

PLATELET-RICH PLASMA AS A PHARMACOPUNCTURE AGENT IN CERVICAL MYOFASCIAL PAIN

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Abstract

Chronic cervical myofascial pain (CMP) is a prevalent musculoskeletal disorder characterized by persistent neck pain, inflammation, functional impairment, and altered pain processing. Conventional treatments, including pharmacological therapy and physical rehabilitation, often provide limited and temporary relief. Increasing evidence suggests that chronic CMP involves not only peripheral nociceptive input but also nociplastic pain mechanisms driven by sustained neuroimmune dysregulation and central sensitization. Pharmacopuncture, combining acupuncture point stimulation with localized injection of therapeutic agents, has evolved with the introduction of regenerative biologics such as platelet-rich plasma (PRP). PRP contains concentrated platelets and bioactive growth factors, including VEGF, PDGF, and TGF- β , which exert anti-inflammatory and tissue-reparative effects. Emerging data indicate that PRP pharmacopuncture may reduce pro-inflammatory cytokines (e.g., IL-1 β and TNF- α), modulate regulated cell death pathways (e.g., apoptosis and pyroptosis), and promote the restoration of myofascial tissue homeostasis. These mechanisms may contribute to both peripheral tissue repair and attenuation of nociplastic pain processing. This narrative review synthesizes current clinical and experimental evidence on the biological mechanisms and therapeutic potential of PRP pharmacopuncture in chronic CMP. Available studies report meaningful improvements in pain intensity and functional outcomes compared with conventional acupuncture or pharmacotherapy alone. However, substantial methodological heterogeneity may arise from PRP preparation protocols, acupoint selection, and outcome measures, limiting the ability to draw definitive conclusions. High-quality randomized controlled trials incorporating standardized protocols and mechanistic biomarkers are required to establish PRP pharmacopuncture as an evidence-based integrative treatment for chronic CMP.

Keywords: platelet-rich plasma, pharmacopuncture, cervical myofascial pain, chronic neck pain, regenerative therapy, inflammation

Introduction

Myofascial pain syndrome is considered the most common non-articular musculoskeletal pain condition and a leading cause of chronic neck pain.¹ Chronic neck pain represents a significant public health challenge, as it not only imposes a substantial personal burden on affected individuals but also exerts broader impacts on families, healthcare systems, and the national economy.² According to the Global Burden of Diseases, Injuries, and Risk Factors (GBD) study, approximately 203 million people worldwide experienced neck pain in 2020. Based on international age-standardized estimates, the global prevalence of neck pain was 2,450 per 100,000 population, while the disability rate associated with neck pain was 244 per 100,000 population. Furthermore, the GBD 2019 report ranked neck pain 11th among 369 conditions contributing to global disability. Individuals with chronic neck pain who develop functional limitations often experience marked reductions in their quality of life, daily functioning, and economic productivity.^{3,4}

In chronic neck pain, inflammatory processes are frequently involved, and cytokines such as IL-1 β and TNF- α may play key roles in sustaining or exacerbating pain. IL-1 β can initiate and prolong inflammatory responses within cervical tissues, thereby contributing to nociceptive sensations. Both cytokines influence the microenvironment surrounding inflamed tissues, leading to persistent or prolonged pain. Assessing IL-1 β in chronic neck pain promotes a better understanding of the inflammatory dimension of this condition. Such information may aid in therapeutic planning and offer additional insights into the pathogenesis of chronic neck pain.^{5,6} Therapeutic strategies capable of simultaneously modulating inflammatory mediators, promoting tissue repair, and restoring neuromuscular function are of increasing clinical interest in the management of chronic neck pain. Conventional conservative therapies often provide only partial or temporary relief, underscoring the need for integrative treatment approaches that address both the biochemical and biomechanical dimensions of persistent pain. In this context, pharmacopuncture has emerged as a promising modality that bridges conventional acupuncture principles with targeted biologically active interventions. Pharmacopuncture involves injecting pharmacological or bioactive agents directly into specific acupoints, thereby enhancing therapeutic effects beyond those achieved with mechanical needle stimulation alone. By combining acupuncture neuromodulation with localized biochemical actions, this technique offers a multimodal approach that may more effectively influence inflammatory pathways, tissue perfusion, and neuromuscular dysfunction.⁷⁻⁹

