Bone Marrow Aspirate Concentrate Is Equivalent to PRP for the Treatment of Knee OA at 1 Year: Letter to the Editor

Dear Editor:

It was with great interest that we reviewed the article by Anz et al[1] published in the *Orthopaedic Journal of Sports Medicine* entitled "Bone Marrow Aspirate Concentrate Is Equivalent to Platelet-Rich Plasma for the Treatment of Knee Osteoarthritis at 1 Year: A Prospective, Randomized Trial." There are numerous concerns regarding most especially the title and conclusions of this manuscript. Both the title and the conclusions would suggest concentrate offers no additional benefits for knee osteoarthritis over standard platelet-rich plasma (PRP). These conclusions would be accepted by the casual reader of this type of paper without a deeper inspection of the methods employed. Specifically, in this study, the methods in obtaining a proper bone marrow aspirate and an appropriate quantification of both the PRP and bone marrow aspirate biologic are severely lacking. The methods of obtaining an appropriate high-yielding bone marrow aspirate are well known and described by various authors, including Philippe Hernigou.[2-4,6,7,9] This technique stresses the importance of using low-volume aspiration using small syringes.[2] In this case, two 30-mL syringes were used from a same single point using what is described as "a traditional 11-gauge, 11-cm Jamshidi needle (Renfrac)."[1] The methods section further describes a technique of "withdrawing and rotating the needle."[1] This is not a method that most clinicians using bone marrow would recommend to optimally obtain a proper bone marrow aspirate.

The authors describe performing quantitative analysis on only 3 of the 49 subjects in the bone marrow aspirate group and only 1 subject in the PRP group. The rationale for this limited number of quantitative analysis was the fact that the study was "initiated before guidelines were issued for minimal reporting of biologic product studies,"[1] referring to the Minimum Information for Studies Evaluating Biologics in Orthopaedics (MIBO) guidelines. They cite Murray et al[10] as the source of the guidelines, however that study was published in 2017, well before the submission of this manuscript. In addition, prior to the minimal reporting of biologic products publication, multiple prominent orthopaedic surgeons and others involved in the use of orthobiologics had noted the importance of quantification of any injected biologic such as PRP and bone marrow aspirate. A quality journal in 2020 should require all publications on orthobiologic treatments include a clear quantification of the biologic injected in all subjects included in the study. An institution such as the Andrews Research & Education Foundation would clearly have the capabilities to provide a quantification of every PRP product and bone marrow aspirate for submitted clinical research studies.

As to the specifics of the orthobiologics employed in this study, it documents a reasonable PRP product in the single sample obtained, which included 1.2×10^6 platelets per milliliter with a low level of red blood cells and granulocytes.[1] This would be a literature-supported type of PRP for the treatment of mild to moderate knee OA.[5] The bone aspirate concentrate result, however, contained large amounts of red blood cell with very few colony-forming units and a very low platelet count.[1] Dose response has previously been reported, and from the data included in this study, the cell counts fall far below what has been reported to ensure optimum outcome with use of bone marrow aspirate concentrate.[4,7-9] It would be appropriate for the authors to acknowledge that the cellular contents of the injectates included in the study were far lower than what has previously been reported and this could have negatively affected the outcome when compared to PRP.[10] Because bone marrow aspirate contains megakaryocytes, and coupled with the less-than-optimum technique thus diluting the aspirate with peripheral blood, it is likely that what was actually injected was bone marrow–derived PRP, and this would explain the authors' results of equivalence of the outcome.[4,6,9] Unfortunately, we will not truly know, as the characterization of each injectate was not performed in this study.

Finally, previous research has noted the negative effects of red blood cells on articular cartilage and the importance of a certain level of either total nucleated cell counts for actual mesenchymal stem cells to have an adequate response in the treatment of knee osteoarthritis.[4] Therefore, the title and conclusions of this manuscript are not accurate and likely misleading to the casual reader. A more accurate title and conclusion would be that a bone marrow aspirate with a low number of mesenchymal stem cells may be equivalent to PRP in the treatment of mild to moderate knee osteoarthritis lasting approximately 12 months. This would be quite similar to the now-known literature regarding PRP in mild to moderate osteoarthritis. Unfortunately, the Anz et al[1] study does not add to the literature regarding the utility of a properly performed bone marrow aspirate. As in all areas of medicine, appropriate methods and techniques are paramount to determine the efficacy of any specific treatment.

