Review

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Intradiscal steroid therapy in chronic discogenic pain: a systematic review of literature

Abstract

Background: This article aims to conduct a systematic review of the present literature and assess the use of intra-discal steroids injection (IDSI) for patients suffering from chronic discogenic back pain irresponsive to conservative treatment.

Methods: The search was conducted in PubMed, PubMed Central, Cochrane, Scopus, Embase, and Google Scholar databases between 1990 and 2021. Included were studies assessing the administration of IDSI to adults suffering from chronic discogenic back pain. Studies evaluating combination interventions were excluded. The quality of evidence was determined by the GRADE assessment. The PROSPERO registration number for the review is CRD42022307690.

Results: Eight studies enrolling a total of 548 patients were finally included in the systematic review. A significant reduction in pain scores after IDSI was calculated one month after intervention [standardized mean difference (SMD) −1.32 (−2.32, −0.31), p = 0.01, I^2 = 89%]. This effect was not sustained at three- six- and twelve-month assessments. The analysis revealed no therapeutic benefit of intra-discal steroids for disability and activity limitation at one month, [SMD −0.76 (−1.88, 0.36), p = 0.18, I^2 = 92%], three-, six- or twelve-months intervals. Overall, the quality of effect estimates was found to be moderate.

Conclusions: The authors believe that Intradiscal steroid therapy can only be used as a bridge therapy for short-term pain relief while the patient with chronic discogenic pain awaits another intervention or surgery.

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Keywords: intradiscal injection, low back pain, intradiscal steroids, discogenic pain, systematic review, palliative care

Introduction

Low back pain (LBP), also called lumbago, is the most common musculoskeletal problem globally [1]. Low back pain is an overlapping entity covering a range of different pain types including neuropathic, nociceptive, nociplastic, and non-specific. Various components within the lumbar spine can contribute

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to LBP like the involvement of soft tissue, vertebrae, intervertebral discs, joints (zygapophyseal and sacroiliac), and neurovascular elements [2]. Discogenic pain is defined as pain occurring due to some pathology in the intervertebral disc (IVD). Discogenic pain is a different entity than pain due to disc herniation and radiculopathies. The Intervertebral disc is composed of three parts: inner nucleus pulposus (NP), outer annulus fibrosus (AF), and endplates made of hyaline cartilage [3]. Discogenic pain is characterized by low back pain, in the presence of radiologically confirmed degenerative disc disease, with or without the symptoms of radiculopathy in the lower limb. Degenerative disc disease term can be used for a degenerated disc that is also painful. Pain occurs due to the chemical irritation of nerve endings present in the annulus or endplate following a disruption. This pain can further be classified into acute (< 6 weeks), sub-acute (6–12 weeks), or chronic (> 12 weeks) [4].

Earlier, LBP was found mainly in the elderly population. However, due to a change in lifestyle and environmental conditions, this entity is increasingly affecting the young and middle age population as well. The major problem is the hampering of quality of life, work disability associated with LBP, and the consequent economic burden. Within the last few decades, several minimally invasive treatment modalities have surfaced and triggered major interest. These include intradiscal radiofrequency thermocoagulation, intradiscal electrothermal therapy, epidural steroid injections, and intradiscal steroid injections [5].

The rationale for the use of intradiscal corticosteroids is by exerting their anti-inflammatory effect and suppressing the inflammation inside the IVD, hence, improving the symptoms [6]. A study published in 1993 concluded that intradiscal steroids lead to a progressive degeneration of the intervertebral disc, followed by tissue contraction and stabilization of the surrounding spinal segment. This results in clinical improvement [7]. Several trials have evaluated the scope of use and efficacy of intra-discal steroid injection for the treatment of chronic discogenic pain [8, 9]. However, they all have presented varied results.

The present research aims to conduct a systematic review of the present literature and assess the use of intra-discal steroids injection for patients suffering from chronic discogenic back pain showing no or poor response to conservative treatment. To the best of the authors' knowledge, there is no systematic review in the literature on specifically this treatment approach. The research question is whether intradiscal steroids have a beneficial effect on chronic discogenic pain in terms of pain relief and reduction in disability.

Methods

Protocol and registration

This review was registered on the International Prospective Register of Systematic Reviews (PROSPERO). It is accepted under the registration ID CRD42022307690. Ethical approval was not required for this research.

Literature search strategy

The secondary data was collected from different studies and trials by two independent reviewers. The studies involving intra-discal steroid injections conducted between the years 1990 to 2021 were searched. The search strategy comprised of a combination of various keywords which are as follows: "discogenic pain", "intra-discal steroids", "low back pain", "back pain", "disc disruption", "hydrocortisone", "methylprednisolone", "betamethasone", "corticosteroid" and "intra-discal injection". A systematic literature search was conducted for this review in the online databases of PubMed, PubMed Central, Cochrane, Scopus, Embase and Google Scholar. A well-formulated PICOS framework was employed to execute this research. Titles and abstracts were reviewed independently for the selection of the full-text review. The reviewers also independently reviewed the full text of relevant studies to decide on eligibility. This systematic review has followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (Figure 1).

