Can Botulinum Toxin A Injections into the Paravertebral Muscles Reduce Pain in Patients with Refractory, Chronic Muscular Lower Back Pain?

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Answer: Probably
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Level of evidence: B
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Summary of the issue

Chronic low back pain is extremely common. Complaints of low back pain account for approximately 15 million clinician office visits per year. It is estimated that as many as 90% of adults experience back pain at some point during their lives. The cost to the American economy is estimated at $50 billion per year. This does not include the cost to society associated with lost worker productivity, the psychosocial stress of being unable to work, and the state of dependency experienced by many of these patients.

In a majority of cases (70 – 90%), low back pain resolves with supportive therapy within five weeks. Currently effective pharmacologic therapy is limited to nonsteroidal anti-inflammatory agents, corticosteroids, anti-depressants, muscle relaxants, and opioids. These medications are often not effective, and opiates might trigger addictive behavior. Surgery and manipulative therapy often fails to provide pain relief, and surgery may even exacerbate the problem.

Botulinum toxin is a presynaptic neuromuscular blocking agent that, when administered intra-muscular, causes a temporary clinical denervation of the muscle by blockade of acetylcholine release from the motor nerve terminals. After injection, muscle weakness begins within a week, peaks within two weeks and then plateaus. The plateau is usually prolonged followed by a gradual, slow recovery to baseline as the neuron sprouts new axons and regains the ability to release acetylcholine. The dose administered affects both the duration of the plateau period and the intensity of the denervation. Typically the effects last three to four months after the injection of botulinum toxin.

Botulinum toxin has already been shown to alleviate the pain associated with cervical dystonia and other conditions characterized by muscle spasticity. It appears to be safe with the advantage of providing pain relief directly to the site of the pain without systemic side effects.

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Summary of the evidence

Foster, et al conducted a randomized, double-blind study investigating the efficacy of botulinum toxin A in patients with chronic low back pain.[1] Inclusion criteria consisted of a) low back pain (L1 – S1), b) pain duration of six months or longer and c) pain laterality (either unilateral or if bilateral, showing a left or right predominance). Exclusion criteria included a) age under 18 years, b) presence of a systemic inflammatory condition, c) acute pathology on MRI, d) known allergy or sensitivity to botulinum toxin A, e) current or planned pregnancy, f) disorders of neuromuscular transmission, g) anesthetic or corticosteroid injection within 12 weeks prior to enrollment and h) involvement in litigation, disability procedures or with evident secondary gain. All patients were encouraged to continue their current medications and not to change their dosage during the study.

Of the 31 patients enrolled in the study, 15 patients received 200 units of botulinum toxin type A, 40 units at five lumbar paravertebral levels on the side of maximum discomfort and 16 patients received normal saline in the same fashion. Base level of pain and degree of disability was documented using the visual analogue scale (VAS) with a range from "no low back pain" to "worst low back pain" and the Oswestry Low Back Pain Questionnaire (OLBPQ). The OLBPQ records information about both pain and functional ability regarding tasks of daily living. Each item is graded from 0 to 5 with 0 being normal and 5 being most affected. The items include pain, personal care, walking, sitting, standing, lifting, sleeping, social life, sexual life, and traveling. The researchers reevaluated the patients at 3 and 8 weeks (VAS) and at 8 weeks (OLBPQ).

Pain intensity prior to treatment ranged from 6 to 10 (mean, 7.5) as measured by VAS in the botulinum A toxin group and 5 to 10 (mean, 7) in the normal saline group. There was no significant difference in the OLBPQ scores between the two groups prior to treatment. At 3 weeks, 11 of 15 patients (73%) who received botulinum toxin A had more than 50% pain relief (VAS score) compared to 4 of 16 (25%) in the normal saline group. ($p = 0.012$).

The difference between these groups was 48% (95% CI, 11.7% to 80.1%). At 8 weeks, 9 of 15 (60%) in the botulinum toxin group vs. 3 of 16 (25%) in the saline group experienced pain relief reported as greater than 50%. ($p = 0.009$), the difference being 47.5% (95% CI, 10.5% to 79.1%). Repeat OLBPQ at 8 weeks showed improvement in 10 of 15 patients (66.7%) in the botulinum toxin group vs. 3 out of 16 (18.8%) in the saline group ($p = 0.011$), a difference of 47.9% between the two groups (95% CI, 10.9% to 79.6%). No patient experienced side effects from the treatment. Two patients in the normal saline group reported increased pain after treatment and none in the botulinum toxin group.

