Treatment of at-level spinal cord injury pain with botulinum toxin A

Audrey Chun1 · Isaiah Levy2 · Ajax Yang3 · Andrew Delgado1,4 · Chung-Ying Tsai1 · Eric Leung5 · Kristell Taylor1 · Stephanie Kolakowsky-Hayner1 · Vincent Huang1 · Miguel Escalon1 · Thomas N. Bryce1

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Abstract

Study design Randomized, double-blinded, placebo-controlled, cross-over study.
Objective To explore whether botulinum toxin A (BoNTA) could be effective for treating at-level spinal cord injury (SCI) pain.
Setting Outpatient SCI clinic, New York, USA.
Methods Participants were randomized to receive subcutaneous injections of either placebo or BoNTA with follow-up (office visit, telephone, or e-mail) at 2, 4, 8, and 12 weeks to assess the magnitude of pain relief post injection. Crossover of participants was then performed. Those who received placebo received BoNTA, and vice versa, with follow-up at 2, 4, 8, and 12 weeks.
Results Eight participants completed at least one of the two crossover study arms. Four completed both arms. The median age of the eight participants was 45 years (range 32–61 years) and 75% were male. All had traumatic, T1-L3 level, complete SCI. Although our data did not meet statistical significance, we noted a higher proportion of participants reporting a marked change in average pain intensity from baseline to 8 and 12 weeks post-BoNTA vs. post-placebo (33% vs. 0%). At 2 and 4 weeks post-BoNTA, almost all participants reported some degree of reduced pain, while the same was not seen post-placebo (83% vs. 0%).
Conclusion The subcutaneous injection of BoNTA may be a feasible approach for the control of at-level SCI pain and is worthy of further study.
Sponsorship The onabotulinumtoxinA (BOTOX) used in this study was provided by Allergan (Irvine, CA).

Introduction

At-level spinal cord injury (SCI) pain is neuropathic pain perceived at the neurological level of injury (NLI) or within three levels below the NLI and is thought to be a result of damage to the spinal cord or its nerve roots [1]. It has been reported to occur in approximately one third of individuals with SCI [2, 3]. Various pharmacological agents used for treating at-level SCI pain have been shown to have only limited efficacy at best [4, 5]. Therefore, a significant need for the investigation of potential new treatments for at-level SCI pain remains.

Botulinum toxin A (BoNTA) is a neurotoxin protein produced by the bacterium *Clostridium botulinum*. It acts at the neuromuscular junction and its onset of action occurs within 24–72 h after administration, with peak clinical effect occurring 4–6 weeks after administration, then 2–6 months of effect duration [6]. At the level of peripheral nerves, BoNTA may inhibit the synaptic release of local neuropeptides associated with pain transmission, such as glutamate, substance P, and calcitonin gene-related peptide [7]. At the level of the central nervous system, retrograde effects of BoNTA on the spinal cord via axonal transport have been proposed [8, 9].
BoNTA therapy has so far been shown to have some effectiveness in treating various peripherally mediated neuropathic pains, but the literature on BoNTA remains limited for treating centrally mediated pain [10]. To date, one randomized, double-blinded, placebo-controlled study has successfully been able to demonstrate that subcutaneous BoNTA may reduce neuropathic pain in persons with SCI. This study by Han et al. evaluated patients with neuropathic pain associated with SCI, both at-level (\(n = 9\)) and below-level (\(n = 29\)), and found participants demonstrated significantly reduced pain at 4 and 8 weeks after BoNTA injections compared with after placebo with saline. They also showed a marginal trend towards improvements on the physical health domain of the World Health Organization Quality of Life Instrument (WHOQOL-BREF abbreviated form) at 4 weeks post-BoNTA vs. post-placebo [7].

BoNTA has been shown to have a favorable safety and tolerability profile across a broad spectrum of therapeutic uses [11, 12]. Adverse effects (AEs) associated with BoNTA are generally related to the mechanism of action of the toxin (e.g., dose-dependent focal weakness when injected intramuscularly). Other local side effects include temporary injection associated pain, edema, erythema, ecchymosis, headache, and short-term hyperesthesia. Systemic side effects include nausea, fatigue, malaise, rash, and flu-like symptoms [12]. In summary, a significant percentage of persons with SCI report at-level SCI pain but there is a lack of effective treatment to date, and BoNTA has shown preliminary evidence of effectiveness for neuropathic pain after SCI in one clinical trial while having a favorable safety and tolerability profile. Our study sought to further explore whether the subcutaneous injection of BoNTA could be a feasible approach for the control of at-level SCI pain.

