9 Management of Hyperhidrosis

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Introduction

Hyperhidrosis is characterized by sweating in excess of the physiologic amount necessary to maintain thermal homeostasis. For those affected, this condition is extremely debilitating with significant impairment in activities of daily living, social interaction, and occupational activities. Hyperhidrosis is divided into primary or idiopathic hyperhidrosis and secondary due to a variety of causes. This classification is further categorized as generalized or focal with respect to its clinical presentation. Primary or idiopathic hyperhidrosis is usually focal and limited to the axillae, palms and soles, and face. Secondary hyperhidrosis can be focal or generalized, affecting the entire body. The focus of this chapter is on the diagnosis and management of hyperhidrosis, with a focus on primary focal idiopathic hyperhidrosis. With a reported prevalence of 2.8% of the population, and associated significant psychosocial morbidity, it is imperative that physicians recognize this disease entity and understand the various treatment modalities that are available. Treatment strategies for hyperhidrosis include topical, oral, surgical, and nonsurgical treatments. These treatment modalities differ with respect to their therapeutic efficacy, duration of effect, side effects, as well as cost of therapy.

Problem being treated

A standard definition of excessive sweating has not yet been established. Quantification of sweat production in studies has ranged from normal being defined as less than 1 mL/m^2/min to the production of less than 100 mg of sweat in one axilla within 5 min, or less than 50 mg within 1 min. The fundamental criticism of these measurement parameters is the fact that they fail to take into account surface area. As a consequence, smaller people may end up falling below this quantitative definition, despite excessive and debilitating sweating. For practical purposes,any degree of sweating that interferes with activities of daily living can be viewed as hyperhidrosis.

Clinical presentation

Symptoms of excessive sweating generally begin in adolescence but may present even earlier. In a study of Taiwanese patients with palmar hyperhidrosis, 75% had a childhood onset, with the rest presenting in puberty. A recent survey of a nationally representative sample of 150 000 households in the USA revealed an average age of onset of 25. The average age of onset for axillary hyperhidrosis was 19 years, and 13 years for palmar hyperhidrosis. In some patients, sweat production can be as high as 40 times the normal rate of 1 mL/m^2/min, as defined in one study. Patients generally present with sweating of one or more anatomic regions such as axillae, palms, soles, or face. The US survey revealed that 51% of patients with hyperhidrosis had axillary involvement alone or in combination with another site, and 9.5% reported axillary involvement alone. Palmar hyperhidrosis alone or in combination with another site was reported in 24% of patients, and only 1% reported palmar hyperhidrosis alone. Plantar hyperhidrosis alone or in combination with another site was reported in 30% of patients. Facial hyperhidrosis was reported in 10% of patients.

Because there is no well established definition of hyperhidrosis, it is reasonable to diagnose this condition in people who report excessive sweating that interferes with activities of daily living. A high index of suspicion is critical to diagnose this condition, as a significant proportion of patients do not realize that they have a medical issue or feel too embarrassed to seek help. Canadian data reported that 75% of men and 64% of women with hyperhidrosis had not consulted their physician about the condition.

An essential component of the clinical assessment of patients with hyperhidrosis is the realization of the significant impact of this condition on the quality of life of patients. A recent survey in the USA reported that 34–47% of patients felt that their sweating had a moderate to severe effect on limitations at work, meeting people, and in romantic or intimate situations. This study also reported that 32% of patients with axillary hyperhidrosis indicated that their sweating is barely tolerable or intolerable, and frequently or always interferes with their daily activities. A reported 35% of patients decreased the amount of time spent in leisure activities. Over 50% of patients with axillary hyperhidrosis in the US survey reported feeling less confident, 34% reported feeling unhappy, 38% reported feeling frustrated with daily activities, and 20% reported feeling depressed.

Hyperhidrosis has a profound impact on social interactions and work-related acitivites. Routine social interactions such as holding hands, shaking hands, or hugging become awkward. Patients report a sense of humiliation and embarrassment associated with soaked or stained clothing as well as perceived odours. Palmar hyperhidrosis can dramatically affect occupational and social activities. Patients report difficulty with holding tools, drawing or writing, and often paper ends up being stained with sweat or smeared ink. Occupations involving contact with paper, metal or electrical equipment were noted in a study to be unattainable for patients with palmar hyperhidrosis. Patients with axillary hyperhidrosis treated with botulinum toxin (BTX) in a large multicenter study were assessed using the Hyperhidrosis Impact Questionnaire. A total of 71% of patients reported being less confident than they would like to be, 49% were unhappy or depressed, 30% were frustrated with daily activities, 25% missed social gatherings with loved ones, 32% felt at least moderately limited with regard to sexual activities, and 81% felt limited with respect to meeting people for the first time. As one would expect, a great deal of time is invested in coping with this problem, with resulting negative consequences both socially and economically.

