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Review Article

The effectiveness of intradiscal corticosteroid injection for the treatment of chronic discovertebral low back pain: a systematic review

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Abstract

Objective: Determine the effectiveness of intradiscal corticosteroid injection (IDCI) for the treatment of discovertebral low back pain.

Design: Systematic review.

Population: Adults with chronic low back pain attributed to disc or vertebral end plate pain, as evidenced by positive provocation discography or Modic 1 or 2 changes on magnetic resonance imaging.

Intervention: Fluoroscopically guided or computed tomography–guided IDCI.

Comparison: Sham/placebo procedure including intradiscal saline, anesthetic, discography alone, or other active treatment.

Outcomes: Reduction in chronic low back pain reported on a visual analog scale or numeric rating scale and reduction in disability reported by a validated scale such as the Oswestry Disability Index.

Methods: Four reviewers independently assessed articles published before January 31, 2023, in Medline, Embase, CENTRAL, and CINAHL. The quality of evidence was evaluated with the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework. The risk of bias in randomized trials was evaluated with the Cochrane Risk of Bias tool (version 2).

Results: Of the 7806 unique records screened, 6 randomized controlled trials featuring 603 total participants ultimately met the inclusion criteria. In multiple randomized controlled trials, IDCI was found to reduce pain and disability for 1–6 months in those with Modic 1 and 2 changes but not in those selected by provocation discography.

Conclusion: According to GRADE, there is low-quality evidence that IDCI reduces pain and disability for up to 6 months in individuals with chronic discovertebral low back pain as evidenced by Modic 1 and 2 changes but not in individuals selected by provocation discography.

Study registration: PROSPERO (CRD42021287421).

Keywords: end plate; vertebrogenic; Modic; spine; steroid.

Introduction

Low back pain (LBP) is among the most common musculoskeletal conditions and affects almost all individuals at some point in their lives. Chronic low back pain (CLBP) is the leading cause of disability and work nonattendance,[1–4] and costs associated with treatment have been estimated to be in excess of 100 billion dollars per year as recently as 2016.[5] CLBP is a complex multidimensional condition, and it has been a pursuit of clinicians and researchers to categorize its multiple etiologies better to develop more targeted and effective treatments. Although CLBP can be multifactorial, in a proportion of individuals, it can be attributed to nociception arising from the intervertebral disc.[6,7] Historically, discogenic pain was thought to be related to degenerative intervertebral disc changes leading to structural and biomechanical instability, inflammation, and nerve ingrowth.[8,9] However, clinical and anatomic evidence indicates that the vertebral end plates contribute to CLBP in patients classically diagnosed with "discogenic" pain.[10,11] Nociceptive signals are transmitted from the vertebral end plates by the basivertebral nerve, a branch of the sinuvertebral nerve.[12–14]

An updated paradigm of anterior element spinal pain describes the intervertebral disc and vertebral end plate as a structural and functional unit known as the discovertebral complex; injuries to either one of these structures can affect the other.[15] The vertebral end plate is a porous structure with capillaries that aid in nutrient transport to the avascular intervertebral disc.[16,17] Injuries or chronic stresses to the vertebral end plate can lead to an inflammatory response mediated by cytokines and other inflammatory factors when nucleus pulposus migrates through the end plate and into the vertebral body. This inflammatory response gives rise to neovascularization, increased basivertebral nerve termini density, and increased density of nociceptive receptors at these termini,

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leading to pain sensitization.[18] These changes might be observed radiographically as Modic type 1 changes (fibrovascular replacement) or Modic type 2 changes (fatty marrow replacement).[19]

The current treatment options for discovertebral CLBP are limited. Guidelines for the treatment of axial LBP generally recommend a 6- to 12-week course of conservative treatment, including physical therapy, analgesic medications, acupuncture, and chiropractic treatment, before an interventional paradigm of injections or surgical treatment is considered. For those who do not respond to first-line treatments, interventional treatments that historically have been used include chymopapain injection, intradiscal electrothermal annuloplasty, nucleoplasty, methylene blue injection, ozone injection, and fibrin sealant injections.[20–24] Ablation of the basivertebral nerve via a transpedicular approach, though effective for specific patients, requires specialized training and is often performed with the patient under deep sedation or general anesthesia.[25–30] Intradiscal injections of disc allograft and allogeneic mesenchymal cells have also shown promising early results.[31,32] These more recently developed treatments are characteristically expensive and not yet covered by most payers. Some patients with recalcitrant discovertebral pain might ultimately undergo costly and potentially ineffective spinal fusion surgery. Intradiscal glucocorticoid injection is purported to target local inflammation within the discovertebral complex, thereby reducing pain and associated disability.[33–35] Intradiscal corticosteroid injection (IDCI) could provide a relatively affordable and effective treatment strategy in carefully selected patients with discovertebral pain, but a systematic review has not been performed to determine whether adequate evidence supports this practice.

Objectives and rationale

The objective of this systematic review was to identify and evaluate the quality of studies on the efficacy of IDCI for the treatment of chronic discovertebral LBP.

Methods

Protocol and registration

This review was registered on PROSPERO (CRD42021287421) on November 24, 2021. For transparency and reproducibility, this review adheres to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines for reporting of the protocol, searches, and review.[36–38] The review was conducted with methodological guidance from the *Cochrane Handbook for Systematic Reviews of Interventions* (version 6.2).[39]

Eligibility criteria

Population

The eligible population consisted of adults 18 years of age or older with CLBP attributed to disc or vertebral end plate pain as evidenced by positive provocation discography or by Modic 1 or 2 changes on MRI, respectively. Studies including patients with radicular pain were excluded.

Intervention

Eligible interventions were (1) fluoroscopically–guided or computed tomography (CT)–guided IDCI or (2) adjunctive treatment in addition to IDCI. Peridiscal or epidural administrations of steroids were excluded. In cases in which an adjunctive treatment was provided in addition to IDCI, a random-effects meta-analysis was planned to assess heterogeneity related to the adjunct.

Comparison

Eligible comparisons were sham/placebo procedures including intradiscal saline, anesthetic, provocation discography alone, or other active treatment. The protocol was amended to include active treatments as eligible for inclusion during the literature search, as few sham-controlled trials were identified.

Outcome

Outcomes were reduction in CLBP reported on a visual analog scale (VAS) or numeric rating scale (NRS) and reduction in disability reported by validated scales such as the Oswestry Disability Index (ODI). When the data were available, the percentages of patients reporting at least 50% reduction in index pain and greater than 15-point ODI reduction at short-term (up to 6 months) and medium-term (6 to 12 months) time points were calculated, along with 95% confidence intervals, with a primary endpoint of 3 months.

Studies

This review was designed to evaluate randomized controlled trials (RCTs). Nonrandomized studies with or without an internal control were captured and reported narratively but were not eligible for meta-analysis. Case reports and expert opinion pieces were excluded. Unpublished and non–English-language studies were excluded.

Information sources and search

An information specialist (M.M.M.) developed the search for our primary database, Medline, from exemplar articles and team feedback, and then translated the search to the other databases. A library colleague peer-reviewed search strategies using the Peer Review of Electronic Search Strategies (PRESS) guidelines.[40]

Clinical outcome studies on the effectiveness of IDCI for the treatment of chronic discovertebral LBP were obtained by searching Medline (Ovid) 1946–2023, Embase (embase.com) 1974–2023, CENTRAL—Cochrane Central Register of Controlled Trials (Wiley) 1898–2023, and CINAHL Complete (Ebscohost) 1937–2023 with a combination of keywords and subject terms. No date limits or methodological filters were applied. Searches were first conducted on December 9–12, 2021, and were updated January 31, 2023. See Supplementary File S1 for search strategies. Literature was also identified from the cited references of included publications. No additional studies or data were sought by contacting authors or experts.

