

ORIGINAL ARTICLE

Reduced Neck Muscle Strength and Altered Muscle Mechanical Properties in Cervical Dystonia Following Botulinum Neurotoxin Injections: A Prospective Study

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ABSTRACT

Objective To evaluate changes in the strength and mechanical properties of neck muscles and disability in patients with cervical dystonia (CD) during a 12-week period following botulinum neurotoxin (BoNT) injections.

Methods Eight patients with CD volunteered for this prospective clinical cohort study. Patients had received BoNT injections regularly in neck muscles at three-month intervals for several years. Maximal isometric neck strength was measured by a dynamometer, and the mechanical properties of the splenius capitis were evaluated using two myotonometers. Clinical assessment was performed using the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) before and at 2, 4, 8, and 12 weeks after the BoNT injections.

Results Mean maximal isometric neck strength at two weeks after the BoNT injections decreased by 28% in extension, 25% in rotation of the affected side and 17% in flexion. At four weeks, muscle stiffness of the affected side decreased by 17% and tension decreased by 6%. At eight weeks, the muscle elasticity on the affected side increased by 12%. At two weeks after the BoNT injections, the TWSTRS-severity and TWSTRS-total scores decreased by 4.3 and 6.4, respectively. The strength, muscle mechanical properties and TWSTRS scores returned to baseline values at 12 weeks.

Conclusions Although maximal neck strength and muscle tone decreased after BoNT injections, the disability improved. The changes observed after BoNT injections were temporary and returned to pre-injection levels within twelve weeks. Despite having a possible negative effect on function and decreasing neck strength, the BoNT injections improved the patients reported disability.

Key Words Muscle strength; Muscle characteristics; Disability; Neck.

Cervical dystonia (CD) is a focal dystonia causing involuntary activation of neck and shoulder muscles resulting in abnormal, sustained and painful posturing that may lead to physical disability and social withdrawal.¹ In recent years, botulinum neurotoxin (BoNT) has become the first line therapy for CD.² A subjective feeling of neck weakness has been reported as one of

the most common localized adverse events of BoNT.²⁻⁷ In clinical practice, this may sometimes be reported as having difficulty keeping the head upright. Although the effects of BoNT have been widely studied,^{2,5} there have been no prospective studies quantifying changes in maximal isometric neck muscle strength. Objective strength measurements may help identify patients

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with neck weakness after BoNT injections that causes difficulties in daily living and therefore need additional strength training. Additionally, even though CD patients have frequent complaints of neck tension, only one study⁸ has provided quantitative data about the effects of initial BoNT injections on the passive mechanical properties of skeletal muscle in a clinical setting, despite that measurement devices have been developed for this purpose. Myotonometers may provide an objective, non-invasive tool to quantify changes in muscle properties after BoNT injections that were previously obtained using subjective methods. The aim of this study was to evaluate the changes in neck strength, the mechanical properties of neck muscles, and disability over a twelve-week period following BoNT injections in patients with CD who had a two-year history of BoNT treatment. We hypothesized that the mechanical properties of muscle fluctuate after BoNT injection, and this fluctuation is reflected in decreased muscle power and tension, as well as disability.

MATERIALS & METHODS

Patients

Twenty-two patients who were receiving BoNT injections in their neck muscles in an outpatient rehabilitation clinic were invited by mail to volunteer for this prospective clinical cohort study. Eight patients (3 women, 5 men) volunteered. Ten patients denied because of the long-distance travel required for regular visits, and four patients denied for personal reasons. The mean age (standard deviation, SD) of the participants was 57 (10) years; the mean body mass index (SD) was 24.7 (5.4) kg/m². The mean duration (SD) from the onset of CD was 14 (12) years, and the mean duration from the start of regular BoNT injections was 2.3 (1.6) years. The predominant component of the CD was rotation or laterocollis of the neck, which was toward the left side in four patients and toward the right side in the remaining four patients. The local ethics committee approved the study. All subjects gave their written consent before participating in the study.

