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Injection Therapies for Rotator Cuff Tears: A Comprehensive Literature Review

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ABSTRACT

Introduction: Rotator cuff tears are one of the primary cause of shoulder pain and disability. Conventional non-operative treatments often provide only short-term symptomatic relief without addressing the underlying degenerative pathology, while surgical intervention carries its own risks. This has led to increased interest in injection therapies, notably dextrose prolotherapy and biologic therapies derived from mesenchymal stem cells (MSCs).

Objective: To synthesize and compare the current evidence regarding dextrose prolotherapy versus cell-based and cell-free (secretome) therapies for the treatment of partial-thickness rotator cuff tears.

Methodology: A comprehensive literature review was conducted to compare injections of dextrose prolotherapy, cell-based therapy, and MSC-derived secretome (cell-free therapy). Primary outcomes included functional measures (pain, range of motion, validated scores) and evidence of structural or biological healing (imaging, histology, biomarkers).

Results: Dextrose prolotherapy consistently demonstrated significant long-term improvements in pain and function compared to placebo or conventional care. Cell-based therapies using adipose-derived products were found to be safe and is functionally superior to corticosteroids. As a surgical augment, results were mixed, showing either short-term functional gains or improved long-term structural integrity (reduced retear rates). Cell-free secretome therapy showed strong preclinical evidence for potent anti-inflammatory, anti-apoptotic, and pro-regenerative effects, with early clinical evidence suggesting rapid functional improvement.

Conclusion: Both dextrose prolotherapy and biologic therapies are promising non-operative treatments for rotator cuff tears. Dextrose prolotherapy is a viable and effective option for symptomatic relief. Cell-based and secretome therapies show greater potential for true biological tissue regeneration but require more robust clinical data.

KEYWORDS: Rotator Cuff Tear, Prolotherapy, Secretome, Cell-based therapy

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BACKGROUND

Rotator cuff tears are a leading cause of shoulder pain and dysfunction, with a prevalence that increases significantly with age. This condition, particularly partial-thickness tears of the supraspinatus tendon, presents a major clinical challenge. Standard non-operative management—including physical therapy, non-steroidal anti-inflammatory drugs (NSAIDs), and corticosteroid injections—often fails to provide lasting relief and does not alter the natural history of the disease, which can include tear progression and muscle atrophy. Surgical repair is typically reserved for cases refractory to conservative treatment but is associated with a lengthy recovery and a notable rate of healing failure or retear. 1

The limitations of these conventional approaches have fueled intensive research into novel biologic and regenerative strategies. The goal of these new therapies is to move beyond mere symptom management and create an optimal biological environment that promotes true physiological healing of the tendon. Among the most studied emerging injection therapies are dextrose prolotherapy, a stimulative therapy designed to trigger the body's natural healing cascade, and biologic therapies, which use a patient's own cells or cellular products to directly facilitate tissue regeneration. This review aims to synthesize the current evidence for these non-conventional injection therapies to compare their mechanisms, clinical effectiveness, and potential roles in managing partial rotator cuff tears. 2,3

METHODOLOGY

This comprehensive literature review was conducted by synthesizing evidence from a curated collection of preclinical and clinical studies. The search included randomized controlled trials (RCTs), cohort studies, systematic reviews and meta-analyses, case reports, and in vivo animal studies. The literature was categorized based on the primary intervention investigated.

The interventions of interest were: (1) Dextrose Prolotherapy, defined as Injections of hypertonic dextrose solution, with or without an anesthetic agent, administered to the site of tendon pathology. (2) Cell-Based Biologic Therapy, defined as Injections of autologous, adipose-derived products, including freshly isolated regenerative cells (UA-ADRCs) or microfragmented lipoaspirate tissue, used either as a standalone therapy or as a surgical augment. (3) Cell-Free Biologic Therapy (Secretome), defined as Injections of products secreted by Mesenchymal Stem Cells (MSCs), such as conditioned medium or isolated exosomes, used to harness the paracrine effects of stem cells without transplanting live cells.

The primary outcomes analyzed across the studies were categorized into functional and structural domains. Functional outcomes included changes in pain levels (e.g., Visual Analog Scale/VAS), shoulder function scores (e.g., ASES, SPADI, WORC), and range of motion (ROM). Structural and biological outcomes included evidence of tendon healing on imaging (MRI or Ultrasound), histological improvements in animal models, and changes in the expression of relevant biomarkers for tenogenesis.

