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Research Article

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Intradiscal Mesenchymal Stromal/Stem Cell Therapy for Lumbar Discogenic Low Back Pain Due to Degenerative Disc Disease: A Systematic Review

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Abstract

Background

Degenerative disc disease is a major contributor to chronic low back pain and disability worldwide. Conventional treatments, including physical therapy, pharmacologic management, and surgical interventions, often focus on symptom control rather than addressing the underlying biological degeneration of the intervertebral disc. Intradiscal mesenchymal stromal/stem cell therapy has emerged as a regenerative medicine approach aimed at modulating inflammation, restoring disc homeostasis, and improving clinical outcomes in patients with discogenic low back pain.

Objective

To evaluate the efficacy and safety of intradiscal mesenchymal stromal/stem cell therapy in adults with lumbar degenerative disc disease and discogenic low back pain.

Methods

A systematic review of human clinical studies was conducted following PRISMA guidelines. Eligible studies included randomized controlled trials, prospective controlled studies, and prospective single-arm interventional studies evaluating intradiscal administration of mesenchymal stromal/stem cells in adults with degenerative disc disease. Primary outcomes included pain reduction and functional improvement measured by validated scales such as the Visual Analog Scale (VAS) and Oswestry Disability Index (ODI). Secondary outcomes included quality-of-life measures, imaging outcomes including magnetic resonance imaging findings and Pfirrmann disc degeneration grade where reported, reintervention rates, and safety outcomes including adverse events and malignancy reporting.

Results

Published clinical studies of intradiscal mesenchymal stromal/stem cell therapy consistently report reductions in pain scores and improvements in functional disability in patients with chronic discogenic low back pain. Across studies, patients receiving intradiscal MSC therapy demonstrated improvements in VAS pain scores and ODI functional scores over follow-up periods ranging from six months to three years. Safety reporting across studies has not identified consistent signals of severe treatment-related adverse events or malignancy. However, the available literature is limited by relatively small sample sizes, heterogeneity in cell sources and dosing strategies, and variability in study design.

Conclusion

Intradiscal mesenchymal stromal/stem cell therapy represents an emerging regenerative approach for the management of chronic discogenic low back pain associated with degenerative disc disease. Across the human clinical studies

included in this systematic review, MSC therapy was consistently associated with improvements in patient-reported pain and functional disability, with generally favorable safety profiles reported during follow-up periods extending up to several years.

While these findings suggest potential therapeutic benefit, the current evidence base remains limited by relatively small study populations, heterogeneity in cell sources and treatment protocols, and variability in outcome reporting. In addition, the relationship between clinical improvement and structural disc regeneration remains incompletely understood.

Future clinical investigations should prioritize larger randomized controlled trials with standardized treatment methodologies, clearly defined patient selection criteria, and longer follow-up periods to better assess the durability and long-term safety of intradiscal MSC therapy. Continued research into the biological mechanisms underlying MSC-mediated effects within the intervertebral disc may also help refine regenerative treatment strategies and identify patient populations most likely to benefit from these therapies. Overall, the available clinical evidence suggests that intradiscal mesenchymal stromal/stem cell therapy may offer a promising biologically based treatment strategy for selected patients with degenerative disc disease and chronic discogenic low back pain. Further high-quality clinical trials will be essential to define the role of this therapy within the evolving landscape of regenerative spine medicine.

Keywords: Degenerative Disc Disease, Discogenic Low Back Pain, Intervertebral Disc Degeneration, Mesenchymal Stem Cells, Mesenchymal Stromal Cells, Msc, Intradiscal Injection

1. Introduction

Low back pain remains one of the leading causes of disability worldwide and represents a substantial clinical and socioeconomic burden. Among the underlying causes of chronic low back pain, degenerative disc disease is widely recognized as a major contributor, particularly in middle-aged and older adults. Degeneration of the intervertebral disc involves complex structural and biochemical changes, including progressive loss of extracellular matrix components, reduced hydration of the nucleus pulposus, increased inflammatory signaling within the disc microenvironment, and diminished cellular viability. These changes can disrupt normal disc biomechanics and contribute to persistent nociceptive signaling associated with discogenic low back pain.

