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## Special Considerations for Children with Hyperhidrosis



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#### **KEYWORDS**

• Hyperhidrosis • Iontophoresis • Botulinum toxin • Pediatric population

#### **KEY POINTS**

- Primary hyperhidrosis has traditionally been considered a medical and psychosocial problem for adult patients, with estimates suggesting that 1.6% of adolescents and 0.6% of prepubertal children are affected by this condition.
- A thorough history and physical examination should be performed to help rule out an underlying causation for secondary hyperhidrosis before initiating treatment.
- Quality of life in the pediatric population can be significantly improved by early diagnosis and therapy.
- Many therapeutic options for primary pediatric hyperhidrosis exist including topical and systemic therapies, iontophoresis, and botulinum toxin injections.

#### INTRODUCTION

Hyperhidrosis is a condition characterized by excess sweat production affecting children and adults. Primary focal hyperhidrosis is currently considered to be idiopathic, affecting areas of the body including the axillae, palms, soles, and face. Primary hyperhidrosis is believed to occur as a result of a hyperactive sympathetic nervous system.<sup>1</sup> Secondary hyperhidrosis, which usually results from an underlying condition, can present in a focal or generalized pattern. A thorough history and physical examination can help to rule out an underlying causation for secondary hyperhidrosis. The prevalence of hyperhidrosis in the United States has been estimated to be 2.9%, with an average age of onset of 14 to 25 years.<sup>2–4</sup> Primary

hyperhidrosis has traditionally been considered a problem for adults, but estimates show that 1.6% of adolescents and 0.6% of prepubertal children are affected.<sup>2</sup> The primary locations of involvement in pediatric subjects include the palmoplantar and axillary areas.<sup>4,5</sup>

Psychological and social development and well-being are often affected, impacting patient quality of life, which may in turn lead to profound emotional and social distress. <sup>2,5,6</sup> Pediatric subjects with hyperhidrosis can have difficulties handing a writing utensil, keeping papers dry, gripping the handlebar of a bicycle, manipulating a computer mouse, and using a video game controller. <sup>6</sup> Quality of life can be significantly improved by early diagnosis and therapy; however, underdiagnosis and lack of

Funding Sources/Conflict of Interest: Allergan (note: all research funds were paid to The University of Texas Medical School - Houston, Houston, Texas; Protocol Number 191622-075-00, Allergan, 2005 – 2007) (A.A. Hebert); No conflicts to report (B.R. Bohaty).

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knowledge regarding therapeutic options has hindered maximization of therapy in the pediatric population. The medical community is not solely to blame for failure to provide or delayed treatment options. In a survey performed by Strutton and coworkers only 38% of patients with hyperhidrosis had sought medical assistance for their excessive sweating. The risk for concomitant cutaneous disease (eg, verruca vulgaris, dermatophytosis) is increased for patients with hyperhidrosis. This article explores the available therapeutic options for pediatric hyperhidrosis, and expands awareness of this frequently underrecognized medical condition.

#### **TOPICAL THERAPY**

Treatment options for hyperhidrosis in the pediatric population are somewhat limited.7,9 Topical medications are often the first-line therapy and frequently include aluminum salts, which are found in over-the-counter and prescription antiperspirants. Aluminum chloride hexahydrate is the active ingredient found in prescription preparations, whereas a partially neutralized version is used in nonprescription compounds. 10 Topical aluminum chloride preparations are thought to mechanically obstruct eccrine sweat gland pores and lead to atrophy of the secretory cells. 11 Aluminum chloride hexahydrate 20% to 25% preparations in alcohol have been found to be effective first-line treatments for axillary hyperhidrosis. 12,13 Treatment regimen during one study consisted of patients applying the solution nightly for 1 week and then as needed, with most patients needing to reapply only once every 7 to 21 days to maintain adequate control. The only side effect reported during this study was irritation at the application site, which responded to treatment with 1% hydrocortisone for most that were affected. 13 Aluminum chloride therapy is less effective at treating palmar hyperhidrosis. A study published in 1990 by Goh14 found that palmar hyperhidrosis was reduced within 48 hours of treatment with topical aluminum chloride 20%; however, this efficacy was lost 2 days after cessation of treatment. Local irritation and posttreatment pruritus and burning were the major limitations for this treatment modality.

