

Coombes BK, Bisset L, Vicenzino B. Efficacy and safety of corticosteroid injections and other injections for management of tendinopathy: a systematic review of randomised controlled trials. Lancet 2010;376(20):1751-67.

Design: Meta-analysis of randomized clinical trials

PICOS:

- Patient population: Tendinopathy of the rotator cuff, elbow, knee, and ankle
- Intervention: one or more peritendinous injection of any active medication
- Comparison: Injection with placebo (saline or local anesthetic), no intervention (wait and see), NSAIDS, physiotherapy, electrotherapy, or orthotic devices
 - o Excluded were studies of intra-muscular or intra-articular injections
 - o “Rotator cuff” studies excluded those with high proportion of adhesive capsulitis, full thickness tears, or rheumatological conditions
- Outcomes: Pain, function, and patient-related overall improvement
 - o Short-term was defined as up to 12 weeks
 - o Intermediate term was defined as up to 26 weeks
 - o Long term was defined as 1 year or longer
- Study types: Randomized controlled trials only

Study selection:

- Databases included MEDLINE, EMBASE, CENTRAL, CINAHL, and the Physiotherapy Evidence Database through March 2010
- Quality was derived from the PEDro scale, which is similar to the Cochrane scale for risk of bias, with two added items: consistency of timing of outcome measurements and documentation of adverse effects
- If the study had a score of less than 50% in the modified PEDro scale, it was not further considered for evidence of the effect of injections
- If the results from the studies could not be statistically pooled, a qualitative system of strength of evidence was defined
 - o Strong evidence was consistent findings between many high-quality RCTs
 - o Moderate quality was one high-quality RCT
 - o Conflicting evidence was inconsistent findings between many RCTs
 - o No evidence was the absence of any RCT on the intervention
- When data could be pooled, the effect size was reported in standardized mean differences (SMD), where the differences in groups were how many standard deviations (SD) separated the two groups: following general conventions, SMD of

less than 0.5 SD is “small,” SMD between 0.5 and 0.8 SD is “medium,” and SMD greater than 0.8 SD is “large”

Results:

- For all tendinopathies, 41 studies were included in the review; 16 of these were of rotator cuff tendinopathy, and from these, 14 analyses from 10 trials with 780 patients were conducted
- For rotator cuff tendinopathies, most comparisons were short-term only
 - o Pooled data from 3 studies of steroid injection versus placebo showed a medium effect (SMD=0.68 SD) for short-term pain relief in favor of steroid injection
 - o Pooled data from the same three studies showed a similarly medium effect (SMD=0.62) in favor of steroid injection for functional benefit
 - o Pooled data from 6 studies of steroid versus oral NSAID did not show an advantage of steroid over oral NSAID for pain or for functional benefit
 - o 2 studies comparing steroid injection with physiotherapy did not have a pooled effect estimate for pain, but they did have a pooled effect estimate for function, and this was an SMD of 0.09 SD in the short term (a non-significant effect) and an effect of 0.0 SD in the intermediate term: in other words, steroid injection and physical therapy were not different for either pain or function
- Other tendinopathies outside the shoulder were also analyzed; in general, these did not favor steroid injections, and for lateral epicondyle pain, the authors estimated that there was strong evidence that steroid injections were less beneficial than other interventions at 26 weeks

Authors' conclusions:

- There is strong evidence that steroid injection provides short term benefit for common tendinopathies
- However, there is also strong evidence that steroid injections are worse than other treatment options in the intermediate and long term results
- This poses a dilemma because tendinopathy does not have an inflammatory pathogenesis; other mechanisms involving collagen and extracellular matrix molecules could explain the biology of these tendinopathies

Comments:

- The effects of steroid injection for rotator cuff tendinopathy is similar to that which was reported in a Cochrane review by Buchbinder et al, which was last updated in 2003