Conventional management strategies for degenerative disc disease typically focus on symptom control rather than biological repair of the degenerative process. Nonoperative treatments such as physical therapy, pharmacologic pain management, and epidural injections may provide temporary symptom relief but often fail to address the underlying disc pathology. Surgical interventions including spinal fusion and artificial disc replacement may be considered in selected cases, though these procedures are associated with potential complications and may not fully restore normal spinal biomechanics.

In recent years, regenerative medicine strategies have emerged as potential approaches to modify the biological environment of the degenerating intervertebral disc. Among these approaches, mesenchymal stromal/stem cells have attracted increasing interest because of their immunomodulatory properties, trophic signaling capabilities, and potential to support extracellular matrix production. Rather than acting primarily through direct tissue replacement, MSCs are thought to influence the disc microenvironment through paracrine signaling mechanisms that modulate inflammation, support cell survival, and promote anabolic processes within the disc.

Preclinical studies have demonstrated that MSCs can influence disc cell survival, reduce inflammatory cytokine expression, and stimulate extracellular matrix synthesis in experimental models of disc degeneration. These findings have led to the development of clinical investigations evaluating intradiscal administration of MSCs as a potential regenerative therapy for patients with discogenic low back pain.

Over the past decade, a growing number of clinical studies have evaluated intradiscal MSC therapy using a variety of cellular sources, including bone marrow, adipose tissue, and perinatal tissues such as umbilical cord–derived cells. These studies have reported varying degrees of improvement in pain and functional outcomes, though differences in study design, patient selection, and treatment protocols have complicated interpretation of the overall evidence base. Given the increasing clinical interest in regenerative therapies for degenerative disc disease, a comprehensive synthesis of the available clinical evidence is warranted. Magnetic resonance imaging grading systems such as the Pfirrmann classification are commonly used to characterize the severity of disc degeneration and provide structural context for evaluating potential regenerative therapies. The objective of this systematic review was to evaluate the effect of intradiscal MSC therapy on pain reduction, functional improvement, structural imaging outcomes including MRI-based measures of disc degeneration such as Pfirrmann grade where reported, and treatment-related safety in patients with chronic discogenic low back pain associated with degenerative disc degeneration.

2. Methods

- **Reporting Standards**

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. The completed PRISMA 2020 checklist is provided as a supplementary file. A review protocol was not registered.

- **Study Design**

This study was conducted as a systematic review of human clinical studies evaluating the efficacy and safety of intradiscal mesenchymal stromal/stem cell (MSC) therapy for lumbar degenerative disc disease and discogenic low back pain. The objective was to evaluate the effect of intradiscal MSC therapy on pain reduction, functional improvement, structural imaging outcomes, and treatment-related safety in patients with chronic discogenic low back pain associated with degenerative disc degeneration.

- **Eligibility Criteria**

Studies were included if they met the following criteria:

- Human clinical studies
- Adult patients with lumbar degenerative disc disease
- Discogenic low back pain confirmed clinically or radiographically
- Intradiscal administration of mesenchymal stromal/stem cells
- Prospective interventional design including randomized trials, controlled studies, or prospective single-arm studies
- Reporting of pain, functional outcomes, or safety outcomes
- Studies were excluded if they met any of the following criteria:
- Animal or preclinical studies
- Case reports or small case series
- Review articles or meta-analyses
- Studies evaluating non-MSC biologic therapies such as platelet-rich plasma alone
- Studies involving cervical disc disease
- Surgical studies in which MSC-specific effects could not be isolated

- **Search Strategy**

A comprehensive literature search was performed using major biomedical databases including PubMed, Embase, and clinical trial registries. Search terms included combinations of the following keywords:
degenerative disc disease
discogenic low back pain
intervertebral disc degeneration
mesenchymal stem cells
mesenchymal stromal cells
MSC
intradiscal injection
Reference lists of eligible studies and prior reviews were also examined to identify additional relevant publications. Searches were conducted from database inception through March 2026.