A newer formulation of aluminum chloride hexahydrate using a hydroalcoholic gel base containing 4% salicylic acid was evaluated in a study of 238 patients with palmoplantar and axillary hyperhidrosis. This base was chosen to enhance absorption and minimize the irritant side effects associated with the traditional alcohol bases. Patients with palmar, plantar, and axillary disease had excellent-to-good response rates with values of 60%, 84%,

and 94%, respectively. Nonresponders and those with adverse reactions to earlier aluminum chloride preparations demonstrated better tolerance and control of disease with this new hydrogel compound.<sup>15</sup>

Other topical applications, such as astringents (eg, formaldehyde, glutaraldehyde, tannic acid), have shown efficacy in the treatment of hyperhidrosis, but their use is limited because of their propensity to cause staining of the skin and sensitization reactions.<sup>16</sup>

The efficacy and safety of topical treatments has rarely been studied in the pediatric population. However, topical aluminum chloride preparations remain popular among pediatric prescribers because of their relatively benign safety profile and ease of application. Downsides to treatment with topical products include the need for frequent reapplication to maintain efficacy, and local side effects including burning and pruritus. In addition, topical therapy is not effective for all those affected by hyperhidrosis, leaving some to explore other treatment options.

#### **ANTICHOLINERGICS**

Anticholinergic medications have been available for many decades and have widely been used to help minimize secretions perioperatively, and to decrease salivation in pediatric patients with neurologic conditions. The ability of anticholinergic medications to improve hyperhidrosis was inadvertently revealed when patients given preparations from atropine plants developed a decrease in sweat production. Anticholinergic medications competitively antagonize the muscarinic acetylcholine receptors, which are a prominent component of glandular tissue. 20,21

A few case reports have demonstrated efficacy of topical anticholinergic preparations in such conditions as craniofacial hyperhidrosis and diabetic gustatory sweating. However, randomized controlled trials are needed to accurately determine efficacy and safety. 10,22-24

Oral anticholinergic use in the treatment of hyperhidrosis is becoming increasingly more common, and agents include such drugs as glycopyrrolate and propantheline bromide. Annual treatment with generic oral glycopyrrolate at a dosage of 2 mg/day has been estimated to cost \$756 per year, which is a fraction of the cost for treatment with botulinum toxin injections. Side effects of anticholinergic medications can be limiting at the doses required for efficacy and include xerostomia most frequently, and blurred vision, tachycardia, urinary hesitancy, and constipation. 16,25 To help determine the efficacy of oral glycopyrrolate in the treatment of

hyperhidrosis, Bajaj and Langtry<sup>21</sup> conducted a retrospective analysis of 24 adult subjects ages 19 to 62 that were treated with oral glycopyrrolate. This study found that 79% of those treated with glycopyrrolate had a positive response; however, the side effects limited further treatment of some of the participating individuals.<sup>21</sup>

More recently, Paller and coworkers<sup>5</sup> conducted a retrospective analysis of 31 pediatric patients with primary focal hyperhidrosis who were treated with a mean dosage of 2 mg of oral glycopyrrolate daily for an average of 2.1 years. The analysis demonstrated a positive response in 90% of those treated, which was major in 71% of responders. Side effects were experienced by 29% of the treated pediatric subjects, the most common of which included xerostomia (26%) and xeropthalmia (10%). These side effects were noted to be dose-related. The authors concluded that oral glycopyrrolate is an inexpensive, well-tolerated, and painless second-line treatment of pediatric subjects with primary focal hyperhidrosis.<sup>5</sup>

Another institutional review by Kumar and coworkers<sup>26</sup> looked at 12 children with severe, refractory hyperhidrosis treated with oral glycopyrrolate from July 2009 to January 2012. The average length of therapy was 18 months and the most common dosing regimen was 1 mg/day. Eleven (92%) of 12 patients noted improvement, and 9 (75%) of 12 would recommend oral glycopyrrolate to a friend. Seven patients noted side effects, none of which were severe. Dry mouth was the most common side effect and was reported in 50% of those treated (N = 6). Other side effects included constipation (N = 1), dizziness (N = 1), and facial swelling (N = 1). This retrospective analysis provides additional support that oral glycopyrrolate is a safe and effective treatment in children with hyperhidrosis.

