Single CT-Guided Chemodenervation of the Anterior Scalene Muscle with Botulinum Toxin for Neurogenic Thoracic Outlet Syndrome

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Abstract

Objective. To examine pain relief in patients with neurogenic thoracic outlet syndrome (NTOS) after a single, low dose injection of botulinum toxin A (Botox) into the anterior scalene muscle (ASM) under computed tomographic (CT) guidance.

Design. Prospective longitudinal study.

Setting. Academic medical institution.

Patients. Patients 18 years of age and older were evaluated for potential scalenectomy and first rib resection using the transaxillary approach at the study institution between 2005 and 2008. All patients had failed physical therapy. A total of 29 procedures on 27 participants were studied.

Interventions. A single, 20-unit injection of Botox into the ASM under CT-guidance.

Outcome Measures. Short-form McGill Pain Questionnaire (SF-MPQ) prior to and at 1, 2, and 3 months post-Botox toxin injection.

Results. There was a decline in pain during the 3 months subsequent to Botox injection as noted by the following components of the SF-MPQ: sensory (P = 0.02), total (P = 0.05), visual analog scale (VAS (P = 0.04)), and present pain intensity (PPI) score (P = 0.06). The proportion of patients reporting more intense pain scores did not return to the pre-intervention level at 3 months post-Botox injection.

Conclusion. Patients experienced substantial pain relief in months 1 and 2 following a single Botox injection into the ASM. Significant pain reduction was noted for 3 months after Botox injection with respect to both sensory and VAS scores, and the total and PPI scores approximated statistical significance. After 3 months, patients experienced a 29% decrease in the sensory component of their pain as well as an approximate 15% reduction in their VAS score. A single, CT-guided Botox injection into the ASM may offer an effective, minimally invasive treatment for NTOS.

Key Words. Thoracic Outlet Syndrome; Anterior Scalene Muscle; Botulinum Toxin (Botox); Computed Tomographic Imaging (CT); Pain Relief; McGill Pain Questionnaire

Introduction

Thoracic outlet syndrome (TOS) remains a controversial entity without standardized methods or uniform criteria for diagnosis, treatment, patient selection for surgery, indications for surgery, or treatment approaches [1–6]. Some argue that the lack of specific objective diagnostic tests for recognition of the compressed structures exemplifies the real controversy [4,7,8]. No definitive test exists for TOS: electrodiagnostics, radiographs, and magnetic resonance imaging (MRI) cannot establish the diagnosis definitively.
Clinicians have relied upon botulinum toxin A (Botox) for the relief of hypertonic conditions in the cervico-cranial musculature including spasmodic torticollis [23], achalasia [24], and oromandibular dystonia [25]. Symptomatic relief may persist anywhere from 3 to 6 months, but accidental spread of toxin may produce weakness, aspiration, phonation disturbance, or dysphagia. Consequently, techniques that use more precise needle targeting with lower volumes of toxin may reduce the risk of inadvertent adverse effects while permitting effective treatment of the condition.

Prior investigations of Botox injection for the treatment of NTOS have included the injection of 100 units divided into the ASM (12 units), middle scalene muscle (12 units), and trapezius muscle (76 units) [21]; as well as a total of 187 units divided into the ASM (12 units), middle scalene muscle (12–15 units), subclavius muscle (35 units), pectoralis minor muscle (35 units); and between 75–100 units for the trapezius and levator scapula muscles [22]. Another investigator injected 100 units divided into the ASM (25 units), splenius cervicis (25 units), supraspinatus (25 units), and rhomboid major (25 units) [26].

Current literature demonstrates that Botox injection into more than one scalene muscle as well as into the upper thoracic or chest wall muscles has been effective in reducing the symptoms of NTOS [21,22,26]. However, no studies have examined a single, low dose injection of Botox into the ASM under CT-guidance for the purpose of assessing analgesia in patients with NTOS. Interestingly, chemodenervation of the anterior scalene muscle with Botox (15 units) has improved subclavian artery blood flow in a patient with arterial TOS [27].