Pathophysiology of hyperhidrosis

There are approximately 2–4 million sweat glands distributed throughout the skin. The majority, approximately 3 million, are eccrine glands. The remaining are apocrine and apo-eccrine glands. Eccrine glands, responsible for focal hyperhidrosis, are distributed over almost the entire body surface area, with the most numerous being on the soles of the feet and the forehead, followed by the palms and cheek. The main role of the eccrine glands is a thermoregulatory function, which is also affected by emotional and gustatory stimuli. Histologically, eccrine glands are composed of a secretory coil in the deep dermis and superficial fat, a duct that traverses the dermis and an intraepidermal pore that passes between keratinocytes and opens to the skin surface. Of note is that histological studies have revealed no increase in the number or size of eccrine glands in patients who have hyperhidrosis. The eccrine glands are innervated by sympathetic nerve fibers. These fibers originate in the hypothalamus and descend through the ipsilateral brain stem, forming a synapse with the intermediolateral cell nucleus of the spinal cord. The final innervation of the eccrine sweat glands is with unmyelinated postganglionic sympathetic nerve fibers. The primary neurotransmitter released at the periglandular nerve endings is acetylcholine. Periglandular nerve endings also contain catecholamines and neuropeptides; however, their exact role in sweat production is yet to be defined. In light of normal eccrine gland histology in hyperhidrosis, it is believed that hyperhidrosis is due to sympathetic overactivity. Hyperhidrosis may result from a dysfunction of the central sympathetic nervous system that affects the hypothalamic nuclei, prefrontal areas, or their cholinergic connections downstream. The neurogenic overactivity in focal hyperhidrosis may be the result of hyperexcitability of these reflex circuits that are involved in eccrine secretion. There is likely a heritable component to this neurogenic overactivity, as 30–50% of patients have a positive family history.

Apocrine glands are primarily confined to the axillae and urogenital regions. The ratio of apocrine to eccrine sweat glands has been reported as 1 : 1 in the axilla and 1 : 10 in other areas. There are also mixed apo-eccrine glands which develop from eccrine-like precursor glands during puberty. The exact roles of apocrine and apo-eccrine glands in hyperhidrosis remains unclear, although in some patients with hyperhidrosis up to 45% of the axillary sweat glands are apo-eccrine glands.

Etiology

Hyperhidrosis is classified as primary or secondary. The clinical presentation is classified as focal or

generalized. Primary hyperhidrosis is considered idiopathic and generally presents as focal hyperhidrosis. Focal hyperhidrosis is localized to specific body areas such as the axillae, palms, feet, or face. Secondary hyperhidrosis is most commonly generalized (involves the entire body); however, it can present in a localized, focal pattern. Secondary hyperhidrosis, as the name implies, is due to a variety of secondary causes (Table 9.1) These secondary causes may include underlying medical conditions, drugs, or exaggerated physiological responses to heat, humidity, or exercise.

It is beyond the scope of this chapter comprehensively to review all the causes of secondary hyperhidrosis; however, we mention certain conditions that should be kept in mind as one evaluates a patient. Secondary generalized hyperhidrosis is seen with various medical conditions such as endocrine disorders including thyrotoxicosis, diabetes mellitus, hyperpituitarism, pheochromocytoma, acute and chronic infections, malignancies, and conditions associated with a high sympathetic discharge such as cardiovascular shock, respiratory failure, and alcohol or drug withdrawal. Secondary hyperhidrosis can also present as focal or localized hyperhidrosis. Secondary hyperhidrosis in a focal presentation is most commonly related to neurological injury. Acute spinal cord injury with or without autonomic dysreflexia can present with focal hyperhidrosis of the face or upper trunk, seen months to years after the injury. Post-traumatic syringomyelia following spinal cord injury may also cause focal hyperhidrosis. Cerebrovascular accidents involving hemispheric or medullary infarcts can lead to focal hyperhidrosis on the ipsilateral or contralateral sides, respectively. Other causes of secondary focal hyperhidrosis include