**Methods**

**Study design and setting**

This study was designed as a randomized, double-blinded, placebo-controlled, crossover study. Institutional Review Board approval (IRB \#14–01107) was obtained prior to conducting any study related procedures and informed consent was obtained from each participant.

Participants received a subcutaneous injection of either normal saline (placebo) or BoNTA with follow-up (via office visit, telephone, or e-mail) at 2, 4, 8, and 12 weeks post injection (phase 1, P1). Crossover of participants was then performed. Those who received placebo received BoNTA, and vice versa, with follow-up at 2, 4, 8, and 12 weeks (phase 2, P2). Twelve weeks were determined as being the minimum required wash-out period based on the pharmacokinetics of BoNTA [6]. Participants were given the choice to start the P2 course at the time of 12-week follow-up for P1, or to defer the P2 course until a later time point.

All study activities took place in a large tertiary care hospital in the outpatient SCI rehabilitation clinic setting. Portions of this study have been accepted for poster presentation at the 2019 American Congress of Rehabilitation Medicine Annual Conference [13].

**Participants**

Participants were recruited via newsletter advertisements, physician recommendations, and Clinicaltrials.gov (NCT #02736890) between 2016 and 2018. Participants were included if they reported chronic traumatic SCI (duration >6 months) and pain that has been: (1) present continuously for ≥1 month, (2) of at least moderate average intensity over the prior week (numeric pain rating scale [NPRS] score ≥4/10) and (3) diagnosed by an SCI provider as being at-level SCI pain with a high degree of certainty [14]. They were excluded if they were: (1) <18 years old, (2) pregnant, (3) with any contraindications to BoNTA (e.g., neuromuscular junction disease), (4) with a history of intolerance, hypersensitivity, or allergy to BoNTA, its preservatives, or the ethyl chloride used as an analgesic during injections, (5) with a history of BoNTA injections within the past 6 months, (6) with a history of coagulation disorder or current infection, (7) with insufficient command of English, and (8) unable to provide informed consent.

**Study procedure**

Consented participants underwent a pre-procedure evaluation, consisting of a focused history and physical exam, by a physician blinded to whether they would be BoNTA or placebo recipients. Each participant was asked to localize his or her area of worst pain, then to describe and rate the intensity of his or her pain before examination of the indicated painful area. Participants were then screened for the presence of neuropathic pain based on the Douleur Neuropathique 4 and SCI Pain Instrument questionnaires to supplement the focused history and exam [15]. The area of pain was marked using a skin marker and a plastic cut-out template for injection sites separated from each other by a 1 cm radius (Fig. 1).

To marked areas, participants received subcutaneous injections of either BoNTA or placebo. Each 100 unit vial of BoNTA was reconstituted with 4 ml preservative-free sterile 0.9% normal saline solution, for a concentration of 5 units of BoNTA per 0.2 ml injectate, as per manufacturer
recommendations. Placebo consisted of 0.2 ml of the same preservative-free sterile 0.9% normal saline. Syringes were prefilled by an unblinded physician and research assistant in a separate location from where injections and assessments occurred. The physician administering the injection was blinded to syringe contents. The randomized treatment allocation for each patient was kept in a sealed envelope by another research assistant, separate from those preparing and administering injections. The area was sterilized with alcohol then localized topical anesthesia was provided with sterile ethyl chloride. Each injection was given using a 25-gauge needle and administrators were allowed to provide up to 80 injections of 5 units each for a total maximum delivery of 400 units, per participant, per phase injection session. This maximum dose and injection number was determined based on the study team’s review of the BoNTA manufacturer recommendations and the BoNTA literature to date at the time of protocol formation [16–18].

Following the injection procedure, participants were monitored for ≥5 min for immediate AEs. They were reeducated on potential AEs of BoNTA (e.g., local hyperesthesia, weakness, erythema), including all serious ones for which they should seek emergency care (e.g., respiratory distress, systemic illness), and provided with contact information for any questions or concerns that they may develop afterwards. Neither participants nor their insurance providers were charged for the BoNTA and participants did not receive any monetary reimbursement for participation. The BoNTA was stored in a locked refrigerator (2–8 °C), labeled in a location separate from the outpatient SCI clinic.