Study selection

Covidence, a Web-based systematic review platform, was used for screening study selection.[41] Per Cochrane Handbook and PRISMA guidelines,[39,42] the selection of studies for inclusion was performed in tandem by multiple authors (D.C., S.M., M.C., and A.C.) independently and in a blinded fashion through all phases of the review. Disagreements were resolved by consensus or by involvement of an additional reviewer.

Data items and collection

Data extraction was performed in Microsoft Excel by 3 authors (M.C., D.C., S.M.) and checked for accuracy by a

fourth author (A.C.). Disagreements were resolved by consensus or by involvement of a fourth reviewer (A.C.). Information related to the population of interest was extracted, including the method used to determine the presence of discovertebral pain. This included clinical evaluation plus either provocation discography or presence of Modic 1 or 2 changes on MRI. Demographic information related to age, gender, and baseline pain and disability was also collected. In terms of the intervention, items collected included the type of imaging guidance, the location of the injection (ie, the level), and the specific injectate. Outcome data collected included VAS score, NRS score, ODI score, and scores of other validated scales assessing back pain–related disability. Study type and details relating to methodology were also recorded.

Risk of bias and methodological assessment

Risk of bias was assessed with the Cochrane Risk of Bias Tool (version 2.0).[43] This tool was designed to assess risk of bias within 5 domains related to randomization, deviations from the intended intervention, missing outcome data, measurement of the outcome, and selection of the reported results. Within each domain, a judgment of "low risk of bias," "some concerns," or "high risk of bias" was ascertained, which then informed the overall risk-of-bias judgment for the result assessed. Judgments were performed independently in a blinded fashion by 2 reviewers (M.C. and D.C.), with disagreements being resolved by consensus or by involvement of a third reviewer (A.C.).

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system of appraisal was used to evaluate the body of evidence to determine the quality of the evidence for the effectiveness of IDCI.[44] The GRADE system evaluates the body of evidence across multiple domains, which include imprecision, inconsistency, indirectness, risk of bias, and publication bias. GRADE allows for an initial rating of quality based on the best available evidence and allows for upgrading (eg, large magnitude of effect, dose–response gradient) or downgrading (eg, risk of bias, indirectness) of the evidence quality. Judgements were performed independently among 3 reviewers (M.C., S.M., and A.C.), with disagreements being resolved by consensus.

Summary measures and synthesis of results

The primary outcome of interest was reduction in CLBP reported on the VAS or NRS and reduction in disability reported by a validated scale such as the ODI. For categorical variables, we considered a greater than 50% reduction in NRS/VAS scores and a greater than 15-point ODI reduction at 3 months to represent robust, clinically significant improvements.[45,46] Planned summary measures for binary outcomes included risk difference and relative risk. Planned summary measures for continuous data included calculations of standardized mean differences between groups, along with standard deviations and 95% confidence intervals. If an adequate number of studies was discovered, a GRADE evidence profile was planned and was to be based on GRADE assessment and calculation of treatment effect.[44,47,48]

Results

Search results yielded 11 968 records. After removal of duplicates, 7806 were screened by title and abstract, resulting in 32 full-text articles assessed for eligibility. Ultimately, 6 RCTs (total $n = 603$; $n = 319$ steroid, $n = 284$ placebo [saline = 100, contrast alone = 153, contrast+ lidocaine = 22, platelet-rich plasma releasate = 9]) met the inclusion criteria.[49–54] See Figure 1 for an overview of the results. Included studies were organized by the study design and characteristics of individual studies and are summarized in Table 1. Given the paucity and heterogeneity of studies, a meta-analysis was not performed.

In addition to the 6 RCTs, we also captured data from 3 observational studies.[55–57] Of the 9 total studies, 5 studies (4 RCTs and 1 observational study) evaluated the effectiveness of IDCI for the treatment of chronic discovertebral LBP as evidenced by Modic changes.[49,50,52,54,55] The presence of discovertebral pain was determined in the remaining 4 studies by the identification of "disc degeneration" or "degenerative disc disease" (DDD) on MRI with or without provocation discography.[51,53,56,57] Injections were performed under fluoroscopic guidance in all but 1 study, which used CT guidance.[49] Across all studies, intradiscal steroid injections consisted of glucocorticoids (methylprednisolone[51,57]; prednisolone[50,52,55]; betamethasone[49,53,54,56]), with injectate volumes ranging from 1 mL to 3 mL.

The 6 RCTs compared the effectiveness of intradiscal injection with steroid vs that of a placebo injectate (saline[49,51]; contrast alone[50,54]; contrast+ 2% lidocaine[52]) or an active treatment (platelet-rich plasma releasate [PRPr][53]). Among the 3 observational studies, 2 studies had no control group,[55,56] and 1 study compared response to IDCI in patients with Modic I changes to that of a control group of patients diagnosed with DDD in the absence of Modic I changes.[57] Pain outcomes were assessed with VAS scores in all but 1 study, which used NRS scores.[50] Disability was measured with the ODI in 5 studies[49,51–54] and with the Quebec Back Pain Disability Scale (QBPDS) in 3 studies.[50,54–56] Postprocedural follow-up time points ranged from 24 hours to 2 years.[54,57] For the remaining studies, final follow-up visits occurred at 3 months,[56] 6 months,[49,52,55] 12 months,[50,51,53] and an average of 14 ± 2 months.[57]

Randomized controlled trials

In 2011, Cao et al. published results of a double-blinded RCT evaluating CT-guided IDCI with betamethasone or IDCI with betamethasone plus Chinese herbal songmeile compared with CT-guided intradiscal saline injection in 120 adults with CLBP.[49] Participants were adults 21–60 years of age with CLBP without radicular pain and failure of more than 6 weeks of conservative treatment. Radiographic inclusion criteria were MRI showing DDD, Modic type 1 or 2 changes, and subsequent positive provocation discography at the level of interest. Technical details of discography, such as pressure threshold, were not reported. Participants were initially categorized as having either Modic type 1 (Group A, $n = 60$) or type 2 (Group B, $n = 60$) changes. Further subgroup analysis was conducted as follows: Subgroup A1 (saline, $n = 20$); Subgroup A2 (betamethasone, $n = 20$); Subgroup A3 (betamethasone+ songmeile, $n = 20$); Subgroup B1 (saline, $n = 20$); Subgroup B2 (betamethasone, $n = 20$); and Subgroup B3 (betamethasone+ songmeile, $n = 20$). The volume of injectate was 3 mL, but the concentration of betamethasone was not reported. Outcomes of VAS and ODI were collected in each subgroup at 3 and 6 months after the CT-guided injections, with a reported 100% follow-up rate. No outcome data were collected beyond 6 months. Comparisons between the betamethasone and betamethasone+ songmeile treatment