Study inclusion criteria

The eligible studies were the ones including administration of intradiscal steroid injections to adults (> 18 years old) suffering from chronic discogenic back pain with disc changes on MRI and irresponsive to conservative treatment. The review was restricted to Randomised control trials and cohort studies only conducted between 1990 and 2021.

Exclusion criteria

Excluded were the studies in non-English-language papers. Also, the studies evaluating the response of intra-discal steroid injection in combination with any other therapeutic intervention were excluded.

Data extraction and study quality

The extracted data from these trials including study design, sample size, methodology, intervention, and outcomes were stored in a customized Excel database. The included studies were assessed for methodological quality through the "risk of bias" tool of the Review Manager Software version 5.4 (The Cochrane

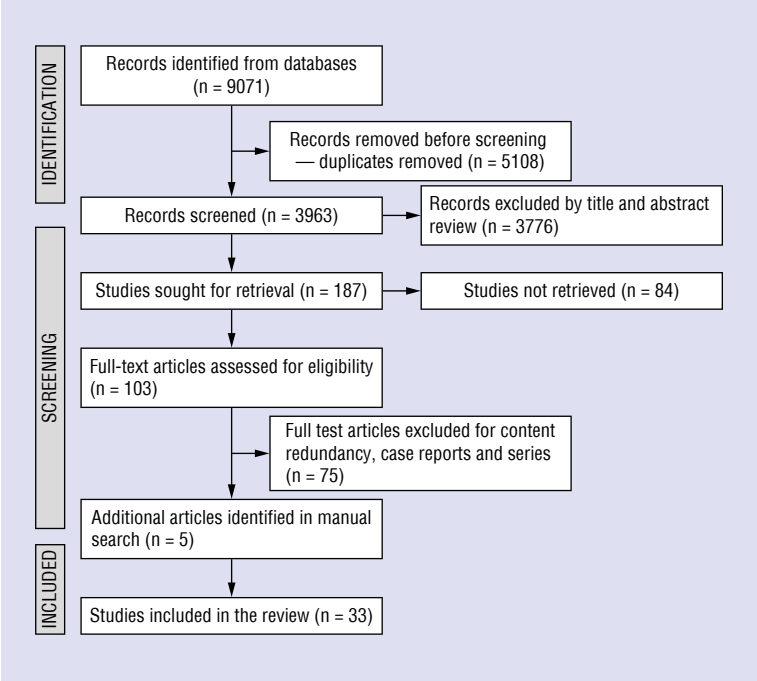

Figure 1. Literature search strategy (PRISMA) flow diagram

14 Collaboration, UK). The quality of each study was independently assessed by two different authors and any disagreements were resolved through discussion. The categories included were allocation concealment and random sequence generation for detection of selection bias, participants blinding for performance bias, any incomplete outcome data for attrition bias, blinding of the outcome assessor for detection bias, selective reporting for reporting bias, and other bias, were further classified into "high", "low" or "unclear" to assess the validity of each included study.

Outcomes

The following outcomes were analysed on a consensus basis. The primary outcome of the research included an evaluation of the relief of pain symptoms after intra-discal steroid intervention. The secondary outcomes included the reduction in disability and the duration of relief after the intervention. Thirdly, an evaluation of the safety profile of the intervention was also done.

Data analysis

The search was performed by giving the highest consideration to systematic reviews and meta-analyses followed by randomized controlled trials (RCTs), and prospective and retrospective cohort studies. There was no systematic review and meta-analysis done on this subject. Of 2080 articles found in the initial search, 20 were finally screened and 8 clinical studies were analysed for the systematic review.

Statistical analysis

This meta-analysis was conducted using Review Manager software (RevMan version 5.4.1). Data entry was done by two reviewers independently. For primary and secondary outcomes, as the effect measure for analyses, the standardized mean difference (SMD) was utilized. SMD contributes to expressing the size of the intervention effect in an individual study relative to the observed variability in that study and additionally allows for comparisons of groups, independent of specific units of measures in them [10].

The results were presented with a 95% confidence interval (CI), p-values, and associated forest plots for different time points of $\leq$ 1 month, 3 months, 6 months and 12 months. The forest plots have been derived for pain and disability comparison at these time points. A p-value of < 0.5 is considered clinically significant. Also, a qualitative synthesis was provided where quantitative synthesis could not be obtained.

Results

Study characteristics

Through this systematic review, eight studies were finally identified. Amongst the identified studies, six were randomized control trials, one retrospective

study and one prospective, non-randomized study. This review includes a total of 548 patients who met the inclusion criteria. The steroids that have been used in the included studies are methylprednisolone, betamethasone, dexamethasone and prednisolone. The characteristics of the included studies have been summarised in Table 1 [11–18].