Outcomes

Our primary outcome measure was patient reported average pain intensity over the prior week in their area of worst pain as indicated above. This measure is part of the International SCI Pain Basic Data Set (ISCIPBDS), whose validity and utility in individuals with SCI have been demonstrated, and it is among the measures recommended for use in SCI clinical trials [19–21]. Participants were asked to rate their average pain using the 0–10 NPRS from 0 (“no pain”) to 10 (“worst pain imaginable”). Secondary outcome measures included other ISCIPBDS items, such as the degree to which pain interfered with: (1) day to day activities, (2) mood, and (3) sleep, all on scales from 0 (“no interference”) to 10 (“extreme interference”). We defined “marked improvement” as a ≥3-point difference based on the minimal clinical important difference (MCID) for the NPRS being ≥3 points [22]. At each follow-up time point, participants were asked to quantify the change in quality of life (QOL) appreciated after injections on a 7-point scale based on the Patient Global Impression of Change scale [19]. Lastly, participants were asked about and monitored for AEs as described above.

Statistical analyses

All collected data were stored in a password-protected REDCap database [23] and all hard copy forms were kept in locked files in the offices of research staff. Statistical analyses were performed using SPSS version 22.0. Power analyses were conducted based on the primary outcome of change in pain intensity from baseline. We determined that MCID on the NPRS would be ≥3 points, that 30% of participants in the placebo group would have positive response to treatment, and that 40% more participants (i.e., 70%) would respond in the treatment group [16, 22, 24]. Assuming a two-sided alpha of 0.05, a sample size of 28 would provide 86% power. Assuming a 15% drop out rate, a sample size of 32 participants was deemed necessary for sufficient power to detect treatment effect. Our study failed to meet target sample size therefore it was determined that our findings would be best presented as a descriptive case series and descriptive statistics were used for participant characteristics and all outcomes.

Results

Participant flow and characteristics

Among 11 enrolled and consented participants, 3 did not proceed to injections because they were deemed ineligible for the study during the pre-procedure history and physical or they declined participation in the study at this point. Among the eight participants who proceeded, five started the study with BoNTA. All participants finished the P1 arm of the study. A single BoNTA recipient withdrew from the
study prior to starting the P2 arm, reporting increased pain after completing P1 (participant was blinded to whether BoNTA or placebo was given). One participant starting the study with BoNTA and two starting with placebo were lost to follow-up during P2. A total of four participants finished both P1 and P2 arms (Fig. 2). Participants had a median age of 45 years (range 32–61 years) and were predominantly male (75%). All had traumatic, thoracic T1 to lumbar L3 level, complete SCI (American Spinal Injury Association Impairment Scale Grade A). Median duration of injury was 8 years (range 2–26 years). Table 1 shows detailed participant demographics and injury characteristics.

**Average pain intensity over the past week**

Participants A–E started with BoNTA injections at P1. Participants F–H received BoNTA at time of crossover P2. For P1 and P2, a total six participants completed post-BoNTA follow-up and six completed post-placebo follow-up. Participant A reported marked improvement in average pain intensity from baseline to 8 and 12 weeks post-BoNTA, but not post-placebo. Participant B reported some degree of reduced pain at all weeks post-BoNTA. Participant C reported some pain reduction at 2 weeks post-BoNTA, marked reduction at 4, 8, and 12 weeks, but not post-placebo. Participant D reported some pain reduction at 2 and 4 weeks post-BoNTA but at the 12-week follow-up, withdrew from the study prior to receiving placebo, reporting increased pain after finishing P1. Participant E reported some pain reduction at 2, 4, and 8 weeks post-BoNTA, but received placebo for P2 some months after 12-week follow-up for P1 then was lost to follow-up. Participant F reported marked pain reduction at 2 and 4 weeks post-BoNTA but not post-placebo. Participant G reported no pain reduction post-placebo, received BoNTA for P2 concurrently with 12-week follow-up for P1, then was lost to follow-up. Participant H reported no pain reduction post-placebo, received BoNTA for P2 some months after 12-week follow-up for P1, then was lost to follow-up (Table 2).

**Pain interference with day to day activities, mood, and sleep**

Participants A and C reported no marked improvements compared with baseline in day to day activities, mood or
sleep, both post-BoNTA and post-placebo. Participant B reported a marked improvement in sleep at 2 weeks post-BoNTA compared with baseline. Participant D reported markedly reduced pain interference with activities at 2 and 4 weeks post-BoNTA; markedly improved mood at 2 weeks post-BoNTA; and markedly improved sleep at 2 and 4 weeks post-BoNTA. Participant E reported markedly improved activities at 2 and 4 weeks post-BoNTA; markedly improved mood at 2, 4, and 8 weeks post-BoNTA; and markedly improved sleep at 4 weeks post-BoNTA. Participant F reported markedly improved activities at all weeks post-BoNTA; markedly improved mood at 2, 4, and 8 weeks post-BoNTA; and markedly improved sleep at all weeks post-BoNTA (Table 3).