A recent retrospective study of pediatric patients aged 10 to 18 years found that subjects with hyperhidrosis who were prescribed glycopyrrolate had on average a three-point improvement (on a five-point scale) in sweating reduction. Most subjects took the medication twice daily to achieve ideal control of sweating. Despite side effects, which included dry mouth (82%), constipation (55%), dry eyes (16%), palpitations (36%), and urinary retention (18%), glycopyrrolate was the preferred treatment of this cohort of patients, because of the rapid onset of action and efficacy of the medication. Additionally, these pediatric patients were remarkably compliant with the glycopyrrolate treatment schedule as prescribed. Half the patients reported refilling their prescription within 1 week of running out of pills. Reasons cited for not taking glycopyrrolate on a regular basis by this pediatric population included being bothered by side effects (62%), lack of efficacy (26%), expense of the medication (15%), and forgetting to take the medication (16%). Of the patients included, 22% were male and 7% were female. Seventy-nine percent of the patients reported their ethnicity to be white, 11% were Hispanic, 7% were Asian, and 3% were of African American descent. Of the patients who participated in the study, 40% had generalized hyperhidrosis, 7% had axillary hyperhidrosis, 41% had palmoplantar hyperhidrosis, 5% had facial hyperhidrosis, and 7% had plantar hyperhidrosis. The duration of hyperhidrosis diagnosis at the time of survey completion was greater than 8 years for 15%, 5 to 8 years for 25%, 1 to 4 years for 48%, and less than 6 months for 12% of responders.<sup>27</sup>

#### **IONTOPHORESIS**

Beginning in the 1930s, electric current has been used to introduce ions into skin in a process known as iontophoresis. For decades this process had been conducted at health care facilities under the supervision of medical staff, but eventually made its way into the home in the year 1984. Unadulterated tap water is the most common medium used to conduct the electric current into the cutaneous tissues. However, anticholinergic drugs can also be added to enhance efficacy at the cost of increasing the risk of systemic adverse effects, such as dry or sore throat. <sup>29</sup>

Despite its many years of effective use, the mechanism of action of iontophoresis remains under debate. Theories for the mechanism range from increased keratinization and plugging of eccrine ducts to alterations in electrochemical signaling, which may prevent the initial stimulus that causes the eccrine gland to perspire. A selective targeting of the eccrine glands because of their locally increased electrolyte concentration has also been proposed, which may lead to protein coagulation and a loss of eccrine function. <sup>29,30</sup>

Iontophoresis has proved effective in the treatment of hyperhidrosis involving the palms and soles. However, treatment of other affected areas, such as the axillae, remains impractical because of the challenges of delivering the iontophoresis to the axillae. The limitations of iontophoresis include the necessity for frequent retreatment to maintain efficacy (which is lost a few weeks after cessation of treatment), and the risk of local and systemic side effects. <sup>16</sup> Local side effects are mild and include erythema, stinging, vesiculation, and papulation at the sites of treatment.

Although iontophoresis has not been studied in the pediatric population specifically, pediatric subjects have been included as members of larger cohorts in more than one study. A single-blind prospective study by Dolianitis and coworkers<sup>29</sup> sought to determine the efficacy of iontophoresis with glycopyrrolate as compared with iontophoresis with tap water alone in 20 subjects ranging in age from 12 to 50 years with moderate to severe palmoplantar hyperhidrosis. Iontophoresis containing glycopyrrolate 0.05% in solution was found to have superior efficacy to iontophoresis with tap water alone. This efficacy was further enhanced and prolonged when treatment was bilateral as opposed to unilateral leading the investigators to hypothesize that a systemic action of glycopyrrolate was contributing to the local effects.<sup>29</sup>

A younger population of patients with hyperhidrosis aged 8 to 32 years was evaluated in a different study that also sought to evaluate the efficacy of iontophoresis. A total of 112 patients were treated and 81.2% were satisfied following the series of eight treatment sessions. More than half the subjects treated noted an improvement in plantar sweating following treatment, even though only the palms were subjected to iontophoresis during the study. This evidence further supports a plausible systemic efficacy for iontophoresis following local treatment alone.

#### **BOTULINUM TOXIN**

The anaerobic bacterium known as Clostridium botulinum is responsible for the production of botulinum toxins. Seven distinct serotypes classified by their antigenic differences work by cleaving proteins necessary for fusion of acetylcholine vesicles with the presynaptic membrane thus inhibiting acetylcholine release from the sympathetic cholinergic nerve terminals. Therefore, a decrease in sweat production is achieved through intradermal botulinum toxin injection, which inhibits neurotransmission by affecting the nerve terminals that innervate sweat glands. The two serotypes of botulinum toxin used most commonly in the clinical realm are toxins A and B, which cleave receptor proteins SNAP-25 and synaptobrevin, respectively. Both have been found to have similar efficacy for the treatment of axillary hyperhidrosis. However, botulinum toxin A had a lower incidence of autonomic side effects and pain at the injection site, which likely contributed to its preferential use by most clinicians. 31,32 Botulinum toxin A (Botox; Allergan, Irvine, CA) was approved by the Food and Drug Administration (FDA) in 2004 for the treatment of severe primary axillary hyperhidrosis in adults. Two newer class A botulinum toxins (Dysport; Ipsen Biopharm, Wrexham, UK; Xeomin; Merz Pharmaceuticals Inc., Greensboro, NC) have

