Comparison of Conventional Dose Versus Superdose Platelet-Rich Plasma for Knee Osteoarthritis: Response

Authors' Response:

We appreciate the valuable comments on our recently published article, "Comparison of Conventional Dose Versus Superdose Platelet-Rich Plasma for Knee Osteoarthritis: A Prospective, Triple-Blind, Randomized Clinical Trial."[8] The author of the letter has raised some genuine concerns, and we would be pleased to thoroughly address all the comments in a comprehensive manner.

Our department has been involved in focused research on various variables concerning intra-articular platelet-rich plasma (PRP) injections for over a decade now.[3,4,7] As far as published literature is concerned, there has been a lot of debate on the dosage and frequency of PRP injections for knee osteoarthritis in recent years.[1,3,5,6] The primary focus of our study was to compare 2 different dosage forms of PRP in terms of ideal volume and quantity of platelets required for a single PRP injection.[8] We agree that the presence of a placebo control group is ideal for such randomized trials. As such, there are multiple studies in the literature clearly establishing superiority of PRP over a placebo.[6,7] In fact, it was a randomized controlled trial (published in 2013) from our department[7] that first established the superiority of a single PRP injection over a placebo injection of normal saline. In recent years, there has been a heightened understanding of the ideal dosage of PRP for osteoarthritis in the knee joint, and many authors have recommended using platelet counts surpassing 5 billion for optimal effectiveness.[3,5,6] The commercially available PRP preparation kits usually yield 3 to 4 mL of injectable product, which may be insufficient for a large joint like the knee; hence, the concept of superdose PRP (7-8 mL of final product) was introduced.[3] Superdose PRP contains nearly 5 billion absolute platelet counts. Our study is valuable, as it challenges the existing commercial kits, which rely on withdrawing less blood and preparing 3 to 4 mL of low-dose PRP.

In the recently published RESTORE trial,[2] which compared commercially available PRP to a placebo injection for symptomatic knee osteoarthritis, the authors concluded that there was no difference in outcomes between the 2 groups. However, this trial included patients with mild to moderate knee osteoarthritis (Kellgren-Lawrence grades 2 and 3), whereas in our study we included only patients with Kellgren-Lawrence grades 1 and 2. We believe that it is imperative to target the inflammation cascade inside the joint by intervening at an early stage to upregulate the anti-inflammatory signals through the growth factors and anti-inflammatory cytokines, which are key components of PRP. Moreover, the PRP used in the RESTORE trial was effectively plasma, with a lower absolute number of platelets.

As far as preinjection physiotherapy is concerned, all patients were initially put on a structured physiotherapy regimen (consisting of isometric quadriceps exercises, hamstring strengthening exercises, and straight-leg raises) and evaluated for response every 6 weeks. We used a threshold of 3 months for the assessment of response to physiotherapy. After the PRP injection, we kept a cooling-off period of 5 to 7 days for subsidence of inflammation inside the joint before resuming the physiotherapy regimen. The postinjection physiotherapy regimen was similar to the preinjection phase, with the inclusion of all exercises for which patient was trained previously.

We would like to thank the author of the letter for raising these valuable comments and suggestions. Hopefully, we have addressed all the queries and concerns regarding our article. We will be happy to answer any additional comments should they arise.

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The authors have declared that there are no conflicts of interest in the authorship and publication of this contribution. AOSSM checks author disclosures against the Open Payments Database (OPD). AOSSM has not conducted an independent investigation on the OPD and disclaims any liability or responsibility relating thereto.

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The Orthopaedic Journal of Sports Medicine, 12(6), 23259671241255962
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