Table 1 Participant demographics and spinal cord injury (SCI) characteristics (total n = 8)

| Demographics                  |         |
|-------------------------------|---------|
| Age at examination (years), median (min–max) | 45 (32–61) |
| Sex, N (%)                    |         |
| Male                          | 6 (75%) |
| Female                        | 2 (25%) |
| Race, N (%)                   |         |
| Black or African American     | 2 (25%) |
| White or Caucasian            | 2 (25%) |
| Latino or Hispanic            | 3 (37.5%) |
| Unknown or not reported        | 1 (12.5%) |
| Injury characteristics         |         |
| Duration of injury (years), median (min–max) | 8 (2–26) |
| Cause of injury, N (%)         | 8 (100%) |
| Spinal cord injury (SCI) category, N (%) |         |
| Traumatic                     | 8 (100%) |
| Thoracic T1–T6 paraplegia     | 4 (50%) |
| Thoracic T7–lumbar L3 paraplegia | 4 (50%) |
| American Spinal Injury Association Impairment Scale (AIS) Grade, N (%) |         |
| AIS A (complete injury)        | 8 (100%) |

Table 2 Participant reported average pain intensity over the past week (primary outcome)

| Pain intensity in the past week? (0–10) | Botulinum toxin A (BoNTA) then placebo | Placebo then BoNTA |
|-----------------------------------------|----------------------------------------|--------------------|
|                                        | A  | B  | C  | D  | E  | F  | G  | H  |
| Baseline (phase 1—week 0)               | 5  | 9  | 8  | 8  | 8  | 8  | 8  | 8  |
| Initial 2-week follow-up                | 5  | 7  | 6  | 7  | 7  | 8  | 8  | 8  |
| Initial 4-week follow-up                | 5  | 6  | 3  | 7  | 7  | 8  | 8  | 8  |
| Initial 8-week follow-up                | 2  | 8  | 4  | 8  | 6  | 8  | 8  | 8  |
| Initial 12-week follow-up               | 2  | 8  | 2  | 8  | 8  | 8  | 8  | 8  |
| Baseline (phase 2—week 0)               | 10 |     |    |    |    |    |    | 7  |
| Crossover 2-week follow-up              | 8  | 8  | 8  | Participant withdrew | Lost to follow-up | 5  | Lost to follow-up |
| Crossover 4-week follow-up              | 8  | 8  | 8  |     |    |    |    | 5  |
| Crossover 8-week follow-up              | 8  | 5  | 7  |     |    |    |    | 6  |
| Crossover 12-week follow-up             | 7  | 8  | 9  |     |    |    |    | 7  |

Intensity reported using numeric pain rating scale, from 0 (“no pain”) to 10 (“worst pain imaginable”)
Table 3  Participant reported pain interference with day to day activities, mood, and sleep

### A  Pain affecting day to day activities? (0–10)

|                  | Botulinum toxin A (BoNTA) then placebo | Placebo then BoNTA |
|------------------|---------------------------------------|--------------------|
|                  | A     | B     | C     | D     | E     | F     | G     | H     |
| Baseline (phase 1—week 0) | 1   | 3   | 0   | 8   | 9   | 8   | 0   | 8   |
| Initial 2-week follow-up | 6   | 3   | 7   | 5   | 6   | 8   | 0   | 0   |
| Initial 4-week follow-up | 6   | 3   | 6   | 5   | 5   | 8   | 0   | 0   |
| Initial 8-week follow-up | 5   | 3   | 4   | 6   | 7   | 8   | 0   | 0   |
| Initial 12-week follow-up | 4   | 3   | 3   | 7   | 7   | 8   | 0   | 0   |
| Baseline (phase 2—week 0) | 10  |       |       |       |       |       |       | 4    |
| Crossover 2-week follow-up | 8   | 5   | 8   |       |       | Participant withdrew | 2   |       |
| Crossover 4-week follow-up | 8   | 4   | 8   |       |       |       | 3   |       |
| Crossover 8-week follow-up | 8   | 4   | 9   |       |       |       | 4   |       |
| Crossover 12-week follow-up | 8   | 3   | 9   |       |       |       | 5   |       |

