

Botulinum Toxin Type A for Pediatric Hyperhidrosis

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Hyperhidrosis is a stigmatizing medical disorder that can present in either adults or adolescents. Many of the treatment options that are approved by the US Food and Drug Administration for use in adults are neither officially approved for use in children nor well described in the literature. This article will provide an understanding of the impact of pediatric hyperhidrosis, review standard treatment options, and discuss the success one pediatric dermatology practice has had with the off-label use of botulinum toxin type A in children with hyperhidrosis.

Hyperhidrosis is defined as excessive sweating; some have even tried to quantify hyperhidrosis by gravimetrically defining the extra sweat as the production of more than 100 mg of sweat per 5 minutes in males and more than 50 mg of sweat per 5 minutes in females.¹ Hyperhidrosis can involve any area of the body but most commonly affects the axillae, hands, and feet and is hence termed *axillary*, *palmar*, or *plantar hyperhidrosis*, respectively. Hyperhidrosis has been noted to run in some families, but most cases are sporadic and not associated with systemic disease or genetically inherited syndromes. The medical disorders that can be associated with hyperhidrosis include thyroid disease, diabetes, pheochromocytoma, and carcinoid syndrome, among others. Several rare syndromes that can present with hyperhidrosis as a feature include localized unilateral hyperhidrosis, Frey syndrome, and Ross syndrome, but the presentation of these syndromes is often focal or unilateral and differs from that of patients with primary hyperhidrosis.² Keeping these syndromes in mind when evaluating a patient with hyperhidrosis should suffice since they are far less common than isolated or idiopathic hyperhidrosis in clinical practice.

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Although untreated hyperhidrosis can result in secondary dermatologic conditions, such as painful maceration, candidiasis, bacterial colonization, and bromhidrosis, the most troublesome aspect of hyperhidrosis is its profound impact on the patient's social functioning.³ Patients with axillary hyperhidrosis often saturate their shirts with sweat repeatedly throughout the day and may compensate by purchasing several of the same garment, changing multiple times as the day progresses to conceal the medical problem from peers or coworkers. They may withdraw from enjoyable physical activities to avoid triggers, placing themselves at risk for social isolation, anxiety, and depression. Individuals with palmar hyperhidrosis complain of difficulty when trying to complete writing tasks, as their sweat blurs the ink on the paper. Some may refrain from shaking hands for fear of revealing their moist palms.

Although most therapies for hyperhidrosis are approved by the US Food and Drug Administration for treating patients 18 years of age and older, a large number of patients with hyperhidrosis present in early adolescence. As is frequently the case in pediatric medicine, providers are compelled to extrapolate safety and efficacy data in order to completely and effectively treat the pediatric patient. This article will focus on the success of botulinum toxin type A (BTX-A) injections for the treatment of hyperhidrosis in children, specifically teenagers. My experience has been derived from the extensive off-label use of BTX-A within the setting of a busy outpatient academic pediatric dermatology practice and by no means

BTX-A FOR HYPERHIDROSIS

should serve as a replacement for well-controlled clinical trials to confirm the safety and utility of this drug in children with hyperhidrosis.

TREATMENT OPTIONS

Current treatment options for hyperhidrosis in children include over-the-counter or prescription topical solutions, oral anticholinergic medications, and surgical procedures aimed at disrupting the structure or innervation of the axillary eccrine ducts.^{4,5} The most common first-line topical therapy is aluminum chloride in concentrations ranging from 10% to 30%. Although some patients find this treatment inexpensive, easy, and effective, many patients require a more potent treatment and complain that the alcohol base in the solution is irritating to their skin, necessitating discontinuation of therapy. Tap water iontophoresis is an over-the-counter alternative in which minerals present in tap water combined with a mild electrical current flow through the skin's surface and thicken the outer layer of the skin, theoretically blocking the flow of sweat. Many patients have found this modality to be both tolerable and highly effective for palmar or plantar hyperhidrosis, but it is more arduous to use in the underarm area and has not gained wide acceptance for treating axillary hyperhidrosis. In addition, iontophoresis is performed using a specialized medical device and thus may not be reimbursed by insurance companies, hindering patient acceptance. Oral anticholinergics and beta-blockers can be effective but are not widely used, based on their unfavorable systemic adverse effect profile at the doses required to achieve efficacy in treating hyperhidrosis. Finally, several surgical options are available to treat axillary hyperhidrosis,⁶ but while they can be useful, they introduce a much higher level of risk. These surgical options include axillary skin excision to remove the eccrine ducts,⁷ liposuction of the axillae to disrupt the function of the eccrine ducts, and sympathectomy.⁸⁻¹¹ Sympathectomy carries the highest risk of these procedures and must be performed by a neurosurgeon with extensive experience. Despite its efficacy, surgical sympathectomy can be associated with postoperative compensatory truncal hyperhidrosis, as well as Horner syndrome, brachial plexus injury, pneumothorax, and scarring.^{10,12,13} We recommend reserving surgical options for those patients who are significantly impaired by hyperhidrosis and who have failed all other medical treatment modalities.