Platelet-rich plasma (PRP) has therefore been increasingly applied in musculoskeletal pain management due to its ability to stimulate tissue repair, attenuate inflammatory activity, and provide sustained analgesic effects. This platelet enrichment facilitates supraphysiological release of various growth factors and bioactive mediators, including

platelet-derived growth factor (PDGF), transforming growth factor- β (TGF- β), insulin-like growth factor (IGF), and vascular endothelial growth factor (VEGF). Collectively, these mediators contribute to enhanced tissue regeneration, modulation of inflammatory responses, and improved healing of both acute and chronic musculoskeletal injuries. VEGF, one of the key components of PRP, plays a central role in angiogenesis, the process of forming new blood vessels from pre-existing vasculature. In chronic inflammatory conditions such as chronic neck pain, elevated VEGF activity may promote pathological angiogenesis in affected tissues. This neovascularization can alter local blood supply and oxygenation, modify the tissue microenvironment, and indirectly sustain inflammatory processes. In several chronic musculoskeletal conditions, aberrant angiogenesis is closely associated with heightened nociceptor activity, tissue hypersensitivity, and persistent pain perception. Consequently, characterizing VEGF in the context of chronic neck pain is essential to better understand the interplay among angiogenesis, chronic inflammation, and prolonged pain pathophysiology.¹⁰ The therapeutic effects of PRP are strongly influenced by its preparation protocol, particularly leukocyte concentration. Leukocyte-rich PRP (LR-PRP) and leukocyte-poor PRP (LP-PRP) exhibit distinct cytokine profiles affecting IL-1 β and TNF- α release. While LP-PRP may reduce acute inflammation, growing evidence indicates that LR-PRP provides superior long-term benefits through sustained immunomodulation, tissue remodeling, and durable functional recovery in chronic myofascial pain.^{11,12}

Despite growing clinical interest in pharmacopuncture incorporating regenerative biologics, the mechanistic basis and therapeutic rationale for integrating PRP into acupuncture-based interventions for chronic neck pain remain insufficiently synthesized. In particular, the ways in which PRP-mediated biological processes—such as modulation of inflammation, tissue regeneration, nociceptor plasticity, and regulated cell death induced neuromodulation have not been systematically reviewed. This narrative review therefore aims to critically consolidate current evidence on PRP pharmacopuncture, identify key mechanistic pathways, and clarify its potential role in advancing multimodal, mechanism-informed management strategies for chronic CMP.

Cervical Myofascial Pain

Cervical myofascial pain (CMP) is a musculoskeletal disorder characterized by pain originating from the muscles and surrounding connective tissues of the neck region. Myofascial pain syndrome is a recurrent form of chronic pain affecting muscles, fascia, or related soft tissues and is frequently accompanied by notable emotional disturbances or functional impairment. It is widely regarded as the most common non-articular musculoskeletal pain syndrome and represents a leading cause of chronic neck pain.^{1,13} Although many cervical spine disorders associated with chronic neck pain demonstrate

detectable structural abnormalities on Magnetic Resonance Imaging (MRI), patients with myofascial pain typically present with normal MRI findings.¹

The current pain classification framework recognizes three principal pain mechanisms, viz., nociceptive, neuropathic, and nociplastic, with an additional category describing mixed pain states. Traditionally, trigger points (TPs) have been considered a source of nociceptive pain. However, growing evidence indicates that in certain individuals, TPs may coexist with predominantly neuropathic or nociplastic pain components. This overlap can complicate clinical assessment and poses challenges in designing effective, mechanism-based treatment strategies for patients.¹⁴ Referred pain (Figure 1), traditionally categorized as either visceral or somatic, describes pain perceived at a location distant from its actual source. Visceral referred pain arises from pathology within internal organs, with the perceived pain distributed to regions innervated by the corresponding sensory nerve roots.¹⁵ Within the TPs framework, each muscle is believed to exhibit a characteristic pattern of referred pain; however, numerous mapped pain patterns indicate that a single muscle may generate multiple referred pain manifestations. These referred pain phenomena can be classified according to their origin into peripheral nerve-mediated referred pain, segmental referred pain arising from the same nerve root, and specific or characteristic referred pain patterns, each representing distinct underlying mechanisms.¹⁶