Etiology of Hyperhidrosis	
Generalized hyperhidrosis	**Focal hyperhidrosis**
Neurologic Parkinson's disease Spinal cord injury Cerebrovascular accident	Primary idiopathic Axillary Palmar Plantar Facial
Endocrine Hyperthyroidism Hyperpittutiarism Diabetes mellitus Menopause Pregnancy Pheochromocytoma Carcinoid syndrome Acromegaly	Gustatory sweating (Frey's syndrome) Associated with neuropathies Secondary to spinal disease/injury
Infectious	
Cardiovascular Shock Heart failure	
Respiratory failure	
Drugs	
Toxic Alcoholism Substance abuse	
Malignancies Myeloproliferative disorders Hodgkin's disease	

Table 9.1 Etiology of Hyperhidrosis

injury to the sympathetic chain due to accessory cervical ribs or an intrathoracic tumor impinging on the sympathetic chain. Frey's syndrome or facial gustatory sweating is also a form of secondary focal hyperhidrosis, due to parotid surgery or trauma. Frey's syndrome is believed to be the result of transection of the postganglionic sympathetic nerve fibers from the otic ganglion that were originally directed to the parotid gland. Following this transection, an aberrant reinnervation of the facial cholinergic sweat glands accounts for the excessive sweating. An awareness of these conditions is helpful in the initial evaluation of a patient with hyperhidrosis. Overall, the most common type of hyperhidrosis remains primary (idiopathic) focal hyperhidrosis, presenting in the axillae, palms, feet, or face.

Patient selection

A recent survey of 150 000 households in the USA revealed that 2.8% of the population or 7.8 million people reported having unusual or excessive sweating. Of those with hyperhidrosis, 62% did not consult a physician for evaluation of their condition. For those with primary focal axillary hyperhidrosis, the numbers are even higher as 61% of women and 73% of men did not consult a physician. Of the 7.8 million people with hyperhidrosis, 2.4 million indicated that their sweating was barely tolerable and frequently interfered with activities of daily living. The prevalence was highest among individuals aged 25–64. No gender differences were noted in prevalence. The average age of onset was 25 years. The average age of onset for axillary hyperhidrosis was 19 years, and 13 years for those with palmar hyperhidrosis. Of note is the fact that other studies have revealed that primary focal hyperhidrosis generally has an onset during childhood or adolescence. A study of 850 patients with axillary, palmar or facial hyperhidrosis revealed that 62% of patients had their symptoms for as long as they could remember, with 33% describing an onset in puberty and 5% with an adult onset. In light of these findings, it would appear that hyperhidrosis is a disease of childhood which appears to peak in early adulthood. Neonatal cases have been described but are not as common. Therefore the early identification and proper management of this debilitating condition is essential to prevent long-term psychosocial morbidity. There is a reported positive family history in 30–50% of patients.

Diagnostic and Treatment Approach

The most common type of hyperhidrosis is primary focal (idiopathic) hyperhidrosis; however, it is critical when evaluating a patient that one is aware of the secondary causes. A thorough history and focused exam will allow one to differentiate primary from secondary hyperhidrosis.

The multispecialty working group on recognition, diagnosis, and treatment of primary focal hyperhidrosis has defined primary focal (idiopathic) hyperhidrosis as focal visible, excessive sweating of at least 6 months' duration without apparent cause with at least two of the following characteristics:

- bilateral and relatively symmetrical
- impairs daily activities
- frequency of at least one episode per week
- age of onset less than 25 years
- positive family history
- cessation of focal sweating during sleep.

Hyperhidrosis associated with symptoms such as fever, night sweats, weight loss, lymphadenopathy, headache or palpitations should alert the physician to evaluate the patient further for possible secondary causes. Therefore, a history focussing on location of excessive sweating, duration of the presentation, associated symptoms or co-morbidities, family history, age of onset, and any specific triggers allows one to differentiate primary from secondary hyperhidrosis.

Once a diagnosis of primary (idiopathic) focal hyperhidrosis is established, the extent of hyperhidrosis can be measured either gravimetrically, as the rate of sweat production (expressed in mg/min), by the iodine starch test, or the ninhydrin test. Gravimetry utilizes a filter paper which is weighed before and after contact with the affected area. Patients are instructed to rest for at least 15 minutes at a room temperature of 21–25 degrees Celsius, before the filter paper is applied to the affected area for 60 seconds and then weighed again. The rate of sweat production in milligrams per minute is then calculated. By gravimetry, axillary hyperhidrosis is defined as > 100 mg/5 min in men and > 50 mg/5 min in women. Palmar hyperhidrosis is defined as > 30–40 mg/min. The starch iodine test is based on the reaction of starch and iodine in the presence of sweat. The area to be tested is dried and iodine solution (1–5%) is applied and after a few seconds starch is sprinkled over this area. The starch and iodine interact in the presence of sweat to develop a