Quality assessment and risk of bias across the included studies

The selection bias risk across the studies was low to moderate as a majority of the studies employed random sequence generation but allocation concealment was not properly achieved. The risk of performance bias was low to moderate due to the lack of proper blinding of personnel and participants for the interventions. Most of the studies failed to report proper blinding for outcome assessment, hence there was a high risk of detection bias. The attrition and reporting bias was calculated to be low to moderate. Another bias was low for the included studies (Figure 2). As the number of eligible studies was inadequate for drafting a funnel plot, hence publication bias could not be assessed. The quality of evidence for the outcome according to the GRADE criteria is discussed ahead in the manuscript [19].

Primary outcome

Comparison of pain scores at different time points

≤ 1 month

Out of five studies evaluated for quantitative analysis, three assessed pain scores within one month of intra-discal steroid injection compared with control. All of them reported a significant reduction in pain scores after IDSI [SMD −1.32 (−2.32, −0.31), $p = 0.01$, $I^2 = 89\%$] (Figure 3) The quality of evidence for this outcome was graded as moderate as per the GRADE assessment (Supplementary Table 1).

3 months

Three of the studies that assessed pain scores at 3 months intervals after intervention demonstrated no significant reduction with steroid injection as compared to the control intra-discal injection. The quality of evidence at 3 months outcomes was graded as moderate as per the GRADE assessment.

6 months

Pain scores at six months were also evaluated by three of the five studies. No significant difference was found between the IDSI and control groups. GRADE assessment judged the outcome evidence quality as moderate.

12 months

Only two studies followed up for twelve months post-intervention. They found that intradiscal steroids offer no significant pain relief compared with control at this time interval. According to the GRADE assessment, the certainty of the effect estimates at twelve months was judged as moderate.

Secondary outcomes

Comparison of disability at different time points

≤ 1 month

The studies which assessed pain scores within one month of intervention, reported no significant improvement in disability and activity limitation after IDSI as compared to control (Figure 4). The GRADE quality of evidence for this outcome is moderate.

3 months

The studies demonstrated no advantage offered with steroid injection as compared to the control intra-discal injection at an intermediate period of three months also. The quality of evidence at 3 months outcomes was graded as moderate as per the GRADE assessment.

6 months

No significant improvement was found in disability with the IDSI as compared with the control groups. GRADE assessment judged the outcome evidence quality as moderate.

12 months

The long-term assessment at twelve months also failed to report any advantage of IDSI over control. According to the GRADE assessment, the certainty of the effect estimates at twelve months was judged as moderate.

Duration of relief

The assessment at different time intervals was performed to decide upon the duration of the therapeutic benefit provided by the use of intra-discal steroids. The statistically significant advantage was offered by IDSI only for one month in terms of analgesia. This effect was not sustained after this short duration.

Safety

Four out of eight included studies did not report complications related to intradiscal steroids. Fayad et al. [13] and Yavuz et al. [16] documented no complications with the IDSI group. Nguyen et al. [17] and Tavares et al. [18] reported adverse events but they were all unrelated to the direct intervention.

Table 1. Summary of the characteristics of the included studies

Study ID	Study design	Study population	Groups			Sample size	Follow-up	Outcomes pain	Disability	Others	Conclusion
Simmone et al., 1992 [11]	RCT	IDD or nuclear prolapse, positive pain response on awake discography	Depo-medrol 80 mg/mL		Bupivacaine, marcaine 5% 1.5 mL	14:10	2 weeks	Decrease in pain score from baseline in both groups but not-significant	Not-significant functional improvement		No significant improvement in pain and disability. No benefit in the use of intradiscal steroids
Khot et al., 2004 [12]	RCT	Chronic discogenic pain	Methylprednisolone injection		Normal saline	60:60	1 year	No significant difference between the two groups ($p = 0.72$)	No significant difference ($p = 0.71$) between two groups		No improvement in clinical outcome was observed with intradiscal steroid as compared to normal saline injection
Fayad et al., 2007 [13]	Retrospective study		Modic I [pure edema endplate changes in MRI]	Modic I-2 [mixture of Modic-I and — II changes but predominantly oedema changes]	Modic II-1 [predominantly fatty changes]	37:25:12	6 months	Significant reduction in pain score at 1 month in Modic I and Modic I-2 groups than in Modic II-1 group (30.2 ± 26.6 and 29.4 ± ± 21.5 *vs.* 5.3 ± ± 25.5; $p = 0.009$ & 0.017, respectively). No significant change at 3 and 6 months		No adverse effects	Effective for short-term in LBP patients predominantly inflammatory endplate changes when conservative treatments failed