- This meta-analysis included the steroid studies analyzed by Buchbinder (Adebajo 1990 and Petri 1987), and in addition pools data from Alvarez 2005, and analyzes the results similarly to Buchbinder
- Homogeneity appears to have been estimated by statistical methods, even though it is not clear that the studies were clinically homogeneous
 - o Specifically, the steroid/oral NSAID comparison for Adebajo 1990 (Table 2 and Figure 3) had the steroid group taking placebo NSAID+ lidocaine injection + steroid injection, while the oral NSAID group took diclofenac + lidocaine injection; this meant that the groups differed on two treatment variables rather than one
- Two studies (Hay 2003, Cloke 2008) compared steroid injection to physiotherapy with exercise, and the functional outcome data was pooled in Table 2, yielding a steroid treatment effect of 0.09 in the short term and a treatment effect of 0.00 in the intermediate term; both are statistically not different from a treatment effect of zero
- A third study, Crawshaw 2010, also reported no difference between steroid injection and physical therapy; data from all three studies can be pooled to yield a treatment effect which does not show any benefit of steroid injections, with a very small advantage of physiotherapy (data taken from the original studies):

Study or Subgroup	Steroid			Physiotherapy			Weight	Std. Mean Difference IV, Fixed, 95% CI	Std. Mean Difference IV, Fixed, 95% CI
	Mean	SD	Total	Mean	SD	Total			
Cloke 2008	-0.96	9.86	27	2.23	7.3	22	18.8%	-0.36 [-0.92, 0.21]	
Crawshaw 2010	14.9	15.73	96	16.87	15.73	96		Not estimable	
Hay 2003	4.55	5.9	103	5.97	5.4	104	81.2%	-0.25 [-0.52, 0.02]	
Total (95% CI)			130			126	100.0%	-0.27 [-0.52, -0.02]	
Heterogeneity: Chi ² = 0.11, df = 1 (P = 0.74); I ² = 0%									
Test for overall effect: Z = 2.15 (P = 0.03)									

- o However, it would be very questionable to infer that the studies steroid injections should be combined in this manner to claim that there is evidence against injections
 - o All three studies used anatomical landmarks to direct the injections; none used ultrasound
 - o The contribution of ultrasound to the therapeutic effect of steroid injections is unsettled at present, but it is likely that they improve the accuracy of the injections
 - o One of the studies (Hay 2003) claimed to be a “pragmatic” trial (one done under conditions which resemble “real world” practice), but in this study, the injection group did not have any rehabilitation program for the first six weeks; they were simply instructed to avoid overuse of the shoulder for the first 48 hours
 - This is a departure from what would be common practice patterns in the real world
 - o The two studies which the authors did combine (Hay and Cloke) had disparate results, which were not included in the authors’ discussion

- Specifically, Hay reported improvements in both the injection group and in the physiotherapy group; the steroid group improved faster, but the PT group caught up later, so that both groups had equal improvement at 6 months
 - However, Cloke randomized participants into four groups, a control group which received NSAIDs, a group which received a course of methylprednisolone injections, a group which received a specific exercise and manual therapy package, and a group which received both interventions
 - None of Cloke's groups improved from baseline to the end of the study, in contrast to Hay, where both groups had significant improvement from baseline to the end of the study
 - Both Crawshaw and Hay reported early improvements in the steroid group which stabilized over time, but which did not deteriorate; it would be an error to infer that injections for rotator cuff tendinopathy are worse than the alternatives
- Similarly to the pattern seen in the trials of steroid versus PT, the three studies (Petri 1987, Adebajo 1990, Alvarez 2005) of steroid versus lidocaine placebo used landmarks to inject the test solutions
 - However, a later RCT (Hong 2011) compared triamcinolone with lidocaine placebo, but used ultrasound guidance during the injection procedure, and reported that 20 mg of triamcinolone was superior to the placebo injection for shoulder pain and disability for up to 8 weeks of observation
 - Again, it is possible that the added accuracy from employing ultrasound guidance leads to a more favorable clinical outcome
- On balance, the evidence from the included studies is that steroid injection is of uncertain benefit after the short term in comparison with local anesthetic injection and physical therapy, but that in the short term up to six weeks, they lead to more rapid functional improvement than placebo or exercise

Assessment: Adequate for strong evidence that steroid injections of rotator cuff tendinopathy have a rapid initial benefit, but inadequate for evidence that they are less effective in the intermediate and long term than alternative treatments (inappropriate pooling of disparate studies)

References:

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