

Hsieh L-F, Hsu W-C, et al. Addition of intra-articular hyaluronate injection to physical therapy program produces no extra benefits in patients with adhesive capsulitis of the shoulder: a randomized controlled trial. Arch Phys Med Rehabil 2012;93:957-64.

Design: Randomized clinical trial

Study question: does the addition of hyaluronic acid (HA) injection to a physical therapy program improve the outcome of physical therapy (PT) in the setting of adhesive capsulitis?

Population/sample size/setting:

- 63 patients (20 men, 43 women, mean age 54) treated for adhesive capsulitis in a department of physical medicine in Taiwan
- Eligibility criteria were unilateral adhesive capsulitis defined as a $\geq 50\%$ loss of passive motion in the shoulder joint compared to the opposite side in at least one of 4 movement directions, and a duration of complaints greater than three months
- Exclusion criteria were prior manipulation of the affected joint under anesthesia, other shoulder conditions (rheumatoid arthritis, osteoarthritis, damage to glenohumeral cartilage, neurologic deficits affecting shoulder function, disorders of cervical spine, elbow, wrist, or hand, allergy to HA, and injection of steroid into the affected shoulder within the past 4 weeks

Main outcome measures:

- All patients were enrolled into a PT intervention consisting of three one-hour sessions lasting 12 weeks, administered by two physiotherapists with at least 5 years' experience
 - o Sessions included heat and electric therapy combined with therapeutic exercise
- Randomization was to intra-articular injection of HA (n=32) or no HA (n=31)
 - o HA was injected without imaging guidance using the posterior angle of the acromial process as a landmark
 - o Treatment consisted of a series of 3 weekly injections of 2 ml of HA at a dose of 20mg of HA
- Primary outcome was the Shoulder Pain and Disability Index (SPADI), with the Shoulder Disability Questionnaire (SDQ), the medical outcomes part of the SF-36, and active and passive ROM as secondary measures
 - o Outcomes were assessed by a physical therapist blinded as to treatment allocation
- Data analysis was completed at 3 months with an interim analysis at 1.5 months
- Both groups improved SPADI, ROM, and SDQ scores between baseline and the 3 month evaluation and the improvement did not depend on whether HA was injected

- For PT alone, total SPADI scores decreased from 49.01 to 24.51; for HA plus PT, the SPADI scores decreased from 51.19 to 28.57 at the 3 month evaluation
- Similarly to the SPADI, the secondary outcomes of passive/active ROM, the SF-36, and the SDQ improved by an equal amount in the two groups

Authors' conclusions:

- Injection of intra-articular HA to PT in the setting of adhesive capsulitis does not add any advantage over PT alone; PT by itself yields the same improvement as PT plus HA
- The addition of HA to PT cannot be justified and may increase unnecessary expenditures

Comments:

- There was no calculation of the power of the study to detect a treatment effect of a given size, leaving the power issue uncertain
- However, the authors did determine that the outcome scores were normally distributed
- Given the sample size (32 per group), it can be estimated that the study had 80% power to detect a treatment effect of 0.7 standard deviations (SD) at a significance level of $p=0.05$
- It is conventional to regard 0.8 SD as a large treatment effect, 0.5 to 0.8 SD as a moderate treatment effect, and 0.2 to 0.5 as a small effect
- The study was probably powered to detect a moderate treatment effect, and the failure to detect that effect makes it likely that any effect of HA would be small
- A misprint in the Methods section gives the concentration of HA as 10 mg/deciliter; this would be a homeopathic dose, but the actual dose of 20 mg is in line with what was used in other studies
- The treatment difference was either HA or no HA (no placebo injection); it is possible that a saline injection would have introduced a placebo response in the PT only group; this does not compromise the conclusion that the PT only group did as well as the PT plus HA group

Assessment: Adequate for evidence that HA added to PT does not improve symptomatic and functional outcomes of adhesive capsulitis over the improvements seen with PT alone