Table 1 (cont.). Summary of the characteristics of the included studies

Study ID	Study design	Study population	Groups			Sample size	Follow--up	Outcomes pain	Disability	Others	Conclusion
Cao et al., 2011 [14]	RCT	Degenerative chronic discogenic pain with positive discography and end plate Modic changes at a single level	120 included patients allocated into Groups A and B a/t type of Modic changes on MRI. Then, patients in Groups A and B were randomized into three subgroups			40:40:40	3, 6 months	No significant decrease in VAS at 3, 6 months after saline injection but a significant reduction at 3, 6 months after diprospan and diprospan + songmeile. However, no significant difference between latter two injection protocol. Similar results obtained in both Modic 1, 2 changes	No significant improvement in ODI at 3, 6 months after saline injection but significant improvement at 3, 6 months after diprospan and diprospan + songmeile. However, no significant difference between latter two injection protocol. Similar results obtained in both Modic 1, 2 changes		Intradiscal corticosteroids short-term efficient alternative for discogenic low back pain patients with end plate Modic changes
			A1 or B1: intradiscal injection of normal saline	A2 or B2: intradiscal injection of diprospan (betamethasone)	A3 or B3: intradiscal injection of mixture of diprospan + songmeile (cervus and cucumis polypeptide injection)						
Yu et al., 2012 [15]	RCT	Discogenic pain with one segmental disc pathology on MRI with negative discography	Provocative discography + intradiscal injection of dexamethasone 5 mg		Intradiscal saline injection	23:22	6 months	VAS score significantly improved during the first 3-month follow-up in the steroid injection group compared to baseline and between groups ($p < 0.05$), but no significant difference after 24-week	Significantly improved ODI score at 3 months but not at 24 weeks		Short-term improvement in discogenic low back pain in steroid injection group. The study also indicated that negative discography in patients with probable symptoms of discogenic pain cannot absolutely exclude the diagnosis of discogenic pain

Table 1 (cont.). Summary of the characteristics of the included studies

Study ID	Study design	Study population	Groups		Sample size	Follow--up	Outcomes pain	Disability	Others	Conclusion
Yavuz et al., 2012 [16]	Prospective non-RCT	Chronic discogenic low backache	1 cc betamethasone injection into the disc	–	18	3 months	Significant reduction in pain intensity between baseline & 2nd week, and between baseline & 3rd month (p = 0.001 & p = 0.002)	Significant improved Disability Scores was seen between baseline & 2nd week, and between baseline & 3rd month (p = 0.001 and p = 0.002)	Significant improvement in finger-tip--to-floor distance & duration of sitting without pain was seen between baseline & 2nd week and 3rd month	Intradiscal steroid injection effective for short-term & mid-term for reducing spinal pain intensity and disability in refractory chronic discogenic low back pain
Nguyen et al., 2017 [17]	RCT	Chronic LBP with active discopathy	GC IDI group (25 mg prednisolone acetate) injected during discography	Discography alone	67:68	12-month	% Of responders (LBP intensity < 40) was higher in the GC IDI group [36/65 (55.4%)] at 1 month than the control group [21/63 (33.3%)]; (p = =0.009). Groups did not differ in LBP intensity at 12 months	Non-significant change	–	Single glucocorticoid (25 mg prednisolone) intradiscal injection reduces chronic LBP with active discopathy At 1 month but not at 12 months

Table 1 (cont.). Summary of the characteristics of the included studies

Study ID	Study design	Study population	Groups		Sample size	Follow-up	Outcomes pain	Disability	Others	Conclusion
Tavares et al., 2020 [18]	RCT	Low back pain and active discopathy	50 mg prednisolone acetate (GC group)	Lidocaine [40 mg (L group)]	24:26	6 months	Significant reduction in pain intensity at 1 month in GC versus L group but not at 3 and 6 months	No significant variation in Oswestry score at follow-up intervals	Groups did not differ in analgesics consumption or professional condition at any time. No serious adverse effects reported	Intradiscal prednisolone acetate injection reduces the discogenic back pain at 1 month but not at 3 and 6 months as compared with intradiscal lidocaine injection

RCT — randomized controlled trials; LBP — low back pain

Discussion

The main findings of the present review are as followed:

1. This review incorporates adult patients with chronic discogenic back pain irresponsive to conservative treatment, who received intradiscal steroid injections.
2. The data were analysed for eight studies with a total of 548 patients.
3. Glucocorticoid intradiscal steroid injections provide a significant advantage in pain relief as compared to a placebo for a duration of up to one month.
4. There was no therapeutic benefit of IDSI with regard to analgesia at three, six- or twelve months post-intervention.
5. Despite a few trials documenting the improvement in disability and activity limitation with steroids, the meta-analyses showed no such benefit at any time interval (short, intermediate, and long-term).
6. The safety of IDSI cannot be clearly commented on as only a few trials have recorded adverse effects. However, no serious adverse effects were noted and the common complication was hospitalization for usual low back pain care or other illnesses.
7. There is a low to moderate risk of selection, performance, and attrition bias across the trials.
8. The quality of evidence (Grade criteria) for the primary and secondary outcomes is moderate for one- three- and six-month point assessments and high for twelve months assessments.
9. As the majority of I^2 is above 89%, (Figures 2, 3) hence the studies are extremely heterogeneous. This is an important finding as it does not allow the observations to be a true reflection of the population. Hence, high-quality homogenous studies are warranted to formulate a genuine consensus on the efficacy of intradiscal steroids in discogenic pain.