### B  Pain affecting mood? (0–10)

|                  | Botulinum toxin A (BoNTA) then placebo | Placebo then BoNTA |
|------------------|---------------------------------------|--------------------|
|                  | A      | B     | C     | D     | E     | F     | G     | H     |
| Baseline (phase 1—week 0) | 6   | 5   | 0   | 8   | 9   | 9   | 0   | 8   |
| Initial 2-week follow-up | 9   | 4   | 9   | 5   | 6   | 8   | 0   | 0   |
| Initial 4-week follow-up | 8   | 4   | 6   | 6   | 5   | 8   | 0   | 0   |
| Initial 8-week follow-up | 5   | 4   | 5   | 6   | 6   | 9   | 0   | 4   |
| Initial 12-week follow-up | 5   | 4   | 4   | 7   | 8   | 9   | 0   | 8   |
| Baseline (phase 2—week 0) | 10  |       |       |       |       |       |       | 5    |
| Cross-over 2-week follow-up | 8   | 5   | 8   |       |       | Participant withdrew | 2   |       |
| Cross-over 4-week follow-up | 8   | 5   | 8   |       |       |       | 3   |       |
| Cross-over 8-week follow-up | 8   | 5   | 9   |       |       |       | 4   |       |
| Cross-over 12-week follow-up | 8   | 3   | 9   |       |       |       | 7   |       |

### C  Pain affecting sleep? (0–10)

|                  | Botulinum toxin A (BoNTA) then placebo | Placebo then BoNTA |
|------------------|---------------------------------------|--------------------|
|                  | A     | B     | C     | D     | E     | F     | G     | H     |
| Baseline (phase 1—week 0) | 0   | 8   | 4   | 8   | 9   | 8   | 4   | 8   |
| Initial 2-week follow-up | 0   | 2   | 9   | 5   | 7   | 8   | 4   | 2   |
| Initial 4-week follow-up | 1   | 7   | 6   | 5   | 6   | 8   | 0   | 2   |
| Initial 8-week follow-up | 5   | 7   | 4   | 6   | 8   | 8   | 4   | 6   |
| Initial 12-week follow-up | 4   | 7   | 4   | 7   | 9   | 8   | 4   | 8   |
| Baseline (phase 2—week 0) | 10  |       |       |       |       |       |       | 10   |
| Cross-over 2-week follow-up | 8   | 8   | 8   |       |       | Participant withdrew | 1   |       |
| Cross-over 4-week follow-up | 8   | 8   | 8   |       |       |       | 3   |       |
| Cross-over 8-week follow-up | 8   | 8   | 8   |       |       |       | 4   |       |
| Cross-over 12-week follow-up | 8   | 5   | 9   |       |       |       | 5   |       |

Degree of interference reported using a numeric scale with endpoints of 0 (“no interference”) to 10 (“extreme interference”)
Participant A reported “thrombosis of a preexisting inferior vena cava filter” and Participant H reported “a fever from a cold”) but both denied feeling the events were related to the study.

Discussion

Our study sought to explore whether the subcutaneous injection of BoNTA is a feasible approach for the control of at-level SCI pain. This study was designed as a randomized, double-blinded, placebo-controlled, crossover study. However, we failed to meet target sample size and determined our findings would be best presented as a descriptive case series. Our data did not meet statistical significance and we were not statistically powered to, but we did note various patterns of improved pain, activities, mood, and sleep among participants after BoNTA.

More participants reported a marked change in average pain intensity from baseline to 8 and 12 weeks post-BoNTA vs. post-placebo (33% vs. 0%). At 2 and 4 weeks post-BoNTA, almost all participants reported some degree of reduced pain; the same was not seen post-placebo (83% vs. 0%) (Table 2). This is consistent with Han et al.’s findings that, at 4 and 8 weeks after BoNTA injections, visual analog scale scores for pain were significantly reduced by 18.6 ± 16.8 and 21.3 ± 26.8, but only reduced by 2.6 ± 14.6 and 0.3 ± 19.5 after placebo injections [7].