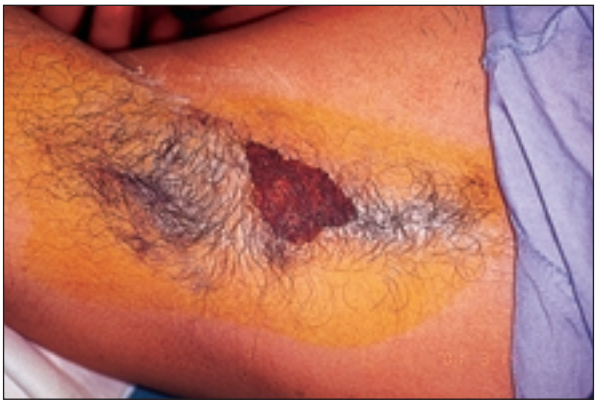

Fig. 9.1 Starch iodine of axillary hyperhidrosis.

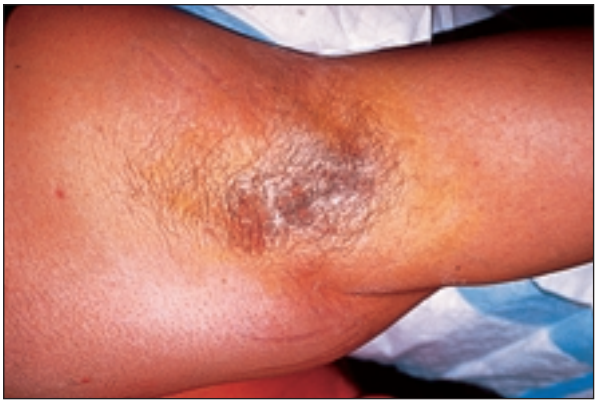

Fig. 9.2 Starch iodine of axilla 2 weeks after treatment with BTX-A.

purplish color. This purple area identifies the orifice of the sweat gland. This test allows the qualitative identification of areas of excessive sweating which can be recorded by pictures taken before and after treatment. In order to obtain good results, the authors recommend thorough drying of the area before applying the iodine solution and allowing it to dry for a few seconds before applying the starch. Simple cornstarch can be used and should be applied through a fine dispenser and lightly dusted on the area. This usually will give the most accurate results (Fig. 9.1). Under procedure, the minor starch iodine test is usually photographed before and after treatment in order to demonstrate the objective evidence of improvement. This test will also increase the accuracy of the injection technique (Fig. 9.2).

Finally, the Ninhydrin test is based on the principal that ninhydrin reacts with amino acids in sweat and the resulting impression is visualized using digital analysis of the image produced on paper. This allows quantification of sweat production.

Treatment techniques and strategies

Treatment of hyperhidrosis can be divided into topical, oral, surgical, and nonsurgical treatments. Each of these therapeutic interventions is different with respect to the indications for its use, therapeutic efficacy, duration of action, side effects, and cost of therapy. Treatment of hyperhidrosis needs to be individualized depending on the clinical presentation and a discussion with the patient as to their preferences is critical to ensure reasonable expectations while avoiding unnecessary frustration.

Topical treatments

Topical treatments for hyperhidrosis are characterized by short-term duration of action, with efficacy limited to mild cases of focal hyperhidrosis. Although there are over 90 different compounds available, aluminum chloride hexahydrate is considered the most effective topical agent. Aluminum chloride is available as a 20–25% solution in water or ethanol. The mechanism of action involves a mechanical obstruction of the eccrine sweat gland pore. Long-term use of aluminum chloride products is associated with histological changes such as atrophy of the secretory cells. Prior to application, the skin is dried to avoid irritation, which appears to be the main limiting side effect of this product. The main indication for aluminum chloride is for focal axillary hyperhidrosis; however, it also appears to have short-term efficacy in palmar hyperhidrosis. Other topical products include glycopyrrolate, a topical anticholinergic product available as topical pads for mild cases of hyperhidrosis.

Other topical agents used for focal hyperhidrosis have included glutaraldehyde 10% and formaldehyde; however, the utility of these products is limited due to an enhanced potential for skin irritation and allergic skin sensitization.

Systemic treatments

Systemic anticholinergic treatments are the primary oral agents available for treatment of hyperhidrosis. The main concern with these agents is the fact that, at doses that may reduce hyperhidrosis, the side effects (including dry mouth, blurred vision,

constipation, urinary retention, and palpitations) are generally not tolerable. Oral glycopyrrolate at doses of 1 mg two or three times a day is a reasonable initial starting regimen. Other anticholinergic agents have included Amitriptyline.

