

Editorial Commentary: Human Granulocyte-Stimulating Factor Increases the Leukocyte Richness of Platelet-Rich Plasma



Daichi Morikawa, M.D., Ph.D.

Abstract: Platelet-rich plasma (PRP) is the most common treatment in orthobiologics, because PRP is safe, low cost, and minimally invasive and could be used to promote the tissue-repair process. The systemic mobilization with human granulocyte-stimulating factor increased concentrations of white blood cells and monocyte but not platelets in PRP. It may enhance the efficacy of PRP therapy via monocytes/macrophages. Improving the efficacy of PRP therapy, bone marrow aspirate, mesenchymal stems cells, or other orthobiologics is not simple because there are many variations in products and patient factors.

See related article on page 2911

Orthobiologics, which include platelet-rich plasma (PRP), bone marrow aspirate (BMA) and concentrate (cBMA), fat grafting, and mesenchymal stem cells (MSCs), are being used increasingly in musculoskeletal diseases such as osteoarthritis and acute/chronic injury of tendon, ligament, and muscle.¹⁻⁶ PRP, which is the most common treatment in orthobiologics, is an autologous blood product that concentrates platelets and contains multiple growth factors and cytokines.^{7,8} PRP therapy is safe, low cost, and minimally invasive and could be used to promote the tissue-repair process.⁸⁻¹¹ PRP products vary widely according to the concentrating system used and patient factors, such as age, sex, and condition.¹² Studies are needed to determine the optimal PRP product for specific pathologies and to improve the efficacy of PRP therapy.

I appreciate the work of the authors, Anz, Matuska, Edison, Abdullah, Dekker, Plummer, Brock, and Goodlett, of the experimental study, "Quantification and Qualification of Stem Cells From Blood After Mobilization With Filgrastim, and Concentration With Using a Platelet-Rich Plasma System."¹³ In this study, they induced

systemic mobilization with human granulocyte-stimulating factor (filgrastim) to increase the efficacy of PRP treatment and called it mobilized platelet-rich plasma (M-PRP).¹³ The authors compared the cellular composition between PRP, M-PRP, and cBMA from 10 healthy young male volunteers. M-PRP showed greater concentrations of white blood cells and monocytes and no significant difference in platelets compared with PRP. Recent studies have shown that PRP promotes recruitment of macrophages in the process of tendon healing by using murine patellar tendon defect models.¹⁴ Although mobilization with filgrastim does not increase the number of platelets, it may enhance the efficacy of PRP therapy via monocytes/macrophages.

BMA/cBMA is an orthobiologic that contains multiple cell lines, including red blood cells, white blood cells, leukocytes, platelets, monocytes, hematopoietic stem cells, endothelial cells, MSCs, and other precursor cells.¹ In the literature, the stem cell content in bone marrow is a small fraction of the total cell yield (0.001%-0.01%).¹⁵ In our in vitro study, we showed that cells derived from subacromial bursa were superior to cells from cBMA in proliferation capacity.¹⁶ Moreover, the cells from cBMA showed lower differentiation ability (chondrogenesis, osteogenesis, and adipogenesis).¹⁶ In the current article, mobilization with filgrastim did not increase mesenchymal progenitor cells or colony-forming ability in PRP.

Improving the efficacy of PRP therapy, bone marrow aspirate, MSCs, or other orthobiologics is not simple

Juntendo University Urayasu Hospital
The author reports no conflicts of interest in the authorship and publication of this article. Full ICMJE author disclosure forms are available for this article online, as [supplementary material](#).

© 2020 by the Arthroscopy Association of North America
0749-8063/201434/\$36.00

<https://doi.org/10.1016/j.arthro.2020.08.020>

because there are many variations in products and patient factors. Additional studies are needed to determine the optimal PRP composition for specific disease pathophysiology.

References

1. Purita J, Lana J, Kolber M, et al. Bone marrow-derived products: A classification proposal—bone marrow aspirate, bone marrow aspirate concentrate or hybrid? *World J Stem Cells* 2020;12:241-250.
2. Hauser RA, Orlofsky A. Regenerative injection therapy with whole bone marrow aspirate for degenerative joint disease: A case series. *Clin Med Insights Arthritis Musculoskelet Disord* 2013;6:65-72.
3. Hernigou P, Flouzat Lachaniette CH, Delambre J, et al. Biologic augmentation of rotator cuff repair with mesenchymal stem cells during arthroscopy improves healing and prevents further tears: A case-controlled study. *Int Orthop* 2014;38:1811-1818.
4. Hernigou P, Poignard A, Zilber S, Rouard H. Cell therapy of hip osteonecrosis with autologous bone marrow grafting. *Indian J Orthop* 2009;43:40-45.
5. Hernigou P, Mathieu G, Poignard A, Manicom O, Beaujean F, Rouard H. Percutaneous autologous bone-marrow grafting for nonunions. Surgical technique. *J Bone Joint Surg Am* 2006;88:322-327 (suppl 1 pt 2).
6. Anz AW, Hubbard R, Rendos NK, Everts 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;8:2325967119900958.
7. Alsousou J, Thompson M, Hulley P, Noble A, Willett K. The biology of platelet-rich plasma and its application in trauma and orthopaedic surgery: A review of the literature. *J Bone Joint Surg Br* 2009;91:987-996.
8. Foster TE, Puskas BL, Mandelbaum BR, Gerhardt MB, Rodeo SA. Platelet-rich plasma: From basic science to clinical applications. *Am J Sports Med* 2009;37:2259-2272.
9. Sanchez-Gonzalez DJ, Mendez-Bolaina E, Trejo-Bahena NI. Platelet-rich plasma peptides: Key for regeneration. *Int J Pept* 2012;2012:532519.
10. Neuwirth J, Fuhrmann RA, Veit A, et al. Expression of bioactive bone morphogenetic proteins in the subacromial bursa of patients with chronic degeneration of the rotator cuff. *Arthritis Res Ther* 2006;8:R92.
11. Werner S, Grose R. Regulation of wound healing by growth factors and cytokines. *Physiol Rev* 2003;83:835-870.
12. Fitzpatrick J, Bulsara MK, McCrory PR, Richardson MD, Zheng MH. Analysis of platelet-rich plasma extraction: Variations in platelet and blood components between 4 common commercial kits. *Orthop J Sports Med* 2017;5:2325967116675272.
13. Anz AW, Matuska A, Edison JL, et al. Quantification and qualification of stem cells from blood after mobilization with filgrastim, and concentration using a platelet-rich plasma system. *Arthroscopy* 2020;36:2911-2918.
14. Nishio H, Saita Y, Kobayashi Y, et al. Platelet-rich plasma promotes recruitment of macrophages in the process of tendon healing. *Regen Ther* 2020;14:262-270.
15. Bieback K, Kern S, Kocaomer A, Ferlik K, Bugert P. Comparing mesenchymal stromal cells from different human tissues: Bone marrow, adipose tissue and umbilical cord blood. *Biomed Mater Eng* 2008;18:S71-S76.
16. Morikawa D, Johnson JD, Kia C, et al. Examining the potency of subacromial bursal cells as a potential augmentation for rotator cuff healing: An in vitro study. *Arthroscopy* 2019;35:2978-2988.