been approved by the FDA in 2009 and 2011, respectively, for the treatment of other conditions (eg, cervical dystonia) but have not yet received FDA approval for the treatment of hyperhidrosis. The FDA approved botulinum toxin B (Myobloc; Solstice Neurosciences, Malvern, PA) for the treatment of cervical dystonia only, thus leaving its use in the management of hyperhidrosis to be categorized as "off label." A lack of FDA approval for the treatment of hyperhidrosis in children often forces affected individuals to pay out-of-pocket for treatment estimated to cost a minimum of \$2400 annually. 5,6,9,33

#### Injection Site Pain

Injection site pain is a major limiting factor for intradermal injections of botulinum toxin, although options exist to help minimize this pain. Application of topical anesthetics and cryotreatment before injection with botulinum toxin are only partially effective but may provide mild shortterm relief. Dichlorotetrafluoroethane-containing refrigerant sprays have been shown to demonstrate some efficacy in reducing injection site discomfort.<sup>34</sup> One effective option for pain control is intravenous regional anesthesia via a procedure termed "Bier's block." This procedure may lack practicality in an outpatient dermatology office because it can lead to cardiovascular and central nervous system toxicity necessitating close cardiac monitoring throughout the procedure.34 Management of palmar and/or plantar hyperhidrosis with digital block anesthesia at the wrists and/or ankles is a safe and effective option and can be performed in the outpatient setting. Nerve block at the median and ulnar nerve can lead to temporary weakness of the hand musculature postprocedure and paresthesias if the needle pierces the nerve during the anesthetizing process. General anesthesia in an operating room setting is arguably the most effective option to minimize pain during treatment; however, the increased cost to the patient and risks of general anesthesia should be weighed against the expected benefits.

#### Adverse Effects

Injection of botulinum toxin may lead to other adverse effects including bruising at the injection site, xerosis, and weakness of hand musculature that tends to be transient. Superficial injection of the toxin may minimize the risk for posttreatment muscle weakness.<sup>34</sup> In 2009, based on a safety evaluation of the botulinum toxin products, the FDA added a Boxed Warning to the prescribing information on this medication class to highlight that botulinum toxin may spread from the area

of injection to produce symptoms consistent with botulism, such as muscle weakness, dysphonia, dysarthria, incontinence, trouble breathing, dysphagia, blurred vision, drooping eyelids, and death. Children treated for spasticity may receive several hundred units of botulinum toxin at a therapeutic session and have the potential for the greatest risk for these symptoms, but the symptomatology can also occur in adults. No definitive serious adverse event reports of distant spread of toxin effect have been associated with dermatologic use of botulinum toxin A at approved doses in children or adults.

#### Safety and Efficacy in Children

The safety and efficacy of botulinum toxin A for the treatment of severe axillary hyperhidrosis was first studied in adults. In a large multicenter 52-week, randomized, placebo-controlled trial in patients aged 18 to 75 with primary axillary hyperhidrosis, repeated botulinum toxin A injections were found to be safe and efficacious substantially reducing impairment in 75% of those treated at 1 month postinjection. Data from this study, coupled with that from a later 3-year open-label extension of greater than 175 adult patients with primary axillary hyperhidrosis treated by intradermal injections of botulinum toxin, elucidated no serious adverse effects. Se

The first report of botulinum toxin treatment of hyperhidrosis in the pediatric population arose in 2002 and described a 13-year-old girl who was treated for refractory hyperhidrosis of the palms.37 Over a 2-year period she received a total of four rounds of injections that were successful in decreasing her palmar sweating, although she did experience an episode of transient muscle weakness of the hands lasting about 3 weeks. Since then, other case reports of successful treatment of refractory palmar hyperhidrosis in the pediatric population have been reported.34 Not until 2005 were injections for hyperhidrosis of the axillae reported in the pediatric literature. A 14-year-old girl with severe refractory hyperhidrosis of the axillae leading to social distress and bad posture was treated with botulinum toxin A injections into each axilla. At follow-up 3 months posttreatment, she was noted to have a significant improvement in symptoms, including improved posture and social functioning.38 Coutinho dos Santos and coworkers<sup>6</sup> conducted the largest case series to date that included a total of nine children or adolescents with palmar hyperhidrosis. All nine of the subjects that received botulinum type A injections demonstrated efficacy 1 month after one to four rounds of treatment. Although

botulinum toxin A has previously been used successfully and safely in the treatment of many other pediatric conditions (eg, cerebral palsy, torticollois, strabismus) randomized controlled trials in the treatment of primary pediatric hyperhidrosis are lacking, and more research is needed to definitively determine safety and efficacy.