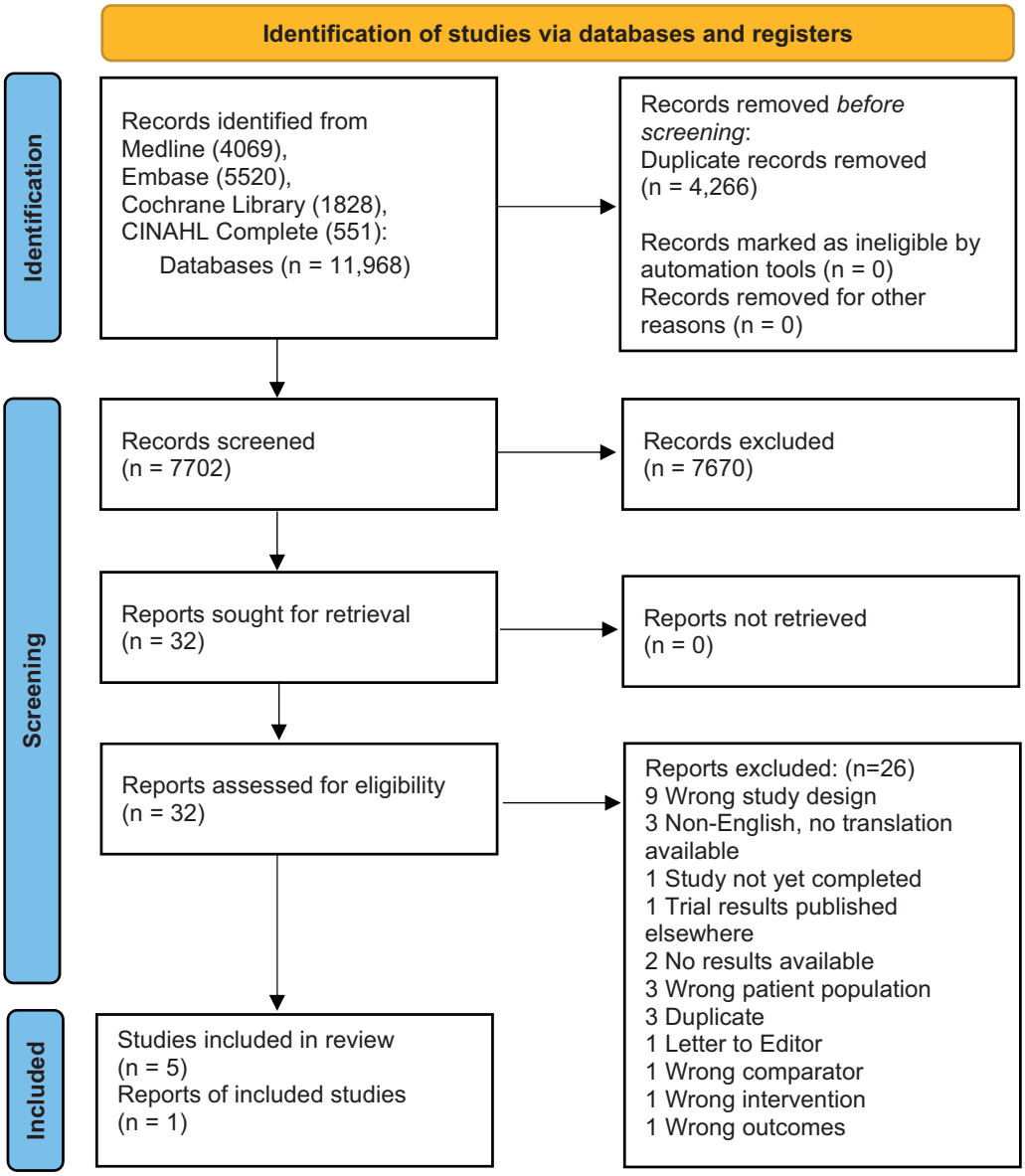

Figure 1. PRISMA 2020 flow diagram for new systematic reviews, which included searches of databases and registers only.

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. https://doi.org/10.1136/bmj.n71

For more information, visit: https://www.prisma-statement.org/.

protocols revealed no significant differences in average VAS or ODI score improvement at either follow-up time point for patients with Modic type 1 (A2 vs A3) or type 2 (B2 vs B3) changes. As such, we have reported outcomes for the Modic type 1 and type 2 betamethasone subgroups (A2 and B2) only. At both 3 and 6 months, significant improvements in both VAS and ODI scores were noted in the betamethasone subgroups when compared with the saline subgroups. In the saline control group with type 1 Modic changes, average VAS scores did not improve significantly from baseline (7.1 ± 1.6) at either 3 months or 6 months (7.0 ± 1.3 and 7.5 ± 1.1, respectively; $P > .05$); this pattern was also observed in the saline control group with type 2 Modic changes (6.5 ± 1.2 at baseline vs 6.8 ± 1.0 and 6.4 ± 1.1 at 3 and 6 months, respectively; $P > .05$). Significant reductions in average VAS scores from baseline occurred in the betamethasone subgroups with type 1 Modic changes (6.5 ± 1.2 at baseline vs 1.8 ± 1.0 and 2.3 ± 1.0 at 3 and 6 months; $P < .05$) and with type 2 Modic changes (6.8 ± 1.3 at baseline vs 1.6 ± 0.8 and 2.1 ± 1.0 at 3 and 6 months; $P < .05$). Results for change in disability as reported on ODI mirrored those for VAS pain scores. No improvements from baseline were observed in average ODI scores for the saline control subgroups with Modic type 1 (37.9 ± 14.7 at baseline vs 42.0 ± 13.9 and 44.4 ± 14.0 at 3 and 6 months, respectively; $P > .05$) or Modic type 2 changes (32.4 ± 9.7 at baseline vs 33.3 ± 10.6 and 33.8 ± 12.0 at 3 and 6 months, respectively; $P > .05$). Average ODI score improvements from baseline were significant at both follow-up time points for the betamethasone subgroups with type 1 (35.7 ± 11.1 at baseline vs 13.1 ± 2.2 and 14.7 ± 3.2 at 3 and 6 months; $P < .05$) and type 2 Modic changes (31.5 ± 5.9 at baseline vs 12.7 ± 2.1 and 13.8 ± 2.3 at 3 and 6 months; $P < .05$). There were no significant differences in these outcomes between those with Modic 1 vs Modic 2 changes at

Table 1. Study characteristics.

Reference	Inclusion criteria	Injectate details	Injection imaging and location(s)	Outcome measures	Follow-up	Adverse events	Funding / author disclosures
Double-blinded RCTs							
Cao et al., 2011	Age 20–60 years; Modic 1 or 2 on MRI at 1 level; positive discography	Treatment groups (A = Modic 1; B = Modic 2): • A2 ($n = 20$): 3 mL betamethasone • A3 ($n = 20$): 1 mL betamethasone+ 2 mL songmeile • B2 ($n = 20$): 3 mL betamethasone • B3 ($n = 20$): 1 mL betamethasone+ 2 mL songmeile Control groups: • A1 ($n = 20$): 3 mL saline • B1 ($n = 20$): 3 mL saline	CT guided at level of positive discography	• Reduction in LBP intensity reported on VAS (0–10 points)[a] • Reduction in disability reported on ODI[b]	3 and 6 months	Not reported	None
Nguyen et al., 2017	Age 18–70 years; failure of conservative treatment (analgesics, NSAIDs) or other spinal steroid injections (epidural or facet joint); intradiscal injection ≥6 months before inclusion; Social Security coverage	Treatment group (GC IDI; $n = 67$): 1 mL iodixanol contrast+ 1 mL (25 mg) prednisolone acetate Control group ($n = 68$): 1 mL iodixanol contrast only	Fluoroscopically guided at lumbar disc level correlating with Modic 1 changes (no provocative discography used)	Primary: percentage of patients with 48-hour average LBP intensity <40 on 11-point NRS at 1 month Secondary: • Reduction in LBP intensity reported on NRS (11-point scale)[a] • Active discopathy on MRI • Reduction in disability reported on QBPDS[b] • MOS SF-12 Physical and Mental Summary scales • HADS • Analgesic and NSAID use in previous week • Employment status • Changes in LBP-related activity limitations	1, 3, 6, and 12 months	SAEs[d] at 12 months: $n = 29$ (GC IDI group), $n = 27$ (control group)	Funded by French Ministry of Health

