Chou W-Y, Ko J-H, et al. Effect of sodium hyaluronate [SH] treatment on rotator cuff lesions without complete tears: A randomized, double-blind, placebo-controlled study. J Shoulder Elbow Surg 2010; 19: 557-563

Design: Randomized clinical trial

Study question: does injection of sodium hyaluronate (SH) improve the pain and Constant scores in shoulders with rotator cuff tendinopathy without complete tears?

Population/sample size/setting:

- 51 patients (32 women, 19 men, mean age 51.5) treated for shoulder pain at a department of orthopedic surgery in Taiwan
- Inclusion criteria were age between 35 and 80, pain around the shoulder with a positive impingement sign, positive imaging diagnosis (MRI or ultrasound) of rotator cuff pathology without a complete tear, and non-response to conservative therapy for 3 months
- Exclusion criteria were rheumatic disease, full-thickness rotator cuff tears, fracture, infection, tumor, hypersensitivity to SH, subacromial injections in the past 3 weeks, and pregnancy or planned pregnancy

Main outcome measures:

- All patients had 5 weekly injections into the subacromial bursa by a single physician who used the posterolateral corner of the acromion as a landmark
- Randomization was to either SH 25 mg (n=25) or 2.5 ml normal saline (n=26)
- Pain and function were assessed each week during the period of injection treatment, but the main outcomes were the Constant score and the pain VAS six weeks after the last injection; at that time, the clinicians and patients were unblinded and patients in the saline group had the option of receiving SH injections for 5 weeks
- Additional outcome was global improvement (physician and patient assessment)
- During the time when injections were being done, both SH and saline groups had improvements from baseline in Constant and pain VAS, and no group differences were recorded at the time of the final injection
    - SH group improved its Constant score from 61.64 to 72.48 as of the final injection; saline group improved its Constant score from 64.89 to 72.42
    - SH group improved its pain VAS from 6.36 to 4.20 as of the final injection; saline group improved from 6.46 to 4.77
    - However, 6 weeks after the final injection, the SH group continued to improve both Constant and VAS: Constant score was79.24 and VAS was 3.04
    - The Saline group had slightly worse Constant and VAS at the 6 week followup compared to the time of the last injection: Constant score was 69.07 and the pain VAS was 5.12

- In contrast to the Constant and VAS scores, the global assessment of improvement done 6 weeks after the last injection did not differ between groups; only one patient (in the SH group) had deteriorated, and the majority of patients in both groups had improved both by their own and by the physician's assessment
- Of the 25 patients in the SH group, 2 had rotator cuff surgery at 3 and 6 months after the injections; 3 patients in the saline group had rotator cuff surgery it 5, 7, and 9 months

Authors' conclusions:

- Subacromial injection of SH leads to better Constant and pain VAS scores than saline 6 weeks after treatment
- A treatment effect of SH is biologically plausible due to its effects in reducing the degradation of matrix components and its stimulation of proteoglycan synthesis; it may also lead to an autocrine stimulation of its own synthesis as has been seen with synoviocytes in vitro

Comments:

- Some sources of potential bias may have influenced the measured outcomes
    - The allocation concealment is not clear; there were envelopes in numeric sequence for the randomization, but these may not have been sealed or opaque
    - Although the allocation was unblinded 6 weeks after the final injection, the injections were done by one physician in syringes which may not have been taped to prevent the injectate from being seen; SH is a clear viscous solution, and if it can be distinguished from normal saline, there is a possibility that blinding could have been compromised if opaque adhesive tape were not used
    - It does appear that the 6 week Constant and VAS were the designated primary outcome, but that is not explicitly stated, and selective outcome reporting cannot be excluded from consideration
- There does not appear to have been any exercise or other shoulder rehabilitation in the treatment program; the injections are the only intervention mentioned
    - This would represent a departure from the overall clinical context in which injections are expected to be done, but it is likely that the patients did receive some instructions for activity which were simply not reported

Assessment: Inadequate for evidence of the effectiveness of hyaluronate in rotator cuff tendinopathy (risks of bias is fairly high)