#### **SURGICAL TREATMENT**

For patients with hyperhidrosis that is absolutely refractory to the less invasive treatments, surgical treatment may be a suitable option.

#### Liposuction

The least invasive of the surgical procedures includes liposuction of adipose tissue or curettage, which functions to remove the eccrine glands from the axillae, thus minimizing the sweat produced in that region over the long term. This procedure does not come without risks. Scarring, surgical site contractures, and infection have been noted; however, there is no risk for the compensatory sweating that can occur following more invasive surgical procedures, such as sympathectomy.<sup>39</sup>

#### **Ultrasound**

Another minimally invasive treatment of hyperhidrosis involves the use of the VASER System (Sound Surgical Technologies, Louisville, CO), which is a third-generation ultrasound system that has widely been used for body-contouring surgery. Treatment of the bilateral axillae takes approximately 1 hour and can be done as an outpatient with local anesthesia only. A prospective pilot-study published in 2009 investigated VASER efficacy in the treatment of 13 adult patients aged 25 to 52 years with significant axillary hyperhidrosis and/or bromidrosis that was refractory to other nonsurgical treatments. A significant reduction in sweat and odor and no recurrence of significant symptoms at 6 months was noted in 11 of 13 subjects who were treated. Two patients noted a decrease in sweat and odor, but the reduction was not as great as they had wished. Although no serious side effects were observed during this pilot study, three complications from the 26 axillae treated included one small seroma, one hyperpigmented area, and one blister (6 mm × 7 mm), all of which resolved spontaneously. Other potential side effects may include dysesthesia, transient or prolonged tissue swelling, bruising, infection, and hematoma formation.<sup>40</sup> Although this treatment option has not yet received FDA approval for the treatment of hyperhidrosis in

children or adults, it seems to show promise as an emerging safe and effective minimally invasive surgical option for the treatment of refractory axillary hyperhidrosis.

#### Thoracic Sympathectomy

More invasive procedures for the treatment of focal hyperhidrosis involve destruction of the sympathetic chain, which in turn prevents neurotransmission to the cholinergic fibers that signal the onset of sweating. This destruction has traditionally been done with a more invasive method termed thoracic sympathectomy, and more recently replaced with less invasive procedures termed video-assisted thoracoscopic sympathectomy or endoscopic thoracic sympathectomy (ETS) that use smaller incisions and modern imaging techniques. Thoracic sympathectomy for the treatment of hyperhidrosis was first performed in Europe in the 1920s. Access to the thorax required division of one or more major muscles of the chest wall along with rib separation, which had the potential to cause significant pain and bone fractures in addition to the complications that are also seen with ETS.39,41 This procedure is uncommonly performed in children today, having been widely replaced by more modern surgical techniques beginning as early as the 1940s.<sup>5,42</sup>

#### Video-Assisted Thoracoscopic Sympathectomy

Video-assisted thoracoscopic sympathectomy is now the most common technique used for the treatment of hyperhidrosis. After two to three incisions (typically no more than 1 cm) are made inferior to the axillae, the patient's lung is deflated, and a telescopic camera is introduced into the thoracic cavity. After the sympathetic chain is located, specific ganglia (ranging from T2 to T4) are destroyed that correlate with the areas of intended treatment effect (palmar vs axillary). Electrocautery and laser are commonly used for this destructive process. 43 Although the video-assisted procedures result in shorter recovery times, decrease postoperative pain, and minimize surgical site scarring, they are not without serious complications. Infection, compensatory sweating in surrounding areas, Horner syndrome, and several lung complications (eg, pneumothorax, hemothorax, atelectasis, subcutaneous emphysema) can occur. 39,41 Postsurgical compensatory hyperhidrosis ranging from mild to severe is common (>70%) and seems to better tolerated in children in turn leading to higher postoperative satisfaction according to at least one study. 44 Severe compensatory hyperhidrosis has been reported to be 40% in patients following ETS<sup>10</sup>; however, this risk can be lowered with a slightly different procedure called a sympathotomy, which interrupts the sympathetic signaling as opposed to destroying the ganglia.<sup>39,41</sup>

