al*. (2003)	Y	Y	Y	Y	Y	Y	6
Manniche *et al*. (1994)	Y	Y	Y	N	Y	N	4
McNeill *et al*. (2005)	Can't tell	Y	N	N	Y	Y	3
Mirzai *et al*. (2002)	Y	Y	N	N	Y	Y	4
Modi *et al*. (2009)	Y	Y	Y	N	N	N	3
Pobereskin *et al*. (1999)	Y	Y	Y	N	Y	Can't tell	4
Rasmussen *et al*. (2008)	Y	Y	N	Y	Y	Y	5
Watters *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	49.33	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 acetonide or 10 mg of TAC acetonide	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	250 mg IV MP + 160 mg 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
Jirarattanaphochai *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; Trimacinolone, 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

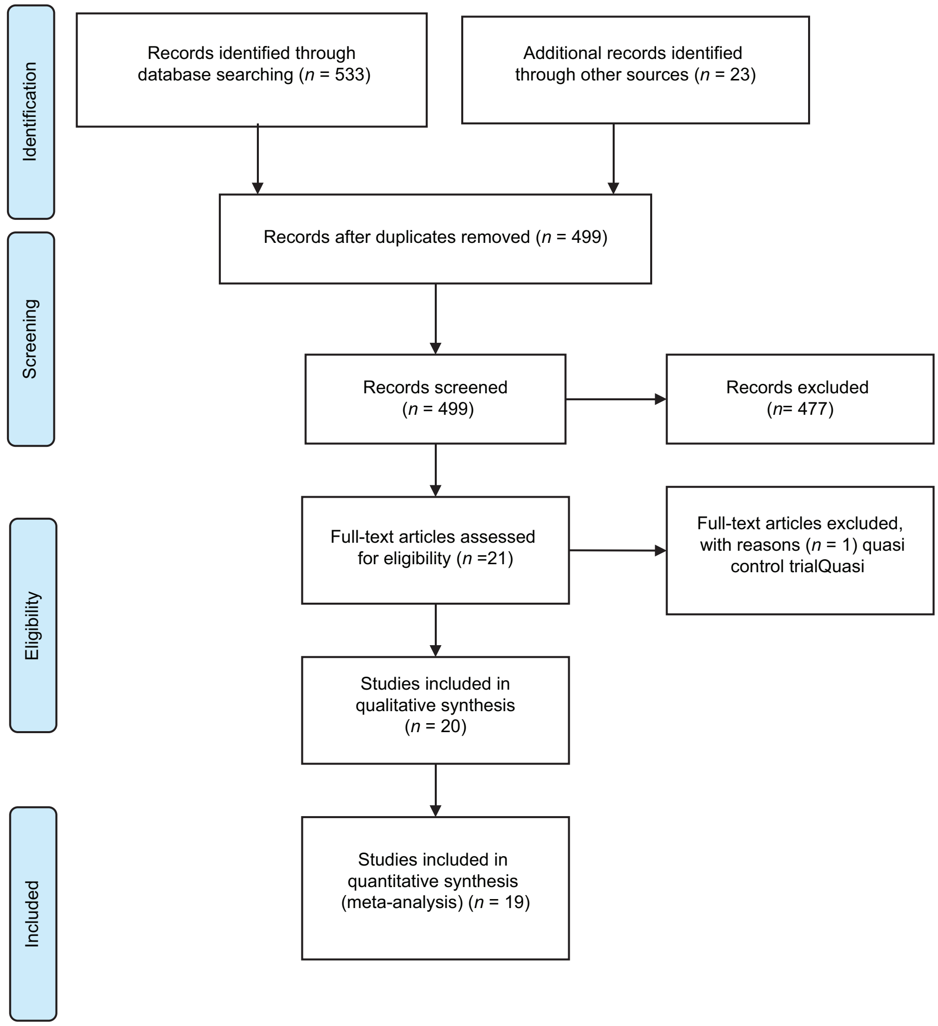

Figure 1: Prisma flow chart – study selection

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).