BOTULINUM TOXIN

Many sources describe the safety and efficacy of BTX-A for the treatment of both axillary and palmar hyperhidrosis in adults.¹⁴⁻²² There are also several reports discussing the similar efficacy of botulinum toxin type B for treating

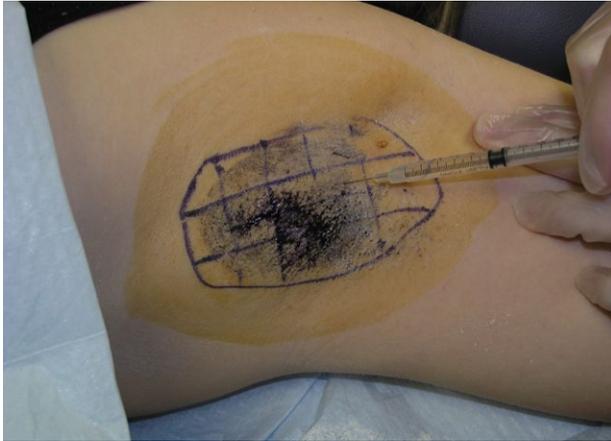
hyperhidrosis in adults.^{23,24} The mechanism of action of BTX-A hinges on its ability to block the presynaptic release of acetylcholine, thus leading to the chemodeneration of eccrine glands. Unlike in the face, the amounts of BTX-A used in the axillae are not sufficient to cause clinically significant relaxation of the large muscles in this region, so weakness has not been described as a common adverse effect. Mild weakness is a potential adverse effect, however, when injecting the hands for palmar hyperhidrosis, and it is imperative to warn patients of the potential risk of mild and usually transient weakness in grip strength after treatment. This slight decrease in strength may be more significant for certain patients, such as musicians or gymnasts, who rely on their grip strength to maximally perform their jobs or hobbies.

BTX-A has historically been used therapeutically in the pediatric population for disorders such as neuromuscular spasticity,^{25,26} especially that associated with cerebral palsy. Experience within pediatric neurosurgery is extensive, and the safety and efficacy of BTX-A in children, with the exception of one report of iatrogenic botulism, have been documented.²⁷ However, only one source in the current literature discusses the use of BTX-A in children with hyperhidrosis, concluding that it is an excellent alternative to other currently available treatment options.²⁸

My pediatric dermatology practice has treated more than 20 adolescents younger than 18 years with axillary BTX-A injections. At the first visit, the social impact of the patient's hyperhidrosis is assessed and documented, and prior treatment failures are discussed and recorded clearly in the medical record. The risks and benefits of axillary BTX-A are then thoroughly discussed with the patient and a legally consenting adult if the patient is younger than 18 years. Alternative therapies, as well as their risks and benefits, are also reviewed. Preauthorization with the patient's insurance company is then sought. Once approved, the vial of BTX-A is ordered, shipped, and refrigerated. After the BTX-A has arrived, the patient is called to return for a procedure-only visit.

AXILLARY BTX-A INJECTION TECHNIQUE

The technique I use is identical to that described in adult patients in that the 100-U vial of BTX-A is diluted with 4 cc of sterile, preservative-free saline and drawn up into four 1-cc syringes. Bilateral axillae are cleansed with povidone-iodine, and the starch-iodine test is performed after the povidone-iodine dries by dusting a thin layer of cornstarch onto each axilla with a cosmetics brush. The hyperhidrotic areas quickly become dark purple, and a grid is then drawn with a sterile surgical marking pen, dividing the positive area into 15 (3 rows of 5) or 16 (4 rows of 4) boxes (Figure).^{29,30} Pediatric patients seem



The dark purple color in the left axilla demonstrates a positive starch-iodine test, around which a grid of 15 boxes is drawn.

to tolerate the procedure best when they engage in a distracting activity during the injections. Therefore, there is a DVD player with a selection of movies in the office. Many patients prefer to bring a digital device to listen to their own music during the procedure. Fifty units of BTX-A (two 1-cc syringes) are injected into each axilla³¹ with a 30-gauge syringe by placing 0.1 cc into the center of each grid box and injecting at a 45° angle into the high dermis until a small bleb is achieved. I prefer to “double up” on the central boxes, where the sweating is usually most concentrated, in order to utilize the remaining 0.4 cc, taking care not to inject directly over the ink grid so as to avoid an iatrogenic ink tattoo. Proceeding efficiently with the injections minimizes patient anxiety and the waste of drug, as the BTX-A solution tends to drip onto the skin if time elapses between injections. The purple ink and starch-iodine are then gently removed with a towel and soap, and the same procedure is performed on the other side.

Axillary BTX-A injections have been extremely well tolerated by the children in my practice and are relatively time efficient, especially when an assistant can prepare the starch-iodine test and help with cleanup, allowing the physician to perform the injections. There have not been any local or systemic adverse effects, with the exception of one patient who experienced tingling in her fingers when her arm was elevated without a rest during the preparation and the procedure. The tingling immediately resolved and did not recur once her arm was lowered. Most patients have a fairly rapid onset of symptom relief, many times even by the day following the procedure, and the therapeutic effect lasts anywhere from 3 to 6 months.^{32,33} However, in my experience, patients who return at 3 months have usually not reached their original level of sweating, as documented by a less deeply positive starch-iodine test. I prefer not to inject more frequently

than every 3 months to minimize the potential development of anti-BTX-A–neutralizing antibodies, which, over time, could render the treatments less effective.³⁴ In my experience, patients and their parents have been universally satisfied with this procedure and tend to return at regular intervals for re-treatment, as their quality of life dramatically improves without the need for daily home therapy.³⁵

FUTURE TRENDS

Even less invasive emerging trends for the treatment of hyperhidrosis in children include the topical application of BTX-A. This approach is currently being researched in the adult population using topical transport peptides, which noncovalently bind BTX-A. If approved, this therapeutic modality would obviously serve as an exciting alternative to a repeated series of injections, especially for the pediatric age group.³⁶

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BTX-A FOR HYPERHIDROSIS

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