Intervention

Two forms of BoNT type A, onabotulinumtoxinA (ona-BoNTA, Botox[®], Allergan, Irvine, CA, USA) ($n = 4$) and abobotulinumtoxinA (abo-BoNTA, Dysport[®],

Ipsen, Paris, France) ($n = 4$), were used according to the most recent recommendations.² The total dose injected into cervical muscles was 100 U for ona-BoNTA and 500 U for abo-BoNTA. All patients received injections in the splenius capitis on the affected side, and the other muscles injected varied according to the distribution and degree of dystonic muscles. The mean number (SD) of injected muscles was 5.4 (1.3). Injections were performed by two physiatrists with several years of experience of BoNT treatment in these patients.

Outcome measures

Neck strength for isometric flexion, extension and rotation was measured while the participant was in the sitting position and using a special neck dynamometer according to the technique reported in previous studies.^{4,9} The best result of three maximal efforts was used in the final analysis.

The mechanical properties of splenius capitis were measured on the affected and non-affected sides with two myotonometers and with the participant in the standard supine position: the head was in a straight neutral position (face down toward the hole of the examination table) and the hands were beside the body. The Myoton-3 (Myoton AS, Tallinn, Estonia) enables measurement of muscle characteristics by recording damped oscillations of the tissue when a mechanical perturbation is applied to the muscle.^{10,11} The Myoton-3, which is placed perpendicular to the muscle, produces a short impulse on the muscle. An acceleration transducer records the damped oscillations of the muscle, and the oscillation frequency (Hz) characterizes the tension in the muscle. A logarithmic decrement of the oscillation characterizes the muscle elasticity, whereas the oscillation stiffness parameter (N/m) characterizes the muscle's ability to resist the force that is shaping it. Measurement of the mechanical properties of splenius capitis using the Myoton is shown in Figure 1. Muscle compliance was measured with a computerized muscle tonometer (CMT) (Medirehabook Ltd., Muurame, Finland).¹² The CMT quantifies the amount of tissue displacement as the probe is pushed down and perpendicular to the muscle.¹² The result of a CMT is expressed as the work performed while the probe compresses the tissue and is calculated as the area under the curve in the force-deformation-graph (mJ). A higher value indicates a higher

compliance of the tissue. Upper trapezius activity was measured simultaneously with myotonometric measurements by surface electromyography (sEMG) using an ME1000 Analyzer (Mega Electronics Ltd., Kuopio, Finland) to assure that only minimal muscular activity was present at rest.

Clinical assessment was performed using the total Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) (0 to 85 points) and its three subscales.¹ The severity scale has 10 items (0 to 35 points), the disability scale has 7 items of activities of daily living (0 to 30 points), and the pain scale has 3 items (0 to

20 points). Higher scores indicate greater impairment. Assessments were performed prior to BoNT injections followed by measurements at 2, 4, 8, and 12 weeks after the injections. All measurements were performed in a standardized manner by the same experienced physiotherapist.

Statistical analysis

The data are reported as the means with SDs. The mean changes with 95% confidence intervals (CI) from baseline to the measurements at follow-ups were calculated. Statistical comparisons of the outcome measurements were performed using paired *t*-tests. No adjustment was made for multiple testing, but this information can be obtained by multiplying the actual *p* value by the number of comparison made. The level of *p* < 0.05 was selected to indicate statistical significance. Statistical analyses were performed with SPSS (version 22.0; SPSS Inc., Chicago, IL, USA).

RESULTS

The mean values for neck strength, the mechanical properties of splenius capitis on the affected side, and the TWSTRS scores are shown in Table 1. There were no significant differences at baseline in rotation strength or the mechanical properties of splenius capitis between the affected and non-affected sides. The mean decrease in neck strength at two weeks after the BoNT injections was -28% (95% CI: -40 to



Figure 1. Measurement of the mechanical properties of splenius capitis using the Myoton.