Botox injection into the scalene muscles has been shown to provide more durable symptom relief than anesthetic blockade. A few prior studies have relied upon electrophysiologically, fluoroscopically, or ultrasonographically guided botox injections of both the ASM and surrounding muscles [21,22,26]. The present study was undertaken to assess pain relief following a single Botox injection into the ASM under computed tomographic (CT) guidance for the treatment of chronic, stable NTOS. It also describes the novel use of a single CT-guided injection of bupivacaine without steroid into the ASM for use in a diagnostic test in advance of surgical decompression of the interscalene triangle.

We hypothesized that patients with NTOS would experience meaningful pain relief, as assessed by the short form McGill Pain Questionnaire (SF-MPQ) [28], after a single, low-dose injection of Botox into the ASM with the assistance of CT-guidance.

**Methods**

This prospective longitudinal study included a total of 29 procedures on 27 participants who were being assessed for potential scalenectomy and first rib resection using the transaxillary approach at the study institution (Johns Hopkins Hospital). Two patients were diagnosed with bilateral NTOS. There was a 4-week interval between bilateral anterior scalene botox injections for one patient and a 6-month interval for the other. For the purposes of the study, each side was treated as an independent subject. Institutional Review Board approval was obtained to study patients 18 years of age and older who presented to an
academic medical institution for diagnosis of TOS between 2005 and 2008. All patients had failed physical therapy.

Subjects were referred from the vascular surgery clinic, demonstrated stable, NTOS, reported no prior scalenectomy/rib resection, and demonstrated no radiographic evidence of significant cervical spine pathology. All patients reported symptoms suggestive of TOS, and physical examination revealed substantial tenderness over the ipsilateral ASM, and a positive elevated arm stress test (EAST). Signs and symptoms of TOS varied between both the upper and lower regions of the brachial plexus. Further, duplex ultrasonography was performed on all patients to exclude arterial or venous sources of TOS. Subjects were followed to determine whether surgical decompression occurred after Botox injection. Any oral opioid use was noted during the period of time before anterior scalene block to 3 months after Botox injection.

CT-Guided Injection Technique

Each patient underwent a CT-guided anterior scalene local anesthetic injection with 1 cc of 0.25% bupivicaine. Patients were then considered for Botox injection if they reported at least a 50% improvement in pain on the numerical analog scale, and an improvement in their ability (i.e. increased length of time before reproduction of symptoms) to perform the EAST. A positive response to blockade of the ASM and a reduction in the patients’ symptoms helped to confirm the diagnosis of NTOS [2,13,17–19]. If these criteria were met, patients then underwent a CT-guided anterior scalene injection with 20 units of Botox using a single-needle approach. Chemodenervation occurred within 4 days to 3 months following local anesthetic blockade. Patients completed the SF-MPQ prior to local anesthetic injection into the ASM and at 1, 2, and 3 months post-Botox injection.

Patients were positioned supine and a biopsy strip was placed on the neck. A scout film was obtained from the C4 to T1 levels using 3-mm slices (Fig. 1). The ASM was identified, the neck was prepared in the usual sterile manner, and a 1.5-inch, 25-gauge needle was inserted into the muscle belly (Fig. 2). A focal area of the neck was rescanned on 1–2 more occasions for evaluation and adjustment of needle position, then 0.1 mL–0.3 mL of radiographic contrast (i.e. omnipaque 180) was injected to verify both needle placement and spread of material within the muscle (Fig. 3). One cc of 0.25% bupivicaine was injected followed by rescanning to confirm selective injection into the ASM.

Botox injections were performed in identical fashion; however, once radiographic contrast confirmed proper needle placement, 20 units of Botox were then injected into the ASM in lieu of local anesthetic. A focal scan of the cervico-thoracic region was performed to verify proper spread of Botox within the muscle (Fig. 4). No other muscles were targeted for local anesthetic or Botox injections. CT exposure time per procedure averaged 25 seconds and did not exceed 60 seconds.

For the 29 procedures performed in the study, CT imaging verified proper needle position into the ASM and no evidence of local anesthetic or Botox leakage into adjacent
None of the patients had other cervico-thoracic injections performed during the study period.