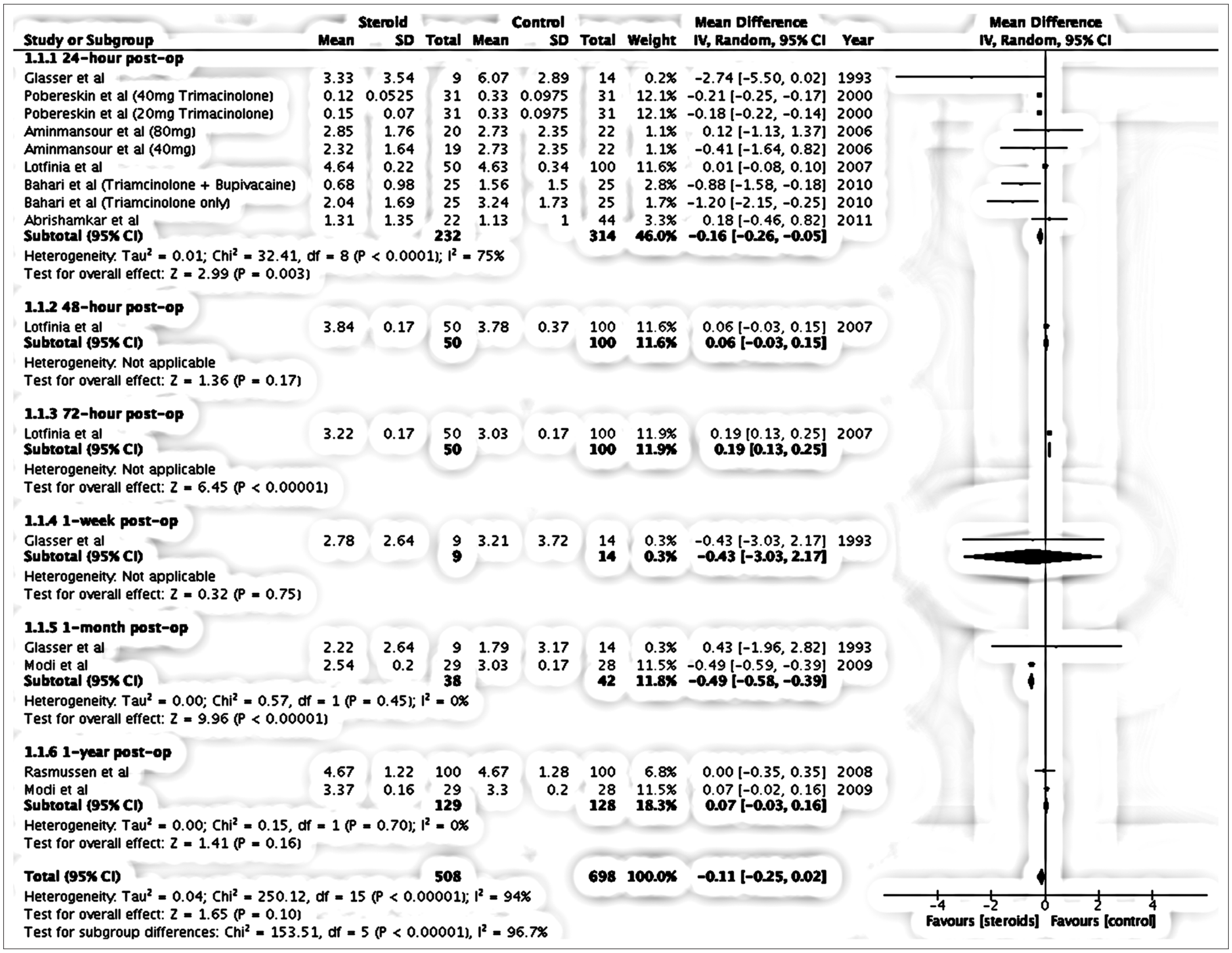

Figure 2: Forest plot – meta-analysis of postoperative back pain

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.*[3] 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 0.39 (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 −0.93 (−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

