Botulinum Toxin for Axillary Hyperhidrosis

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KEYWORDS

• Axillary hyperhidrosis • Excessive underarm sweating • Botox • Botulinum toxin • Neuromodulators

KEY POINTS

- Botulinum toxin has been proved to be safe and effective for the treatment of axillary hyperhidrosis.
- Although its pathophysiology continues to be controversial, the beneficial effect of type-A neuromodulators in temporarily inhibiting localized sweating supports a level A recommendation from evidence-based review.
- Before the procedure, the correct identification of the affected area is mandatory to avoid wastage of drug and neglect of target areas, and to enhance efficacy, as the hyperhidrotic location may not match the hairy axillary region.

INTRODUCTION

Axillary hyperhidrosis is a disease that affects the social and occupational lives of many people on all continents.[1,2] Axillary hyperhidrosis begins during the teenage years and equally affects men and women.[3] When associated with axillary malodor it is known as bromhidrosis.

The pathophysiology of primary focal hyperhidrosis is not well understood. It can result from hyperstimulation of eccrine and, possibly, apoeccrine sweat glands.[4]

Eccrine glands are distributed over almost the entire body surface[5] and are most numerous on the palms, soles, forehead, axillae, and cheeks.[6] Innervated by cholinergic postganglionic sympathetic nerve fibers, they excrete sweat and contribute to regulation of body temperature.[6,7] When comparing patients with excessive sweating with normal controls, histologic studies have not shown any morphologic alterations or increase in the number or size of the sweat glands.[8] However, preliminary findings of a recent study suggest that the eccrine gland's secretory clear cell exercises a main role in fluid transport (the only one equipped with cotransporter and aquaporin channels), and is likely the source of excessive sweating in this form of hyperhidrosis.[9]

Apocrine glands are stimulated by epinephrine and norepinephrine, and are specifically localized at the urogenital regions and the axillae.[9,10] These glands produce a viscid secretion that can become malodorous as a result of bacterial breakdown.[11]

Sato and colleagues[5,12] described apoeccrine glands in 1989 as having morphologic characteristics of both eccrine and apocrine types. According to these investigators, they correspond to 10% to 45% of all axillary glands and respond to cholinergic stimuli, and intensely so to epinephrine and isoproterenol infusion.[7] However, recent histologic studies have failed to show evidence of

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apoeccrine glands in the tissues of the axillary region investigated.[8,9] The existence of these glands remains controversial.[9,13,14]

BOTULINUM TOXIN

Intracutaneous injections of botulinum toxin (BoNT) have been used as a treatment for focal hyperhidrosis since 1996 with safety, efficacy, and high levels of patient satisfaction.[2,15] Two types of botulinum toxins, BoNT type A (BoNT-A) and BoNT type B (BoNT-B), were studied in axillary hyperhidrosis, and both demonstrated effectiveness in temporarily inhibiting sweating, although acting at different target sites. BoNT-A binds to and cleaves the 25-kDa synaptosomal-associated protein (SNAP-25), whereas BoNT-B acts on the vesicle-associated membrane protein (VAMP or Synaptobrevin),[16,17] both blocking the release of acetylcholine from cholinergic neurons that innervate sweat glands.[16,18]

The use of BoNT-A for the treatment of axillary hyperhidrosis was approved in 2004 by the US Food and Drug Administration (FDA),[19] since then a multitude of studies have confirmed its efficacy, beneficial effects, and paucity of side effects.[20–24]

There are many commercial available BoNT-A products available worldwide. The formulations are not identical and present individual potencies, making caution necessary to ensure proper use. In April 2009, the FDA established drug names to reinforce these differences,[25] summarized in **Table 1**.

There is no globally accepted exact ratio among the different formulations. Reviewing the related published literature, the most commonly accepted dose correlation among products are: 1 U onabotulinumtoxinA (OnaA) = 1 U incobotulinumtoxinA (IncoA) = 1 U BoNT-A (Lanzou) = 1 U BoNT-A (Medytox) = 2,5–3 U abobotulinumtoxinA (AboA).

The available BoNT-B (rimabotulinumtoxinB [RimaB]) products are Neurobloc in the European Union and Myobloc in the United States. Unlike BoNT-A, it is not commercially available worldwide, and probably for this reason a limited number of studies of axillary hyperhidrosis being treated with this toxin type have been published. The literature found describes side effects related to distant spread of the toxin, such as dry eyes and dry mouth, which are not commonly described after the use of BoNT-A.[26–28] The dose correlation between BoNT-A and BoNT-B varies from 20 to 100 U of RimaB to 1 U of OnaA.[26–29]

A recent evidence-based review[30] of hypersecretory disorders that searched for botulinum toxin as a treatment of axillary hyperhidrosis found 2 Class I (prospective, randomized, controlled, and with masked outcome assessment clinical trial with strict requirements) studies (1 with OnaA[21] and 1 with AboA[20]) and 5 Class II (similar to Class I trials but lacking 1 or more of the required criteria) studies. The investigators concluded that the evidence supports a level A recommendation for BoNT-A in general and a level B recommendation for OnaA and AboA individually, whereas RimaB and IncoA received a level U recommendation (insufficient data) for axillary hyperhidrosis.

Some studies have compared the use of different toxins for the treatment of axillary hyperhidrosis.

Studies Comparing BoNT-A Products

Kalner[15] performed a prospective same-patient comparison between OnaA in one axilla and AboA in the other, using a conversion factor of 1 U OnaA to 3 U AboA. She noted that OnaA resulted in a faster onset of action, within 1 week,

Table 1
Commercially available botulinum toxin A (BoNT-A)

Botulinum Toxin	Trade Name	Origin
OnabotulinumtoxinA (OnaA)	Botox	(Allergan, Irvine, CA, USA)
AbobotulinumtoxinA (AboA)	Dysport	(Ipsen Biopharm, UK) in USA, Europe, and Latin America
BoNT-A	Prosigne	(Lanzhou, China) in Asia and Latin America
BoNT-A	Neuronox	(Medytox, South Korea) in Asia, Botulift in Latin America
IncobotulinumtoxinA (IncoA)	Xeomin	(Merz Pharma, Germany) in Canada, Germany, USA, Latin America
BoNT-A	PureTox	(Mentor Corp, Santa Barbara, CA, USA) uncomplexed BoNT-A. Phase III studies