**Atroshi I, Flondell M, et al. Methylprednisolone injections for the carpal tunnel syndrome: a randomized, placebo-controlled trial. Ann Intern Med. 2013;159(5);309-17.**

PMID: 24026316

Design: randomized clinical trial

Purpose of study: in patients with clinical carpal tunnel syndrome, to determine the effectiveness of local methylprednisolone injection compared to placebo injection

Population/sample size/setting:

* 111 patients (81 women, 30 men, mean age 28) treated for CTS at a university hospital in Lund, Sweden
* Eligibility criteria were primary idiopathic CTS, age 18-70, symptoms of classic or probable CTS, numbness or tingling in at least 2 of the 4 radial fingers, unsuccessful treatment with 2 months of splinting, referral from a primary care physician for consideration of surgery, and nerve conduction tests showing median neuropathy at the wrist
  + A difference in sensory latency less than 0.6 ms was normal, 0.6 to 0.9 ms was mild, 1.0 to 1.6ms was moderate, and 1.7 ms or greater was severe
  + If nerve conduction studies were normal, 2 independent orthopedic surgeons had to diagnose CTS in order for the patient to be included
* Exclusion criteria were previous steroid injection, thenar muscle atrophy, sensory loss with 2-point discrimination >8 mm, diabetes, thyroid disorder, inflammatory disease, polyneuropathy, previous carpal tunnel release, current pregnancy , surgery on the contralateral hand in the past 2 months, severe illness, and drug or alcohol abuse

Interventions:

* All patients received a single injection of volume 3 ml, and each injection contained 1 ml of lidocaine
  + Injections were administered 1 cm proximal to the wrist crease ulnar to the midline, in a 45 to 60 degree angle to the forearm
* Randomization was to injection with 2 ml methylprednisolone (80 mg) plus 1 ml lidocaine (n=37), 1 ml methylprednisolone (40 mg) plus 1 ml saline and 1 ml lidocaine (n=37), or 2 ml saline plus 1 ml lidocaine (n=37)
* After the injection, patients were instructed to use their hands as tolerated, and no other treatments were given

Outcomes:

* The primary end points were the change in the CTS symptom severity score (SSS) at 10 weeks and the rates of surgery at one year
  + The CTS SSS is the average of 11 items on a scale from 0 (no symptoms) to 5 (worst symptoms); thus the CTS SSS is also rated on a scale from 0 to 5
  + Patients were permitted to pursue surgery (open carpal tunnel release) at any time following 3 months after the injection, for any reason they chose if they did not feel improved
  + Surgery was done by a physician not involved in the trial
* There were assorted secondary end points: the Quick Dash, the SF-6D survey, and a rating of satisfaction on a 100 point scale from 0 (completely dissatisfied) to 100 (completely satisfied)
* All 111 patients had 1-year data and were included in the 12-month analysis
* The 10 week CTS SSS improved more in patients who received methylprednisolone than in those who received placebo
  + The mean change in CTS SSS from baseline to 10 weeks was -0.90 in the 80 mg methylprednisolone group, -1.17 in the 40 mg methylprednisolone group, and – 0.30 in the placebo group
  + The difference between the 80 mg and the 40 mg methylprednisolone groups were not statistically significant, but both methylprednisolone groups were significantly different from placebo
* The rates of surgery also differed between the three groups at one year, even though most patients elected to pursue surgery during the study followup period
  + 73% of the 80 mg methylprednisolone group had surgery, compared with 81% of the 40 mg methylprednisolone group and 92% of the placebo group
  + Time from injection to surgery was longer in the 80 mg and the 40 mg methylprednisolone groups than in the placebo group
* For the secondary outcomes, the methylprednisolone groups had better scores at 10 weeks than the placebo group, but thereafter, the secondary outcome scores did not differ between the three groups
* Pain after injection was reported by 24 patients in the methylprednisolone groups and by 6 patients in the placebo group; the median duration of pain was 2 days, and no serious adverse events were recorded
* Exploratory analyses, not included as primary end points, suggested that the effect of methylprednisolone on CTS SSS were greatest in patients who had more severe nerve conduction abnormalities at baseline; it also appeared that patients who received 80 mg methylprednisolone had greater improvement in pinch strength and monofilament sensation than those who had placebo

Authors’ conclusions:

* There is a large and statistically significant benefit on CTS symptoms of methylprednisolone injection observed at 10 weeks compared to placebo, without a significant difference between 40 mg and 80 mg
* However, most patients had surgery within one year, indicating that the effects of methylprednisolone injection are not highly durable
* Patients who had 80 mg of methylprednisolone had a modestly lower likelihood of having surgery compared to placebo, but even this moderate effect on surgery may prevent a large number of carpal tunnel release operations if methylprednisolone is given to a large population of CTS patients
* A study limitation is that the patients were only seen in one center in a region where primary care physicians do not perform steroid injections
* However, the results are likely to apply to patients who have not responded to splinting for 2 months, and for few other proven treatment options are available

Comments:

* Although the 73% rate of surgery in the 80 mg methylprednisolone group could be seen as modestly lower than the 92% rate in the placebo group, the rates could also be expressed as the rates of avoiding surgery in the first 12 months, and would be 27% in the 80 mg methylprednisolone group but only 8% in the placebo group
* The CTS SSS is only one part of the Boston CTS rating system; there is also a functional rating scale, which was apparently not measured, even though it would have been relevant
* There is a commonality with steroid injection in the setting of lateral epicondylitis, where there appears to be an early benefit which may not endure past the short term
  + However, it is not clear whether there is a deterioration of CTS symptoms and function with steroid injections
  + Table 3, showing changes in the CTS SSS at 5 weeks, 24 weeks, and 1 year, shows that the improvement in SSS is maintained in the steroid groups, and does not regress as often happens with lateral epicondylitis
  + The placebo group shows continued improvement in SSS from 5 weeks through 1 year
  + This is probably due to the fact that almost all of the placebo groups and most of the steroid groups underwent surgery before 12 months, and the final scores show improvements which are mostly attributable to carpal tunnel release rather than injection treatment
* Patients with normal nerve conduction tests could be included if 2 orthopedists diagnosed CTS
  + The number of patients with normal NCS is not clear from Table 1, where normal and mild abnormalities are combined, but it appears that not many patients were qualified for inclusion by orthopedist examination alone
* The source population consisted of CTS cases in the community who had not improved after 2 months of splinting; the size of the source population is not known, and the total number of patients who had improved with splinting is not available; this prevents an estimation of the total number of new cases of CTS are likely to end up with surgery after one year or so from the time of initial presentation to a primary care physician

Assessment : High quality RCT providing good evidence that in patients with CTS who have not improved after 2 months of splinting, an injection of 80 mg of methylprednisolone and of 40 mg of methylprednisolone are equally likely to lead to short-term 5-week improvements in carpal tunnel symptoms compared to placebo, but the success of methylprednisolone in avoiding surgery in CTS patients is modest. Although approximately 92% of placebo-injected patients are likely to require carpal tunnel release within one year, about three quarters of patients who have a methylprednisolone injection are also likely to have surgery; however, this modest difference in rates of surgery may prevent a large number of carpal tunnel release operations if steroid injections are offered to a large population of CTS patients who continue to have symptoms after a 2 month trial of splinting