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## **Hyaluronic Acid and Platelet-Rich Plasma, Intra-articular Infiltration in the Treatment of Gonarthrosis: Letter to the EditorResponse**

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What is This?

# Hyaluronic Acid and Platelet-Rich Plasma, Intra-articular Infiltration in the Treatment of Gonarthrosis

## Letter to the Editor / Response

### Dear Editor:

We read with great interest the article by Cerza et al,<sup>1</sup> "Comparison Between Hyaluronic Acid and Platelet-Rich Plasma, Intra-articular Infiltration in the Treatment of Gonarthrosis" in the December 2012 issue. The authors should be commended for their efforts in performing a randomized study of 120 patients (with 100% follow-up) on a topic highly relevant to many different types of physicians and providers, including sports medicine physicians. We would like to raise 3 points related to study design that may have further strengthened their findings.

First, although this was a level 1 randomized controlled trial,<sup>5</sup> there was no blinding of patients with respect to the treatment received. As we know, patients' outcomes can be influenced by their own preconceptions and expectations regarding their treatment and its purported effectiveness. A recent meta-analysis of patients with osteoarthritis treated with different modalities found an effect size of 51% for the placebo group, with an increase in pain-relieving effect when the treatment was given with injection.<sup>6</sup> It is impossible to determine the exact treatment effect resulting from the absence of blinding, but we suspect it had at least a partial influence on the response rate reported by the authors.

Second, even though the authors excluded participants with platelet counts less than 150,000 cells/ $\mu$ L on initial blood draw, there was no testing of the platelet-rich plasma (PRP) to ensure adequate concentrations of platelets and to guarantee that patients were in fact receiving PRP. Previous investigations reported ranges of 1.99- and 5.19-fold increases in the concentrations of platelets over whole blood in PRP prepared with different devices.<sup>3,4</sup> While no consensus has been reached on the definition of PRP (including concentrations of leukocytes and growth factors), it is possible that some patients may have received an "inadequate" concentration of PRP during their injection.

Third, the authors did not use imaging to verify the accuracy of their knee injections. Although the knee is regularly injected without the aid of imaging, a recent systematic review found that only 79% of knee injections performed without imaging were accurate, as compared with 99% of those performed with the aid of imaging.<sup>2</sup> As no imaging

was used in the current study, we cannot be certain that all injections reached their intended intra-articular location.

We thank the authors for their important investigation comparing the use of hyaluronic acid and PRP on the clinical outcomes of patients with osteoarthritis of the knee. In discussing these topics, we hope to stimulate discussion and highlight methods for conducting future studies which may improve the validity of study findings.

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### Authors' Response:

Thank you for the interesting and perceptive comments received regarding our recent study. Of course, it is always

possible to improve future studies, but we trust that the clarifications below will satisfy the reader.

Concerning the reliability of the study: The guidelines of the Centre for Evidence-Based Medicine outline a level 1 for this kind of study that does not depend exclusively on whether a study is double-blind.<sup>3</sup> In addition, in this particular type of study, there are real difficulties in establishing a reliable double-blind because of the large differences between the preparation procedures. In fact, to ensure the blinding of the patient, it would be necessary to take blood also from the group of patients undergoing treatment with hyaluronic acid. To ensure the blinding of the operator who carries out the intra-articular infiltration, we should use the double syringe used in the PRP group (useful in ensuring the sterility of the product) even for the hyaluronic acid group, masking the syringe to cover for the difference in both color and volume. These evident problems led us not to choose a double-blind approach.

In relation to the placebo effect: We accept that the matter is controversial. In the cited article,<sup>7</sup> among the limitations of the analysis it was stated that the placebo effect was largely determined as the difference between baseline and end point rather than the difference in benefit between placebo and nontreatment groups. In our study, the assessment of effectiveness in relation to the degree of gonarthrosis and the continuous improvement obtained in each subsequent follow-up suggested that any placebo effect was of limited impact. In addition, a recent study<sup>4</sup> showed that treatment with PRP is more effective than placebo for knee osteoarthritis.

Regarding the platelet concentration: Since blood or plasma is a physiological medium, the content and the composition differ inter- and intraindividually. Tests of the platelet concentration for each infiltration would have been financially expensive and of dubious importance, since it is not possible to certify an exact platelet concentration in plasma. This is something very individual, which is also shown in the literature.<sup>5</sup> Specific studies to evaluate the system used by us have shown high levels of platelet concentration and growth factors and low levels of leucocytes.<sup>2,6</sup>

Finally, the infiltration technique used for both groups was the superolateral approach, which has been shown to be the safest, ensuring intra-articular penetration of the

drug in up to 93% of cases. Jackson et al<sup>1</sup> have shown the accuracy rates for needle placement, confirmed with fluoroscopic imaging to document the dispersion pattern of the injected contrast material.

Essentially, we are confident that the comments made by the reader will help guide and improve future studies on the effectiveness of PRP in gonarthrosis. However, we believe that our study was sufficiently reliable to make a valid contribution to the field today and that the care taken in each step of the procedures ensured an accurate reading of the results.

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The authors declared that they have no conflicts of interest in the authorship and publication of this contribution.

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