The Orthopaedic Journal of Sports Medicine, 8(10), 2325967120960706
DOI: 10.1177/2325967120960706

Gerard A. Malanga, MD
Cedar Knolls, New Jersey, USA
Don Buford, MD
Dallas, Texas, USA
William D. Murrell, MD
Dubai, UAE
Brian J. Shiple, DO
Glenn Mills, PA, USA

Address corresponding to Gerard A. Malanga, MD, New Jersey Regenerative Institute, 197 Ridgedale Avenue, Suite 210, Cedar Knolls, NJ 07927, USA. (E-mail: gmalangamd@hotmail.com).

One or more of the authors has declared the following potential conflict of interest or source of funding: G.A.M. has received honoraria from Fidia Pharma and Lipogems USA. D.B. has received grant support from NeuroLogica, education payments from Arthrex, faculty/speaker fees from Linvatec, and consulting fees from Linvatec, Trice Medical, and Flexion Therapeutics. B.J.S. has received honoraria from Trice Medical. 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.

REFERENCES

1. Anz AW, Hubbard R, Rendos NK, Eerts PA, Andrews JR, Hackel JG. Bone marrow aspirate concentrate is equivalent to platelet-rich plasma for the treatment of knee osteoarthritis at 1 year: a prospective, randomized trial. *Orthop J Sports Med*. 2020;8(2):2325967119900958.
2. Bowen JE. Technical issues in harvesting and concentrating stem cells (bone marrow and adipose). *PM R*. 2015;7(4 Suppl): S8-S18.
3. Centeno CJ, Al-Sayegh H, Bashir J, Goodyear S, Freeman MD. A dose response analysis of specific bone marrow concentrate treatment protocol for knee osteoarthritis. *BMC Musculoskelet Disord*. 2015;16:258.
4. Everts PA, Malanga GA, Paul RV, Rothenberg JB, Stephens N, Mautner KR. Assessing clinical implications and perspectives of the pathophysiological effects of erythrocytes and plasma free hemoglobin in autologous biologics for use in musculoskeletal regenerative medicine therapies. A review. *Regen Ther*. 2019;11: 56-64.
5. Filardo G, Madry H, Jelic M, Roffi A, Cucchiarini M, Kon E. Mesenchymal stem cells for the treatment of cartilage lesions: from preclinical findings to clinical application in orthopaedics. *Knee Surg Sports Traumatol Arthrosc*. 2013;21:1717-1729.
6. Friedlis MF, Centeno CJ. Performing a better bone marrow aspiration. *Phys Med Rehabil Clin N Am*. 2016;27(4):919-939.
7. Hernigou P, Homma Y, Flouzat Lachaniette CH, et al. Benefits of small volume and small syringe for bone marrow aspirations of mesenchymal stem cells. *Int Orthop*. 2013;37(11):2279-2287.
8. Kim YS, Choi YJ, Koh YG. Mesenchymal stem cell implantation in knee osteoarthritis: an assessment of the factors influencing clinical outcomes. *Am J Sports Med*. 2015;43(9):2293-2301.
9. Murphy M, Terrazas JA, Buford DA. Bone marrow concentrate and platelet-rich plasma. Acquisition and preparation: why technique matters. *Techniques in Regional Anesthesia and Pain Management*. 2015; 19(1-2):19-25.
10. Murray IR, Geeslin AG, Goudie EB, Petrigliano FA, LaPrade RF. Minimum Information for Studies Evaluating Biologics in Orthopaedics (MIBO): platelet-rich plasma and mesenchymal stem cells. *J Bone Joint Surg Am*. 2017;99(10):809-819.