Jabarri, et al conducted an open label prospective study involving 75 patients, treated with repeated botulinum toxin injections over a period of 14 months, to determine the short- and long-term effects in patients with refractory, chronic lower back pain.[2] Inclusion and exclusion criteria were the same as for the prior study mentioned. Pain intensity (VAS), pain impact (PIQ) and perceived functional status (OLBPQ) were assessed at baseline, 3 weeks and at 2,4,6,8,10,12 and 14 months. Botulinum toxin A was injected into the paraspinal muscles at 4 – 5 sites (L1 – S1 level) unilaterally or bilaterally. The dose per site varied from 40 – 50 units with a total dose range of 200 – 500 units per session. Reinjection was performed at 4 months only if pain recurred. A decrease of 50% or more in the individual VAS maximum score, two or more level improvement in at least one functional subset of the OLBPQ in addition to the pain subset, and more than 30% improvement in the PIQ (pain days), were considered significant.

At 3 weeks, 40 patients (53%) and at 2 months, 39 (52%) demonstrated statistically significant response to treatment. At 2 months, mean group values for VAS average, VAS maximum, OLBPQ score and pain days (in PIQ) 5.5, 8.4, 17.2 and 23.4 fell to 3.6, 5, 12.5 and 11.1 respectively ($p = < 0.005$ for all values). Responders reported improvement in symptoms within 24-96 hours after injection. Comparing responders to non-responders, there was no statically significant difference between the two groups with respect to age, gender, pain intensity, duration, laterality, history of surgery, presence of radicular pain, focal muscle tenderness, neurological deficits, use of opioids or the type of MRI abnormality. Among initial responders, 91% continued responsiveness over the length of the study. Three patients (4%), after the first treatment, had a mild flu-like reaction that lasted 2-5 days.

Ney, et al conducted an open-label prospective study involving 60 patients evaluating the effects of two successive botulinum toxin injections for chronic low back pain.[3] Adults with chronic low back pain received multiple paraspinal muscle injections with a maximum of 500 units botulinum toxin A per session. Responders received a second injection at 4 months. Pain and disability was assessed with VAS, OLBPQ and clinical low back pain questionnaire (CLBPQ) at baseline, 3 weeks, 2 months, 4 months and 6 months after treatment.

Sixty patients, ages 21 to 79 years (mean 46.6 years), with low back pain of mean duration of 9.1 years were included. At baseline the average VAS score (over preceding 28 days) was 5.3 and the mean maximum VAS score was 8.58. The mean OLBPQ score was 17.2 and mean number of days with clinically significant back pain on the CLBPQ was 23.8 (out of past 28 days). Clinically significant improvement in lower back and radicular pain occurred at 3 weeks in 60% and at 2 months in 58% of the cohort. Beneficial response to the first treatment predicted response to reinjection in 94%. A significant minority of patients had a sustained beneficial effect from the first injection at 4 (16.6%) and 6 months (8.3%). Two patients had a transient flu-like reaction after the initial treatment. Statistically significant improvements were noted at 6 months compared to baseline ($p<0.005$ for all comparisons to baseline). VAS average (mean) 5.3 to 2.9 at baseline and 6 months respectively, VAS maximum (mean) 8.58 to 3.79, OLBPQ (mean) 17.2 to 10.9, and CLBPQ (mean days) 23.8 to 7.2.

Comments

Potential biases of the studies discussed include small numbers of patients, only one placebo control group and all three studies were conducted by the same research team.

Search terms

Low back pain, Botulinum toxin A, Botox®, radicular pain, spasm, muscle.

Inclusion and exclusion criteria

From all the articles reviewed, we selected to review only those articles that focused on use of botulinum toxin A to treat chronic lower back pain. Only one study could be found that compared the botulinum toxin A to placebo (normal saline).

List of articles reviewed

1. Foster L, Clapp L, Erickson M, Jabbari B. Botulinum toxin A and chronic back pain. *Neurology* 2001;56(10):1290-3.
2. Jabarri B, Ney J, Sichani A, Monacci W, Foster L, Difazio M. Treatment of refractory, chronic low back pain with Botulinum Neurotoxin A: an open-label, pilot study. *Pain Management* 2006;7(3):260-4.
3. Ney J., Difazio M., Sichani A., Monacci W., Foster L., Jabbari B. Treatment of chronic back pain with successive injections of Botulinum Toxin A over 6 months. *Clin J Pain* 2006;22(4):363-369.