Akeda et al., 2022	Age >18 years; LBP >3 months, VAS >40 mm; ODI score >20% at baseline; painful DDD ≥1 lumbar level from L3–L4 to L5–S1 confirmed by radiographic findings and provocation discography; disc degeneration on MRI (Pfirrmann grade >II); <50% disc height loss; positive provocation discography	Treatment group ($n = 9$): 2 mL PRPr
		Control group (CS; $n = 7$): 2 mg betamethasone sodium phosphate in 2 mL saline
			Fluoroscopically guided at levels L3–L4 ($n = 1$ PRPr group; $n = 3$ CS group), L4–L5 ($n = 5$ PRPr group; $n = 6$ CS group), and L5–S1 ($n = 5$ PRPr group; $n = 1$ CS group)	Primary: reduction in LBP intensity reported on VAS (0–100 mm) for PRPr vs control group at 8 weeks[a]
				Secondary:
				• Change and % change in:
				  • VAS pain score[a]
				  • Disability reported on ODI[b]
				  • RDQ
				  • JOABPEQ
				• Change in disc height index
				• Pfirrmann and modified Pfirrmann classification change
				• PRPr vs CS treatment success ratio (defined as >30% improvement on VAS and ODI, no additional treatment, and no SAEs after injection)
					4, 8, 12, 16, 20, 34, and 60 weeks after initial injection	Two separate instances of post-injection pain: $n = 1$ (PRPr group)	Funded by Okasan-Kato Foundation

Single-blinded RCTs							
Khot et al., 2004	No age requirements reported; discogenic LBP with DDD on MRI; failure of conservative treatment >6 weeks; concordant pain with positive discography	Treatment group (steroid; $n = 60$): 1 mL (40 mg) Depo-Medrone (methylprednisolone) Control group ($n = 60$): 1 mL saline	Fluoroscopically guided at level of positive discography	Primary: Reduction in disability reported on ODI[b] Secondary: Reduction in LBP intensity reported on VAS[a]	12 months	Not reported	None

(continued)

Table 1. (continued)

Reference	Inclusion criteria	Injectate details	Injection imaging and location(s)	Outcome measures	Follow-up	Adverse events	Funding / author disclosures
Tavares et al., 2021	Age 18–80 years; LBP >6 weeks; Modic 1 changes; conservative treatment failure	Treatment group (GC; $n=17$): 0.5 mL contrast dye followed by 2 mL prednisolone acetate Control group ($n=22$): 0.5 mL contrast dye followed by 2 mL lidocaine (2%)	Fluoroscopically guided at levels L2–L3 ($n=5$), L3–L4 ($n=2$), L4–L5 ($n=21$), and L5–S1 ($n=22$)	Primary: Reduction in LBP intensity reported on VAS at 1 month[a] Secondary: • Reduction in LBP intensity reported on VAS[a] • Reduction in disability reported on ODI[b] • DPQ • MOS SF-36	1, 3, and 6 months	Hospitalization for usual care of CLBP: $n=3$ (GC group), $n=4$ (control group)	Funded by CHU Montpellier and CHU Nimes
Nonblinded RCT							
Buttermann, 2004	Age 18–65 years; conservative treatment failure; LBP >1 year with DDD diagnosis based on combination of clinical examination, medical history, and MRI	Treatment group (discography+ ISI): • Patients with inflammatory end plates (Modic I changes; $n=40$): mean 9.7 ± 4.3 mg betamethasone • Patients with noninflammatory end plates (no Modic I changes; $n=46$): mean 8.3 ± 4.4 mg betamethasone Control group (discography): No injectate details provided for either subgroup (Modic I changes, $n=38$; no Modic I changes, $n=47$)	Fluoroscopically guided at level(s) with positive discography	• Reduction in LBP intensity reported on VAS (0–10)[a] • Reduction in disability reported on ODI[b] • Pain diagram area • Pain medication use • Patient assessment of injection success (yes vs no)	1–3 months, 4–6 months, 7–12 months, 1–2 years	Not reported	None
Retrospective case series							
Fayad et al., 2007	Modic changes on MRI; conservative treatment failure ≥3 months	Treatment group ($n=37$ Modic I; $n=25$ Modic I-2; $n=12$ Modic II): 1 mL (25 mg) prednisolone acetate No control	Fluoroscopically guided at levels L2–L3 ($n=6$), L3–L4 ($n=5$), L4–L5 ($n=30$), and L5–S1 ($n=33$)	Primary: Reduction in LBP intensity reported on VAS (0–100 mm) at 1 month[a] Secondary: • Reduction in disability reported on QBPDS[b] • ≥50% reduction in VAS score[c] • PGA of treatment efficacy	1, 3, and 6 months	None	None
Beaudreuil et al., 2012	Conservative treatment failure; underwent lumbar MRI	Treatment group ($n=30$ Modic I-a; $n=37$ Modic I-b): 2 mL methylprednisolone Control group ($n=30$ DDD without Modic I changes): 2 mL methylprednisolone	Fluoroscopically guided at level(s) with Modic changes or DDD	• Reduction in LBP intensity reported on VAS (0–100 mm)[a] • Reduction in radiating pain intensity reported on VAS (0–100 mm) • Patient self-assessed pain improvement (yes vs no)	24 hours, latest follow-up (mean 14 ± 2 months)	Not reported	None
Prospective, observational study							
Yavuz et al., 2012	Conservative treatment failure ≥3 months; DDD on MRI; positive provocation discography	Treatment group ($n=18$): 1 mL betamethasone No control	Fluoroscopically guided at levels T12–L1 ($n=1$), L1–L2 ($n=1$), L3–L4 ($n=2$), L4–L5 ($n=13$), and L5–S1 ($n=3$)	• Reduction in LBP intensity reported on VAS (0–100 mm)[a] • Reduction in disability reported on QBPDS (0–100)[b] • Fingertip-to-floor distance (centimeters) • Duration of sitting without pain (minutes)	2 weeks, 3 months	None	None

Abbreviations: CHU= Centre Hospitalier Universitaire; CLBP= chronic low back pain; CS = corticosteroid; CT= computed tomography; DDD = degenerative disc disease; DPQ = Dallas Pain Questionnaire; GC = glucocorticoid; GC IDI = glucocorticoid intradiscal injection; HADS = Hospital Anxiety and Depression Scale; ISI = intradiscal steroid injection; JOABPEQ = Japanese Orthopaedic Association Back Pain Evaluation Questionnaire; LBP = low back pain; MOS = medical outcomes study; NRS = numeric rating scale; NSAID = nonsteroidal anti-inflammatory drug; ODI = Oswestry Disability Index; PGA = Patient Global Assessment; PRPr = platelet-rich plasma releasate; QBPDS = Quebec Back Pain Disability Scale; RCT= randomized controlled trial; RDQ= Roland-Morris Disability Questionnaire; SAE = serious adverse event; SF-12 = Short Form-12; SF-36 = Short Form-36; VAS = visual analog scale.

None of the included studies reported the prespecified categorical outcome of interest for disability reduction (>15-point reduction on ODI).

[a] Prespecified continuous outcome of interest for pain reduction.

[b] Prespecified continuous outcome of interest for disability reduction.

[c] Prespecified categorical outcome of interest for pain reduction.

[d] SAEs were defined as "any untoward medical occurrence that resulted in death, were life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, or resulted in persistent or clinically significant disability," excluding infections.[50]

any time point for each injection protocol. Adverse events were not reported. No funding disclosure was provided.

