Comment on "Intra-articular Platelet-Rich Plasma vs Placebo Injection on Pain and Medial Tibial Cartilage Volume in Patients with Knee Osteoarthritis: The Restore Randomized Clinical Trial"

To the Editor:

We read with great interest the manuscript by Bennell et al (1) reportedly showing lack of effectiveness of (platelet rich plasma) PRP vs. placebo injection on pain and medial tibial cartilage volume. The study is well designed with appropriate randomization, outcomes, sample size calculation, and statistical analysis. Unfortunately, the preparation of PRP appears to be suboptimal with 20 mL of whole blood yielding 1.2 x platelet concentration with platelet dose of only 325 x 10³ /mm³ versus the more typical 1,000 x 10³ /mm³ platelets drawn from 60 mL of blood. In the trial protocol (2) authors indicate the lack of recommendations for hyaluronic acid, which is commonly used. Weekly injections are utilized only for hyaluronic acid injections. Even local anesthetic injections with or without steroids are injected no more than once in 3 months.

While this study was negative, it demonstrated benefits of PRP with mean change in pain scores that exceeded the placebo group. In addition, the number of participants in the PRP group who reported global improvement was greater than in the placebo group at 2 months as one would expect. Further, more participants in the PRP group than in the placebo group reported global improvement in function at 12-month follow-up.

Earlier systematic reviews and meta-analysis of trials utilizing PRP to treat knee osteoarthritis have shown that PRP improves pain and functional scores (3). Placebo design may induce nocebo effect. It is beyond any reasonable doubt any longer than intra-articular injection of sodium chloride solution is not a placebo. A placebo is an inert solution injected into an inert structure. The knee joint is not an inert structure and sodium chloride solution is not inert when given into a joint or, for that matter, the epidural space (4). The clinical applicability may not be feasible with the study with screening of 2,284 patients, and finally, selecting 288 patients, a 12.6% selection rate for randomization.

RESTORE is a well-designed study the result of which should be the development of protocols that better match PRP real world use.

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