Table 1. Mean values of maximal isometric neck strength, mechanical properties of splenius capitis on the affected side, and TWSTRS scores at baseline and regular intervals following botulinum toxin injections in patients with cervical dystonia

| | Baseline, mean (SD) | At 2 wk, mean (SD) | At 4 wk, mean (SD) | At 8 wk, mean (SD) | At 12 wk, mean (SD) |
|------------------------------|------------------------|-----------------------|-----------------------|-----------------------|------------------------|
| Neck muscle strength | | | | | |
| Flexion (N) | 92.8 (45.2) | 76.7 (37.0)* | 83.2 (37.4) | 90.3 (48.0) | 90.1 (41.0) |
| Extension (N) | 179.4 (73.5) | 128.7 (74.8)* | 127.7 (68.9)* | 148.8 (79.3)* | 172.2 (79.0) |
| Rotation (Nm) | 10.6 (6.6) | 8.0 (5.4)* | 8.6 (5.5)* | 10.2 (7.3) | 10.1 (5.8) |
| Mechanical properties | | | | | |
| Tension (Hz) | 15.6 (3.1) | 14.5 (2.1) | 14.6 (2.5)* | 15.2 (1.2) | 15.4 (2.1) |
| Elasticity | 1.26 (0.18) | 1.34 (0.26) | 1.35 (0.19) | 1.41 (0.13)* | 1.39 (0.12) |
| Stiffness (N/m) | 319 (109) | 274 (93) | 265 (82)* | 278 (53) | 244 (32) |
| Compliance (mJ) | 22.1 (4.7) | 23.8 (4.8) | 24.3 (6.6) | 22.4 (3.1) | 21.7 (5.9) |
| TWSTRS | | | | | |
| Severity (0 to 35) | 12.4 (3.8) | 8.1 (4.3)* | 9.1 (4.0)* | 10.8 (3.0)* | 13.6 (3.0) |
| Disability (0 to 30) | 7.1 (3.9) | 6.0 (2.9) | 6.4 (2.4) | 7.1 (3.9) | 8.1 (2.9) |
| Pain (0 to 20) | 6.3 (4.1) | 5.3 (4.9) | 4.2 (3.4) | 5.3 (4.9) | 5.3 (4.8) |
| Total (0 to 85) | 25.8 (10.3) | 19.4 (9.1)* | 21.0 (5.7) | 23.1 (10.0) | 27.0 (8.4) |

*significantly different from baseline (*p* < 0.05). Hz: hertz, N: newton, m: meter, mJ: millijoule, TWSTRS: Toronto Western Spasmodic Torticollis Rating Scale, SD: standard deviation.

-17) in extension ($p = 0.001$), and -17% (95% CI: -33 to -2) in flexion ($p = 0.032$). No significant change was observed on the non-affected side for rotation strength among consecutive measurements. The rotation strength of the affected side decreased by -25% (95% CI: -41 to -9) at two weeks ($p = 0.008$). After two weeks, however, rotation strength gradually improved. A significant decrease in extension strength was still evident at eight weeks, and a decrease in rotation strength was present on the affected side at four weeks after the BoNT injections. All strength measures returned to the baseline values within 12 weeks.

Muscle stiffness and tension on the affected side were decreased by 17% (95% CI: -32 to -2) ($p = 0.031$) and 6% (95% CI: -12 to -1) ($p = 0.030$), respectively, at four weeks after the BoNT injections. Muscle elasticity on the affected side was increased by 12% (95% CI: 6 to 18) ($p = 0.003$) at eight weeks, showing a reduced elastic capacity. No other significant changes in the muscle mechanical properties were observed after BoNT injections. The sEMG values recorded during these measurements were low at all time-points (range from 0 to 14 mV).

The TWSTRS-severity and TWSTRS-total scores were decreased by 4.3% (95% CI: -6.3 to -2.2) ($p = 0.002$) and 6.4% (95% CI: -9.1 to -3.6) ($p = 0.001$), respectively, at two weeks after the BoNT injections. The TWSTRS-severity score remained significantly improved compared to baseline until eight weeks after the treatment. There were no significant changes in the TWSTRS-disability or pain scores at any time during follow-up. No adverse events were reported with BoNT injections, except neck weakness.