In 2017, Nguyen et al. published results of a multicenter double-blinded RCT comparing fluoroscopically guided IDCI (25 mg prednisolone acetate) with intradiscal iodixanol contrast (control) in 135 adults with CLBP.[50] Participants were adults 18–70 years of age referred for management of CLBP with last-48-hour average NRS greater than 40/100 and Modic 1 changes on MRI for less than 6 months. Exclusion criteria were previous disc surgery, current oral steroid treatment, ankylosing spondylitis, sciatica, previous or going infectious spondylodiscitis, fever, and multilevel Modic type 1 changes on MRI. Outcome measures, including NRS and QBPDS, were obtained at 1, 3, 6, and 12 months after the index injection. At 1 month, the mean reduction in LBP intensity from baseline as reported on the NRS (range 0–100) was significantly greater for the IDCI group than for the control group (–32.5 [CI –38.2 to –26.8] vs –17.5 [CI –23.3 to –11.7]; $P < .001$). At 12 months, however, this between-group difference was no longer significant (–18.2 [95% CI –24.2 to –12.2] for IDCI vs –24.8 [95% CI –30.9 to –18.7] for control; $P = .122$). Between-group comparisons of mean reduction in disability from baseline as reported on the QBPDS (range 0–100) were not statistically significant at 1-month (–11.9 [95% CI –16.0 to –7.8] for IDCI vs –6.7 [95% CI –10.8 to –2.7] for control; $P = .069$) or 12-month (–6.9 [95% CI –11.6 to –2.2] for IDCI vs –7.6 [95% CI –12.4 to –2.8] for control; $P = .83$) follow-up time points. These and additional study outcomes are reported in Table 2. No cases of infection or discitis were reported in either group. One case of sciatica, which was deemed possibly related to the intervention, was reported in the control group. Funding was provided by a research grant from the French Ministry of Health.

In 2004, Khot et al. published results of a single-blinded RCT comparing fluoroscopically guided IDCI (methylprednisolone acetate) with intradiscal saline injection in 120 adults with CLBP.[51] Participants were adults with "discogenic" LBP without radicular pain and failure of at least 6 weeks of conservative treatment without previous surgery. Radiographic inclusion criteria were MRI showing DDD and concordant pain on provocation discography of a "degenerative disc." The presence or absence of Modic changes was not reported. All fluoroscopically guided injections were performed at levels associated with positive provocation discography and were comprised of 1 mL of 40 mg/mL methylprednisolone or 1 mL saline. Outcomes including VAS and ODI were reported but only at the 12-month time point. At 12 months, no significant differences were noted between the 2 groups for either median change in LBP intensity on VAS (0 [IQR –0.25 to 1] for the steroid group vs 0 [IQR –1 to 1] for the saline control group; $P = .72$) or mean change in disability on the ODI (2.3 [SE 2.5] for the steroid group vs 3.4 [SE 1.8] for the saline control group; $P = .71$). Adverse events were not reported. The authors reported no funding for support of the study.

In 2021, Tavares et al. published results of a multicenter, single-blinded RCT comparing fluoroscopically guided IDCI (prednisolone acetate) with intradiscal lidocaine injection in 50 adults with CLBP.[52] Participants were adults 18–80 years of age with at least 6 weeks of LBP associated with single-level type 1 Modic changes that had not improved with conservative treatment. Those with multilevel Modic changes were excluded. All fluoroscopically guided injections were performed at levels with type 1 Modic changes. Outcomes included VAS, ODI, Dallas Pain Questionnaire, analgesic treatment, and work status at weeks 1–4 and at 3 and 6 months after injection. Collection of patient outcome data was concluded at the 6-month follow-up time point. With regard to the primary outcome, mean change in LBP intensity as reported on VAS was significantly greater at 1 month for the IDCI group than for the lidocaine control group (–2.7 ± 2.3 vs 0.1 ± 2.0; $P < .001$), but no significant differences were found between the 2 groups at 3 and 6 months ($P = .31$ and .45, respectively). No between-group differences in disability reduction as reported on the ODI were significant at 1, 3, or 6 months ($P = .3$, .2, and .4, respectively). There were significant differences in the daily activities of the Dallas Pain Questionnaire in favor of the active group, with the mean "daily activity" subscore improving in the active group by 21.2 and 30.6 points at 1 and 3 months, respectively, compared with 3.3- and 9.4-point improvements in the control group. Adverse events were defined as "hospitalization for usual care of chronic LBP" and reported as 3 in the study group and 4 in the control group. The study was supported by a research grant from Centre Hospitalier Universitaire Montpellier and Centre Hospitalier Universitaire Nimes. It was stated that funders had no role in study design, conduct, or reporting.

In 2022, Akeda et al. published results of a double-blinded RCT comparing fluoroscopically guided IDCI (methylprednisolone [CS]) with autologous PRPr in 16 adults with CLBP, with 15 patients receiving an optional PRPr injection 8 weeks after the first injection.[53] Participants were adults 18 years of age or older with CLBP lasting at least 3 months, a VAS >40 mm, ≥1 lumbar disc (L3/4 to L5/S1) with evidence of degeneration on MRI, and ≥1 symptomatic disc, with these levels confirmed by "standard provocative discography." The primary outcome was changes in VAS from baseline at 8 weeks, with secondary outcomes being pain, disability, quality of life, and safety for up to 60 weeks. At 8 weeks, both the PRPr (–30.9 ± 22.7) and CS (–26.3 ± 29.8) groups' VAS scores had decreased significantly from baseline ($P < .01$), with no significant differences between groups. Reductions in disability at 8 weeks as captured by ODI did not differ significantly between the PRPr (–14.5 ± 11.6) and CS groups (–7.7 ± 8.9); however, the study authors did not indicate whether these changes in ODI scores represented significant decreases from baseline values. Additional secondary outcomes, after optional PRPr injection in 15/16 participants at 8 weeks, are shown in Table 2. Post-injection pain was the only adverse event reported during this study. This study was supported by a grant from the Okasan-Kato foundation.

In 2004, Buttermann published results of a nonblinded RCT comparing fluoroscopically guided discography with or without concurrent administration of IDCI (betamethasone) in 171 adults categorized according to the presence ($n = 78$) or absence ($n = 93$) of inflammatory end plate (Modic type 1) changes on MRI.[54] Participants, who were 18–65 years of age, were part of a larger study population receiving epidural steroid injections to treat CLBP lasting at least 1 year that was refractory to conservative care. All were diagnosed with DDD on the basis of a combination of clinical examination, medical history, and MRI. Patients whose CLBP did not improve with epidural steroid injections were deemed potential spinal fusion surgery candidates and subsequently randomized to provocative discography, either as a standalone procedure or

Table 2. Pain and disability improvement outcomes data as reported on NRS/VAS and ODI/QBPDS for individual studies.