More participants reported markedly reduced pain interference with day to day activities at 2 and 4 weeks post-BoNTA vs. post-placebo (50% vs. 17%). More participants reported markedly reduced pain interference with mood post-BoNTA vs. post-placebo at 2 (50% vs. 17%), 4 (33% vs. 17%), and 8 (33% vs. 17%) weeks. More participants reported markedly reduced pain interference with sleep post-BoNTA vs. post-placebo at 2 (50% vs. 17%), 4 (50% vs. 33%), 8 (17% vs. 0%) and 12 (17% vs. 0%) weeks (Table 3). Lastly, more participants reported at least moderate improvements in QOL post-BoNTA vs. post-placebo at 2 (33% vs. 0%) and 4 (33% vs. 0%), 8 (17% vs. 0%), and 12 (33% vs. 0%) weeks (Table 4). This too supports Han et al.’s trend towards improvements at 4 weeks post-BoNTA ($p = 0.0521$) on the physical health domain of the WHOQOL-BREF, which includes facets like activities of daily living and sleep [7].

Our data was statistically insufficient to draw conclusions regarding the effects of BoNTA on at-level SCI pain. Despite this, we managed to demonstrate several interesting patterns within our participants’ reports on how they felt post-BoNTA. Participants also denied any significant AEs.

| Table 4: Participant reported change in quality of life following injections |
|----------------------------------|-------------------|-------------------|
|                                  | Botulinum toxin A (BoNTA) then placebo | Placebo then BoNTA |
|                                  | A    | B    | C    | D    | E    | F    | G    | H    |
| Baseline (phase 1—week 0)        | N/A  |      |      |      |      |      |      |      |
| Initial 2-week follow-up         | 0    | 3    | 0    | 5    | 3    | 0    | 1    | 0    |
| Initial 4-week follow-up         | 0    | 3    | 3    | 4    | 2    | 0    | 1    | 0    |
| Initial 8-week follow-up         | 4    | 0    | 2    | 2    | 2    | 0    | 0    | 0    |
| Initial 12-week follow-up        | 4    | 0    | 4    | 1    | 1    | 0    | 0    | 0    |
| Crossover 2-week follow-up       | 0    | 0    | 0    |      | Participant withdrew | Lost to follow-up | 5    | Lost to follow-up |
| Crossover 4-week follow-up       | 0    | 0    | 0    |      | 5    |      |      |      |
| Crossover 8-week follow-up       | 0    | 0    | 0    |      | 3    |      |      |      |
| Crossover 12-week follow-up      | 0    | 0    | 0    |      | 1    |      |      |      |

Amount of change in quality of life appreciated after injections on a scale of 0–6, with corresponding verbal descriptions as below:

0 = “no change, or condition got worse”
1 = “almost the same, hardly any change at all”
2 = “a little better, but no noticeable change”
3 = “somewhat better, but the change has not made any real difference”
4 = “moderately better, a slight but noticeable change”
5 = “moderately better, a definite improvement that has made a real worthwhile difference”
6 = “a great deal better, a considerable improvement that has made all the difference”

*aItem data could not be obtained for participant C at 8 weeks follow-up for phase 1 (P1)*
from receiving BoNTA injections, consistent with the drug’s favorable safety and tolerability profile demonstrated in the literature to date [11, 12]. One withdrew from the study reporting worsened pain following BoNTA injections, but it was later noted this participant had initially reported improvements in pain, activities, mood, sleep, and QOL post-BoNTA.

The largest limitation to our study was our failure to meet target sample size due to low recruitment and retention rates. BoNTA injections were offered for free but the time, planning, and costs required of participants to coordinate injection visits were inadequately accounted for. Coordinating follow-ups also proved to be difficult once participants received injections, possibly because patients lost incentives to continue participating. These issues could be better addressed with more resources for both improved recruitment and retention in the future. Based on our findings, we encourage the field to continue considering BoNTA as a potential option for treating at-level SCI pain. We further hope that sharing our limitations may facilitate additional investigations into this treatment method throughout the field.

**Conclusion**

Several encouraging patterns among participants with respect to self-reported average pain levels; pain interference with day to day activities, mood, and sleep; as well as overall QOL as related to pain were observed post-BoNTA injections. These findings are consistent with the literature to date and incite us to continue investigating subcutaneous BoNTA as a feasible approach for the control of at-level SCI pain.

**Data availability**

Survey data are available from the corresponding author upon reasonable request.

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**Author contributions** All listed authors have met all of the following authorship criteria: (1) Conceived and/or designed the work that led to the submission, acquired data, and/or played an important role in interpreting the results. (2) Drafted or revised the paper and approved the final version. (3) Agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

**Compliance with ethical standards**

**Conflict of interest** The authors declare no conflict of interest.

**Ethical approval** We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during the course of this research.

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