**Pain Assessment**

The SF-MPQ [28,29] was scored as follows: the sensory pain component score was the sum of the first 11 items (“throbbing” through “splitting”) and the affective component score was the sum of the remaining 4 items (“tiring-exhausting” through “punishing-cruel”). The total pain score was the addition of the sensory and affective pain components. The visual analog scale (VAS) was converted into a quantitative score by measurement in millimeters; values were divided by the measurement of the entire line in order to standardize the results. The present pain intensity (PPI) score was the final component of the SF-MPQ; scores ranged from 0 to 5 and were used to describe overall pain experience.

**Statistical Analysis**

A sample size of 20 patients was required in order to detect a 21% difference in pain scores before and after the intervention, with a power of 95%. Descriptive statistics were performed for pain scores before and after the intervention. Boxplots were used to examine the distribution of data and outliers. Reported pain scores were non-normally distributed and log transformation did not improve normality. Therefore, non-parametric methods were employed for analyses and each component of the SF-MPQ was analyzed separately. Percentage change in median pain scores was calculated using the pre-Botox score compared with 1, 2, and 3 months post-Botox injection. The Wilcoxon signed rank test was used to test differences in the median pain scores reported at each time period. The Kruskal-Wallis procedure was used for pairwise comparison of median pain scores for the pre-Botox pain score compared with each month subsequent to the intervention.

**Results**

Study participants ranged in age from 19 to 58 years with a mean age of 39.5 and 79% were female. Twenty-eight percent (28%) of patients reported opioid use during the study period; most were using short-acting agents only. Forty-eight percent (48%) of patients eventually proceeded with surgical decompression via scalenectomy and first rib resection.

**Figure 2** Needle insertion into the anterior scalene muscle.

**Figure 3** Contrast accumulation in the anterior scalene muscle.

**Figure 4** Spread of contrast after botulinum toxin injection into the anterior scalene muscle.
Table 1 displays median pain scores, derived from the SF-MPQ, reported by patients before and after a single Botox injection into the ASM. There was a decline in pain during the 3 months subsequent to Botox injection as noted by the following components of the SF-MPQ: sensory (P = 0.02), total (P = 0.05), VAS (P = 0.04), and PPI score (P = 0.06).

According to the four SF-MPQ components that suggested significant pain relief, median pain scores dropped 30–42% for the first month after the intervention. During the second month, participants reported 29–47% less pain compared with before the Botox injection and during the third month, reported pain scores were 14–33% lower than before the intervention. For months two and three after the intervention, pain scores were still below those levels reported before the Botox injection, with the exception of the affective component.

Pairwise comparisons were performed to examine the difference in pain scores reported for each of the four time periods compared with each other (pre-Botox, 1 month post-Botox, 2 months post-Botox, 3 months post-Botox). The most significant reductions in pain scores occurred after the first and second months post-intervention (P < 0.04 for each period) for the sensory, total, VAS, and PPI components of the SF-MPQ. By the third month after the Botox injection, the difference between the pre- and post-intervention scores was no longer statistically significant.

Before Botox injection, approximately 75% of the participants reported “more intense” pain (defined as a score of 3, 4, or 5) on the PPI scale (Table 2). After Botox injection, the distribution of pain severity shifted such that fewer than 50% of participants reported “more intense” pain for 3 months (45% at month 1, 38% at month 2, and 48% at month 3). Even at 3 months post-Botox injection, the proportion of patients reporting more intense pain scores did not return to the pre-intervention level.

In general, patients experienced few side effects associated with Botox injection into the ASM. The most frequent side effect was neck weakness which was minimal and did not interfere with activities of daily living. There were no clinically significant complaints of dysphagia, phonation disturbance, or aspiration over the 3 months following Botox injection.

