

# Emerging Nonsurgical Treatments for Hyperhidrosis

Anastasia O. Kurta, DO, Dee Anna Glaser, MD\*

## KEYWORDS

- Hyperhidrosis • Thermolysis • Laser • Ultrasound scan • Anticholinergic drugs • Botulinum toxin • Iontophoresis

## KEY POINTS

- Botulinum toxin is easy to deliver and provides excellent and predictable results with minimal side effects.
- Tap water iontophoresis therapy is a cost-effective treatment modality, especially useful for palmo-plantar hyperhidrosis.
- Devices delivering energy to destroy sweat glands in the axillary region provide long-lasting reduction in sweating with a good safety profile.
- Topical anticholinergic agents are being investigated and may provide efficacy with fewer systemic adverse effects.
- Despite new therapies, more research is needed to further enhance hyperhidrosis treatment.

## INTRODUCTION

Primary focal hyperhidrosis is characterized by excessive sweating greater than what is required for normal physiologic temperature regulation and that cannot be attributed to secondary medical conditions or medications. Hyperhidrosis affects approximately 3% of the global population and negatively influences quality of life and physical and emotional well-being.<sup>1</sup> Areas commonly affected are axillae, palms and soles, face, scalp, inframammary region, and groin. Its impact on affected individuals' quality of life is comparable to many common dermatologic disorders such as psoriasis and acne.<sup>2</sup> The effect of hyperhidrosis on quality of life can be assessed in multiple ways. Two commonly used measures are the Dermatology Life Quality Index and the Hyperhidrosis

Disease Severity Scale (HDSS), a 4-point, validated scale that measures the severity of patients' hyperhidrosis based on how it affects daily activities (**Box 1**).<sup>3</sup>

A variety of treatment options exist for hyperhidrosis, some depending on the anatomic region that is affected. Therapies can include the use of:

- Botulinum toxins
- Tap water iontophoresis
- Microwave energy thermolysis
- Externally applied ultrasound
- Lasers
- Anticholinergic drugs
- Alpha-2 adrenergic agonists (such as clonidine)
- Beta blockers
- Endoscopic thoracic sympathectomy

A.O. Kurta is serving as a sub-investigator for Allergan and Ulthera. D.A. Glaser has served as advisor for Allergan, Galderma, Miramar Labs, and Unilever. She has been an investigator for Allergan, Miramar Labs, and Ulthera and received a research grant from Allergan.

Department of Dermatology, Saint Louis University School of Medicine, 1755 South Grand Boulevard, St Louis, MO 63104, USA

\* Corresponding author.

E-mail address: [glasermd@slu.edu](mailto:glasermd@slu.edu)

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**Box 1**  
**Hyperhidrosis disease severity scale**

*"How would you rate the severity of your hyperhidrosis?"*

1. My sweating is never noticeable and never interferes with my daily activities.
2. My sweating is tolerable but sometimes interferes with my daily activities.
3. My sweating is barely tolerable and frequently interferes with my daily activities.
4. My sweating is intolerable and always interferes with my daily activities.

This review focuses on therapies that have been approved or cleared by the US Food and Drug Administration (FDA) and potential treatments that are undergoing promising clinical investigation.

### CHEMODENERVATION

Although several botulinum toxins are commercially available with published data on treating hyperhidrosis, only onabotulinumtoxin A (onabotA), (BOTOX; Allergan Inc, Irvine, California), was FDA approved in 2004 for the treatment of severe primary axillary hyperhidrosis in adults. Numerous studies show the efficacy and safety of onabotA to treat axillary hyperhidrosis. One multicenter, randomized, controlled, double-blind study, compared effects of onabotA with placebo in 320 subjects 18 and older. This study found that greater than 90% of participants experienced at least a 50% reduction in axillary sweating 4 weeks after treatment.<sup>4</sup> The safety profile of onabotA was similar to that in the placebo group.

Another study evaluated the efficacy and safety of onabotA in adolescents ages 12 to 17 years with severe primary axillary hyperhidrosis. Up to 72% of patients experienced at least a 2-grade improvement in the HDSS score at 4 and 8 weeks after each of the first 2 treatments.<sup>5</sup> The median duration of effect ranged from 134 to 152 days. Less than 6% of patients experienced treatment-related adverse effects.<sup>5</sup> Overall, this study found that the efficacy and safety of onabotA can also be extended to adolescents.

Botulinum toxins can be used off label to treat hyperhidrosis in other body regions, including but not limited to the face/scalp, inguinal region, or palms/soles.<sup>6,7</sup> Each anatomic location presents unique challenges, but in the palms, the injections tend to cause more pain and can be associated with risk of muscle weakness when injecting over the thenar eminence.<sup>7</sup>

Possible new topical formulations of botulinum toxin are under investigation by at least 2 different companies, Revance Therapeutics (Newark, California) and Transdermal Corp (Birmingham, Michigan).

Glogau's randomized, blinded, vehicle-controlled study of 12 patients using 200 U of onabotA in a proprietary vehicle delivery system developed by Revance Therapeutics found a statistically significant 65% reduction in sweating reported at 4 weeks compared with 25.3% in the vehicle-treated axilla.<sup>8</sup> No systemic adverse events were reported, and very few local adverse events were observed, none of which were considered related to the treatment.

A second company, Transdermal Corporation, is developing a topical agent based on ionic nano-particle technology.<sup>9</sup> This agent consists of micelles that entrap the active ingredient with no changes in its chemical composition; this creates particles that are smaller than skin pores. Data from clinical trials are scarce, and more information is needed to evaluate its efficacy in hyperhidrosis.

### TAP WATER IONTOPHORESIS THERAPY

Tap water iontophoresis is a first line option to treat palmoplantar hyperhidrosis, a lifelong, socially embarrassing, and occupationally disabling condition. Iontophoresis uses the passage of a direct electrical current onto the skin and can serve as an effective treatment option. Side effects are typically minor and related to higher amperage. Skin erythema, minor pain or paresthesias in the treated areas, and minor burns can occur.<sup>10</sup> For patients who have any breaks in the skin, it is recommended to apply petroleum jelly to those areas to reduce irritation and the passage of current through the open skin. The underlying mechanism of iontophoresis is not fully understood. One hypothesis is that iontophoresis may induce a hyperkeratotic plug in the eccrine duct and obstruct sweat flow and secretion.<sup>11</sup> Another proposed mechanism includes impairment of the electrochemical gradient of sweat secretion.

Tap water iontophoresis should be performed every 48 to 72 hours. Successful reduction in sweating usually requires the application of 15 to 20 mA.<sup>12</sup> Each treatment takes approximately 30 to 40 minutes to perform (15–20 minutes for the palms and 15–20 minutes for the soles). We generally suggest treating one hand and one foot together, so one free hand is available to control the unit (**Fig. 1**). Once therapeutic effect is achieved, treatments can be performed once weekly for maintenance. A controlled trial of 112

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