The point prevalence of low back pain was found to be nearly 7.5% globally in the year 2017 [20]. Around 40 to 50% of chronic LBP is attributed to discogenic causes [21]. Approximately 70% of the years lost through disability have been found in the working-age population (20–65 years) [22]. Out of the total costs incurred by LBP, around 80% are attributed to indirect costs like loss of productivity and payments associated with disability [23, 24]. Minimally invasive percutaneous procedures offer the benefits of fewer side effects, elimination of perioperative complications related to surgery and anaesthesia, absence of post-surgical scarring, less expensive, shorter hospital stay, and earlier return to work [25].

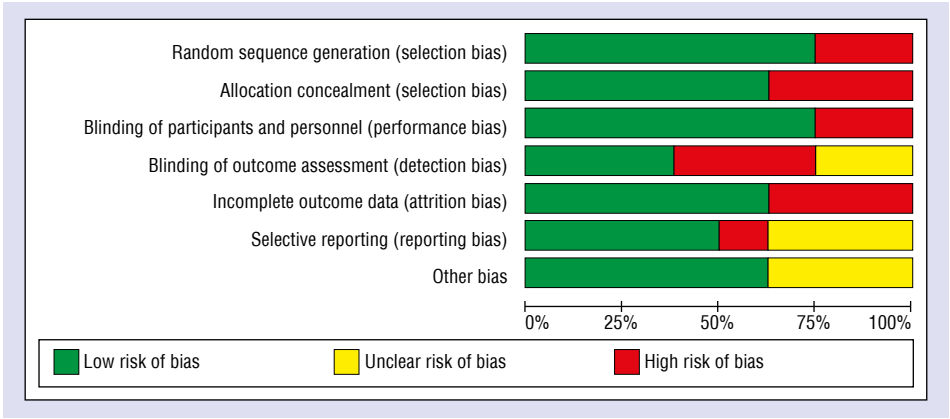

Figure 2. Risk of bias across included studies

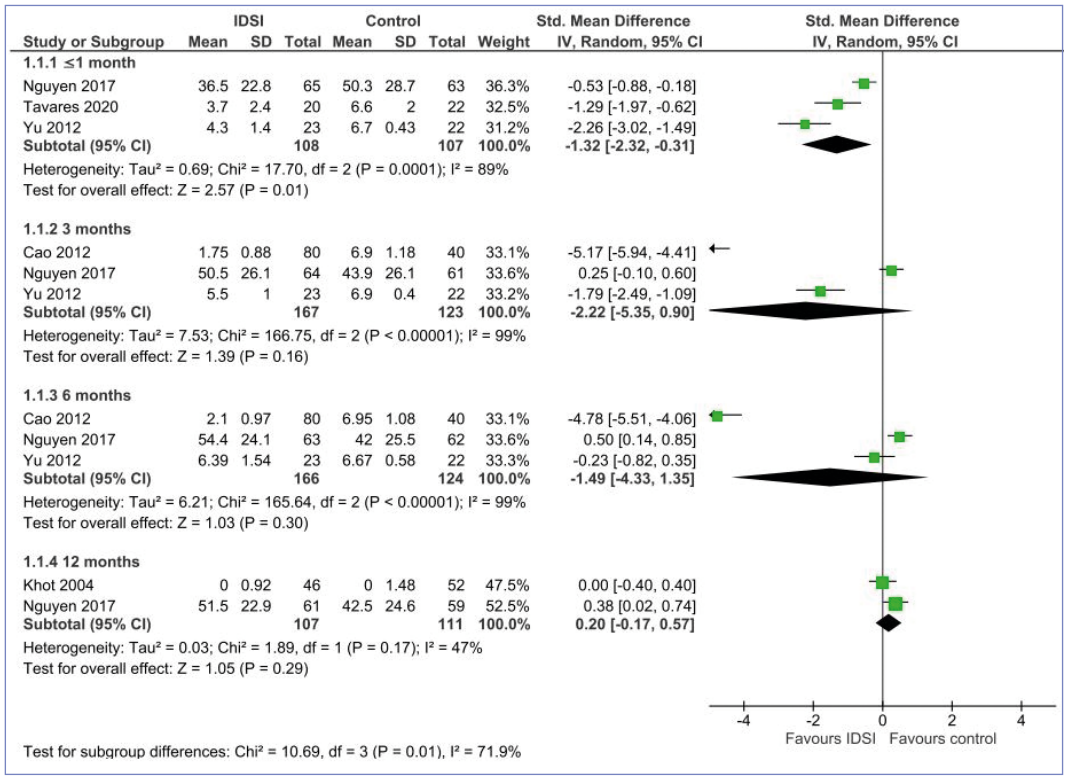

Figure 3. Forest plot for the primary outcome — pain at ≤ 1 month, 3 months, 6 months and 12 months. CI — confidence interval; SD — standard deviation; IDSI — intradiscal steroid injection

