Botulinum toxin: An effective treatment for prosthesis-related hyperhidrosis in patients with traumatic amputations

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ABSTRACT

Hyperhidrosis-related to prosthesis use in patients who have suffered a traumatic limb amputation presents itself as a barrier to comfort, prosthesis use and overall quality of life. This review intends to encourage dermatologists to consider the use of botulinum toxin A or B for the treatment of hyperhidrosis in the residual limb and may serve as a stimulus for a modern, in-depth, and more comprehensive study. A review of the literature was conducted using the PubMed database, focusing on hyperhidrosis treatment after traumatic limb amputation. Articles discussing hyperhidrosis treatment for amputations secondary to chronic medical conditions were excluded. Seven case studies published over the last 12 years have demonstrated positive outcomes of this treatment strategy. Overall, there is little data examining this topic and current publications focus primarily on small case series. A larger, double-blind, placebo-controlled study would likely benefit veterans, service members, and civilians.

Key words: Amputation, botulinum toxin, hyperhidrosis, prosthesis comfort, trauma-related amputation

INTRODUCTION

The United States Department of Defense and Department of Veteran Affairs are dedicated to providing superior rehabilitation care for veterans and service members who have suffered combat-associated traumatic limb loss.[1] Current literature reports that 70% of amputees with multiple limb loss are bothered by sweating and skin irritation inside of the prosthesis socket.[1,2] We present a review of the literature examining the effectiveness of botulinum toxin A (BTX-A) and BTX-B for the treatment of hyperhidrosis related to prosthesis use.[3-8] While both BTX-A and BTX-B are approved by the Food and Drug Administration (FDA), indications for use are limited.[9] Hyperhidrosis continues to be a significant barrier to prosthesis comfort,[1] and treatment with BTX has the potential to address this concern.

A review of the literature was conducted using the PubMed database, focusing on hyperhidrosis treatment after a traumatic limb amputation. We used the key search words: BTX; hyperhidrosis; amputation; trauma-related amputation; prosthesis comfort. Articles discussing hyperhidrosis treatment for axillary, palmar, plantar and amputations secondary to chronic medical conditions were excluded.

BOTULINUM TOXIN A

Botulinum toxin A is currently approved by the FDA as Botox (Allergan, Inc., Irvine, California, USA) supplied in 50 and 100 unit vials, and Dysport (IPSEN, Berkshire, United Kingdom) supplied in 300 and 500 unit vials, to treat cervical dystonia, severe primary axillary hyperhidrosis, strabismus, blepharospasm, and for temporary improvement of moderate to severe glabellar lines.[9] The benefits of using BTX-A for these conditions is well-established and it has few adverse effects at their respective therapeutic doses, which range from 20 to 360 units. The most common adverse effects reported are muscle weakness, fatigue, flu-like symptoms, dry mouth, dizziness, discomfort at the injection site and skin rash.[9] Large volume injections of BTX-A > 600 units have been associated with systemic weakness related to injection dose and frequency, which should be a consideration in the treatment of the residual limb hyperhidrosis.[10]

Current literature emphasizes the positive effects of BTX-A on pain perception, itch and inflammation while simultaneously producing an anhidrotic effect.[11] A study conducted by Charrow *et al*.[3] found that injections of BTX-A successfully reduced residual limb hyperhidrosis and improved prosthesis fit and function when evaluated three weeks after treatment. In this study, 300-500 units of BTX-A at a dilution of 100 units in 1 mL of 0.9% isotonic saline were injected intradermally with 2-3 units at 1 cm intervals in a circumferential pattern on the skin covered by the prosthesis socket. This approach however, did not have any effect on the residual limb pain (RLP) or phantom limb pain (PLP). However, Jin *et al*.[12] demonstrated in three cases that injection of BTX-A at 200, 300, or 500 units using electromyographic guidance and targeting areas of the residual limb where strong fasciculations were present achieved marked improvement in RLP and PLP lasting up to three months.