RESULTS

Dextrose Prolotherapy

The evidence for dextrose prolotherapy is supported by several RCTs and systematic reviews. Clinically, it is significantly more effective than placebo (saline injection) and conventional exercise therapy for long-term pain reduction and functional improvement 4,5. A network meta-analysis by Lin et al. (2019) identified prolotherapy as the superior injection therapy for long-term pain relief compared to corticosteroids and PRP. When compared directly with corticosteroids, results are mixed, with some studies showing equivalent or superior short-term outcomes 6,7. However, the effect of prolotherapy on the physical structure of the tendon remains a point of contention. While some studies have reported sonographic evidence of improved tendon morphology 8, Higher-quality studies have failed to find significant structural changes, suggesting its primary benefit is symptomatic rather than regenerative 4,7,9.

Biologic Therapies

Cell-Based (Lipid-Derived) Therapy

Therapies using a patient's own adipose (fat) tissue have been consistently shown to be safe. Their efficacy, however, appears to depend heavily on the application. As a standalone, non-operative treatment, a single injection of uncultured, adipose-derived regenerative cells (UA-ADRCs) was found to be significantly superior to a corticosteroid injection for improving long-term shoulder function10. When used as an augment during arthroscopic surgery, the results are less clear. One RCT found that augmenting repair with microfragmented adipose tissue accelerated functional recovery in the short term (at 6 months) but offered no long-term clinical or structural advantage 11. In contrast, another study using adipose-derived MSCs mixed with fibrin glue reported a significantly lower rate of tendon retear, indicating a structural benefit, but this did not translate to superior clinical scores at final follow-up12.

Cell-Free Therapy (Secretome)

The secretome, containing the paracrine factors secreted by MSCs, represents a promising frontier. Preclinical evidence is strong. In vitro studies show that the secretome has potent anti-inflammatory and cytoprotective effects on tendon cells exposed to inflammatory conditions 13. Animal studies have demonstrated that the secretome can modulate the local immune environment by promoting anti-inflammatory macrophage polarization (Chen et al., 2021) and upregulate key biomarkers for tendon formation, such as Tenomodulin (TNMD) and RUNX2 14. Furthermore, exosomes, a key component of the secretome, have been shown to prevent muscle atrophy and fatty infiltration associated with chronic rotator cuff tears in animal models 15,16. Clinical evidence in humans is still emerging, but is encouraging. A case report documented significant pain reduction and functional improvement within one week of a secretome injection, although immediate structural changes were not visible on ultrasound17.

DISCUSSION

The collected evidence reveals a clear distinction between the therapeutic approaches for rotator cuff tendinopathy. Dextrose prolotherapy has established itself as a reliable, low-cost option for long-term symptomatic relief. Its mechanism, likely a non-specific stimulation of the local healing environment, consistently improves pain and function, making it a strong alternative to corticosteroids, which offer only transient benefits. However, its inability to reliably produce structural regeneration suggests it may not alter the underlying pathology.

In contrast, biologic therapies, both cell-based and cell-free, are aimed directly at tissue regeneration. The consistent safety profile of autologous lipid-based products is a major advantage. The conflicting results between standalone injections (showing functional benefit) and surgical augmentation (showing mixed functional/structural benefits) highlight that the timing and method of application are critical variables that need further investigation. The secretome represents the most targeted biological approach, with a strong preclinical rationale for modulating inflammation and promoting tenogenesis. Its potential to be an "off-the-shelf" product without the complexities of live cell therapy makes it a particularly attractive avenue for future research.

The primary limitation across this body of literature is the absence of direct, head-to-head comparative trials. Without studies comparing dextrose prolotherapy directly against secretome therapy or cell-based injections, it is difficult for clinicians to make evidence-based decisions about which regenerative option may be superior. Furthermore, the heterogeneity in protocols—including dextrose concentration, cell preparation methods, and injection techniques—complicates the comparison of results across different studies.

CONCLUSION

Dextrose prolotherapy and biologic therapies (cell-based and secretome) are valuable and promising alternatives to conventional treatments for partial rotator cuff tears. Dextrose prolotherapy is a clinically effective, safe, and affordable option for patients seeking long-term pain relief and functional improvement. Biologic therapies, particularly those derived from adipose tissue and the MSC secretome, show greater potential for true tissue regeneration and disease modification. However, they require more robust clinical evidence and standardization of protocols before they can be widely adopted. Future research must prioritize high-quality, head-to-head randomized controlled trials to definitively establish the comparative effectiveness of these promising therapies.

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