Discussion

Our study demonstrates that patients experienced substantial pain relief in months 1 and 2 following a single Botox injection into the ASM under CT guidance. Further, there was continued pain relief after the third month of the intervention, but it was no longer significantly different from pre-Botox pain levels. However, pain scores following month 3 did not reach pre-Botox levels with the exception of the affective component of the SF-MPQ. Statistically significant pain reduction was noted for 3 months after Botox injection with respect to both sensory

<table>
<thead>
<tr>
<th>SF-MPQ Component</th>
<th>Time Post-Botox</th>
<th>% Change from Pre-Botox 1 Month</th>
<th>% Change from Pre-Botox 2 Months</th>
<th>% Change from Pre-Botox 3 Months</th>
<th>% Change from Pre-Botox 3 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensory</td>
<td>11 (5–15)</td>
<td>3 (1–4)</td>
<td>0 (1–4)</td>
<td>35 (1–4)</td>
<td>35 (2–4)</td>
</tr>
<tr>
<td>Affective</td>
<td>14 (5–19)</td>
<td>13 (5–20)</td>
<td>13 (5–20)</td>
<td>35 (1–4)</td>
<td>35 (2–4)</td>
</tr>
<tr>
<td>VAS</td>
<td>61 (44–75.7)</td>
<td>35 (21–46)</td>
<td>35 (21–46)</td>
<td>52 (30–70.8)</td>
<td>52 (30–70.8)</td>
</tr>
<tr>
<td>PPI</td>
<td>3 (2–4)</td>
<td>2 (1–3)</td>
<td>2 (1–3)</td>
<td>2 (2–4)</td>
<td>2 (2–4)</td>
</tr>
</tbody>
</table>

* P-value derived from Wilcoxon signed rank test. VAS = visual analog scale; PPI = present pain intensity.
and VAS scores, and the total and PPI scores approximated statistical significance. Even after 3 months, patients experienced a 29% decrease in the sensory component of their pain as well as an approximately 15% reduction in their VAS score. It is important to note that patients continued to report lower pain intensity 3 months post-intervention based on the SF-MPQ overall intensity scores (VAS and PPI) [28].

All previous investigators have injected Botox into more than just the ASM for the treatment of NTOS [21,22,26]. Moreover, they have used at least 100 units of Botox or greater. In all of these studies, both cervical and upper thoracic muscles were treated. Our study focused on the injection of just 20 units of Botox into the ASM which produced statistically significant pain relief over a 3-month period. This duration of action compares favorably with prior studies using larger doses of Botox [21,22,26] and with current understanding of a mean of 3–4 months duration of action [30]. Larger doses of Botox, frequent use, and higher protein load increase the likelihood of developing neutralizing antibodies [30]. Furthermore, both the duration of action and the maximal therapeutic effect typically decrease with the formation of antibodies. Therefore, it may be clinically meaningful to use the lowest effective dose over the longest interval while still achieving a reasonable duration of pain relief. Analgesia associated with a single Botox injection into the ASM may provide an alternative to multiple injections into several muscles while reducing the risk of immunogenicity.

Selective neuromuscular blockade for the control of excessive muscle contraction or spasm in patients with NTOS is an important effect of Botox [31]. The results of our study suggest that ASM relaxation alone is effective in mitigating the symptoms associated with neurogenically compromised tissues associated with the interscalene triangle. Though these sites of potential neurovascular compression exist [32,33], imaging analyses suggest that brachial plexus compression typically occurs in the costoclavicular space or interscalene triangle [32,33]. In fact, histologic studies of the scalene muscles in NTOS patients reveal that either ASM or middle scalene muscle injury is the prime cause of most of these cases [13,34,35]. Moreover, surgical interventions for TOS target decompression of the interscalene and costoclavicular spaces. Hence, it seems prudent to target injection therapies to the scalene muscles. Muscle fibrosis is the most prominent histologic finding upon examination of excised scalene muscles of NTOS patients, and the degree of scar tissue present is three times greater than controls [34,35]. Interestingly, preclinical data suggest that Botox may improve wound healing from injured muscles and thereby reduce the risk of scarring [36], and human data show benefit from Botox injection into muscles affected by radiation fibrosis syndrome [37]. Aside from its beneficial neuromuscular actions, Botox may be involved in reducing inflammation and pain by inhibiting the release of neuropeptides (e.g., substance P, calcitonin gene-related peptide, glutamate) that are involved in nociceptive transmission and central sensitization processes [38–41].

