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Comment on "clinical benefit of intra-articular saline as a comparator in clinical trials of knee osteoarthritis treatments: A systematic review and meta-analysis of randomized trials"

To the Editor,

We read with great interest the systematic review and meta-analysis by Altman et al. [1]. The findings presented in this review were very compelling, demonstrating that intra-articular (IA) saline is not a true placebo control in randomized controlled trials (RCTs) of osteoarthritis (OA). Their systematic review and meta-analysis provides a more homogeneous examination of the "placebo" effect of IA saline in RCTs than what was previously described in the literature [2]. The authors identified 40 RCTS, of which 31 trials examined IA corticosteroids, 8 trials examined hyaluronic acid, and only 1 trial examined IA platelet rich plasma.

As researchers in the field of IA treatment of painful knee OA, we believe the authors would have provided a more accurate systematic review of the literature by either (a) expanding their search criteria to include all RCTs of IA saline vs. all IA therapies for painful knee OA, or (b) removing the sole article of platelet rich plasma, and revising the title and objectives of the systematic review to reflect the more limited inclusion of trials of corticosteroids and hyaluronic acid therapies.

Our own research examining the effect of IA saline vs. IA comparator, a biologic derived from the low molecular weight fraction of human serum albumin, identified a large effect of saline on short-term pain relief (12 weeks in our trial), which was more pronounced in patients with minor OA defined by Kellgren–Lawrence grade II [3]. In our publication, we describe the saline arm as "saline vehicle control" rather than "placebo control" because of the antinociceptive effects of saline that have been reported, particularly with IA injection [2].

As the authors point out, non-surgical treatments including IA injections are an integral management strategy in clinical practice. With the questionable benefits of some commonly used IA therapies (viscosupplementation in particular [4]), there are newer therapies for treating pain due to knee OA. We suggest all trials of IA therapies be described to improve the accuracy and validity of a systematic review of the literature on IA saline in clinical trials of knee OA.

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