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ORIGINAL ARTICLE

Effect of Electrical Stimulation on Botulinum Toxin A Therapy in Patients With Chronic Myofascial Pain Syndrome: A 16-Week Randomized Double-Blinded Study

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Abstract

Objective: To evaluate the effect of different intensities of electrical stimulation on botulinum toxin A (BTX-A) injection at trigger points (TrPs) in patients with chronic myofascial pain syndrome (MPS).

Design: Double-blind randomized trial.

Setting: Outpatient rehabilitation clinic.

Participants: Patients (N = 76) with chronic MPS of the neck and shoulder regions.

Interventions: Patients were randomly assigned to 1 of 2 intervention groups: BTX-A injection followed by (1) electrical stimulation that induces visible muscle contraction (MOTOR group); or (2) electrical stimulation with an intensity just above the sensory threshold (SENSORY group). Electrical stimulation was administered for 30 minutes a day for 3 consecutive days after injection.

Main Outcome Measures: The primary outcome was the visual analog scale (VAS) for pain. Secondary outcomes included the Neck Pain and Disability Scale (NPAD), Global Assessment of Improvement Scale (GAS), and pressure pain threshold (PPT).

Results: The VAS scores decreased significantly at 4, 8, 12, and 16 weeks from the baseline in both groups. Significant changes in the NPAD score over time were noted only in the SENSORY group at 8, 12, and 16 weeks. The SENSORY group showed lower VAS and NPAD scores at 16 weeks ($P = .043$ and $P = .041$, respectively), and higher treatment success rates at 12 and 16 weeks ($P = .039$ and $P = .024$, respectively) than the MOTOR group. There was no significant result in the GAS and PPT.

Conclusions: Short-term electrical stimulation may affect the reduction in pain after BTX-A injection at TrPs in patients with chronic MPS of the neck and shoulder regions. Based on the results, it seems that sensory electrical stimulation was superior to motor electrical stimulation as an adjuvant therapy to BTX-A injection in patients with chronic MPS. Further studies are warranted to investigate the method facilitating the effect of BTX-A on MPS.

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Myofascial pain syndrome (MPS) is one of the most common causes of musculoskeletal pain in general practice.[1] MPS is characterized by myofascial trigger points (TrPs) in skeletal muscle. A TrP is defined as a hyperirritable spot associated with a hypersensitive palpable nodule in a taut band.[2] Although the pathogenesis of TrPs is still unclear, based on histologic and electrophysiologic studies, it has been suggested that excessive release of acetylcholine from dysfunctional motor endplates is the underlying etiology of TrPs.[2,3] TrP injection has been widely used for treatment, with several investigations supporting its effectiveness.[4] The hypothesis of dysfunctional motor endplates has given rise to the idea of treatment with botulinum toxin A (BTX-A) injection, which inhibits presynaptic acetylcholine release.[5]

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BTX-A is one of the toxins produced by *Clostridium botulinum*. It binds and cleaves synaptosomal-associated protein-25 (SNAP-25), a protein of the presynaptic membrane, which results in abolition of acetylcholine exocytosis.[6] This leads to reversible chemodenervation in the injected muscles and subsequently reduces muscle tension and pain.[7] BTX-A has been used in several chronic pain conditions associated with muscle disorders including cervical dystonia, piriformis syndrome, chronic lower back pain, and MPS.[8] However, recent studies[9-16] have shown contradictory results about the efficacy of BTX-A on myofascial pain. In particular, a large multicenter randomized controlled trial[9] (RCT) in 145 patients with upper back MPS showed better outcomes with BTX-A injection than normal saline injection. By contrast, other small RCTs[10,11] showed no favorable outcome of BTX-A injection on myofascial pain when compared with normal saline injection. Based on these trials, a recent Cochrane review[17] concluded that "there is inconclusive evidence to support the use of BTX-A in the treatment of MPS."[17(p2)]

Previous animal experiments[18,19] demonstrated that muscle inactivity delayed the onset of BTX-A action, and electrical stimulation enhanced BTX-A absorption and accelerated the onset of the effect of BTX-A at the neuromuscular junctions. Several human studies showed that electrical stimulation with a frequency of 20Hz and an intensity that is sufficient to induce visible muscle contraction facilitated the effect of BTX-A on healthy muscles[20] and spastic muscles.[21-24] Based on these findings, electrical stimulation may also facilitate the effect of BTX-A on muscles with dysfunctional endplates, such as those in MPS. To our knowledge, no study has been performed to explore the effect of electrical stimulation and BTX-A in patients with MPS.

