



Muscle Strain Injuries: Comparative Evaluation of Platelet-Rich Plasma, Platelet-Rich Fibrin, and Prolotherapy

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Abstract

Context: Muscle injuries are among the most common sports-related traumas, accounting for 30%–55% of all athletic injuries. This review evaluates the therapeutic efficacy of three regenerative approaches—platelet-rich plasma (PRP), platelet-rich fibrin (PRF), and prolotherapy—in the treatment of muscle strains.

Evidence Acquisition: This narrative review synthesized current clinical and mechanistic evidence on PRP, PRF, and prolotherapy in the management of muscle strain injuries. A targeted search of the relevant literature was performed to identify influential and representative studies. The aim was to summarize key patterns, physiological mechanisms, and clinical implications rather than to conduct a systematic or exhaustive analysis.

Results: Platelet-rich plasma demonstrated promising regenerative effects through growth factor-mediated modulation of inflammation and tissue repair; however, clinical outcomes varied because of differences in preparation protocols. Platelet-rich fibrin may provide a fibrin-based scaffold with sustained release of bioactive molecules, making it a potential option for chronic or severe injuries; however, high-quality clinical trials remain limited. Prolotherapy, by inducing controlled inflammation, may provide symptomatic improvement, but its regenerative impact appears less consistent than that of platelet-based therapies. Across all modalities, methodological variability and limited comparative studies remain major challenges.

Conclusions: Current evidence suggests that PRP and PRF may be beneficial treatment options for muscle injuries. However, owing to heterogeneity in study design and preparation protocols, as well as the limited number of high-quality comparative trials, definitive conclusions regarding their superiority or routine clinical use cannot yet be established. Protocol standardization remains crucial. Future research should prioritize direct comparative studies and the evaluation of combination therapies with novel regenerative approaches.

Keywords: Platelet-rich Plasma, Platelet-rich Fibrin, Prolotherapy, Muscle Strain, Muscle Injuries, Sports Injuries, Acute Muscle Strains, Chronic Muscle Strains

1. Context

Muscle injuries are common among athletes and physically active individuals, accounting for approximately 30%–55% of all sports-related injuries (1). Among these injuries, muscle strains are particularly prevalent, with up to 92% affecting major lower-limb muscle groups, such as the hamstrings, quadriceps, and gastrocnemius. These injuries typically result from excessive stretching or sudden, forceful contractions,

making them a frequent concern in high-intensity and team sports (1).

The hamstring muscles are particularly susceptible to injury and are often affected during high-speed activities such as sprinting and kicking. Other commonly affected muscles include the adductors, quadriceps, and calf muscles. Muscle strains can range from mild, self-limiting injuries to severe, career-threatening conditions. They pose substantial challenges in sports medicine because of slow healing

and frequent incomplete functional recovery. Achieving full recovery and return to play is essential not only for athletic performance but also for minimizing financial and professional consequences, such as lost wages and sponsorship opportunities.

A major barrier to complete muscle regeneration is the development of scar tissue and fibrosis, which can impair muscle repair. To address these challenges, various regenerative strategies have been explored. Platelet-rich plasma may promote muscle healing by releasing growth factors and cytokines from platelets, thereby enhancing tissue regeneration. Platelet-rich fibrin, a second-generation platelet concentrate, may offer additional advantages, including prolonged growth factor release and potentially improved healing outcomes, and is increasingly used because of its autologous nature and straightforward preparation (2, 3). Prolotherapy, which involves the injection of irritant solutions to stimulate tissue repair, has also been used for musculoskeletal injuries, although its efficacy relative to PRP and PRF remains under investigation (4, 5). This review evaluates the mechanisms of action, clinical efficacy, and comparative outcomes of PRP, PRF, and prolotherapy and provides clinicians and researchers with a comprehensive perspective to inform optimal treatment selection.

2. Evidence Acquisition

2.1. Research Design

This study was conducted as a narrative review to summarize current evidence on PRP, PRF, and prolotherapy for the management of muscle strains, with a focus on clinical outcomes and mechanistic insights.

2.2. Search Strategy

A narrative literature search was conducted using major biomedical databases and relevant published literature to identify representative and influential studies on PRP, PRF, and prolotherapy for muscle strain injuries. The purpose of this narrative review was to provide conceptual and clinical insight rather than to conduct a systematic or exhaustive search. Studies were selected based on relevance to mechanisms, clinical applications, and emerging trends in regenerative therapies. Keywords included “platelet-rich plasma,” “platelet-rich fibrin,” “prolotherapy,” and “muscle strain injuries.” The aim was not to identify all available studies systematically but to prioritize articles

providing clinically relevant evidence, mechanistic insights, or comprehensive reviews.

2.3. Data Extraction and Synthesis

Relevant information from the selected studies was qualitatively analyzed. Key themes, mechanistic insights, clinical outcomes, and controversies were identified to provide a narrative synthesis of regenerative therapies for muscle strains.