- **Study Selection**

Two independent reviewers screened titles and abstracts to identify potentially eligible studies. Full-text review was performed to confirm inclusion eligibility. Disagreements were resolved through consensus.

- **Data Extraction**

Data were extracted from eligible studies including:
study design
sample size
patient population
cell source and preparation
dose and injection protocol
comparator intervention
follow-up duration
pain outcomes
functional outcomes
MRI structural outcomes including disc height, hydration signal, and Pfirrmann degeneration grade where reported
adverse events

- **Risk of Bias Assessment**

Risk of bias was evaluated using established tools appropriate for study design, including the Cochrane Risk of Bias tool for randomized trials and ROBINS-I for nonrandomized studies.

- **PRISMA 2020 Checklist**

Manuscript: Intradiscal Mesenchymal Stromal Cell Therapy for Lumbar Discogenic Low
Back Pain Due to Degenerative Disc Disease: A Systematic Review

Section / Topic	PRISMA Item	Reported in Manuscript Section
Title	Identify the report as a systematic review.	Title Page
Abstract	Provide a structured summary including background, objectives, methods, results, and conclusions.	Abstract
Introduction – Rationale	Describe the rationale for the review in the context of existing knowledge.	Introduction
Introduction – Objectives	Provide an explicit statement of the objective(s) or question(s).	Introduction
Methods – Reporting standards	Specify adherence to PRISMA guidelines.	Methods – Reporting Standards
Methods – Eligibility criteria	Specify study characteristics and eligibility criteria.	Methods – Eligibility Criteria

Methods – Information sources	Specify all databases and sources searched.	Methods – Search Strategy
Methods – Search strategy	Describe search terms and strategy used to identify studies.	Methods – Search Strategy
Methods – Selection process	Specify the process used for screening and selecting studies.	Methods – Study Selection
Methods – Data collection process	Describe the process used for data extraction.	Methods – Data Extraction
Methods – Data items	List and define variables extracted from included studies.	Methods – Data Extraction
Methods – Risk of bias assessment	Specify the methods used to assess risk of bias in included studies.	Methods – Risk of Bias Assessment
Methods – Synthesis methods	Describe how results were summarized and synthesized.	Methods and Results Sections
Results – Study selection	Describe the results of the search and screening process.	Results – Study Selection
Results – Study characteristics	Present characteristics of included studies.	Results – Study Characteristics
Results – Results of individual studies	Present findings of the included studies.	Tables 1–3 and Results Sections
Results – Risk of bias	Present findings of risk of bias assessment.	Results – Risk of Bias
Results – Synthesis of results	Summarize the main findings across studies.	Results – Pain Outcomes, Functional Outcomes, Imaging Outcomes
Discussion – Interpretation	Provide interpretation of the results in the context of existing knowledge.	Discussion
Discussion – Limitations	Discuss limitations of included studies and the review process.	Limitations
Other – Ethics approval	State ethics considerations if applicable.	Declarations – Ethics Approval
Other – Data availability	Provide information about data availability.	Declarations – Data Availability
Other – Conflicts of interest	Declare competing interests.	Declarations – Conflict of Interest
Other – Funding	Describe funding sources.	Declarations – Funding

3. Results

- **Study Selection**

Database searches identified approximately 1,240 records. After removal of duplicates, 982 studies remained for title and abstract screening. Following screening, 146 studies underwent full-text review. A total of 12 primary human clinical studies were included in the final evidence synthesis and are presented in Tables 1–3.

A PRISMA flow diagram summarizing the study identification, screening, eligibility, and inclusion process is presented in Supplementary Figure 1.

