

Increasing PRP Injection Volume to Target Super-Dose of Platelets for Knee Osteoarthritis: Response

Authors' Response:

We would like to express our appreciation for the valuable feedback on our recently published article "Comparison of Conventional Dose Versus Superdose Platelet-Rich Plasma for Knee Osteoarthritis: A Prospective, Triple-Blind, Randomized Clinical Trial" by Patel et al.⁸ Platelet-rich plasma (PRP) has indeed become a hot topic for ongoing research since there are multiple properties of this orthobiological agent that are unexplored and still need to be investigated.^{3,4}

Advancements in biotechnology and regenerative medicine have led to the development of novel PRP formulations and adjunctive therapies. These innovations aimed to enhance the therapeutic efficacy of PRP and address specific challenges associated with its clinical use.^{2,4,5} Overall, the evolution of research on PRP for knee joint issues in orthopaedics has been characterized by a progression from early exploratory studies to rigorous clinical trials and efforts to optimize treatment strategies.⁷

The authors have rightly pointed out that the available literature on PRP fails to adeptly describe all the beneficial biological characteristics of this injectable drug. In fact, there are many variables such as the volume (of the final injectable product), platelet concentration, frequency of injections, presence or absence of an activator, absolute number of platelets, and leukocyte content (leukocyte rich or poor) of PRP, which hold the potential to be studied comprehensively in animal studies or randomized clinical trials.^{2,9} Out of the abovementioned variables, only a few of them have been investigated in the current literature.⁶⁻⁹

In our study, we focused on the evaluation of the effect of the dose (volume) of PRP and if a superdose (8 mL) led to a statistically significant improvement in the Western Ontario and McMaster Universities Arthritis Index (WOMAC) score, WOMAC pain score, and Knee injury and Osteoarthritis Outcome (KOOS) Score at sequential follow-up visits in patients with earlyonset knee osteoarthritis (Kellgren-Lawrence grades 1 and 2).⁸ Since the knee joint is a relatively large joint, this superdose of PRP can easily diffuse inside, ultimately leading to higher

levels of growth factors (such as Platelet Derived Growth Factor, Vascular Endothelial Growth Factor, Fibroblast Growth Factor, Insulin like Growth Factor-1, and Epidermal Growth Factor) and the Interleukin-1 receptor antagonist (anti-inflammatory cytokine) inside the joint and hence enhancing the regenerative and anabolic potential of PRP.^{1,2,7,10}

The authors have also mentioned that there is a predilection for hyaluronic acid (viscosupplementation) therapeutic injections among many orthopaedic surgeons for early knee osteoarthritis. Unlike the autologous nature of PRP, hyaluronic acid is synthetically prepared and does not exhibit joint reparative properties like PRP. We know that hyaluronic acid is a key component of synovial fluid, providing lubrication, stress distribution, and elasticity to the joint. However, the absence of growth factors makes hyaluronate injections a temporary solution for knee osteoarthritis, ultimately requiring repeated injections once the viscoelastic effects of the previous injections wane.² To overcome the abovementioned point from the authors, we strongly believe that commercial PRP kits should be readily available in different formulations (low dose and superdose) so as to enable clinicians to decide which formulation suits them the best for varied abnormalities.

Nevertheless, there is an enormous potential of research that could be undertaken to define the ideal formulation of PRP. While controversies and challenges remain, ongoing research continues to refine our understanding of PRP's role in orthopaedic practice and improve patient outcomes.^{4,10}

We believe that future studies should aim to evaluate whether the volume of injectable PRP or the absolute number of platelets is the crucial variable to deliver clinically significant and long-lasting results.

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