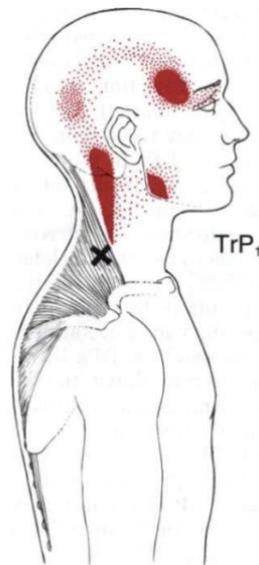


Figure 1. Referred pain pattern of the upper trapezius trigger point.¹⁷

Inflammation plays a critical role in the pathophysiology of neck pain, particularly when it originates from myofascial sources. Key inflammatory mediators implicated in this process include interleukin-1 β (IL-1 β), IL-6, IL-8, tumor necrosis factor- α (TNF- α), substance P, bradykinin, norepinephrine, calcitonin gene-related peptide, and serotonin. The myofascial tissue constitutes a continuous connective-tissue network throughout the body, providing stabilization and structural linkage to muscles and anchoring them to the

overlying skin. This connective layer is composed primarily of dense collagen fibers, which confer structural integrity, and elastin, which enables elasticity. Fibroblasts are the predominant cell type in the myofascial matrix and play a central role in tissue injury and repair. Adipocytes and various leukocyte populations may also be present within the myofascial tissue.⁶ IL-1 β has been extensively investigated and is well recognized for its ability to enhance multiple fibroblastic functions, particularly those involved in tissue repair and inflammatory responses. Recent studies demonstrate that IL-1 β influences extracellular matrix metabolism and modulates several forms of regulated cell death (RCD), including apoptosis, pyroptosis, and ferroptosis. IL-1 β expression is significantly elevated in degenerative compared with non-degenerative conditions, as supported by immunohistochemical evidence. Moreover, its expression levels show a positive correlation with both patient age and disease severity, underscoring its relevance in the progression of degenerative musculoskeletal disorders.^{18,19}

Pharmacopuncture

Pharmacopuncture is a relatively new acupuncture-based therapeutic technique that integrates the benefits of pharmacological agents with the principles of conventional acupuncture. Whereas conventional acupuncture relies on physical stimulation of specific acupoints, pharmacopuncture involves injecting pharmacologically active substances directly into selected acupoints. This approach offers several advantages over conventional acupuncture, including a more rapid onset of action, greater flexibility in adjusting dosages, and the potential for synergistic therapeutic effects arising from combined pharmacological and acupuncture stimulation.^{7,8}

Although pharmacopuncture has been applied across a broad spectrum of clinical conditions, its most frequent and extensively studied use is in the management of musculoskeletal disorders. In this domain, its therapeutic effects in modulating inflammation, alleviating pain, and promoting tissue recovery have been investigated more systematically than in other areas.⁷ In addition to its clinical efficacy, pharmacopuncture demonstrates notable economic benefits in chronic neck pain management. Compared with usual care, it provides slightly better quality-of-life outcomes while reducing societal costs by approximately USD 1,157, with a 100% probability of being cost-effective at a willingness-to-pay threshold of USD 26,374. From the healthcare system perspective, pharmacopuncture also shows lower incremental costs and an 83.7% likelihood of cost-effectiveness. These findings indicate that pharmacopuncture is a more cost-effective option than standard care and should be considered as a viable therapeutic alternative.²⁰

The primary mechanism of pharmacopuncture involves the synergistic interaction between the mechanical stimulation of acupuncture points and the biochemical effects of the injected pharmacological solution.²¹ In an experimental study employing

pharmacopuncture with a transient receptor potential (TRP) agonist at acupoint ST36, the intervention demonstrated a significant antinociceptive effect compared with the control group receiving normal saline.²² An animal study evaluated the analgesic effects of *Datura Flos* Pharmacopuncture (DFP). *Datura Flos* is an herbal substance composed primarily of alkaloids distributed throughout the plant. These alkaloids exert analgesic activity through interactions with the opioid system. Opioids produce analgesia by inhibiting neurons in the gray matter of the brainstem and spinal cord. The study concluded that DFP provides short-term analgesic effects, indicating its potential utility in pain management.²³