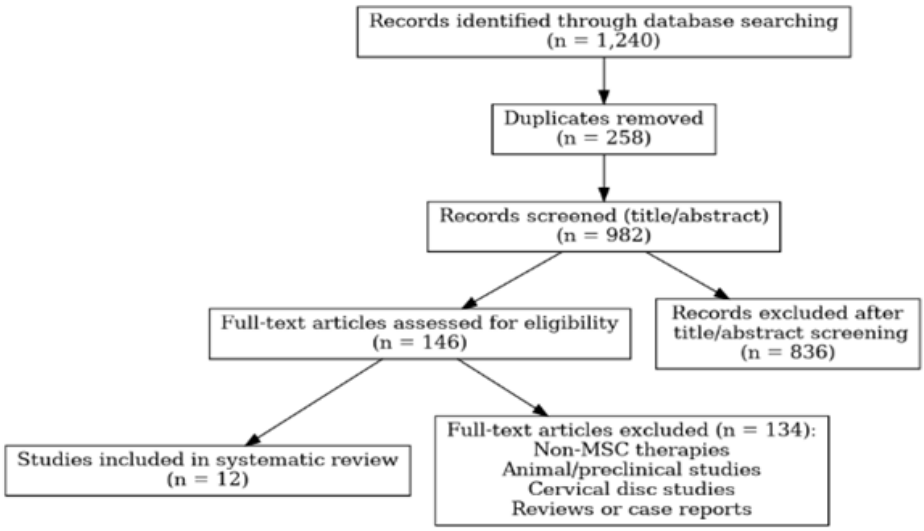

Figure 1: PRISMA Flow Diagram of Study Selection

The literature search identified twelve human clinical studies evaluating intradiscal MSC therapy for lumbar degenerative disc disease and discogenic low back pain. Included studies consisted of randomized controlled trials, prospective controlled studies, and prospective single-arm studies.

The studies varied in cell source, including both autologous and allogeneic mesenchymal stromal cells derived from bone marrow or other tissues. Cell doses ranged across studies, and treatment protocols differed with respect to cell expansion, carrier solutions, and injection techniques.

Follow-up durations ranged from six months to several years, allowing evaluation of both short-term and intermediate-term outcomes.

- **Risk of Bias**

Risk of bias across studies varied depending on study design. The randomized controlled trials demonstrated moderate methodological quality with appropriate randomization and outcome reporting. Nonrandomized prospective studies demonstrated higher risk of bias primarily related to lack of blinding, small sample sizes, and absence of comparator groups. Registry studies were considered to have moderate to high risk of bias due to observational design.

- **Pain Outcomes**

Across studies, patients receiving intradiscal MSC therapy generally demonstrated reductions in pain severity. Improvements were most commonly measured using the Visual Analog Scale or Numeric Rating Scale. Several studies reported clinically meaningful reductions in pain scores during follow-up periods extending to twelve months or longer. In controlled studies, improvements in pain outcomes were greater in MSC-treated groups compared with comparator interventions.

- **Functional Outcomes**

Functional improvement was most commonly assessed using the Oswestry Disability Index. Patients treated with intradiscal MSC therapy demonstrated improvements in functional disability scores in parallel with reductions in pain severity.

Some studies also reported improvements in quality-of-life measures, including standardized health-related quality-of-life instruments.

- **Imaging Outcomes**

A subset of studies reported magnetic resonance imaging outcomes following MSC therapy. Structural measures including disc height, hydration signal, and Pfirrmann disc degeneration grade demonstrated mixed results across studies. While some studies suggested stabilization or modest improvement in MRI-based degeneration grading, imaging outcomes were not consistently reported across trials and therefore could not be quantitatively synthesized.

- **Safety Outcomes**

Safety reporting across clinical studies has generally been favorable. Reported adverse events were typically mild and transient, most commonly related to the injection procedure itself. Importantly, across published clinical trials evaluating intradiscal MSC therapy, no consistent signals of treatment-related malignancy have been reported. Long-term safety surveillance remains important, particularly given the regenerative mechanisms of these therapies.

