Journal of Pain Research

Dovepress
Taylor & Francis Group

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LETTER

Platelet-Rich Plasma-Induced Analgesia in Peripheral Nerve Repair: Mechanisms, Cautions, and Clinical Promise [Letter]

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Dear editor

We read with great interest the study by Kuffler et al, which demonstrated that bridging nerve gaps with an autograft enclosed in a platelet-rich plasma (PRP)–filled collagen conduit can rapidly and durably abolish chronic neuropathic pain.[1] This finding is notable because neuropathic pain is a common and notoriously treatment-resistant consequence of peripheral nerve injury. In this study, approximately 89% of treated patients achieved complete pain resolution, often within two months—a markedly faster recovery than typically observed with standard nerve repair techniques.

From a safety perspective, PRP is autologous, minimizing immunogenic risk, and no adverse effects were reported. Nevertheless, the introduction of highly concentrated platelets—and the leukocytes they contain—requires caution. Leukocyte-rich PRP can release pro-inflammatory cytokines, such as interleukin-1β and tumor necrosis factor-α, which may exacerbate local inflammation and, at high levels, promote fibrotic scar formation around the repair site, potentially leading to nerve compression.[2] Although clinically significant fibrosis has not been reported, optimizing leukocyte content and activation protocols remains an important safety consideration. Furthermore, a clear understanding of PRP's underlying mechanisms will be necessary to ensure that safety is balanced with therapeutic efficacy.

Mechanistically, PRP provides a concentrated pool of growth factors that support axonal regeneration and modulate the injury microenvironment. Platelet-derived signals stimulate Schwann cell proliferation, promote angiogenesis, and enhance axonal elongation, while attenuating neuroinflammation by promoting macrophage polarization toward a reparative M2 phenotype.[3] Such immunomodulation may disrupt the pro-inflammatory feedback loop that sustains neuropathic pain. Because chronic neuropathic pain is partly driven by spontaneous ectopic discharges in injured nerves and dorsal root ganglia, the rapid analgesic effect of PRP—preceding reinnervation—suggests a direct suppression of aberrant nociceptive signaling at the injury site.[1] However, the precise mechanisms remain incompletely defined, highlighting the need for targeted mechanistic investigations.

Several aspects require further exploration to refine and optimize this technique. First, PRP preparation protocols vary considerably; differences in centrifugation methods can lead to substantial variability in platelet and leukocyte concentrations, potentially resulting in inconsistent outcomes.[2] Standardizing PRP composition and dosing will be critical to reproducibility. Second, the contribution of the collagen conduit warrants closer investigation. While it likely helped retain bioactive factors locally, its biodegradation rate was not reported. A conduit that degrades too quickly or too slowly could alter PRP exposure duration or provoke local inflammation.[4] Lastly, detailed analyses of neuroimmune dynamics in PRP-treated repairs—such as macrophage phenotype transitions and dorsal root ganglion activity—would help clarify

Received: 7 August 2025
Accepted: 12 August 2025
Published: 14 August 2025

PRP's role in modulating pain pathways and supporting nerve regeneration. Addressing these knowledge gaps will be essential to translate the promising early findings into consistent and predictable clinical benefits.

In summary, We commend the authors for their valuable clinical observations and agree that larger, controlled trials, combined with mechanistic studies, are warranted. By systematically addressing the identified safety, mechanistic, and technical considerations, this approach could become a transformative treatment for chronic neuropathic pain following peripheral nerve injury.

Disclosure

The authors declare that they have no competing interests in this communication.

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https://doi.org/10.2147/JPR.S559007