ORIGINAL ARTICLE

Therapeutic Use of Botulinum Toxin Type A in Treating Neck and Upper-Back Pain of Myofascial Origin: A Pilot Study

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ABSTRACT. Lew HL, Lee EH, Castaneda A, Klima R, Date E. Therapeutic use of botulinum toxin type A in treating neck and upper-back pain of myofascial origin: a pilot study. Arch Phys Med Rehabil 2008;89:75-80.

Objective: To determine the efficacy of botulinum toxin type A (BTX-A) in treating neck and upper-back pain of myofascial origin.

Design: A randomized, double-blind, placebo-controlled pilot study.

Setting: Outpatient physical medicine and rehabilitation clinic of a university-affiliated tertiary hospital.

Participants: A total of 29 subjects enrolled from among 45 screened patients. No subject withdrawal due to serious adverse events occurred.

Intervention: Subjects were evaluated at baseline, received a 1-time injection of either BTX-A (treatment group) or saline (control group), and were followed up at 2 weeks and at months 1, 2, 3, 4, and 6.

Main Outcome Measures: Visual analog scale (VAS) for pain, the Neck Disability Index (NDI), and the Medical Outcome Study 36-Item Short-Form Health Survey (SF-36).

Results: Improvements in the VAS and NDI scores were seen in the treatment group but were not significant when compared with the controls. Statistically significant improvements for the treatment group were seen in the SF-36 bodily pain (at months 2 and 4) and mental health (at month 1) scales but not in the other scales, nor in the summary measures. No serious adverse events were reported.

Conclusions: Trends toward improvements in VAS and NDI scores of the BTX-A group are encouraging, but they were possibly due to a placebo effect and were not statistically significant. The BTX-A subjects, at certain time points, showed statistically significant improvements in the bodily pain and mental health scales of the SF-36 compared with controls. Our study had limited power and population base, but the results could be used to properly power follow-up studies to further investigate this topic.

Key Words: Back pain; Botulinum toxin type A; Myofascial pain syndromes; Rehabilitation.

AS THE LEADING CAUSE of job-related disability and the second leading cause for all disabilities in the United States, neck and back pain are major public health problems.[1] It has been estimated that neck and back pain affect up to 70% of adult Americans during their lifetimes.[1]

The most common medications currently available to alleviate neck and back pain include muscle relaxants, nonsteroidal anti-inflammatory drugs, antidepressants, and opioids. In recent years, there has been a growing interest in the use of botulinum toxin type A (BTX-A) for the treatment of neck and back pain. Various clinical studies[2-4] suggest that BTX-A may provide effective analgesic effect for muscular pain conditions, particularly those due to myofascial pain syndrome (MPS), which is a common cause of muscular pain in the neck and back and is characterized by shortened muscle length, increased tone or tension, and trigger points.

Prospective randomized studies have been conducted on the efficacy of BTX-A on neck and back pain of myofascial origin, but these are few in number. We found 3 randomized, placebo-controlled studies[5-7] regarding the effects of BTX-A on neck and upper-back myofascial pain and only 1 controlled study[8] concerning BTX-A effects on lower back pain that have been published to date.

In a small randomized study of 6 subjects, Cheshire et al[5] reported that BTX-A treatment of myofascial neck pain resulted in improvement compared with saline. On the other hand, Ojala et al[6] did not find statistically significant results in neck pain and pressure pain threshold between the treatment and control groups in their study of 31 subjects. Gobel et al[7] conducted a larger, more recent study in 120 subjects with myofascial upper-back pain and reported that BTX-A injection resulted in significant pain reduction and significant pain-free days for the treatment group compared to those in the placebo group.

Foster et al[8] studied the efficacy of BTX-A on chronic low back pain (CLBP) in 31 subjects who were randomly assigned to treatment or placebo groups. By using the visual analog scale (VAS) as a subjective measure of pain intensity, Foster showed that 73% of BTX-A subjects and 25% of placebo subjects had 50% or more pain relief. Foster's study likewise showed that more subjects in the treatment group (66.7%) experienced improvement (as measured by the Oswestry Disability Index [ODI]) compared with 18.8% among the placebo group.

Other related studies have been mostly open-label trials, but these showed promising results. Vasan et al[9] injected BTX-A into the myofascial trigger points of 16 subjects with chronic neck pain. A significant reduction in pain was noted among patients in this prospective, open-label study. Jabbari et al[10] conducted an open-label prospective study on the short- and long-term effects of BTX-A injections on paraspinal muscles in 75 patients. They reported that BTX-A was beneficial in patients with CLBP.

The findings of positive benefits with BTX-A for myofascial pain warrant further investigations using a randomized, placebo-

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controlled design that could yield valid clinical evidence to support the use of BTX-A for relief of neck and back pain. We report the results of a pilot study in which we used a randomized, double-blind, placebo-controlled design and set out to evaluate the therapeutic efficacy of BTX-A in the treatment of neck and upper-back pain of myofascial origin. The hypothesis was that the subjects treated with BTX-A would experience greater pain relief and clinical benefit than those who received placebo.