Benodiazepines such as clonazepam have been reported in cases with a significant emotional component; however, their use has been limited due to the potential for sedation. Other oral agents that have been tried include diltiazem, clonidine, and nonsteroidal anti-inflammatory drugs; however, their efficacy to date has largely been confined to isolated case reports.

Overall, the exact role for oral treatments has not yet been clearly defined in hyperhidrosis. Larger case series or randomized controlled data are needed to determine the true efficacy and role of these agents.

Iontophoresis

Iontophoresis is defined as the introduction of an ionized substance (usually tap water) through intact skin by means of an electrical current. Alternatives to tap water include anticholinergics such as glycopyrrolate or atropine sulphate. This method of treatment is mainly indicated for palmar and plantar hyperhidrosis. The mechanism of action appears to be distal duct blockage. Iontophoresis has several advantages as a means of treatment as there is no systemic use of drugs and patients can utilize this treatment at home. The main disadvantages include the one-off cost, which can range from US$ 600 to 1000 and the time-consuming frequency of treatments (can be several times a week for 30–40 minutes). Iontophoresis has an efficacy of up to 90% in palmar and plantar hyperhidrosis with multiple treatments. This treatment is generally well tolerated with the potential for mild irritation and dryness. A randomized, controlled double-blind study of iontophoresis in 11 patients with palmar hyperhidrosis and sham treatment of the other hand reported a 38% reduction in sweat production by gravimetry with 10 initial treatments at 4 mA. Maintenance treatments over a 3-month period at 10 mA resulted in an 81% reduction in sweat production.

Iontophoresis is a safe and effective treatment for palmar and plantar hyperhidrosis. The frequency of treatment is generally three to four times a week for approximately 30 minutes. Efficacy has been reported in the range of 80–90% within 3 months; however, long-term maintenance therapy is generally required. The main contraindications for this treatment modality include a pacemaker, orthopedic prosthesis, heart arrhythmias, and pregnancy. Iontophoresis is indicated as a second-line treatment for palmar or plantar hyperhidrosis following topical treatments.

Surgical treatments

Surgical treatments for hyerhidrosis include excision of the axillary vault to remove eccrine glands, curettage or liposuction to remove glandular tissue and, finally, sympathectomy. Appropriate patient selection and detailed patient information is critical in light of the associated postoperative morbidity and complications. Surgical treatment options are generally reserved for patients who fail to respond to all other therapeutic modalities.

Excision of the axillary vault to remove eccrine glands is reported to have an efficacy in the range of 50–90%. Various surgical techniques have been described; however, there are no randomized, controlled trials evaluating this method of treatment. Excision of the axillary vault can be complicated by infection, bleeding, delayed healing, flap necrosis, and significant scarring. Subcutaneous curettage of the axillae was attempted to decrease the postoperative morbidity associated with excisional techniques. Curettage of the axilla is done using a small incision, with a goal to destroy eccrine glandular tissue. Results with this procedure have been mixed as reported attempts at duplicating the initial results have been disappointing, with high relapse rates and poor patient satisfaction. Axillary liposuction has also been advocated in an attempt to destroy and remove glandular tissue, with acceptable efficacy and fewer side effects than traditional techniques. Liposuction tends to cause minimal scarring compared to excision and has a lower risk of bleeding. With all these surgical axillary techniques, the potential for scarring that may subsequently restrict superior arm rotation is present.

Endoscopic thoracic sympathectomy (ETS) destroys the sympathetic ganglia by excision, ablation or clipping. ETS has been performed most frequently for palmar hyperhidrosis and success rates are reported as high as 98%. Several studies validate the efficacy of ETS in palmar and axillary hyperhidrosis. Of note, however, is that long-term

outcome studies have reported that patient satisfaction declined over time, with 67% of patients being completely satisfied and 27% partially satisfied after a mean follow-up of 16 years. The main complications with sympathectomy include compensatory sweating, phantom sweating, gustatory sweating, Horner syndrome, and neuralgia. Compensatory sweating in other regions can occur in up to 90% of patients undergoing this procedure. The compensatory sweating is generally mild but has been reported to be severe in up to 40% of patients. Patients in this category generally prefer their premorbid condition over the compensatory hyperhidrosis. Recurrence rates following ETS have been reported in up to 2% of patients and immediate postsympathectomy failure rates are in the range of 0–2%. Failure rates have been attributed to a failure to ablate or resect the second thoracic ganglion; however, recent literature has also shown that preservation of this second thoracic ganglion may lead to a reduction in the incidence of compensatory sweating. Because compensatory sweating is usually irreversible and can be severely debilitating to patients, this necessitates explicit and detailed counselling of patients prior to undertaking this surgical procedure. Newer techniques include the use of clips instead of complete transsection of the nerve but reversal is not always possible as nerve destruction can be quick and compensatory disease may not be immediate. At present, the role for ETS appears to be in patients with palmar or axillary hyperhidrosis who have failed all other therapeutic modalities, including BTX.