In this study, we attempted to evaluate the effect of different intensities of electrical stimulation on botulinum toxin A (BTX-A) injection at TrPs in patients with chronic MPS of the neck and shoulder regions. We hypothesized that motor electrical stimulation after BTX-A injection would facilitate the effect of BTX-A on MPS when compared with sensory electrical stimulation, because BTX-A mainly exhibits its action on the motor nerve endings.

Methods

Design overview

This study was a prospective, randomized, double-blind study to investigate the effect of different intensities of electrical stimulation, administered for a short period, on a single BTX-A (Dysport) injection at TrPs in patients with chronic MPS. Written informed consent was obtained from each patient before enrollment. The study was approved by the institutional review board of Seoul National University Hospital.

List of abbreviations:

BTX-A	**botulinum toxin A**
CI	**confidence interval**
GAS	**Global Assessment of Improvement Scale**
MPS	**myofascial pain syndrome**
NPAD	**Neck Pain and Disability Scale**
PPT	**pressure pain threshold**
RCT	**randomized controlled trial**
TENS	**transcutaneous electrical nerve stimulation**
TrP	**trigger point**
VAS	**visual analog scale**

Setting and participants

This study was conducted in the Outpatient Department of Rehabilitation Medicine at the Seoul National University Hospital and Seoul National University Boramae Medical Center. Eligible patients were recruited between April 2005 and March 2007.

Seventy-six patients participated in this study. Subjects were included if they (1) had chronic neck and shoulder pain for at least 6 months that was refractory to other conservative treatments; (2) presented at baseline with a pain score >5 on a visual analog scale (VAS); and (3) had an active TrP. An active TrP was defined as a tender spot localized in a taut band of muscle fibers associated with (1) tenderness; (2) referred pain, which was recognized by the patient, into well-defined areas that were remote from the TrP area at palpation; and (3) preferably, the presence of a local twitch response, the jump sign, or both, on palpation. The exclusion criteria were as follows: (1) age <21 years; (2) disk or bone disease; (3) any history of neck surgery; (4) neurologic deficits; (5) current or planned pregnancy; (6) neuromuscular junction disorder; (7) motor neuron disease; (8) systemic inflammatory disease; (9) hypersensitivity to BTX-A; (10) received anesthetic injections at the target TrP within 4 weeks of study enrollment, or corticosteroid injections within 3 months; (11) diffuse tender points or a diagnosis of fibromyalgia; (12) previous electrical stimulation; and (13) previous injection of BTX-A within 6 months of study enrollment.

Randomization and interventions

The 3 (or 6 when bilateral) most painful and active TrPs of the cervical and shoulder muscles were identified by a physician. In all the study participants, for each TrP, BTX-A (Dysport 500U) reconstituted with 3.0mL of normal saline was injected with a total volume of 1.0mL (or 0.5mL when bilateral). Electrical stimulation on the injected muscles was given for 30 minutes a day for 3 consecutive days after BTX-A injection with 1 of the following 2 intensities: (1) for the MOTOR group, an intensity large enough to induce visible muscle contraction of the injected muscle; and (2) for the SENSORY group, an intensity just above the sensory threshold. Subjects were randomly assigned to the MOTOR group or SENSORY group by stratified block randomization. Separate randomization procedures were performed within each of 6 subsets (sex and age subsets) of participants, with a block size of 4 and an allocation ratio of 1:1. A multichannel device with continuous trains (3s) of rectangular biphasic current pulses was used for stimulation. The stimulation pulse frequency and width were set to 20Hz and 200μs on the basis of a previous study.[21] These stimulation parameters were adequate to induce moderate muscle contraction with less muscle fatigue. Surface electrodes were placed on the motor point of each muscle. Both physicians and patients were blinded to the treatment used. All the patients discontinued both medication and physical therapy for myofascial pain during the entire study period.

Outcomes and follow-up

Patients were evaluated at baseline, at 1 and 3 days, and at 1, 2, 4, 8, 12, and 16 weeks postinjection by a researcher blinded to the groups. The primary outcome measure was a 10-cm VAS, with 0 indicating no pain and 10, maximum pain. Secondary outcome measures for treatment efficacy included a modified version of the