Intradiscal steroids have been debated to promote stabilization of the spinal segment through disc degeneration. Several trials documented this re-stabilization to result in decreased pain and disability [26, 27]. A practical advantage of using intradiscal steroid therapy is that the intervention can be simultaneously performed with the diagnostic discogram (single sitting). This further saves time, expense and reduces morbidity. The use of intradiscal steroids has been associated with various complications including infection, spondylodiscitis, haematoma, spinal canal and epidural ossifications and loss of disc height [14, 17]. Some early studies have also demonstrated the long-term risks associated with the use of intra-discal steroids. These included a low risk of spinal canal ossification, calcification and necrotic granulomatous lesions [27, 28]. In the present review, Nguyen et al. [17] reported the safety outcomes of disc steroid injections. They documented 25 adverse events in the steroid intradiscal injection group and 29 in the control group but these all included hospitalizations for chronic LBP usual care or other causes like exi-

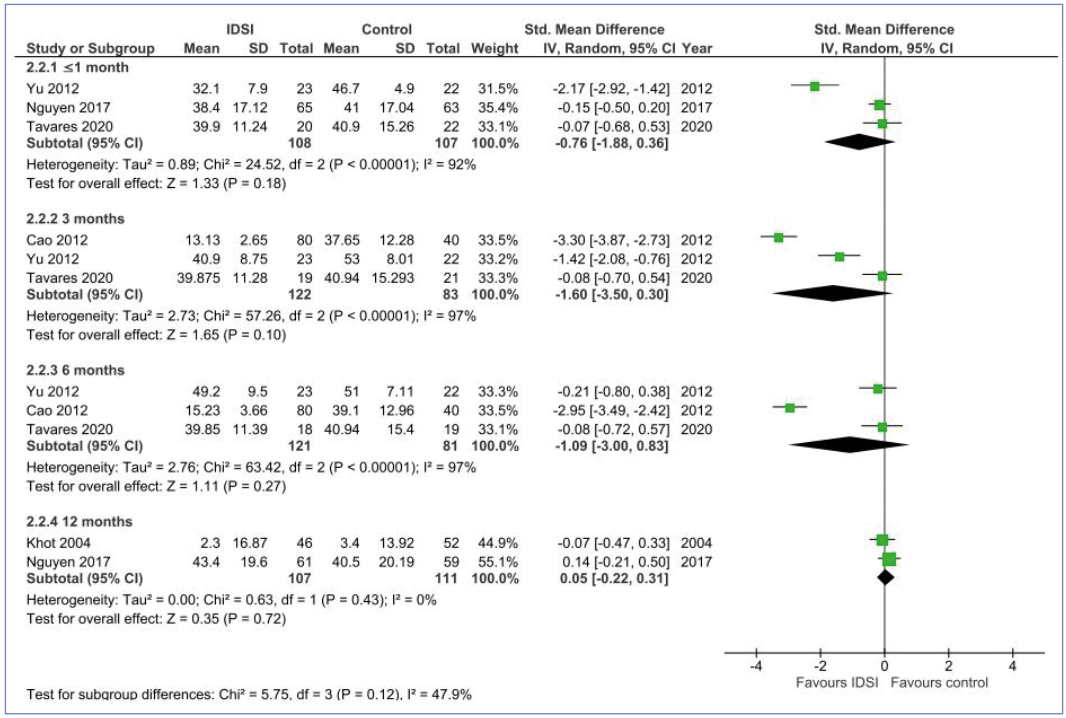

Figure 4. Forest plot for the secondary outcome. Comparison of disability with IDSI versus control at ≤ 1 month, 3 months, 6 months and 12 months. CI — confidence interval; SD — standard deviation; IDSI — intradiscal steroid injection

sting comorbidities (not directly intervention related). Tavares et al. [18] also reported adverse events only as hospitalization for usual care of LBP (three in the steroid group and four in the control group). Studies have shown IDSI beneficial for analgesia for up to six months [13, 29–31]. Improvement in functional activity has also been found in earlier trials for as long as up to one year [30]. The included studies have utilized different measures for the assessment of functional disability. These include a) Oswestry Disability Index which employs Oswestry Low Back Pain Disability Questionnaire [32]; b) the Quebec disability score [33]; c) the modified Schober test and finger-tip-to-floor test [13]. With this view in context, there are few trials with encouraging results and some documenting the least benefits with the use of IDSI [12–16].

This article provides an updated systematic review of the minimally invasive approach of intra-discal steroid injection for patients with chronic discogenic pain, who are irresponsive to conservative therapy or unwilling to invasive surgery.

Clinical importance of the review

The authors believe that the use of steroids in the intervertebral disc space has been empirical. In consideration of the present findings, intra-discal steroids can be offered as a bridge therapy for pain relief to patients awaiting another therapy or surgical intervention. Intradiscal steroid therapy should not be expected or offered to provide any improvement in functional disability. Moreover, there can be potential concerns related to the long-term effects of steroids in the disc space which have yet not been studied. The risk of bias in the included studies and the high heterogeneity also emphasizes the need to conduct high-quality randomized control trials to resolve the uncertainties and improve the evidence base.