BTX treatment

Multiple studies have validated the efficacy of BTX for the treatment of hyperhidrosis. Intradermal injections are clearly safe and well-tolerated and represent a viable alternative in the treatment of hyperhidrosis. BTX is produced by the anaerobic bacterium *Clostridium botulinum*. Seven different botulinum neurotoxins have been identified; however, BTX- appears to be the most potent and is currently available as two commercial preparations (Botox and Dysport). One unit of Botox is estimated to be equal to 3–4 units of Dysport. The mechanism of action of BTX involves the inhibition of acetylcholine release at the neuromuscular junction and in cholinergic autonomic neurons. BTX injection results in a localized, prolonged, yet reversible, decrease in cholinergic transmission. BTX-B (Myobloc) has also been used in a few studies for the treatment of hyperhidrosis. It seems to have a faster onset of action and greater diffusion. A higher incidence of local and systemic side effects have limited its use in the treatment of hyperhidrosis.

BTX for axillary hyperhidrosis

BTX for the treatment of axillary hyperhidrosis has been evaluated by two large randomized, controlled clinical trials in 465 patients. One trial in 145 patients with axillary hyperhidrosis unresponsive to topical therapy, defined as a rate of sweat production greater than 50 mg/min were randomized to BTX-A 200 units (Dysport) or placebo. After a 2-week period, the treatments were revealed and the axilla treated with placebo was injected with 100 units of BTX. Overall, there was an 81.4% decrease in sweat production with 200 units and a 76.5% decrease with 100 units; however, follow-up measurements of the rates of sweat production showed no advantage with the higher dosage. Sixty-three percent of patients reported being completely satisfied, 29% reported being satisfied, and 8% reported being partially satisfied. Of note is the fact that 98% of patients stated they would recommend this treatment to others. BTX-A (Botox) was evaluated in another randomized, controlled study with 320 axillary hyperhidrosis patients. Patients were treated with either 50 units of BTX-A or placebo in each axilla. Treatment assessments were done at baseline and 16 weeks' post-treatment. Overall, the trial reported an 89% response rate at 1 week and a 93% response rate throughout the rest of the study period. During the post-treatment period dramatic and statistically significant improvements were noted in the treatment group with respect to various quality of life measures such as emotional status, ability to participate in daily and social activities, productivity at work, and number of clothing changes per day. Pain associated with these intradermal injections is reported to be minimal but a topical anesthetic can be used to further minimize the discomfort. Several smaller noncontrolled studies have also validated the above results in patients with axillary hyperhidrois. BTX-A is a safe, well-tolerated, and highly efficacious treatment for axillary hyperhidrosis in patients who have failed to respond to topical therapy. The mean duration of effect is 6–7 months.