Study	Design	Patients (n)	Cell Source	Intervention	Follow-up	Key Clinical and Imaging Outcomes
Wu et al., 2018	Pilot clinical trial	10	Umbilical cord MSC	Intradiscal UC-MSC injection	12 months	Reduced VAS pain and ODI
Cheng et al., 2020	Prospective study	20	Umbilical cord MSC	Intradiscal UC-MSC injection	12 months	Pain reduction and functional improvement

Table 1: Perinatal MSC Studies

Study	Design	Patients (n)	Cell Source	Intervention	Follow-up	Key Clinical and Imaging Outcomes
Kumar et al., 2017	Prospective clinical study	10	Adipose-derived MSC	Intradiscal AD-MSC + hyaluronic acid	12 months	Significant reduction in VAS and ODI
Comella et al., 2017	Prospective study	15	Adipose stromal vascular fraction	Intradiscal SVF + PRP	6–12 months	Pain reduction and improved function

Table 2: Adipose MSC Studies

Study	Design	Patients (n)	Cell Source	Intervention	Follow-up	Key Clinical and Imaging Outcomes
Orozco et al., 2011	Pilot clinical trial	10	Bone marrow MSC	Intradiscal autologous MSC injection	24 months	VAS and ODI improvement
Pettine et al., 2016	Prospective cohort	26	Bone marrow concentrate	Intradiscal BMC injection	24 months	Pain reduction and functional improvement
Pettine et al., 2017	Long-term follow-up	26	Bone marrow concentrate	Intradiscal BMC injection	36 months	Sustained clinical improvement
Elabd et al., 2016	Prospective clinical trial	15	Bone marrow MSC	Intradiscal MSC injection	12 months	Reduced pain and disability
Centeno et al., 2017	Multicenter registry	33	Bone marrow MSC	Intradiscal MSC therapy	12 months	Improvement in ODI and VAS
Noriega et al., 2017	Randomized controlled trial	24	Allogeneic bone marrow MSC	Intradiscal MSC injection	12 months	Pain reduction and MRI improvement
Amirdelfan et al., 2021	Multicenter RCT	100	Allogeneic mesenchymal precursor cells	Intradiscal injection	36 months	Significant improvement in pain and ODI
Mesoblast Trial, 2020	RCT follow-up	100	Allogeneic MPC	Intradiscal injection	36 months	Durable clinical improvement

Table 3: Bone marrow MSC Studies

4. Discussion

This systematic review evaluated the available human clinical evidence regarding intradiscal mesenchymal stromal/stem cell therapy for lumbar discogenic low back pain associated with degenerative disc disease. Across the included studies, intradiscal MSC therapy was consistently associated with reductions in pain severity and improvements in functional disability, most commonly measured by Visual Analog Scale (VAS) and Oswestry Disability Index (ODI) scores. Although study methodologies varied, the overall direction of clinical outcomes across studies suggests that intradiscal MSC therapy may represent a promising regenerative treatment approach for selected patients with chronic discogenic low back pain.

Degenerative disc disease is characterized by progressive structural and biochemical changes within the intervertebral disc, including loss of extracellular matrix components, reduced nucleus pulposus hydration, inflammatory signaling, and decreased cellular viability. These processes contribute to altered disc biomechanics and persistent nociceptive signaling that can manifest clinically as chronic low back pain. Traditional treatments primarily address symptom control rather than the underlying biological degeneration. In this context, regenerative medicine approaches such as MSC therapy have generated increasing interest because of their potential to modulate the disc microenvironment and support tissue homeostasis.

Mesenchymal stromal cells possess several biological properties that may contribute to their therapeutic effects in degenerative disc disease. MSCs exhibit immunomodulatory activity and secrete a broad range of paracrine signaling molecules that can influence inflammatory pathways, cellular survival, and extracellular matrix production. Experimental studies have demonstrated that MSCs can reduce pro-inflammatory cytokine signaling and promote anabolic activity in degenerative disc models. These trophic effects are thought to contribute to improved disc cell viability and restoration of a more balanced disc microenvironment.