METHODS

Participants

Twenty-nine adult subjects with diagnoses of cervical or upper-back pain of myofascial origin participated in the study. Through flyers and advertisements, subjects were recruited from the general population and the patient population of the physical medicine and rehabilitation clinic in a university-affiliated tertiary hospital. The study was approved by the institutional review board of the hospital's affiliated university. Subjects were included if they (1) had been diagnosed as having neck or upper-back pain of myofascial origin within the past 2 to 6 months or had a previous diagnosis of neck or upper-back pain of myofascial origin but had experienced an exacerbation of pain symptoms within the same period, (2) were aged 18 to 70 years, and (3) had a VAS pain score of 5 or greater for the 4-week period before injection. The exclusion criteria were the following: (1) allergy to BTX-A; (2) any medical condition that put a subject at risk with exposure to BTX-A; (3) acute pathology such as infection, inflammation, cervical radiculopathy, or any operative pathology, as shown on physical examination or magnetic resonance imaging; (4) use of aminoglycoside antibiotics, curare-like agents, or other agents that may interfere with the neuromuscular junction; (5) history of gastroesophageal reflux disease (GERD); (6) abnormal swallowing test results on baseline; and (7) pregnancy, breastfeeding, or planned pregnancy. Use of concomitant pain medication and physical therapy was allowed, and no instructions were given to subjects to alter their current regimen.

Subjects were referred by other physicians and their history, physical examinations, and pertinent laboratory and other examination results were reviewed during the screening visit. Initial screening included history taking to include medication and surgical history and duration of pain, as well as completion of preinjection assessments for the VAS for average and maximum pain, the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) to assess functional status, and the Neck Disability Index (NDI). In addition to the screening review, a physical examination was performed to determine the most tender cervical or upper-back muscles and to rule out operative, radiculopathic, and other contraindicated conditions.

Study Intervention

Qualified, consenting subjects were randomized to the control group (injection with normal saline solution) or the treatment group (injection with BTX-A [Botox]). A computer-generated randomization scheme was used. Subjects were assigned a randomization number, which corresponded to a treatment allocation schedule and was stored by the hospital's research pharmacist. Hence, for each injection, both the subject and the investigator were blinded. Fourteen subjects were included in the treatment group, and 15 subjects participated in the control group (fig 1). Each vial of BTX-A (100U) or saline was reconstituted by 2mL of normal saline. The BTX-A or saline vials were prepared and reconstituted before receipt by the investigator, who received them in identically appearing syringes, which ensured that he remained blinded as to whether the syringe contained medication or placebo.

The dose per injection site was 50U. The total dose did not exceed 200U per treatment and 100U per side. No more than 2 muscles were selected on each side, and only painful muscles were injected. Trigger points were determined before the injection procedure by deep finger pressure. Injections were performed without electromyographic guidance at the site of the trigger points. The muscles that were injected include the trapezius, levator scapulae, splenius capitis, and other posterior neck muscles. For the control group, the same determined volume was injected, but with normal saline. Injection sites were sterilized, and BTX-A or normal saline was administered by a disposable 27-gauge needle with disposable syringe. Each injection was performed slowly, over 15 seconds per location.

The following outcome measures were used: (1) VAS for pain, (2) SF-36, and (3) NDI. Evaluations were performed at baseline, week 2, and months 1, 2, 3, 4, and 6. Subjects were monitored for possible adverse events after BTX-A injection by telephone follow-up at 3 and 10 days postinjection. Monitoring of adverse events continued throughout the entire study period.

Outcome Assessment

Subjects were evaluated at baseline, then at 2 weeks, and at 1, 2, 3, 4, and 6 months postinjection. For the baseline and second-week assessments, subjects were evaluated in person. For the succeeding evaluation periods, subjects were requested to complete the questionnaires for the outcome measures and to return them by mail to the study coordinator. The study used the following outcome measures to determine subjective pain relief as reported by each patient.

VAS for pain. The VAS for pain measures the amount of pain experienced by a subject with a continuous range from none to extreme, using 0 for no pain and 10 for maximum pain. It has been validated as a "reliable, generalizable and internally consistent measure of clinical and experimental pain."[11(p217)] Subjects were asked to indicate the pain levels (average and maximum pain) which they experienced within the specified evaluation time periods.

The SF-36. The SF-36 is a validated measure of health status widely used in clinical practice and research.[12] It has 36 items under 8 categories assessing general health concepts: physical functioning, role limitation due to physical health, bodily pain, general health perception, vitality, social functioning, role limitation due to emotional problems, and mental health.[12]

Neck Disability Index. This is a modified pain index derived from the ODI and is designed to describe how much a subject's neck pain affected his/her ability to manage everyday activities.[13]

Data Analysis

The results of the study were analyzed by an independent data management group. SAS software[a] was used for statistical analysis. Patients were included in the analysis on the basis of intention to treat. The hypothesis, that the efficacy in pain relief would be better with BTX-A, was tested through between- and within-group comparisons in the average pain VAS, SF-36, and NDI scores. The normality of variables was tested using Shapiro-Wilk tests. According to the normality of variable, the 1-sided *t* test (Wilcoxon rank-sum test) and 2-sided paired *t* test (Wilcoxon signed-rank test) were used for between- and