ETS has most commonly been used as an immediate and permanent treatment of primary palmar hyperhidrosis, although its use in the treatment of primary axillary hyperhidrosis shares those characteristics, with cure rates reportedly in the range of 96% for each location. Some patients have reported a decrease in plantar sweating following ETS even though this was not the intended target of the treatment. 10,30,31 This success has led some to suggest that early surgical treatment in children with severe primary palmar hyperhidrosis could avert the psychosocial and physical symptoms that are so disabling. 45

Several studies support the use of ETS for severe palmar hyperhidrosis in children. One report published in 1995 looked at a period of 14 months where 23 ETS operations were performed on children aged 9 to 17. Intraoperative time was 12 to 25 minutes and uneventful for all patients. Most patients (18 of 23) had no postoperative difficulties and were sent home on postoperative Day 1. One patient developed a pneumothorax, was treated appropriately, and returned home on postoperative Day 3. All patients were able to resume their daily school routine 3 to 5 days following the procedure. Complete postprocedure satisfaction was obtained in 90% of those treated in up to 13 months of follow-up. There were two subjects (9%) who complained of moderate compensatory hyperhidrosis. A larger retrospective study published 1 year later (1996) examined patients aged 5.5 to 18 that were treated with ETS from 1992 to 1995 for severe primary palmar hyperhidrosis. Immediate and permanent resolution of palmar hyperhidrosis was observed in 98% of patients. Postoperative complications occurred in only two patients who developed pneumothorax that required 24-hour intercostal drainage.<sup>45</sup>

Another retrospective study conducted in the United Kingdom analyzed data from a total of 44 children (median age, 12.8 years) who underwent video-assisted thorascopic sympathectomy (85 total procedures) for the treatment of palmar hyperhidrosis over a 21-year period. The procedures performed included bilateral T2-T3 sympathectomy in 87% (38 of 44), bilateral T2-T5 sympathectomy in 9% (4 of 44), and right-sided thoracoscopic (left-sided done open) in 1% (0.5 of 44). Video-assisted thorascopic sympathectomy was not possible in 3% (1.5 of 44) of cases. Postoperative hospital stay ranged from 1 to 5 days (median, 2) and follow-up time ranged from 0.2 to 4.7 years (median, 1.3 years). During the follow-up period, 21% (9 of 44) of those treated developed severe hyperhidrosis of other parts of body (eg, plantar, axillary, or whole body). Postoperative complications were seen in about one-half (21 of 44) of those treated, which included postoperative pain (requiring >2 days hospital stay) in 18% (8 of 44), Horner syndrome in 18% (8 of 44), and recalcitrant palmar hyperhidrosis in 11% (5 of 44) of cases. Some patients (5 of 44) chose to repeat the procedure. Overall, the success rate for thoracoscopic sympathetectomy was 93% (79 of 85).<sup>46</sup>

Based on these and many other studies, videoassisted thorascopic sympathectomy seems to be an immediate and permanent treatment of severe palmar hyperhidrosis in children and adolescents that carries a low rate of morbidity and minimal risk for mortality. Some studies, however, do not have long-term follow-up regarding satisfaction with the outcome of the surgery or the degree and impact of compensatory hyperhidrosis on the patient. The compensatory hyperhidrosis has been characterized, at times, as a worse entity than the original hyperhidrosis for the patient.

### CALCIUM-CHANNEL BLOCKERS, CLONIDINE, α-ADRENOCEPTOR ANTAGONISTS, BENZODIAZEPINE

Other medical treatments for hyperhidrosis have been tried with some success. Calcium-channel blockers, clonidine, and α-adrenoceptor antagonists have all been found to have efficacy in hyperhidrosis; however, these data are largely limited to isolated case reports and further research is needed to determine the appropriate role they should play in treating hyperhidrosis in children.<sup>28</sup> Another medical treatment involves benzodiazepine use for those patients whose hyperhidrosis is emotionally induced or anxiety driven. Physicians should be cautious when prescribing benzodiazepines in the pediatric population, however, because they can cause common side effects, such as dizziness, impaired coordination, and sedation, followed by dependency over the long term. 16,25

#### **SUMMARY**

Primary hyperhidrosis often affects the psychological and social development of children, impacting quality of life, and can lead to profound emotional and social distress. Quality of life can be significantly improved by early diagnosis and therapy; however, underdiagnosis and lack of knowledge regarding therapeutic options has traditionally hindered maximization of therapy in the pediatric population. The current therapeutic options for primary pediatric

hyperhidrosis, including topical and systemic therapies, iontophoresis, botulinum toxin injection, and surgical interventions, comprise an expanding knowledge regarding the management of hyperhidrosis in children and adolescents. Even though many different therapeutic options are available, further studies in the pediatric population are needed to help guide appropriate management.

