Ferrante EM, Bearn L, et al. Evidence against Trigger Point Injection Technique for the Treatment of Cervicothoracic Myofascial Pain with Botulinum Toxin Type A. Anesthesiology 2005;103:377-83.

Design: Randomized clinical trial

Population/sample size/setting:

- 132 patients (52 men, 70 women, mean age 45) treated for cervical or shoulder myofascial pain at a department of anesthesiology at UCLA
- Eligibility criteria were at least 6 months of myofascial pain in the surface muscles of the neck and shoulder
- Exclusion criteria were (more than 5 active trigger points, (2) more than two trapezius trigger points on any one side of the body, (3) more than one trigger point in any other single surface muscle on any on e side of the body, (4) pregnancy, (5) age under 18, and (6) history of intolerance to NSAIDs

Main outcome measures:

- All participants were weaned from all pain drugs (NSAIDs, antidepressants, muscle relaxants, and opioids) for 2 weeks prior to any injection
- All participants were placed on 10 mg amitriptyline 2 hr before bedtime for 1 week, then 25 mg for 1 week, then 50 mg for 2 weeks, then 75 mg for 2 weeks
- Each patient also was to take 800 mg ibuprofen qid and 1 tablet propoxyphene-acetaminophen q4h p.r.n. for pain
- Participants received these medications together with physical therapy focused on myofascial release techniques for the duration of the study
- Trigger points were identified by palpation reproducing the pain and by acupressure at the same point eliminating the pain
- All participants were received 0.5 ml of injectate with a 22 gauge needle, randomized to either saline or 10, 25, or 50 U of botulinum toxin type A (BTX)
    - A maximum of 5 trigger points could be injected in any participant
    - Therefore, the maximum dose in each group was 0, 50, 125, or 250 U BTX per participant
- Four outcomes were measured
    - Pain VAS in the past 24 hours, recorded in diaries the same time each day, and returned at 1, 2, 4, 6, 8, and 12 weeks after injection, when patients were interviewed and re-examined
    - Use of propoxyphene-acetaminophen p.r.n. for pain recorded in same logs
    - Pain threshold measure by pressure algometry at the same follow-up interviews; each point on the skin was marked with methylene blue at the time of injection and at each examination
    - SF-36 quality of life at baseline and at each follow-up interval
- All outcome measures improved over time, sowing significant improvement in VAS scores, analgesic use, and pressure algometry

- For these outcomes, placebo and BTX groups improved equally, with no observed difference between treatment groups
- On the SF-36, BTX patients had an improvement in the Role Emotional subscale compared with placebo ($p < 0.05$), with trends toward significance for Vitality and Social Functioning subscales; no dose-response effect was seen for any subscale
- Few adverse effects were seen; 3 BTX patients had transient flu-like symptoms which resolved during the course of the study

Authors' conclusions:

- Injection of BTX directly into trigger points does not appear to improve pain relief in patients with cervicothoracic myofascial pain syndrome; although the passage of time led to improvements, the injection did not
- The role of injection method and technique may influence the response to BTX
    - The site of action of BTX could be the neuromuscular junction, the neuromuscular spindle, or (via axonal transport) the CNS
    - The size of the area of chemodenervation depends on dose and volume of the injectate
    - The motor endplate zones are not known for most muscles
- Biomechanical functional relations may influence the functional consequences of chemodenervation; for example, weakening neck flexors without weakening the extensors could produce postural abnormalities

Comments:

- While many data analyses are done informatively, there is insufficient description of the method of randomization (and allocation concealment) to make it clear that the risk of bias is low
    - Failure of allocation concealment, with its attendant possibility of allocation bias, raises more concerns when a treatment effect is reported than when no group differences are reported
- Baseline data shows mean VAS scores for each treatment group, but participants can have up to five trigger points, and it is not clear whether the baseline VAS represents the score for the most painful trigger point, or if it represents some other kind of value (e.g., an average of the VAS for all active trigger points)
- The nature of the physical therapy co-intervention is described only as focusing on myofascial release techniques; if any active PT (stretching, exercises, etc) were done during the study, it is not described
- Pharmacological co-interventions (amitriptyline and ibuprofen) may have provided sufficient pain relief to mask any effects of BTX and make the placebo and BTX results more similar
    - This could also be interpreted to mean that BTX adds little to the management of myofascial pain if adequate pharmacologic treatment is being used in the treatment plan

- Trigger points were called “active” if palpation reproduced the pain and acupressure eliminated it; it is not clear whether this determination was done by only one observer, or if different clinicians might have determined the “active” status of the suspected trigger points
- The sample size is probably sufficient to detect a large treatment effect, but the power of the study is not reported
- No outcome is reported in terms of proportion of responders (patients who have a clinically important change in pain, such as a 30% or a 50% reduction in pain); because group comparisons of average pain scores may be statistically inefficient, the lack of a statistically significant difference of average pain scores may obscure response differences of clinical significance
- Unlike several studies of tennis elbow, where the effect of BTX on extensor strength was reported, no measurement of motor strength is reported
    - This would be of greater concern in a study which reports a benefit of BTX than in a study which reports no pain benefit

Assessment: Inadequate for evidence statement that BTX is ineffective for myofascial pain (power of study unclear)