In this study, CT imaging permitted the efficient localization of the ASM and surrounding musculature as well as osseous and vascular structures that may be implicated in the etiology of TOS. Compared with ultrasound guidance, the use of CT does expose patients to radiation and the potential for nephrotoxic and allergic responses to the iodinated contrast agent. However, we limited radiation exposure to 60 seconds and did not exceed 0.5 cc of the non-ionic contrast agent, iohexal 180 mg/mL (omnipaque). CT imaging may indeed be emerging as a preferred method of evaluating the thoracic outlet and uncovering the underlying pathophysiologic process of TOS based on functional anatomic imaging studies [8,42] and 3D-CT (spiral) imaging [43]. While ultrasound can typically reveal venous and arterial abnormalities, obesity and adjacent osseous structures may obscure an accurate interpretation and diagnosis [44]. Further, it is very difficult to appreciate neural compression and fibrous bands with ultrasound [44]. Although there is a belief that MRI may be the method of choice for diagnosing TOS [45], the promise of high-speed multidetector CT studies with contrast may more clearly define the etiology of TOS [46]. Furthermore, CT produces a faster image with better special resolution than MRI.

The CT-guided injection of 1 cc of 0.25% bupivicaine into the ASM served as a diagnostic indicator of NTOS among study participants. No delay in reporting pain improvement or performing the EAST was noticed with bupivicaine despite its prolonged onset compared with prior studies using lidocaine [16–22]. Although not specifically

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**Table 2** Number (%) of participants reporting present pain intensity score

<table>
<thead>
<tr>
<th>Pain Description</th>
<th>Pre-Botox</th>
<th>Month 1</th>
<th>Month 2</th>
<th>Month 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pain (0)</td>
<td>0</td>
<td>0</td>
<td>1 (3.4)</td>
<td></td>
</tr>
<tr>
<td>Mild (1)</td>
<td>1 (3.4)</td>
<td>8 (27.6)</td>
<td>6 (20.7)</td>
<td>4 (13.8)</td>
</tr>
<tr>
<td>Discomforting (2)</td>
<td>7 (24.1)</td>
<td>8 (27.6)</td>
<td>12 (41.4)</td>
<td>10 (34.5)</td>
</tr>
<tr>
<td>Distressing (3)</td>
<td>9 (31.0)</td>
<td>7 (24.1)</td>
<td>5 (17.2)</td>
<td>4 (13.8)</td>
</tr>
<tr>
<td>Horrible (4)</td>
<td>10 (34.5)</td>
<td>4 (13.8)</td>
<td>4 (13.8)</td>
<td>7 (24.1)</td>
</tr>
<tr>
<td>Excruciating (5)</td>
<td>2 (6.9)</td>
<td>2 (6.9)</td>
<td>2 (6.9)</td>
<td>3 (10.3)</td>
</tr>
</tbody>
</table>
studied, the use of bupivicaine may help identify candidates for surgical decompression given that 48% of our patients proceeded with successful scalenectomy and first rib resection. The longer duration of action may afford patients a better ability to determine whether the block has made a meaningful difference in pain and function. A sustained, positive response may in turn provide more convincing evidence to the patient and surgeon that a surgical option is prudent.

The diagnosis and management of NTOS remains elusive. Because the operative treatment of TOS risks serious complications in some cases [47,48], accurate patient selection is crucial. Surgical success rates as high as 90% with complications as low as 1% have been reported for (non-specific) NTOS [10], while persistent disability in 60% of patients 1 year following surgery with a greater than 30% complication rate has also been described [49]. Therefore, an alternative intervention that aids the management of TOS can be of value for those suffering from the syndrome. For instance, patients who are unable to benefit from conservative therapy often suffer from limitations in activities of daily living, working, or sleeping, and cannot reduce their pain to a comfortable level with medications. Our study suggests that a single, CT-guided Botox injection into the ASM may offer an effective, minimally invasive treatment for NTOS. This may be of value to those who are non-surgical candidates, wishing to add to a conservative approach to therapy, or interested in bridge therapy to surgical intervention.

References


CT-Guided Chemodenervation of the ASM with Botox