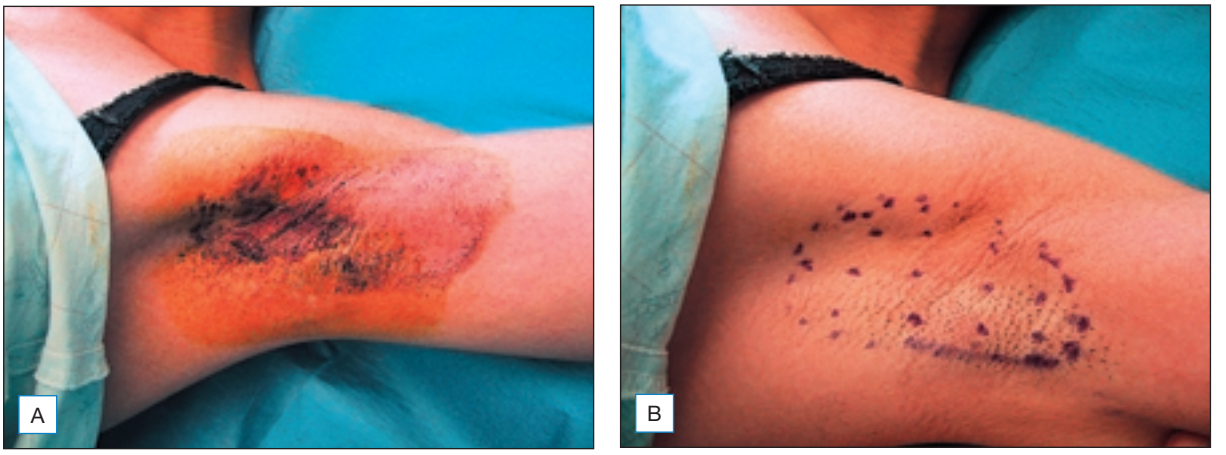

Fig. 9.3 (**A**) Starch iodine of axilla premarking. (**B**) Marking of affected area and sites of injection.

Injection procedure

As noted above, specific studies on BTX-A for axillary hyperhidrosis have used different preparations (Botox or Dysport), different dosages, and different dilution techniques. Botox should be diluted with preserved normal saline (containing benzyl alcohol) in order to decrease the pain on injection. Different dilutions have been suggested for use in hyperhidrosis; however, a range of 2.5–5.0 cc is commonly used for every 100 units or vial of Botox. Dosages for injection range from 50 to 200 units/axilla. The usual starting dose is 50 units/axilla. It seems that the dose may have more to do with the distribution of drug in the given area of disease rather than the degree of disease severity. Larger surface areas of involvement may require more drug. A starch iodine test should be done to properly delineate the affected area. This will increase the accuracy of injection and results. As mentioned earlier, the area should be thoroughly dried and iodine solution (1–5%) should be evenly spread over the entire vault. Starch should then be sprinkled lightly over the area and the area of purple–black discoloration marked. This area can be further delineated with a surgical pen if needed. A digital picture can be helpful for future injections and monitoring efficacy.

After the area requiring treatment has been delineated (Fig. 9.3A), the drug is injected intradermally using a half-inch 30-gauge needle. This should be administered in a grid-like pattern in order to cover the entire area of involvement. Spacing should be approximately 1–2 cm apart (Fig. 9.3B). Some will mark injection sites to ensure the drug is distributed evenly throughout the treatment area. To minimize discomfort, topical anesthetics may be used ahead of time but may alter the effectiveness of the starch iodine test. It is also recommended to change the needle if it becomes dull. Side effects include rare bruising and minimal discomfort.

BTX for palmar hyperhidrosis

Two randomized, double-blind studies have evaluated the efficacy of BTX-A in palmar hyperhidrosis. A total of 30 patients were treated, with an overall response rate of greater than 90%. One study was with Dysport 120 mU diluted with 0.5 mL of 0.9% sterile saline and injected subcutaneously into one palm. Another bilateral paired second study used Botox 100 units diluted with 1.5 mL of 0.9% sterile saline, injected intradermally into each palm. The main side effects were pain at the site of injection and transient minor weakness of intrinsic hand muscles lasting 2–5 weeks with the Dysport but not with the Botox study. Other studies have reported a minor weakness of finger grip in two-thirds of patients. Patients have reported resolution of the reduced grip strength in days to weeks. Other noncontrolled trials have validated the high efficacy rate and safety of BTX-A in palmar hyperhidrosis. The duration of effect generally exceeded the length of the trials and is reported to be an average of 4–6 months.

Techniques and dosages of BTX-A differ among the studies for palmar hyperhidrosis as well. Intradermal injections spaced approximately 1–2 cm apart appear to give the best results (Fig. 9.4). It

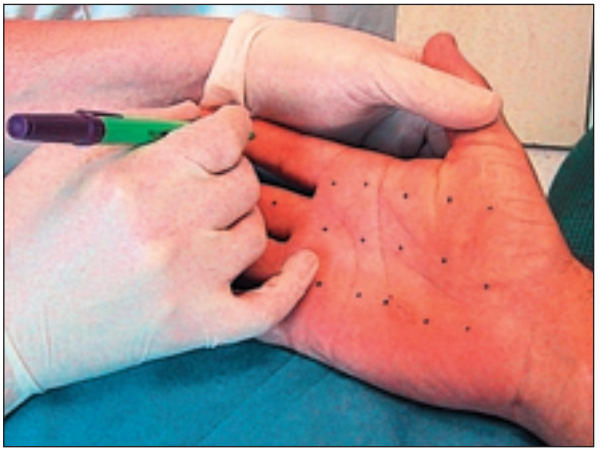

Fig. 9.4 Markings of injection sites for palmar injections.