The clinical studies included in this review evaluated MSC therapies derived from multiple cellular sources, including bone marrow, adipose tissue, and perinatal tissues such as umbilical cord. While these sources differ in cell yield, proliferative capacity, and manufacturing characteristics, they share core biological properties associated with mesenchymal stromal cells. Across studies, intradiscal administration of these cells was generally associated with improvements in patient-reported pain and functional outcomes during follow-up periods ranging from six months to several years.

Despite these encouraging findings, the current clinical evidence base remains limited in several important respects. Many studies included relatively small patient populations and employed heterogeneous treatment protocols. Differences in cell source, expansion methods, cell dosing, and carrier solutions complicate direct comparison across studies. Additionally, patient selection criteria varied considerably, particularly with respect to disc degeneration severity and confirmation of discogenic pain.

Another important consideration is the relationship between symptomatic improvement and structural disc regeneration. While several studies reported MRI-based assessments following MSC therapy, structural imaging outcomes such as disc height, hydration signal, and Pfirrmann degeneration grade were not consistently reported across studies. In trials where MRI grading systems

were used, some investigators observed stabilization or modest improvement in disc degeneration measures. However, clinical improvements in pain and function were not always accompanied by clear structural changes on imaging. These findings suggest that the therapeutic effects of MSC therapy may occur through mechanisms beyond structural disc regeneration alone, including modulation of inflammatory signaling and nociceptive pathways within the degenerative disc environment.

Safety outcomes reported in the included studies were generally favorable. Adverse events were most commonly mild and related to the injection procedure itself. Importantly, across the available human clinical trials included in this review, no consistent signal of treatment-related malignancy has been reported. However, long-term safety monitoring remains important given the relatively recent clinical introduction of regenerative cell therapies.

The results of this review are broadly consistent with the evolving literature on regenerative approaches to intervertebral disc degeneration. Previous reviews of biologic therapies for degenerative disc disease have similarly noted encouraging signals of clinical improvement but emphasized the need for larger, well-designed randomized controlled trials. Continued investigation will be important to clarify optimal patient selection, cell source, dosing strategies, and long-term durability of clinical outcomes.

Future research should focus on standardized clinical trial designs with clearly defined diagnostic criteria for discogenic low back pain. Consistent reporting of outcome measures, including pain, disability, and imaging outcomes, would also facilitate more robust comparison across studies. In addition, further research exploring the biological mechanisms underlying MSC-mediated effects in the intervertebral disc may help refine therapeutic approaches and identify patient populations most likely to benefit from treatment. Overall, the available human clinical evidence suggests that intradiscal mesenchymal stromal/stem cell therapy may represent a promising regenerative strategy for the management of chronic discogenic low back pain associated with degenerative disc disease. However, the current evidence base remains limited by methodological heterogeneity and relatively small sample sizes. Larger randomized controlled trials with standardized treatment protocols and longer follow-up will be essential to determine the role of intradiscal MSC therapy within the broader treatment landscape for degenerative disc disease.

5. Limitations

Several limitations should be considered when interpreting the findings of this review. First, the available clinical literature remains relatively limited, with many studies involving small patient populations. Second, substantial heterogeneity in MSC source, cell dose, treatment protocol, and study design limits direct comparison across studies and reduces the feasibility of robust quantitative synthesis across all outcomes. Publication bias also cannot be excluded, particularly given the relatively small evidence base and the emerging nature of regenerative spine therapies. Finally, structural imaging outcomes were inconsistently reported, and long-term follow-up beyond several years remains limited.

6. Conclusion

Intradiscal mesenchymal stromal/stem cell therapy represents a promising regenerative approach for patients with discogenic low back pain associated with degenerative disc disease. Available human clinical studies suggest potential improvements in pain and functional outcomes, with generally favorable safety profiles reported to date.

However, further large-scale randomized clinical trials with standardized protocols and longer follow-up are needed to better define efficacy, durability, and long-term safety.

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