Reference	Outcome measures	Follow-up	Pain reduction outcomes	Disability reduction outcomes
Double-blinded RCTs				
Cao et al., 2011	VAS, ODI	• 3 months • 6 months	• Betamethasone subgroup: Significant decrease in VAS scores from baseline at 3 and 6 months for both Modic type I (6.5 ± 1.2 at baseline vs 1.8 ± 1.0 and 2.3 ± 1.0 at 3 and 6 months) and II (6.8 ± 1.3 at baseline vs 1.6 ± 0.8 and 2.1 ± 1.0 at 3 and 6 months) groups. • Betamethasone+ songmeile subgroup: Significant decrease in VAS scores from baseline at 3 and 6 months for both Modic type I (6.6 ± 1.4 at baseline vs 2.0 ± 0.8 and 2.2 ± 1.0 at 3 and 6 months) and II (7.1 ± 1.2 at baseline vs 1.6 ± 0.8 and 1.8 ± 0.9 at 3 and 6 months) groups. • Saline (control) subgroup: No change in VAS scores at any follow-up time point for either Modic type I (7.1 ± 1.6 at baseline vs 7.0 ± 1.3 and 7.5 ± 1.1) or type II (6.5 ± 1.2 at baseline vs 6.8 ± 1.0 and 6.4 ± 1.1 at 3 and 6 months) group. • No significant difference in pain reduction between betamethasone and betamethasone+ songmeile subgroups at any follow-up time point. • No significant difference in pain reduction between Modic type I and II groups for any intervention at any follow-up time point.	• Betamethasone subgroup: Significant decrease in ODI scores from baseline at 3 and 6 months for both Modic type I (35.7 ± 11.1 at baseline vs 13.1 ± 2.2 and 14.7 ± 3.2 at 3 and 6 months) and II (31.5 ± 5.9 at baseline vs 12.7 ± 2.1 and 13.8 ± 2.3 at 3 and 6 months) groups. • Betamethasone+ songmeile subgroup: Significant decrease in ODI scores from baseline at 3 and 6 months for both Modic type I (36.6 ± 12.7 at baseline vs 13.6 ± 3.1 and 16.9 ± 4.5 at 3 and 6 months) and II (34.2 ± 7.8 at baseline vs 13.1 ± 3.2 and 15.5 ± 4.7 at 3 and 6 months) groups. • Saline subgroup: No change in ODI scores at any follow-up time point in either Modic type I (37.9 ± 14.7 at baseline vs 42.0 ± 13.9 and 44.4 ± 14.0 at 3 and 6 months) or type II (32.4 ± 9.7 at baseline vs 33.3 ± 10.6 and 33.8 ± 12.0 at 3 and 6 months) group. • No significant difference in disability reduction between betamethasone and betamethasone+ songmeile subgroups at any follow-up time point. • No significant difference in disability reduction between Modic type I and II groups for any intervention at any follow-up time point.
Nguyen et al., 2017	NRS, QBPDS	• 1 month • 3 months • 6 months • 12 months	• Primary study outcome: Significantly higher responder rate in GC IDI group (36/65 [55.4%]) than in control group (21/63 [33.3%]), based on <40 NRS LBP score at 1 month. • Significantly greater decrease in mean NRS LBP scores from baseline at 1 month for GC IDI group (–32.5 [95% CI –38.2 to –26.8]) vs control group (–17.5 [95% CI –23.3 to –11.7]). • No difference in LBP pain improvement on NRS from baseline at 12 months between GC IDI (–18.2 [95% CI –24.2 to –12.2]) and control (–24.8 [95% CI –30.9 to –18.7]) groups.	• No difference in mean QBPDS score change from baseline between GC IDI group and control group at 1 month (–11.9 [95% CI –16.0 to –7.8] vs –6.7 [95% CI –10.8 to –2.7]) or at 12 months (–6.9 [95% CI –11.6 to –2.2] vs –7.6 [95% CI –12.4 to –2.8]).
Akeda et al., 2022	VAS, ODI	• 4 weeks • 8 weeks[a] • 12 weeks • 16 weeks • 20 weeks • 32 weeks • 60 weeks	• Primary study outcome: Significant decreases in VAS LBP scores from baseline at 8 weeks for both PRPr (–30.9 ± 22.7) and CS (–26.3 ± 29.8) groups; no significant difference in VAS score change between groups. • No significant differences in VAS LBP score change or % change from baseline between PRPr and CS groups for any follow-up time point.	• No significant differences in ODI score change or % change from baseline between PRPr and CS groups for any follow-up time point.
Single-blinded RCTs				
Khot et al., 2004	VAS, ODI	• 12 months	• No significant difference between steroid group and control group in median VAS pain score change from baseline at 12-month follow-up (0 [IQR –0.25 to 1] vs 0 [IQR –1 to1]).	• Primary study outcome: No significant difference in mean percentage disability change on ODI from baseline between steroid group and control group at 12-month follow-up (2.28 [SE 2.5] vs 3.4 [SE 1.8]).
Tavares et al., 2021	VAS, ODI	• 1 week • 2 weeks • 3 weeks • 1 month • 3 months • 6 months	• Primary study outcome: Significant difference in mean VAS LBP score changes from baseline between GC and control groups at 1-month follow-up (–2.7 ± 2.3 for GC vs 0.1 ± 2.0 for control). • Significantly greater pain reduction in steroid group than in control group according to VAS LBP score changes from baseline at weeks 2 and 3. No between-group differences at week 1 or months 3 and 6.	• No significant between-group differences in ODI score changes from baseline at 1, 3, or 6 months.
Nonblinded RCT				
Buttermann, 2004	VAS, ODI	• 1–3 months • 4–6 months • 7–12 months • 1–2 years	• Significantly greater reduction in VAS LBP scores from baseline at the 1- to 3-month follow-up time period for patients with and without Modic I changes treated with discography+ ISI compared with discography alone. • Significant reductions in VAS LBP scores from baseline at all follow-up time periods for patients with Modic I changes treated with discography+ ISI. • Significantly greater decreases in VAS LBP scores from baseline for patients with Modic I changes than for patients without Modic I changes at 1- to 3- and 4- to 6-month follow-up time periods.	• Significantly greater reduction in ODI scores from baseline at the 1- to 3-month follow-up time period for patients with and without Modic I changes treated with discography+ ISI compared with discography alone. • Significant reductions in ODI scores from baseline at all follow-up time periods for patients with Modic I changes treated with discography+ ISI. • Significantly greater decreases in ODI scores from baseline for patients with vs patients without Modic I changes at all follow-up time periods.

(continued)

Table 2. (continued)

Reference	Outcome measures	Follow-up	Pain reduction outcomes	Disability reduction outcomes
Retrospective case series				
Fayad et al., 2007	VAS, QBPDS	• 1 month • 3 months • 6 months	• Primary study outcome: Significantly greater mean VAS LBP score decreases from baseline to 1 month in Modic I and I-2 groups (30.2 ± 26.6 and 29.4 ± 21.5) than in Modic II-1 group (5.3 ± 25.5). No difference between Modic I and I-2 groups. • No significant between-group differences in VAS LBP changes from baseline at 3 or 6 months. • Significantly greater proportion of responders (defined as ≥50% pain reduction on VAS) at 1 month in Modic I and I-2 groups than in Modic II-1 group (54.5% and 52.0% vs 9.1%).	• No significant differences between groups in QBPDS score changes at any follow-up time point.
Beaudreuil et al., 2012	VAS	• 24 hours • Latest follow-up (mean 14 ± 2 months)	• Modic I-a group: Significant decrease in mean VAS LBP score from baseline at 24 hours (52 [SE 5] vs 28 [SE 5]). No difference in VAS radiating pain score from baseline at 24 hours or last follow-up. • Modic I-b group: Significant decrease in mean VAS LBP score from baseline at 24 hours (62 [SE 4] vs 37 [SE 5]). No difference in VAS radiating pain score from baseline at 24 hours or last follow-up. • Control group: No significant change in VAS LBP score or radiating pain score from baseline at either follow-up time point.	
Prospective, observational study				
Yavuz et al., 2012	VAS, QBPDS	• 2 weeks • 3 months	• Mean VAS spinal pain score decreased significantly from baseline (66.4 ± 13.7) at both 2-week (37.5 ± 17.1) and 3-month (39.2 ± 19.6) follow-up time points.	• Mean QBPDS score improved significantly from baseline (35.1 ± 15.9) at both 2-week (23.7 ± 14.5) and 3-month (24.4 ± 13.8) follow-up time points.

Abbreviations: CI = confidence interval; CS = corticosteroid; GC IDI = glucocorticoid intradiscal injection; IQR = interquartile range; ISI = intradiscal steroid injection; LBP = low back pain; NRS = numeric rating scale; ODI = Oswestry Disability Index; PRPr = platelet-rich plasma releasate; QBPDS = Quebec Back Pain Disability Scale; RCT= randomized controlled trial; SE = standard error; VAS = visual analog scale.