#### **REFERENCES**

- Fealey RD, Hebert AA. Disorders of the eccrine sweat glands and sweating. In: Goldsmith LA, Katz SI, Gilchrest BA, et al, editors. Fitzpatrick's dermatology in general medicine. 8th edition. New York: McGraw Hill; 2012. p. 936–47. Chapter 84.
- Strutton DR, Kowalski JW, Glaser DA, et al. US prevalence of hyperhidrosis and impact on individuals with axillary hyperhidrosis: results from a national survey. J Am Acad Dermatol 2004;51:241–8.
- Hamm H, Naumann MK, Kowalski JW, et al. Primary focal hyperhidrosis: disease characteristics and functional impairment. Dermatology 2006;212: 343–53.
- Lear W, Kessler E, Solish N, et al. An epidemiological study of hyperhidrosis. Dermatol Surg 2007;33: S69–75.
- Paller A, Shah P, Silverio A, et al. Oral glycopyrrolate as second-line treatment for primary pediatric hyperhidrosis. J Am Acad Dermatol 2012;67(5): 918–23.
- Coutinho dos Santos LH, Gomes AM, Giraldi S, et al. Palmar hyperhidrosis: long-term follow-up of nine children and adolescents treated with botulinum toxin type A. Pediatr Dermatol 2009;26:439–44.
- Gelbard CM, Epstein H, Hebert A. Primary pediatric hyperhidrosis: a review of current treatment options. Pediatr Dermatol 2008;25:591–8.
- Walling HW. Primary hyperhidrosis increases the risk of cutaneous infection: a case-control study of 387 patients. J Am Acad Dermatol 2009;61:242–6.
- Bellet JS. Diagnosis and treatment of primary focal hyperhidrosis in children and adolescents. Semin Cutan Med Surg 2010;29:121–6.
- Cohen JL, Cohen G, Solish N. Diagnosis, impact, and management of focal hyperhidrosis: treatment review including botulinum toxin therapy. Facial Plast Surg Clin North Am 2007;15:17–30, v-vi.
- Kreyden O, Böni R, Burg G. Hyperhidrosis and botulinum toxin in dermatology. Basel (Switzerland): Karger; 2001.
- Shelley WB, Hurley HJ Jr. Studies on topical antiperspirant control of axillary hyperhidrosis. Acta Derm Venereol 1975;55:241–60.
- Scholes KT, Crow KD, Ellis JP, et al. Axillary hyperhidrosis treated with alcoholic solution of aluminium chloride hexahydrate. Br Med J 1978;2:84–5.

- Goh CL. Aluminum chloride hexahydrate versus palmar hyperhidrosis. Evaporimeter assessment. Int J Dermatol 1990;29:368–70.
- Benohanian A, Dansereau A, Bolduc C, et al. Localized hyperhidrosis treated with aluminum chloride in a salicylic acid gel base. Int J Dermatol 1998;37: 701–3.
- Connolly M, de Berker D. Management of primary hyperhidrosis: a summary of the different treatment modalities. Am J Clin Dermatol 2003;4:681–97.
- Stern LM. Preliminary study of glycopyrrolate in the management of drooling. J Paediatr Child Health 1997;33:52–4.
- Blasco PA, Stansbury JC. Glycopyrrolate treatment of chronic drooling. Arch Pediatr Adolesc Med 1996;150:932–5.
- Mijnhout GS, Kloosterman H, Simsek S, et al. Oxybutynin: dry days for patients with hyperhidrosis. Neth J Med 2006;64:326–8.
- Matsui M, Yamada S, Oki T, et al. Functional analysis of muscarinic acetylcholine receptors using knockout mice. Life Sci 2004;75:2971–81.
- Bajaj V, Langtry JA. Use of oral glycopyrronium bromide in hyperhidrosis. Br J Dermatol 2007;157: 118–21
- 22. Seukeran DC, Highet AS. The use of topical glycopyrrolate in the treatment of hyperhidrosis. Clin Exp Dermatol 1998;23:204–5.
- 23. Luh JY, Blackwell TA. Craniofacial hyperhidrosis successfully treated with topical glycopyrrolate. South Med J 2002;95:756–8.
- Shaw JE, Abbott CA, Tindle K, et al. A randomised controlled trial of topical glycopyrrolate, the first specific treatment for diabetic gustatory sweating. Diabetologia 1997;40:299–301.
- 25. Haider A, Solish N. Focal hyperhidrosis: diagnosis and management. CMAJ 2005;172:69–75.
- Kumar M, Foreman R, Berk D, et al. Oral glycopyrrolate for refractory pediatric and adolescent hyperhidrosis. Pediatr Dermatol 2014;31:e28–30.
- Diaz L, Bicknel L, McNiece K, et al. Poster presentation. Society for Pediatric Dermatology Poster Presentation. Milwaukee (WI), July 11-14, 2013.
- 28. Eisenach JH, Atkinson JL, Fealey RD. Hyperhidrosis: evolving therapies for a well-established phenomenon. Mayo Clin Proc 2005;80:657–66.
- 29. Dolianitis C, Scarff CE, Kelly J, et al. Iontophoresis with glycopyrrolate for the treatment of palmoplantar hyperhidrosis. Australas J Dermatol 2004;45: 208–12.
- Karakoc Y, Aydemir EH, Kalkan MT, et al. Safe control of palmoplantar hyperhidrosis with direct electrical current. Int J Dermatol 2002;41:602–5.
- 31. Jeganathan R, Jordan S, Jones M, et al. Bilateral thoracoscopic sympathectomy: results and long-