DISCUSSION

This is the first follow-up study to quantify the effect of BoNT injections on neck strength in patients with CD. At the doses used in the present study, BoNT injections caused partial paralysis of the muscles injected,^{2,5} and thus the reduction in strength was expected. We found no previous reports that quantify changes in neck muscles that could be compared with our results. The present study showed that the fluctuation in neck strength between consecutive BoNT injections is substantial. At two weeks after treatment, the decrease in neck strength was the largest in extension, almost as large as that in rota-

tion, and was less pronounced in flexion. The time required for neck strength to recover in the different movements varied, and this was probably due to the muscles that were injected. Strength in all movements was normalized to pre-injection levels at twelve weeks. Häkkinen et al.⁴ showed that CD patients with BoNT-treated neck muscles show significantly lower peak neck strength compared to healthy matched controls. In their study, the strength measurements were performed just prior to the next injection. However, according to the findings of the present study, this was when neck strength was highest in the CD patients. Thus, the results suggested that BoNT injection may have long-term effects on maximal neck strength. The present study shows that maximal neck strength is considerably lower two weeks after injection. The current neck strength values at two weeks after BoNT injections were approximately 50 to 60% of the maximal isometric strength that was previously reported in healthy subjects with comparable age groups.^{13,14} Strength measurements in the present study were performed with the same equipment and test protocol that were used for the healthy subjects in previous studies, and thus the results are comparable. Fortuna et al.¹⁵ have shown that BoNT injections cause severe muscle atrophy and loss of contractile tissue in not only the injected muscles but also the non-injected muscles. Muscle weakness may be partly due to chronic neck pain, which as was previously shown in patients with chronic mechanical neck pain.⁹ It is important to note that the patients in the present study had received BoNT injections at three months intervals for approximately two years.

The muscle mechanical properties measured in this study were altered after BoNT injections. Muscle tension and stiffness values decreased at four weeks after BoNT injections, and elasticity values increased at eight weeks after BoNT injections. The results of the present study are somewhat similar to the results reported by Marvulli et al.,⁸ who combined BoNT injections and physiotherapy for the treatment of CD in 15 patients. They performed clinical evaluation and myotonometric measurements using the Myoton-3 before and at one, two, and three months following BoNT injections. Their study found that muscle tension, stiffness, and elasticity values measured with the Myoton were decreased after BoNT injections at one, two, and three months

after injections. However, the differences in study designs between that study and the present study may partly explain the differences in results. Patients in the present study had been receiving BoNT injections for years, whereas patients in the study of Marvulli et al.⁸ received their first BoNT injections. It has been reported that long-term use of BoNT results in a decrease in contractile tissue and an increase in connective tissue,¹⁵ thus making the muscle more rigid. Consequently, acute changes in muscle properties would become less obvious. No changes were observed in the muscle compliance values. This result may be methodological: it was difficult to position the measurement device on a small, round muscle. The CMT technique is probably more suitable for larger muscles.¹¹

The findings in our study on disability are consistent with those of previous studies reporting short-term functional improvement in CD after BoNT injections.^{2,3,5-7} In the present study, the TWSTRS-total and TWSTRS-severity scores were significantly lower at two weeks compared with the pre-injection scores. These findings also showed that the scores return to pre-injection state over the course of the three-month follow-up, as was reported in earlier studies.^{2,3,5-7} The present study shows that the changes in clinical scores are associated with objectively measured changes in muscle properties. Furthermore, the results show that, despite a possible negative effect on function that included decreased neck strength, the BoNT injections improved the patients reported disability.

The fact that the group of patients who were treated in the present study had been undergoing regular therapy with BoNT injections for several years indicates their baseline disability scores were probably less severe than those without treatment. Therefore, the changes in the treatment group were smaller than those in the untreated groups.^{3,7} However, in this study, the aim was to evaluate changes in the patient group with the long-term use of BoNT. The small and heterogeneous study group used in the present study may not have provided sufficient power to detect small changes in outcome measures. Further research with a larger study group and a longer follow-up period is needed to study the effects of BoNT injections on muscle strength and the mechanical properties of muscles.

This study showed that although maximal strength,

tension, stiffness, and elastic capacity were reduced in neck muscles after BoNT injections, the severity of neck complaints decreased in patients with CD. Neck muscle strength, muscle mechanical properties and disability scores returned to pre-injection levels within twelve weeks.

Conflicts of Interest

One of the co-authors, Jari Ylinen, has developed the Computerized Muscle Tonometer, and is one of the owners of the company Medirehabook Ltd. No other potential conflict of interest declared.

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