Intradermal Botulinum Toxin Type A Injection Effectively Reduces Residual Limb Hyperhidrosis in Amputees: A Case Series

Alexandra Charrow, BA, Marc DiFazio, MD, Leslie Foster, DO, Paul F. Pasquina, MD, Jack W. Tsao, MD, DPhil


Objective: To study the effectiveness of botulinum toxin type A (BTX-A) therapy for residual limb hyperhidrosis, prosthesis fit and function, and residual and phantom limb pain in patients with limb amputation.

Setting: Outpatient physical medicine and rehabilitation clinic.

Participants: Walter Reed Army Medical Center patients (N = 8) with unilateral traumatic upper- or lower-limb amputation.

Intervention: BTX-A was injected transdermally in a circumferential pattern around the residual limb by using a 1-cm matrix grid.

Main Outcome Measure: A 10-cm continuous Likert visual analog scale was used to assess residual limb sweating and pain and prosthesis fit and function before and 3 weeks after BTX-A injections.

Results: Patients reported a significant reduction in sweating and improvement in prosthesis fit and function after treatment. However, residual limb and phantom pain were unaffected by treatment.

Conclusions: BTX-A may be an effective treatment for residual limb hyperhidrosis, resulting in subjective improvement in prosthesis fit and functioning. BTX-A should be considered as a method to manage excessive sweating in the residual limb of traumatic amputees.

Key Words: Amputation; Botulinum toxin type A; Hyperhidrosis; Pain; Phantom limb; Rehabilitation.

© 2008 by the American Congress of Rehabilitation Medicine and the American Academy of Physical Medicine and Rehabilitation

HYPERHIDROSIS HAS BEEN widely reported in patients with limb amputation, with estimates of upward of 50% of upper-limb amputees being affected and listing it as their primary complaint. The etiology in amputees is likely to be multifactorial. Heat dissipation is compromised in the amputee because of decreased body surface area and complicated by residual limb coverage with various nonpermeable sockets and liners, limiting the comfort and use of the prostheses.

Surgery has been used to treat hyperhidrosis, as well as noninvasive treatments including topical creams and oral anticholinergic drugs. Injections of BTX-A have been very effective in treating axillary hyperhidrosis with effects lasting up to 6 months before additional treatment was needed. In an extension of a large double-blind study of 320 patients, 5 of 20 patients needed only 1 injection of botulinum toxin in 18 months. BTX-A has also been reported in several cases to be effective at reducing phantom limb pain in amputees and improving pros thesis use. In this report, we examined further the effects of BTX-A on stump hyperhidrosis, prosthesis use, and residual and phantom limb pain in amputees. We hypothesized that BTX-A would be effective not only in reducing hyperhidrosis and pain but also in improving prosthesis fit and use.

METHODS

Eight consecutive patients with traumatic limb amputation and hyperhidrosis (table 1) were treated by using BTX-A (Botox) after topical agents failed to reduce sweating. Hyperhidrosis is defined as dysfunctional sweating exceeding the amount necessary for thermoregulation, and all patients reported excessive sweating leading to soaking of socks and liners throughout the day. Patients were referred by their therapists or prosthetists because of excessive sweating interfering with prosthetic training. None of the patients reported that pain interfered with prosthetic wear or function at the time of treatment.

The effectiveness of the treatment on hyperhidrosis and phantom and residual limb pain was assessed both before and 3 weeks after treatment. A 10-cm continuous Likert visual analog scale, with 1 being low and 10 being high, was used to assess the following questions: (1) How much sweating are you experiencing in your residual limb? (2) How much does the sweating interfere with your prosthesis functioning? (3) How much does the sweating interfere with your prosthetic training? (4) What is your average amount of phantom pain? and (5) What is your average amount of residual limb pain? After obtaining institutional review board approval for this study, data analysis was performed comparing pre- and posttreatment values by using paired t tests with significance established by a P level of less than .05.

BTX-A (300–500U of Botox at a dilution of 100U in 1mL of 0.9% isotonic saline) was injected intradermally at 2 to 3U a site and in a circumferential manner at 1-cm intervals.

List of Abbreviations

<table>
<thead>
<tr>
<th>BTX-A</th>
<th>botulinum toxin type A</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

From the Department of Neurology, Uniformed Services University of the Health Sciences, Bethesda, MD (Charrow, Tsao); and Departments of Physical Medicine and Rehabilitation (Charrow, Foster, Pasquina) and Neurology (DiFazio), Walter Reed Army Medical Center, Washington, DC.

Supported by the Defense Advanced Research Projects Agency.

A commercial party having a direct financial interest in the results of the research supporting this article has conferred or will confer a financial benefit on the author or one or more of the authors. DiFazio’s spouse is an employee of Allergan, manufacturer of Botox, a drug used in this study.

Reprint requests to Jack W. Tsao, MD, DPhil, Dept of Neurology, Uniformed Services University of the Health Sciences, 4301 Jones Bridge Rd, Room A1036, Bethesda, MD 20814, e-mail: jacktsao@earthlink.net.

0003-9993/08/0907-00432$34.00/0
doi:10.1016/j.apmr.2007.11.054
BTX-A was effective in reducing hyperhidrosis of the residual limb at 3 weeks (table 2). Patients also reported that sweating that interfered with both prosthetic function and fit was diminished after BTX-A treatment. However, no effect on either phantom limb or residual stump pain was noted.

**DISCUSSION**

BTX-A (Botox) is approved for the treatment of axillary hyperhidrosis, cervical dystonia, and cosmesis. Although several studies have reported the effectiveness of BTX-A in treating axillary hyperhidrosis, only 3 case studies comprised of 6 patients have reported its use to treat amputee residual limb hyperhidrosis. Four of the patients also reported significantly decreased residual limb and phantom limb pain. BTX-A has been reported to relieve dysesthetic pain in several cases and is thought to act through inhibiting substance P. Because hyperhidrosis has been reported to affect prosthesis use, this was chosen to be our primary outcome measure. Our results support a treatment effect of BTX-A on residual limb hyperhidrosis and prosthesis use as suggested by a previously published case series. We did not find a beneficial effect on either residual limb or phantom limb pain as previously reported. However, our injection technique was different because we used a grid pattern rather than targeting trigger points.

**Study Limitations**

The primary limitations of this study are its small sample size, open-label design, and subjective nature of the patients’ reports on prosthesis fit and function. One potential limitation of this technique is that patients will require repeat injections of toxin after several months, with some studies on axillary hyperhidrosis reporting a duration of effect of up to 6 months. Although BTX-A significantly reduced the amount of sweating our patients experienced and improved prosthetic fit and function, it did not affect the severity of residual limb or phantom limb pain, suggesting that hyperhidrosis may be a limiting factor in prosthetic use. The mechanism of action of BTX-A on residual limb sweating may be similar to its effects on axillary hyperhidrosis, namely, a direct reduction of acetylcholine release from sympathetic nerve fibers in the skin.

**CONCLUSIONS**

The reduction of residual limb hyperhidrosis may have an effect on prosthesis use through improving fit and, consequently, function. BTX-A may be considered as part of the clinical armamentarium for controlling residual limb hyperhidrosis after amputation. Based on these results, we believe that a larger double-blind, placebo-controlled study is warranted to determine the effectiveness of BTX-A on residual limb hyperhidrosis.

**Acknowledgment:** The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Departments of the Navy, Army, or Defense.

**References**