2.4. Narrative Comparative Overview

This review compares PRP, PRF, and prolotherapy across three dimensions: 1) mechanisms, including biological pathways that promote tissue repair and regeneration; 2) efficacy, including clinical outcomes such as pain reduction, functional recovery, and return to activity; and 3) limitations, including practical and methodological constraints such as variability in preparation protocols, cost, and accessibility. This comparative overview is intended to provide a conceptual and clinical perspective rather than to establish definitive comparative effectiveness.

3. Results

3.1. Platelet-Rich Plasma

3.1.1. Mechanism of Action

Platelet-rich plasma is an autologous plasma fraction with a platelet concentration higher than baseline levels (150000 - 450000/ μ L) (6, 7). It contains platelets, clotting factors, cytokines, chemokines, growth factors, including vascular endothelial growth factor, transforming growth factor beta, and platelet-derived growth factor, as well as plasma proteins (8-11). These bioactive molecules regulate tissue repair by modulating inflammation, angiogenesis, stem cell recruitment, and cellular proliferation (12, 13).

Transforming growth factor beta 1 has a dual role: it supports tissue repair through fibroblast proliferation and extracellular matrix synthesis but may also contribute to fibrosis if unregulated (14-17). Therefore, PRP functions as both a reservoir of growth factors and a signaling system that influences proliferation, differentiation, chemotaxis, and tissue morphogenesis. Heterogeneity in platelet concentration, leukocyte content, and activation methods affects clinical outcomes.

3.1.2. Clinical Efficacy

Platelet-rich plasma is used in acute muscle strains to accelerate the return to play (18, 19). Some studies have reported faster recovery and reduced pain, whereas others, including Hamilton et al., found no significant benefit compared with standard care (18). Meta-analyses indicate shorter recovery in some studies; however, results remain inconsistent, particularly for hamstring injuries (21, 22).

In chronic muscle injuries, PRP has shown potential benefits, including pain reduction and functional improvement, particularly when ultrasound-guided injections are used (23-25). However, variations in platelet concentration, centrifugation, leukocyte content, and patient-related factors limit the generalizability of these findings (26, 27).

3.1.3. Limitations

The main limitations of PRP include heterogeneity in preparation protocols and patient-related factors that influence outcomes (26, 27). The limited number of high-quality randomized controlled trials restricts definitive conclusions regarding dosing, timing, and long-term efficacy (18, 21, 27).

3.2. Platelet-Rich Fibrin

3.2.1. Mechanism of Action

Platelet-rich fibrin is a second-generation platelet concentrate comprising platelets, leukocytes, and growth factors embedded within a fibrin matrix (28). It is prepared without anticoagulants, maintaining a fully autologous composition (29, 30). Its fibrin matrix acts as a scaffold, allowing sustained release of growth factors and supporting proliferation, differentiation, angiogenesis, and tissue regeneration (31).

3.2.2. Clinical Efficacy

Platelet-rich fibrin is primarily applied in chronic or surgical muscle repair. Studies suggest potential benefits in tissue healing, pain reduction, and functional recovery when combined with rehabilitation (27, 31-33). However, the evidence mainly comes from small cohorts or case series, and variability in preparation and application limits comparability.

3.2.3. Limitations and Gaps

The preparation of PRF can be more complex than that of PRP, which may limit feasibility (34). Long-term outcomes are largely unknown (35). Variability in centrifugation, clot handling, and injection technique

also affects efficacy (21, 28-31). Standardized preparation methods and high-quality trials are needed to confirm the efficacy of PRF (28, 29, 31, 33, 35, 36, 37, 38).

3.3. Prolotherapy

3.3.1. Mechanism of Action

Prolotherapy involves the injection of irritant solutions, such as dextrose or saline, to induce controlled inflammation and stimulate tissue repair (5). Unlike PRP and PRF, prolotherapy does not directly deliver growth factors.

3.3.2. Clinical Efficacy

Evidence for prolotherapy is limited primarily to chronic muscle strains. Studies have reported potential benefits in pain reduction and functional improvement compared with placebo or exercise therapy (4, 5). For example, more than 50% pain reduction was reported in 73% of patients with chronic hamstring injuries following dextrose prolotherapy (4).

3.3.3. Limitations and Gaps

The inflammatory mechanism of prolotherapy may limit structured tissue regeneration (5). Outcomes vary according to injury type, chronicity, and injection technique (5). In addition, limited high-quality evidence restricts the generalizability of the available findings (4).

3.4. Comparative Overview

Platelet-rich plasma is the most extensively studied modality. It may be effective in acute and chronic injuries, but outcomes vary because of preparation methods, injection timing, and muscle-specific responses (19). Platelet-rich fibrin provides scaffold support and sustained growth factor release and may be beneficial in chronic injuries, although high-quality trials are lacking (21, 28-31, 33, 35, 38). Prolotherapy is primarily used in chronic injuries through inflammation-mediated repair, but its evidence base is limited and less predictable (4, 5). Critical gaps include a lack of standardized protocols, limited high-quality trials, and the need for muscle-specific studies.