Strengths and limitations

This systematic review provides an updated report, followed a pre–specified protocol that has been registered in advance, and summarised the outcome quality of the evidence using the GRADE criteria. The authors acknowledge that as discussed, there was a moderate degree of bias across the various included trials that hampers the quality of these studies. The high heterogeneity is another limitation of the review. It is also admitted that the present review has a limitation in that the studies included in the review were performed over a long-time span and the technology used for the diagnosis and treatment may have evolved over that time.

Conclusions

— The available evidence suggests that IDSI is associated with a decrease in pain intensity in patients suffering from chronic discogenic pain for a short duration of up to one month.
— However, these beneficial effects do not extend beyond one month and hence, are not suitable for long-term relief.
— Moreover, IDSI does not seem to provide any advantage in improving disability and activity limitations.
— Hence, as per the present analysis, intradiscal steroid therapy can only be used as a bridge therapy for pain relief while the patient with chronic discogenic pain awaits another intervention or surgery.
— Finally, this review demonstrates the need to perform high-quality rigorously conducted RCTs to conduct a meta–analysis to formulate results that could be accurately generalized to a bigger population.

Article information and declarations

Declaration of conflict of interest

The authors declare that there is no conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://journals.viamedica.pl/palliative_medicine_in_practice/article/view/PMPI.a2023.0014.

References

1. Balagué F, Mannion AF, Pellisé F, et al. Non-specific low back pain. Lancet. 2012; 379(9814): 482–491, doi: 10.1016/S0140-6736(11)60610-7, indexed in Pubmed: 21982256.
2. Knezevic NN, Cohen SP, Knezevic NN, et al. Low back pain. Lancet. 2021; 398(10294): 78–92, doi: 10.1016/S0140-6736(21)00733-9, indexed in Pubmed: 34115979.
3. Huang YC, Hu Y, Li Z, et al. Biomaterials for intervertebral disc regeneration: Current status and looming challenges. J Tissue Eng Regen Med. 2018; 12(11): 2188–2202, doi: 10.1002/term.2750, indexed in Pubmed: 30095863.
4. Fujii K, Yamazaki M, Kang JD, et al. Discogenic back pain: literature review of definition, diagnosis, and treatment. JBMR Plus. 2019; 3(5): e10180, doi: 10.1002/jbm4.10180, indexed in Pubmed: 31131347.
5. Zhou Y, Abdi S. Diagnosis and minimally invasive treatment of lumbar discogenic pain — a review of the literature. Clin J Pain. 2006; 22(5): 468–481, doi: 10.1097/01.ajp.0000208244.33498.05, indexed in Pubmed: 16772802.
6. Muzin S, Isaac Z, Walker J. The role of intradiscal steroids in the treatment of discogenic low back pain. Curr Rev Musculoskelet Med. 2008; 1(2): 103–107, doi: 10.1007/s12178-007-9015-y, indexed in Pubmed: 19468881.
7. Kato F, Mimatsu K, Kawakami N, et al. Changes in intervertebral disc after discography with intradiscal injection of corticosteroids observed with MRI. J Neurol Orthop Med Surg. 1993; 14: 210–216.
8. Leao L. Intradiscal injection of hydrocortisone and prednisolone in the treatment of low back pain. Rheumatism. 1960; 16: 72–77, indexed in Pubmed: 13759932.
9. Feffer HL. Therapeutic intradiscal hydrocortisone. A long-term study. Clin Orthop Relat Res. 1969; 67: 100–104, indexed in Pubmed: 4243380.
10. Chapter 6: types of data and effect measures. In: Higgins JPT, Green S, editors. Cochrane handbook for systematic reviews of interventions version 6. The Cochrane Collaboration; 2019. www.handbook.cochrane.org (10.05.2020).
11. Simmons JW, McMillin JN, Emery SF, et al. Intradiscal steroids. A prospective double-blind clinical trial. Spine (Phila Pa 1976). 1992; 17(6 Suppl): S172–S175, indexed in Pubmed: 1385902.
12. Khot A, Bowditch M, Powell J, et al. The use of intradiscal steroid therapy for lumbar spinal discogenic pain: a randomized controlled trial. Spine (Phila Pa 1976). 2004; 29(8): 833–836; discussion 837, doi: 10.1097/00007632-200404150-00002, indexed in Pubmed: 15082979.
13. Fayad F, Lefevre-Colau MM, Rannou F, et al. Relation of inflammatory modic changes to intradiscal steroid injection outcome in chronic low back pain. Eur Spine J. 2007; 16(7): 925–931, doi: 10.1007/s00586-006-0301-y, indexed in Pubmed: 17216228.
14. Cao P, Jiang L, Zhuang C, et al. Intradiscal injection therapy for degenerative chronic discogenic low back pain with end plate Modic changes. Spine J. 2011; 11(2): 100–106, doi: 10.1016/j.spinee.2010.07.001, indexed in Pubmed: 20850390.
15. Yu Y, Liu W, Song D, et al. Diagnosis of discogenic low back pain in patients with probable symptoms but negative discography. Arch Orthop Trauma Surg. 2012; 132(5): 627–632, doi: 10.1007/s00402-011-1448-5, indexed in Pubmed: 22228279.
16. Yavuz F, Taşkaynatan MA, Aydemir K, et al. The efficacy of intradiscal steroid injections. Turk J Phys Med Rehab. 2012; 58(2): 88–92, doi: 10.4274/tftr.33602.
17. Nguyen C, Boutron I, Baron G, et al. Intradiscal glucocorticoid injection for patients with chronic low back pain associated with active discopathy: a randomized trial. Ann Intern Med. 2017; 166(8): 547–556, doi: 10.7326/M16-1700, indexed in Pubmed: 28319997.
18. Tavares I, Thomas E, Cyteval C, et al. Intradiscal glucocorticoids injection in chronic low back pain with active discopathy: A randomized controlled study. Ann Phys Rehabil Med. 2021; 64(2): 101396, doi: 10.1016/j.rehab.2020.05.003, indexed in Pubmed: 32461125.
19. Balshem H, Helfand M, Schünemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol. 2011; 64(4): 401–406, doi: 10.1016/j.jclinepi.2010.07.015, indexed in Pubmed: 21208779.
20. Wu A, March L, Zheng X, et al. Global low back pain prevalence and years lived with disability from 1990 to 2017: estimates from the Global Burden of Disease Study 2017. Ann Transl Med. 2020; 8(6): 299, doi: 10.21037/atm.2020.02.175, indexed in Pubmed: 32355743.
21. DePalma MJ, Ketchum JM, Saullo T. What is the source of chronic low back pain and does age play