[a] The primary study endpoint occurred at 8 weeks after the initial injection of either CS or PRPr. At this time point, all study participants were offered an optional PRPr injection. Subsequent time point (12–60 weeks) analyses of outcome data were conducted only for participants who received the optional injection.

accompanied by simultaneous injection of intradiscal steroid. All injections were performed at levels with concordant pain upon provocation discography. Pain and disability outcomes were assessed with VAS and ODI, respectively, at follow-up time periods of 1–3 months, 4–6 months, 7–12 months, and 1–2 years. Additional outcomes included reductions in total area covered on pain diagrams, use of analgesic medications, and patients' assessment of whether the injection was successful (yes vs no) at treating their LBP symptoms. No prespecified primary or secondary outcomes were defined. Reporting of study outcomes and measures of statistical significance was limited to figures, with no supporting information provided in tables or the main text with regard to the magnitude or significance levels of changes to patient pain and functioning. Reductions from baseline in both LBP intensity on VAS and disability on ODI were significantly greater at 1–3 months for participants who received IDCI at the time of discography than for those who received discography alone ($P < .005$), regardless of whether they were identified as having Modic 1 changes at study initiation. However, precipitous study dropout rates by participants in the discography control group precluded statistical comparisons for time periods beyond 3 months. Among participants in the discography+ IDCI treatment group, individuals with Modic 1 changes had significantly greater reductions from baseline in VAS LBP scores at 1–3 months and 4–6 months ($P < .05$) and ODI disability scores at all follow-up time periods ($P < .04$) than did participants without Modic 1 changes. Mean VAS LBP and ODI scores were significantly decreased from baseline at all follow-up time periods for participants with Modic 1 changes in the discography+ IDCI group ($P < .05$), while mean VAS LBP scores for participants without Modic 1 changes showed significant improvements from baseline at 1–3 months and 4–6 months after discography+ IDCI. Adverse events were reported for 6 patients (all were dural punctures during epidural steroid injection), but it is unclear whether these individuals were among the subset of surgical candidates randomized to either of the provocative discography study groups. No study funding was reported.

Observational studies

In 2007, Fayad et al. published results of a single-center, retrospective, observational study of fluoroscopically guided IDCI (prednisolone) in 74 adults with CLBP.[55] Participants were adults 32–70 years of age with disabling CLBP with Modic changes on MRI of the lumbar spine, not responding to at least 3 months of conservative treatment. All fluoroscopically guided injections were performed at levels with Modic changes (type I = pure end plate edema, I-2 = mixture of type 1 and type 2 but predominantly edema changes, and II-1 = predominantly fatty changes). The primary outcome was change in LBP intensity, measured by VAS, from baseline to 1 month after injection. Secondary outcomes included change in LBP intensity recorded at 3 and 6 months and change in disability score at 1, 3, and 6 months, as well as the proportion of responders with at least 50% reduction in pain intensity at 1 month and the patient's global assessment of treatment efficacy at 1 month. Of note, data were available for 93.2% of patients ($n = 69$) at 1 month and for 81.1% and 75.7% of patients at 3 and 6 months, respectively. The primary outcome of pain intensity decreased from baseline to 1 month by a mean of 30.2 ± 26.6 in the Modic I group, 29.4 ± 21.5 in the Modic I-2 group, and 5.3 ± 25.5 in the Modic II-1 group, with reductions significantly higher in the Modic I and I-2 groups than in the Modic II group ($P = .009$ and .017). At 1 month, 54.5% of Modic I, 52% of Modic I-2,

and 8.3% of Modic II-1 participants had at least 50% reduction in pain. The patient's global assessment of treatment efficacy was rated as excellent or good in 54.4% of patients ($n = 18$) in the Modic I group, 32% of patients in the Modic I-2 group, and 10.2% of patients in the Modic II-1 group. The reduction in disability was greater in the Modic I and Modic I-2 groups than in the Modic II-1 group but not with statistical significance. Of note, at 3 and 6 months, both the Modic I and I-2 groups tended to have better results for all outcome measures than did the Modic II-1 group, but the result was not statistically significant. No adverse events of infection or hematoma were reported. Sources of funding were not reported.

In 2012, Yavuz et al. published results of a prospective, single-arm observational study of fluoroscopically guided IDCI (betamethasone) in 18 adults with CLBP and positive provocation discography who had failed to improve after at least 3 months of conservative treatment and who were noted to have DDD findings on MRI.[56] Clinical parameters were recorded at baseline, 2 weeks, and subsequently 3 months after treatment and included LBP intensity on VAS, QBPDS, fingertip-to-floor distance, and duration of sitting without pain. Mean VAS scores were found to have decreased significantly from baseline (66.4 ± 13.7) at 2 weeks and 3 months after treatment with IDCI (37.5 ± 17.1 and 39.2 ± 19.6, respectively; $P = .001$ and .002). Similar decreases in mean patient QBPDS scores from baseline (35.1 ± 15.9) were observed at 2 weeks and 3 months (23.7 ± 14.5 and 24.4 ± 13.8, respectively), again showing statistical significance at both time points ($P = .001$ and .002). Other secondary outcomes, including the mean fingertip-to-floor distance and mean duration of sitting without pain, showed statistical significance at both the 2-week and 3-month follow-up time points. No adverse events of infection or hematoma were reported. The authors reported no conflicts of interest and reported no funding for the study.

In 2012, Beaudreuil et al. published results of a retrospective study of fluoroscopically guided IDCI (methylprednisolone) in 97 adults with CLBP.[57] Participants were adults with severe, disabling CLBP whose disease had not responded to usual conservative treatments and who lacked evidence of systemic inflammatory disorder, metabolic bone disease, local infection, or malignancy, and all had undergone lumbar spine MRI with T1- and T2- weighted sequences. Participants were divided into 3 groups on the basis of MRI evaluations of Modic changes. Individuals with type I Modic changes were categorized by whether they had no history of disc surgery or nucleolysis treatment (Modic I-a) or had undergone one or both of these interventions ≥6 months before IDCI treatment (Modic I-b). A final control group consisted of patients with DDD but no Modic type I changes. Outcome measures including self-assessed improvement (yes vs no) and VAS scores (range 0–100 mm) for back and radiating pain were obtained at 24 hours after the index injection and then subsequently at the latest mean follow-up of 14 ± 2 months. Although both Modic I groups' VAS scores showed significant decreases in LBP intensity from baseline at 24 hours (Modic I-a, 52.0 ± 5.0 vs 28.0 ± 5.0; Modic I-b, 62.0 ± 4.0 vs 37.0 ± 5.0; $P < .05$), these improvements were not maintained through long-term follow-up. At a final mean follow-up of 14 ± 2 months, VAS LBP scores did not significantly differ from baseline for any of the 3 groups ($P > .05$). No discussion of adverse events was reported. The authors reported no conflicts of interest.

GRADE quality assessment

According to GRADE, there is low-quality evidence that IDCI provides short-term reduction in pain and disability in patients with discovertebral CLBP as evidenced by type 1 or type 2 Modic changes at involved segments. Although multiple RCTs have evaluated IDCI in patients with Modic changes, the body of evidence is limited by small study sizes (imprecision), risk of bias (only 1 RCT without concern for risk of bias[49]), and inconsistency of results. There is low-quality evidence that IDCI is ineffective at reducing pain and disability at 1 year in those with discovertebral pain as evidenced by positive provocation discography in the absence of Modic changes on MRI. There was insufficient evidence to provide a GRADE evidence quality rating for IDCI in those with discovertebral pain as evidenced by positive discography (without Modic changes) at short and intermediate time points; the sole RCT reported outcomes only at 1 year.[51] On the basis of a single RCT with high risk of bias and small sample size,[53] there is very-low-quality evidence to suggest that PRPr and intradiscal steroid produce similar reductions in pain and disability in those with discovertebral pain selected by positive provocation discography for up to 1 year. Given the paucity of RCTs, a GRADE evidence profile was not constructed. See Supplemental File S2 for results of the risk of bias assessment.

