**Monfort J, Rotes-Sala D, et al. Comparative efficacy of intra-articular hyaluronic acid and corticoid injections in osteoarthritis of the first carpometacarpal joint: results of a 6-month single-masked randomized study. Joint Bone Spine. 2015 Mar;82(2);116-21.**

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Design: randomized clinical trial

Purpose of study: in patients with osteoarthritis of the first carpometacarpal joint, to compare the effectiveness of two intra-articular injections: hyaluronate acid (HA) versus corticosteroid (CS)

Population/sample size/setting:

* 88 patients (11 men, 77 women, mean age 63) treated for thumb OA at a rheumatology service in Barcelona
* Eligibility required age over 18 with a diagnosis of thumb OA for at least 90 days, requiring treatment with analgesics or NSAIDs, with a confirmatory radiologic diagnosis with in the previous six months
* Exclusion criteria were pregnancy, physical therapy performed by a PT at home or in a specialized center, history of any surgical procedure at the trapeziometacarpal joint, OA of the trapezioscaphoid joint or microcrystalline arthritis, participation in a clinical trial in the past three months, presence of any medical condition (e.g., renal or hepatic disease) judged to preclude entry into the study, allergy to low molecular weight HA, oral or parenteral corticosteroid therapy, or any corticosteroid injection in the past three months

Interventions:

* All patients received one cycle of echographic-guided injections spaced one week apart: HA (n=48) or CS (n=40) from one investigator
  + HA injections contained 0.5 cc of 5 mg HA (molecular weight 500 to 1000 kDa)
  + CS injections contained 0.5cc of solution with 1.5 mg betamethasone disodium phosphate and 1.5 mg betamethasone acetate

Outcomes:

* Followup was done at 30 days, 90 days, and 180 days after initiation of treatment by a blinded investigator
* Primary endpoint was the clinical improvement (change score) on the algofunctional index for hand OA (FIHOA), which is a physician-administered questionnaire containing ten items concerning daily activities of the hand, in which 0 represents no difficulty and 3 represents an inability to do the activity; thus, the best score is 0 and the worst score is 30
* There were some secondary outcomes as well: pain relief on the VAS, the physical and mental components of the SF-36 and global assessment of overall condition by patients and investigators
* For both groups, there were improvements in the VAS and the FIHOA during followup, but no changes in the SF-36 scores
  + There were no differences in the mean changes between groups
  + However, the HA group had a greater difference of median FIHOA scores (4 points at 90 days and 3 points at 180 days) than the CS group (1 point at 90 and at 180 days), p=0.071at day 90
* The physician assessment of overall condition at 90 days and 180 days was more favorable for the HA than the CS group (‘good’ or ‘very good’ general condition in 61.6% of the HA group vs 30.8% of the CS group at 90 days, 53.4% of the HA group versus 28.6% of the CS group at 180 days)
* In a subset of 77 patients who had FIHOA scores >5 and VAS scores >3 at baseline, there were greater changes in the median FIHOA scores at 90 and 180 days
  + Another subset of 65 patients with FIHOA scores >5 and VAS scores >5 at baseline also fared better with HA than CS with respect to FIOHA score changes
* Treatment was well-tolerated and no serious adverse events were reported apart from injection pain in 5 HA patients and 5 CS patients

Authors’ conclusions:

* Although the analysis of the overall series of patients encountered no statistically significant differences between HA and OA, patients with a baseline FIHOA score greater than 5 and a baseline VAS greater than 5 did show greater FIHOA improvement with HA than with CS injections
* A limitation of the study is that there was no placebo group
* HA could be a good alternative to CS in patients with moderate to severe thumb OA, and HA has been reported to have a better safety profile than CS

Comments:

* The pre-specified primary outcomes (FIHOA scores) did not differ between groups, and the differences which were observed appear to have arisen from post-hoc analyses of subsets of the data
* It appears that there was no minimum pain or FIHOA scores for entry into the study, with a significant participation from patients with mild OA; this places the study at risk of floor effects (not enough room on the scale to show improvement over time), and it would have been better to set minimum symptom criteria for study entry
* This means that the study’s conclusions about the greater effectiveness of HA over CS are best regarded as hypothesis-generating rather than hypothesis-confirming, and may have arisen from selective patient subset formation after the initial comparisons fell short of nominal statistical significance
  + It is possible that there was some element of data-dredging in search of a p value which would be less than 0.05, a practice which is generally discouraged and which entails a risk of bias due to selective outcome reporting and emphasis
* HA may be an acceptable alternative to CS, as the authors suggest, but this study cannot support evidence that HA is superior to CS or even to placebo

Assessment: inadequate for evidence of effectiveness of intra-articular hyaluronic acid over intra-articular betamethasone injections for patients with carpometacarpal osteoarthritis (post-hoc outcome analyses do not confirm hypothesis unless subgroup analyses were specified in advance)