a role? Pain Med. 2011; 12(2): 224–233, doi: 10.1111/j.1526-4637.2010.01045.x, indexed in Pubmed: 21266006.
22. Global Health Group Data Exchange. http://ghdx.healthdata.org/gbd-results-tool (22.02.2022).
23. Tymecka-Woszczerowicz A, Wrona W, Kowalski P, et al. Indirect costs of back pain – review. Polish Annals Med. 2015; 22(2): 143–148, doi: 10.1016/j.poamed.2015.07.003.
24. Dutmer AL, Schiphorst Preuper HR, Soer R, et al. Personal and societal impact of low back pain: the groningen spine cohort. Spine (Phila Pa 1976). 2019; 44(24): E1443–E1451, doi: 10.1097/BRS.0000000000003174, indexed in Pubmed: 31369481.
25. Vaishnav AS, Othman YA, Virk SS, et al. Current state of minimally invasive spine surgery. J Spine Surg. 2019; 5(Suppl 1): S2–SS10, doi: 10.21037/jss.2019.05.02, indexed in Pubmed: 31380487.
26. Aoki M, Kato F, Mimatsu K, et al. Histologic changes in the intervertebral disc after intradiscal injections of methylprednisolone acetate in rabbits. Spine (Phila Pa 1976). 1997; 22(2): 127–131; discussion 132, doi: 10.1097/00007632-199701150-00001, indexed in Pubmed: 9122791.
27. Ito S, Usui H, Maruyama K, et al. Roentgenographic evaluation of ossification and calcification of the lumbar spinal canal after intradiscal betamethasone injection. J Spinal Disord. 2001; 14(5): 434–438, doi: 10.1097/00002517-200110000-00010, indexed in Pubmed: 11586144.
28. Menei P, Fournier D, Alhayek G, et al. Rev Rhum Mal Osteoartic. 1991; 58(9): 605–609.
29. Buttermann GR. The effect of spinal steroid injections for degenerative disc disease. Spine J. 2004; 4(5): 495–505, doi: 10.1016/j.spinee.2004.03.024, indexed in Pubmed: 15363419.
30. Graham CE. Chemonucleolysis. A preliminary report on a double blind study comparing chemonucleolysis and intradiscal administration of hydrocortisone in the treatment of backache and sciatica. Orthop Clin North Am. 1975; 6(1): 259–263, indexed in Pubmed: 123053.
31. Zhuang Cy, Cao P, Zheng T, et al. [Intradiscal interventional therapy for degenerative chronic discogenic low back pain with end-plate Modic changes]. Zhonghua Yi Xue Za Zhi. 2009; 89(35): 2490–2494, indexed in Pubmed: 20137437.
32. Fairbank JC, Pynsent PB. The Oswestry Disability Index. Spine (Phila Pa 1976). 2000; 25(22): 2940–52; discussion 2952, doi: 10.1097/00007632-200011150-00017, indexed in Pubmed: 11074683.
33. Kopec JA, Esdaile JM, Abrahamowicz M, et al. The Quebec Back Pain Disability Scale. Measurement properties. Spine (Phila Pa 1976). 1995; 20(3): 341–352, doi: 10.1097/00007632-199502000-00016, indexed in Pubmed: 7732471.