Discussion

Clinicians and researchers have made efforts to comprehend and classify the diverse causes of LBP, recognizing it as an often multifaceted and intricate condition. As the understanding of the underlying causes of CLBP has advanced, there has been a shift in focus toward the development of target-specific treatments. Increasing knowledge of the inflammatory nature of pathological discovertebral degeneration has prompted a number of new studies testing biological agents and a resurgence of interest in IDCI for those with chronic discovertebral pain.[16,58,59]

The aim of this systematic review was to identify and evaluate the quality of studies examining the effectiveness of IDCI for the treatment of chronic discovertebral LBP as evidenced by provocation discography or Modic type 1 or 2 changes. The review ultimately yielded 6 RCTs (total $n = 603$; $n = 319$ steroid, $n = 284$ placebo [saline = 100, contrast alone = 153, contrast+ lidocaine = 22, platelet-rich plasma releasate = 9]) that met the inclusion/exclusion criteria. The quality of the evidence supporting the use of IDCI for discovertebral LBP was considered "low." Short-term effectiveness of IDCI based on outcomes reported up to 6 months was found in all included studies other than Khot et al.; however, that study assessed outcomes only at 12-month follow-up and not before that time point.[51] Evaluations of effect duration with regard to improvements in both pain and disability ranged from 1 to 6 months, but not thereafter, in all studies. It is possible that the short-term effectiveness of IDCI is secondary to a systemic corticosteroid effect, but intramuscular injection of corticosteroid has been shown to produce clinically significant reductions in pain in only a minority of patients (21%) at 1 month.[60]

To provide precise and effective treatment, it is imperative to establish an accurate diagnosis of the underlying cause of CLBP. All studies in the present systematic review met the minimum eligibility requirement of selecting patients for IDCI treatment on the basis of Modic changes (type 1 or 2) or positive provocation discography at concordant levels. These diagnostic criteria were often combined with clinical findings, as well as radiographic evidence of DDD, to confirm that a patient's CLBP was indeed discovertebral in origin. Previous studies have shown DDD in 37% to 96% of asymptomatic individuals, with prevalence increasing with age.[61] Further research investigating the complex innervation and signaling pathways in both healthy and injured discovertebral segments could enhance our ability to appropriately provide sustained treatment of DDD by targeting the intervertebral disc only. In the present review, along with clinical suspicion, different imaging parameters were used with mixed prognostic results: IDCI was restricted to patients with Modic changes in 3 of 6 RCTs and 1 of 3 observational studies,[49,50,52,55] whereas IDCI administration in the remaining studies was based on "disc degeneration" findings with or without provocation discography.[51,53,54,56,57] Four studies (2 RCTs and 2 observational studies) investigated whether Modic changes had predictive value for patient outcomes. Buttermann observed that LBP and disability were significantly reduced in patients with inflammatory end plate changes (Modic type 1) compared with patients without Modic 1 changes.[54] Between-group disparities with regard to LBP improvement persisted through 6 months, whereas significant differences in disability reduction were still present at the final study follow-up period of 1–2 years. However, these findings were likely influenced by patients dropping out from the study: Attrition rates at 1- to 2-year follow-up were 68% and 76% among patients with and without Modic 1 changes, respectively. In a retrospective analysis comparing IDCI treatment outcomes in patients with and without Modic 1 changes, Beaudreuil et al. found no significant differences in LBP improvement at the average latest follow-up time of 14 months.[57] Cao et al. also observed no statistically significant difference in outcomes between participants with Modic I and II changes[49]; however, Fayad et al. did show statistically significant improvements in patients with Modic type I changes compared with those with Modic type II changes at all time points assessed.[53] These observations warrant further clinical investigation.

As is evidenced in this systematic review, our current understanding of imaging and pain sources in CLBP relies largely on clinical suspicion combined with imaging and potentially provocation discography. Clinical suspicion based on patient history and physical examination is inadequate for diagnosing discogenic pain.[62,63] The high prevalence of disc degeneration and disruption in asymptomatic individuals makes advanced imaging a similarly insufficient diagnostic tool.[64,65] When performed and interpreted according to current clinical guidelines from the Spine Intervention Society (SIS) / International Association for the Study of Pain (IASP), provocation discography provides superior diagnostic value for discogenic pain with low false positive rates.[7] Because no included studies provided necessary technical details (eg, pressure threshold, pain response, etc.) for determining whether discography procedures and subsequent interpretation of results met these standards, we cannot make inferences about the utility of provocation discography for predicting IDCI treatment outcomes. Evidence suggests that surgical outcomes for discectomy and spinal fusion are improved when patient selection criteria include a guideline-concordant positive discography response compared with clinical and imaging findings alone.[7] However, the prognostic value of discography for assessing the likelihood that a patient will benefit from IDCI remains undetermined. The limitations of these diagnostic approaches underscore the need for consistent implementation and reporting of protocols when discography is used to confirm suspected discogenic sources of CLBP.

Although IDCI does appear to provide short- to medium-term pain relief, effective and durable treatments are needed in this difficult-to-treat population. A previous systematic review for "regenerative" therapies, including intradiscal platelet-rich plasma and stem cells, suggested mixed results and overall very low-quality evidence.[66] Results from the Akeda et al. study were included in the present review.[53] This RCT investigated outcomes at 8 weeks for patients who had received either IDCI or PRPr injections. Both the IDCI and PRPr groups showed statistically significant improvement in VAS pain scores from baseline, with no differences between groups. However, all subjects were offered an optional PRPr injection at 8 weeks regardless of their original injection type; 15 out of 16 patients elected to receive the optional injection, making further outcomes analysis of IDCI difficult past that time point.

As discussed, the present systematic review provides evidence of potential short-term pain relief after IDCI. In addition to intradiscal treatments, targeting the intraosseous portion of the basivertebral nerve has emerged as a safe and effective treatment for pain arising from the discovertebral complex.[12,13,59,67] In contrast to the short-term relief observed in multiple studies discussed previously, research has shown that an updated technique for the basivertebral nerve ablation procedure might provide long-term effectiveness for vertebrogenic pain, as studied up to 5 years.[25,68,69]

With IDCI exhibiting short-term effectiveness, consideration and reporting of adverse events are important, and reporting was absent in 2 of 6 included RCTs and 1 of 3 cohort studies. One study suggested adverse events rates of 39% to 43% between groups[50]; although the authors explicitly stated that none of the adverse events were infections, they provided no further explanation for the study's unexpectedly high adverse event rate compared with those reported in the literature.[70,71]

Limitations of the present review and its findings must be acknowledged. Despite the exhaustive search strategy, this review yielded only 6 RCTs and 3 cohort studies of IDCI for the treatment of discovertebral pain. This small number inherently limits our ability to draw firm conclusions. It also is worth mentioning that the steroid injectate differed among RCTs ($n = 1$ methylprednisolone; $n = 2$ prednisolone; $n = 3$ betamethasone), which might have influenced the observed results in these studies.

Conclusion

According to GRADE, there is low-quality evidence that IDCI provides a short-term reduction in pain and disability in those with chronic discovertebral LBP as evidenced by Modic 1 and 2 changes. There is low-quality evidence that IDCI does not provide reduction in pain and disability in those with chronic discovertebral LBP when selected by positive provocation

discography alone. IDCI does not appear to be effective beyond 6 months, regardless of selection method.

Supplementary material

Supplementary material is available at *Pain Medicine* online.

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