Platelet-Rich Plasma

Autologous PRP is a processed peripheral blood derivative containing platelet concentrations substantially above baseline levels. PRP therapy has been utilized across a wide range of clinical indications for more than three decades, generating considerable interest in its regenerative potential and its applicability within contemporary regenerative medicine.²⁴ PRP contains a wide range of biologically active factors, including PDGF, TGF- β , IGFs, VEGF, and epidermal growth factor (EGF).²⁵ Normal human serum contains approximately 150,000–450,000 platelets per microliter. Although PRP was initially defined as any preparation with a platelet concentration above baseline, current evidence suggests that a minimum concentration of approximately 1,000,000 platelets per microliter is required to meaningfully enhance healing responses within the musculoskeletal system.²⁶

PRP contains a variety of growth factors that promote tissue repair and regeneration, enhance angiogenesis, and play essential roles in mediating anti-inflammatory and analgesic effects.^{26,27} The cascade of tissue healing involves multiple interacting components, including platelets with their growth factors and cytokine-rich granules, leukocytes, the fibrin matrix, and various other cytokines that function synergistically. Throughout this cascade, a complex coagulation process occurs, comprising platelet activation followed by the release of dense and α -granule contents, the polymerization of fibrinogen (released from platelets or circulating in plasma) into a fibrin mesh, and the formation of a platelet plug.²⁸ Tissues treated with activated PRP are exposed to an influx of platelet-derived growth factors (PGFs), cytokines, and other lysosomal mediators. Fibroblasts proliferate in response to cytokines and platelet-derived factors, including IL-1, IL-6, IL-4, TNF- α , FGF-2, and TGF- β 1. These observations indicate that PRP application can induce a pronounced pro-inflammatory response within the target tissue. Interestingly, IL-10 is also present in higher-than-expected concentrations following PRP administration. Furthermore, upon degranulation, platelets release substantial amounts of serotonin (5-HT), a key modulator of pain signaling. In concentrated PRP (C-PRP), platelet counts are elevated by approximately five- to seven-fold compared with peripheral blood, resulting in markedly increased 5-HT release. The 5-HT system is known to exert bidirectional effects on nociception, either amplifying or attenuating pain following noxious stimulation.

Alterations in both peripheral and central 5-HT signaling pathways have been reported in patients with chronic pain. Recent studies have therefore increasingly focused on elucidating the roles of 5-HT and its receptors in danger-signal processing and nociceptive modulation.^{10,29}

Importantly, the biological activity of PRP is strongly determined by its leukocyte content, which critically regulates IL-1 β signaling. IL-1 β is a central mediator linking inflammation to extracellular matrix remodeling and the activation of multiple RCD pathways, including apoptosis, pyroptosis, and the increasingly recognized ferroptosis pathway. Differences between LR-PRP and LP-PRP directly translate into distinct effects on IL-1 β -driven cellular fate decisions. While LP-PRP may attenuate short-term inflammatory responses, accumulating evidence suggests that LR-PRP induces more durable modulation of IL-1 β -dependent RCD, facilitating sustained tissue remodeling and long-term functional recovery. This mechanism is particularly relevant in chronic myofascial pain, where persistent inflammation, nociplasticity, and dysregulated cell death converge to drive chronic pain states.^{11,12,18,19}

Conclusions

This narrative review highlights the emerging potential of PRP as a pharmacopuncture agent in the management of CMP. Current evidence indicates that PRP contains a concentrated reservoir of growth factors, cytokines, and bioactive molecules that modulate inflammation, enhance angiogenesis, promote fibroblast activity, and facilitate tissue regeneration. When delivered through pharmacopuncture, PRP may offer synergistic benefits by combining the mechanobiological effects of acupoint stimulation with the regenerative and anti-inflammatory properties of autologous platelet concentrates.

Overall, PRP pharmacopuncture represents a biologically plausible and clinically relevant integrative therapy with potential advantages over conventional pharmacopuncture solutions. Future well-designed clinical trials are required to clarify its efficacy, determine optimal protocols, and establish its role within the broader framework of multimodal management for CMP.

Competing Interests

The authors declare no competing interests.

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