Increasing PRP Injection Volume to Target Super-high Dose of Platelets for Knee Osteoarthritis: Letter to the Editor

Dear Editor:

We read with great interest the randomized controlled trial (RCT) conducted by Patel et al[10] comparing the efficacy of a conventional 4-mL injection of platelet-rich plasma (PRP) with that of an 8-mL injection, corresponding to a higher volume and platelet dose and called by the authors "superdose of PRP" in patients presenting with early knee osteoarthritis (OA).

First, we want to congratulate Patel et al[10] for this work that moves research forward on this crucial topic and that is in line with recommendations from rigorous scientific societies by detailing biological settings of PRP injected.[5,9] Indeed, there is still a lack of evidence on which PRP biological formulation is the best for patients presenting with knee OA. Among them, platelet dose remains a parameter that is poorly studied, whereas the majority of the articles fail to appropriately describe the biological characteristics of PRP injected, which is a major flaw in the field.

This RCT demonstrates higher benefits from an 8-mL PRP injection containing 5.6 billion platelets compared to a 4-mL PRP injection containing 2.8 billion platelets. Interestingly, Bansal et al[2] proposed an even higher standardized platelet dose of 10 billion in 8 mL, necessitating a double-spin protocol that is more complex to introduce in daily practice with available medical devices. It is interesting to note that Prost et al[11] recently introduced the concept of a very high volume in a retrospective study, taking advantage of a large amount of data collected from real-life injections. The idea was to reach the target platelet dose of 10 billion by increasing the volume of PRP injected, considering the large-volume capacity of the knee joint. Thus, the authors described a significant benefit at 18 months using a single injection of PRP with a mean volume of 17 mL, containing a mean dose of 9 billion platelets, and reported a trend that an increased volume and dose of platelets are safe and could lead to prolonged benefits over time compared to a lower volume/dose.

Although increasing the total volume of an injectable product for knee OA to such a proportion is not common for physicians, whose habits have been modeled by historical procedures using hyaluronic acid (ie, low volume and repeated injections), a certain number of scientific elements could justify investigating the potential benefit of very high-volume PRP injections:

(1) The intra-articular capacity of the knee joint has been estimated to be around 103.5 mL (healthy knee) and 131.5 mL (knee with OA and inflammation).[8,13]
(2) Safety and tolerance seem to be similar, as only slightly adverse events (brief and spontaneously resolved) have been reported when the injected volume is increased.[10]
(3) Neuromuscular inhibition has been reported in the quadriceps because of a knee joint injury or simulated joint effusion. This phenomenon, called arthrogenic muscle inhibition, has never been reported with an injected volume < 20 mL.[6,7]
(4) Increasing the volume injected in the knee would favor better diffusion among all the damaged areas compared to a lower volume.[12]
(5) Increasing the volume of PRP injected will also increase the plasma fraction, which could have beneficial effects particularly by bringing specific growth factors (insulin-like growth factor-1 and hepatocyte growth factor),[3,4] cytokines (interleukin-1 receptor antagonist),[14] or some extracellular vesicles whose role needs to be defined[1] and mainly contained in the plasma fraction.

In conclusion, we take the opportunity of the brilliant work from Patel et al[10] to introduce the concept of very high-volume injections that we defined as a volume of PRP between 10 and 20 mL with a target dose of 10 billion platelets. We encourage the scientific community to continue its effort to refine the best PRP formulation for patients presenting with knee OA using either RCTs or real-life registries with the same rigor as Patel et al[10] or Prost et al[11] recently did.

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One or more of the authors has declared the following potential conflict of interest or source of funding: J.B., A.P., J.M., and D.P. own shares in Remedex. J.M. has received educational support from Fidia, Horiba, Macopharma, Arthrex, and Horus. J.B., A.P., A.S., and D.P. have received educational support from Fidia. The

The Orthopaedic Journal of Sports Medicine, 12(8), 23259671241264283
DOI: 10.1177/23259671241264283

manufacturers had no role in the development of this letter or its decision for publication. 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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