4. Discussion

This narrative review evaluated the current evidence on PRP, PRF, and prolotherapy for muscle strain injuries, highlighting their distinct mechanisms, clinical applications, and comparative advantages. These

biologic therapies are increasingly used in sports medicine to support tissue repair and functional recovery in frequently injured muscle groups, such as the hamstrings, quadriceps, and gastrocnemius (1, 23, 24).

Platelet-rich plasma remains the most extensively studied regenerative modality. Its therapeutic effects are primarily mediated by concentrated platelets and associated bioactive molecules, which regulate inflammation, enhance angiogenesis, recruit stem cells, and stimulate cellular proliferation and differentiation (6-13). However, clinical outcomes with PRP remain heterogeneous. Some studies have reported accelerated return to play, reduced pain, and improved functional recovery (16, 17, 19, 22), whereas others, particularly in hamstring injuries, have shown no significant advantage over conventional rehabilitation (18, 20, 21). This variability largely reflects differences in PRP preparation protocols, including centrifugation speed, leukocyte content, activation methods, and injection timing, as well as patient-specific factors such as age, baseline platelet count, and comorbidities (26, 27, 32).

As a second-generation platelet concentrate, PRF offers mechanistic advantages over PRP, including a three-dimensional fibrin scaffold and sustained growth factor release, which may support tissue integration, angiogenesis, and long-term regeneration (28-31, 35). Although PRF has shown encouraging outcomes in chronic muscle injuries and surgical applications, including reduced pain and improved functional recovery (27, 31-33), clinical evidence remains limited because of small cohort sizes, heterogeneity in preparation protocols, and a lack of high-quality randomized controlled trials (34, 35, 37). The autologous nature, relative ease of handling, and favorable safety profile of PRF make it an attractive option, particularly for chronic or severe injuries in which sustained regenerative signaling may be beneficial (29, 30).

Prolotherapy represents a mechanistically distinct approach. It induces controlled inflammation through the injection of irritant solutions, such as dextrose, to stimulate endogenous tissue repair (4, 5, 31). Evidence for prolotherapy is mainly derived from chronic musculoskeletal conditions and suggests potential benefits of pain reduction and functional improvement (4, 5). However, its regenerative capacity appears less robust than that of PRP or PRF because it does not provide exogenous growth factors. Outcomes are also highly context dependent and influenced by factors such as injury chronicity, injection technique, and patient selection (5, 31). Despite these limitations, prolotherapy may provide a cost-effective alternative,

particularly for patients with financial constraints or contraindications to platelet-based therapies.

Platelet-rich plasma is generally preferred for acute muscle injuries because of its rapid delivery of growth factors and established clinical familiarity (23, 29). Platelet-rich fibrin may be more advantageous in chronic or severe injuries because it provides scaffold support and prolonged release of growth factors that facilitate sustained tissue regeneration (31, 33). Prolotherapy is primarily used in chronic injury management and may complement rehabilitation when platelet-based therapies are unavailable or contraindicated (4, 5). Emerging evidence suggests that combining regenerative modalities may offer synergistic benefits by integrating growth factor signaling from PRP or PRF with inflammatory priming from prolotherapy to enhance tissue repair (31, 35). Furthermore, combining platelet-derived therapies with advanced regenerative approaches, such as mesenchymal stem cells or exosome-based treatments, shows promise for accelerating functional recovery, modulating inflammation, and promoting structured tissue regeneration (25, 30, 35).

4.1. Limitations and Future Directions

Despite growing interest in regenerative injections, important gaps remain. Heterogeneity in preparation methods, injection protocols, and outcome measures limits reproducibility and cross-study comparisons. The lack of high-quality randomized trials, especially those evaluating head-to-head comparisons of PRP, PRF, and prolotherapy, limits definitive conclusions regarding their relative efficacy.

Future research should prioritize standardizing preparation and administration protocols, conducting muscle-specific and injury-grade-specific studies, evaluating long-term functional outcomes to determine the durability of therapeutic effects, and investigating combination therapies, as well as integrating regenerative injections with advanced regenerative strategies. Importantly, current evidence does not support definitive recommendations regarding the routine use or superiority of PRP, PRF, or prolotherapy over standard rehabilitation. Clinicians should interpret available findings cautiously and consider individual patient factors, injury severity, and clinical context when selecting regenerative injection therapies.

5. Conclusions

Platelet-rich plasma, PRF, and prolotherapy are minimally invasive regenerative approaches for muscle

strain injuries. Current evidence suggests that these therapies may provide benefits in pain reduction and functional recovery, particularly in selected clinical contexts. However, owing to heterogeneity in study designs, variability in preparation protocols, and the limited number of high-quality randomized comparative trials, their comparative effectiveness and clinical superiority in routine practice cannot yet be definitively established. Clinicians should interpret the current evidence with caution and consider these therapies as adjunctive or emerging options rather than standard first-line treatments. Further well-designed randomized controlled trials, standardized protocols, and long-term studies are essential to clarify their optimal clinical role, validate efficacy, optimize treatment selection, and establish clinical guidelines.

Footnotes

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