Three separate case studies[5,6,8] utilized a starch-iodine test to identify hyperhidrotic areas on a residual limb, then injected BTX-A at 100 U in 5-10 unit aliquots,[6,8] or 300 units in 25 units aliquots.[5] In all three reports, BTX-A was diluted in preservative-free saline and produced anhidrotic effects lasting three months. These treatments at our facility cost $5.36/unit of Botox as of April 2014. Because our facility is a government-funded hospital with extensive medical coverage for military personnel, poor prosthesis satisfaction due to hyperhidrosis is the only indication needed for treatment. While large volume injections can be costly, the literature has shown that improving prosthesis comfort is directly correlated with an improved quality of life.[1]

To inject BTX-A at 1-2 cm intervals in a grid-like pattern over a surface area of 600 cm^2 would require over 140 intradermal injections, typically achieved with a 30-gauge needle.[6] The procedure lasts up to 30 min and is criticized as painful.[13] A recent study by Torrisi *et al*.[13] investigated the use of pocketed microneedles (PMN) as an intradermal delivery system for BTX-A. The width of the PMN used in this study is 340 μm, which could serve as a less invasive administration method of BTX-A in hyperhidrotic areas.[13] Table 1 shows a comparison of data.

BOTULINUM TOXIN B

Botulinum toxin type B, supplied in 2500, 5000, and 10,000 units vials is approved by the FDA as Myobloc (Solstice Neurosciences, Inc., South San Francisco, CA, USA) to treat cervical dystonia.[9] The use of BTX-B for the treatment of palmar hyperhidrosis was deemed effective by Baumann *et al*.[14] and further studied by Kern *et al*.[4] in the treatment of the residual limb hyperhidrosis for lower limb amputees. BTX-B administered in a low dose is believed to have a higher affinity for sympathetic nerve endings and better diffusion[15] than BTX-A. Furthermore, BTX-B and was found to be effective in reducing residual limb sweating in nine lower limb amputees.[4]

Kern *et al*.[4] treated nine lower limb amputees with 1750 units of BTX-B injected intracutaneously using a 27-gauge needle (20 injection sites 2-4 cm apart). In addition to subjective identification of hyperhidrotic areas, a starch-iodine test was used on six participants, to help guide injection locations. Participants in the Kern *et al*.[4] study reported a significant reduction in residual limb sweating and a significant improvement in use of the prosthetic device, duration of use and quality of life evaluated 4 weeks and 3 months after treatment. There were no relevant differences between participants evaluated with the starch-iodine test.[4] Kern *et al*.[16] published in a separate study that intradermal low dose BTX-B also decreased RLP and PLP as well as improved quality of life and prosthesis use.

An additional case series published by Kern *et al*.[17] reports that BTX-B injections in muscular trigger points decreased RLP and involuntary movements of the stump for 4-12 weeks, which was dependent on the BTX-B dose and location of amputation. Two of the four patients had a trauma-related amputation, and all found the injections very painful. Table 2 compares the results from both studies by Kern *et al*.[4,17]

CONCLUSION

Current literature investigating the use of BTX to treat hyperhidrosis in trauma-related amputations is limited. However, current case studies[3-8] all report positive outcomes related to treating hyperhidrosis with either BTX-A or BTX-B. Hyperhidrosis, discomfort, and skin irritation related to prosthesis use in trauma-related limb loss remains a topic deserving of more attention as a larger, double-blind, placebo-controlled study evaluating the efficacy of BTX-A and BTX-B in treatment.[1,3]

Table 1: Summary of effects of botulinum toxin A

Reference	Dose	Injection technique	Conculsion
Charrow *et al*.[3]	300-500 units	Circumferential pattern at 1 cm intervals	Anhidrotic effect lasted 3 weeks
Jin *et al*.[12]	200, 300, or 500 units	Electromyographic guidance targeting fasciculations	Improvement in residual limb pain and phantom limb pain lasting up to 3 months
Gratrix and Hivnor[5]	300 units in 25 units aliquots	Starch-iodine test	Anhidrotic effects lasting 3 months
García-Morales *et al*.[6]	100 units in 5-10 units aliquots	Starch-iodine test	Anhidrotic effects lasting 3 months
Wollina *et al*.[8]	100 units in 5-10 units aliquots	starch-iodine test	Anhidrotic effects lasting 3 months

Table 2: Summary of effects of botulinum toxin B

Reference	Dose	Injection technique	Conclusion
Kern *et al*.[4]	1750 units	20 injection sites 2-4 cm apart	Significant anhidrotic effect and a significant improvement in use of the prosthetic device, duration of use and quality of life evaluated after 4 weeks and 3 months
Kern *et al*.[17]	2500 units in 3 cases, 5000 units in 1 case	4-5 injections into muscular trigger points	Decreased residual limb pain and involuntary movements of the stump lasting 4-12 weeks

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