- term follow-up. Interact Cardiovasc Thorac Surg 2008;7:67-70.
- Baumann LS, Halem ML. Botulinum toxin-B and the management of hyperhidrosis. Clin Dermatol 2004; 22:60–5.
- Reisfeld R, Berliner KI. Evidence-based review of the nonsurgical management of hyperhidrosis. Thorac Surg Clin 2008;18:157–66.
- Vazquez-Lopez ME, Pego-Reigosa R. Palmar hyperhidrosis in a 13-year-old boy: treatment with botulinum toxin A. Clin Pediatr (Phila) 2005;44:549–51.
- 35. Lowe NJ, Glaser DA, Eadie N, et al. Botulinum toxin type A in the treatment of primary axillary hyperhidrosis: a 52-week multicenter double-blind, randomized, placebo-controlled study of efficacy and safety. J Am Acad Dermatol 2007;56:604–11.
- 36. Glaser DA, Coleman WP, Loss R, et al. 4-Year longitudinal data on the efficacy and safety of repeated botulinum toxin type A therapy for primary axillary hyperhidrosis. Presented at the 65th American Academy of Dermatology Conference 2007. Washington, DC, February 1–5, 2007.
- Bhakta BB, Roussounnis SH. Treating childhood hyperhidrosis with botulinum toxin type A. Arch Dis Child 2002;86:68.
- Farrugia MK, Nicholls EA. Intradermal botulinum A toxin injection for axillary hyperhydrosis. J Pediatr Surg 2005;40:1668–9, 414.
- Ram R, Lowe NJ, Yamauchi PS. Current and emerging therapeutic modalities for hyperhidrosis, part 2: moderately invasive and invasive procedures. Cutis 2007;79:281–8.
- Commons G, Lim A. Treatment of axillary hyperhidrosis/bromidrosis using VASER ultrasound. Aesthetic Plast Surg 2009;33(3):312–23.
- 41. Moya J, Ramos R, Morera R, et al. Thoracic sympathicolysis for primary hyperhidrosis: a review of 918 procedures. Surg Endosc 2006;20:598–602.
- 42. Kestenholz PB, Weder W. Thoracic sympathectomy. Curr Probl Dermatol 2002;30:64–76.
- Cohen Z, Shinar D, Levi I, et al. Thoracoscopic upper thoracic sympathectomy for primary palmar hyperhidrosis in children and adolescents. J Pediatr Surg 1995;30:471–3.
- 44. Steiner Z, Cohen Z, Kleiner O, et al. Do children tolerate thoracoscopic sympathectomy better than adults? Pediatr Surg Int 2007;24:343–7.
- Cohen Z, Shinhar D, Mordechai J, et al. Thoracoscopic upper thoracic sympathectomy for primary palmar hyperhidrosis. Harefuah 1996;131: 303-5.
- Sinha C, Kiely E. Thoracoscopic sympathectomy for palmar hyperhidrosis in children: 21 years of experience at a tertiary care center. Eur J Pediatr Surg 2013;23:486–9.