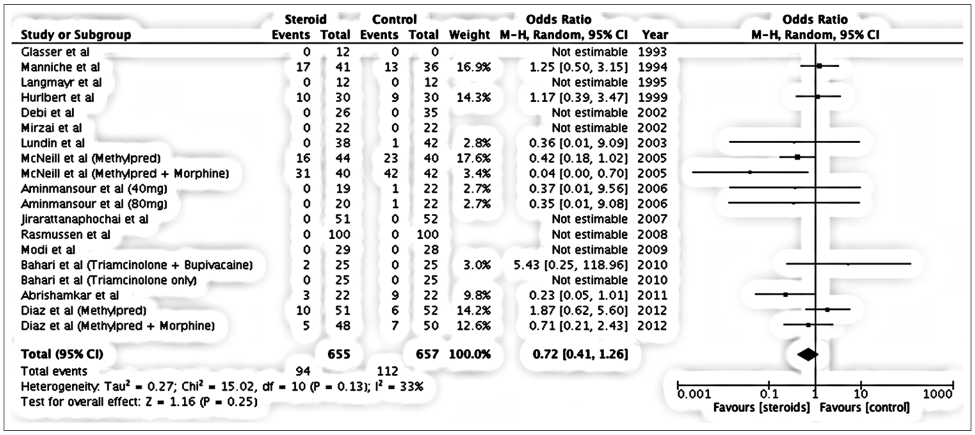

Figure 3: Forest plot – meta-analysis of adverse effects

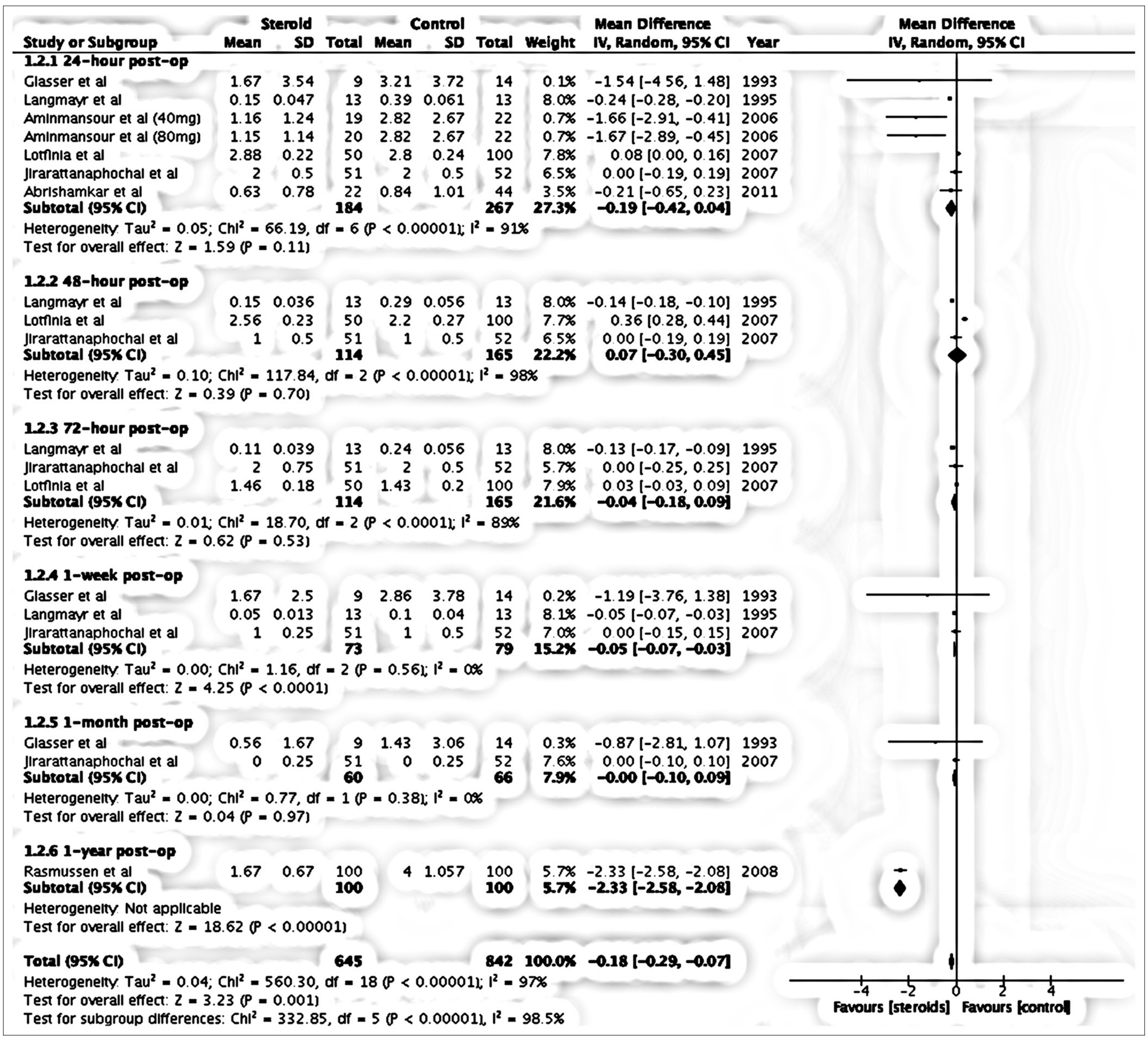

Figure 4: Forest plot – meta-analysis of postoperative leg pain

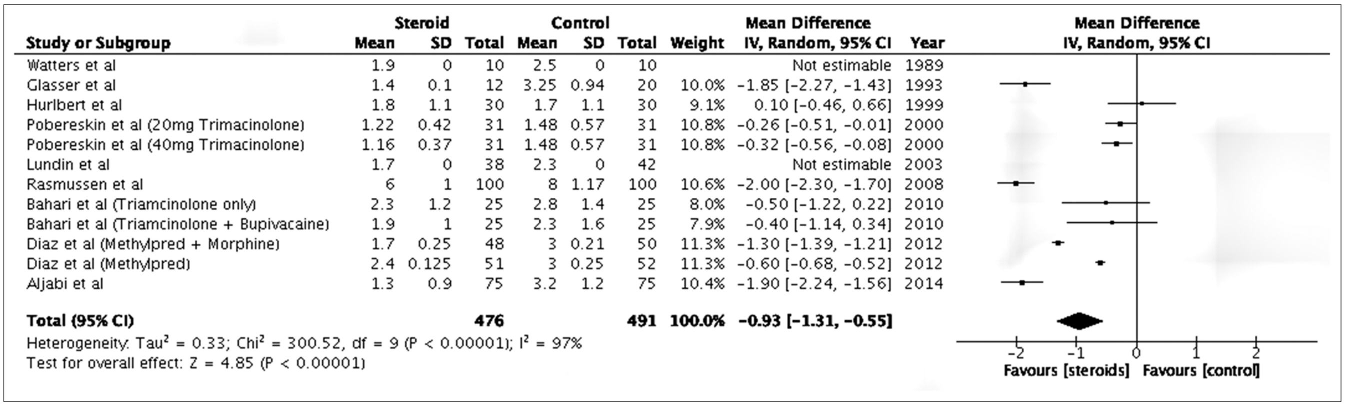

Figure 5: Forest plot – meta-analysis of total hospital length of stay

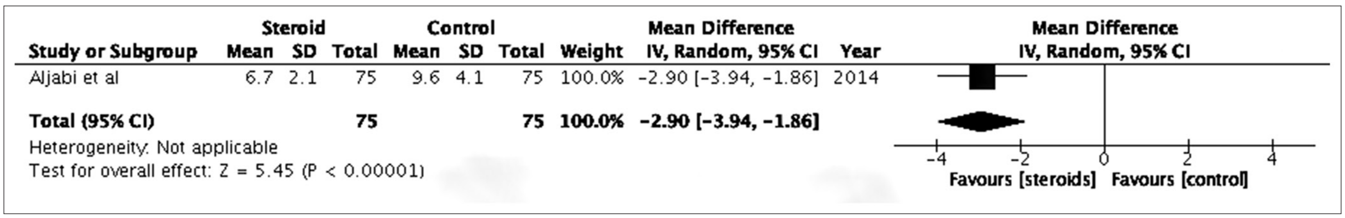

Figure 6: Forest plot – meta-analysis of return to work

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[15] 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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Nil.

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 “post operative”[All Fields]) OR (“postoperative period”[MeSH Terms] OR (“postoperative”[All Fields] AND “period”[All Fields]) OR “postoperative period”[All Fields] OR “postoperative”[All Fields])))) OR (((“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] OR “surgery”[All Fields] OR “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