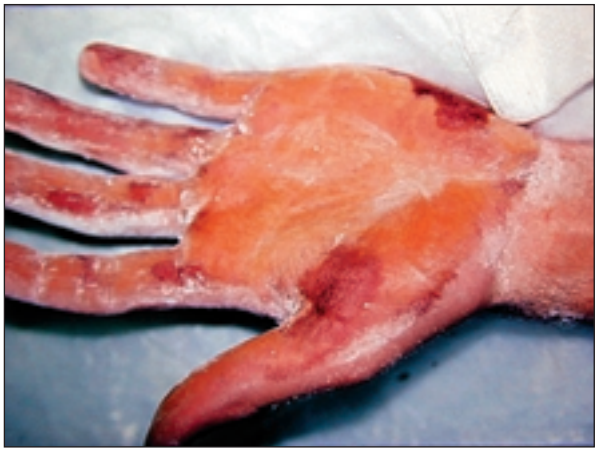

Fig. 9.5 Starch iodine of hand 2 weeks after treatment with BTX-A.

seems to be more efficacious to treat palm size, adjusting for dose and number of injections based on surface area of involvement, rather than having a standard number of injection sites. A starch iodine test may not be required when injecting the palms when the entire surface area is involved. In the opinion of the authors, 100 units of Botox are enough for either palm but up to 200 units may be required for larger extremities. Spacing should be 2 cm apart and approximately 2 units of Botox are injected per site as required. Smaller syringes facilitate administration of the drug into this thick dermis. The use of a 50- or 100-unit insulin syringe with an ultrafine needle allows for easier injection and less spillage or reverse flow of the BTX out of the dermis. BTX-A injections for palmar hyperhidrosis represent a highly efficacious treatment alternative in patients who have failed to respond to topical therapies or iontophoresis (Fig. 9.5). The main limitation of this treatment method is the fact that most patients find the injections quite painful and therefore require regional nerve blocks. Side effects include bruising, mild discomfort and, rarely, temporary weakness of intrinsic hand muscles.

Regional anesthesia is achieved by a median, ulnar, and radial nerve block at the level of the wrist. The median nerve is located medial to the flexor carpi radialis tendon and just below the palmaris longus tendon at the level of the wrist crease. A skin wheal is raised at this site to block the palmar cutaneous branch of the median nerve. The needle is subsequently placed between the tendons. A total of 3–5 mL of local anesthetic (1% lidocaine) is injected approximately 0.5 cm below the surface. The ulnar nerve is located radial to the flexor carpi ulnaris. To block this nerve, the needle is inserted medial to the tendon, directing the needle towards the ulnar styloid. The superficial branch of the radial nerve can also be anesthetized by placing local anesthetic subcutaneously lateral to the radial artery as it extends towards the dorsum of the wrist or simply within the anatomic snuff box. It is very important that if any pain is felt in the distribution of the nerves when passing the needle into the wrist or upon injection of the anesthetic, it must be assumed that the needle has entered the nerve. The needle must be withdrawn and redirected to avoid neural damage. Patients should be warned that they cannot drive until the anesthesia has resolved.

The Bier block, which involves the insertion of a venous catheter into a distal vein, and application of a tourniquet followed by the injection of an anesthetic into the vein has been demonstrated to be superior to regional block anesthesia for plantar hyperhidrosis. This technique is reported to provide excellent pain control for palmar hyperhidrosis as well. This procedure usually requires the expertise of an anesthesiologist.

Recent reports of high intensity vibration in the areas of injection have significantly reduced injection pain. These devices held against the palms during injections are reasonably effective in minimizing pain.

BTX for plantar hyperhidrosis

There are currently no randomized, controlled trials evaluating BTX-A in plantar hyperhidrosis. Small case series and reports have demonstrated efficacy

and improvement with dosages similar to those used in palmar studies, with a duration of effect between 4 and 6 months. Regional nerve block is generally required for anesthesia and involves the posterior tibial and sural nerves. A sural nerve block is achieved by injecting 3–5 mL of local anesthetic (1% lidocaine) subcutaneously between the lateral malleolus and the Achilles tendon. A posterior tibial nerve block uses a point located midway between the Achilles tendon and the medial malleolus. The needle is passed medially towards the tibia where approximately 5 mL of local anesthetic is injected. Following a nerve block, patients may have some instability when walking and cannot drive until the anesthesia has resolved. The authors have again used high-intensity vibration devices during the injection of BTX with acceptable pain control in some patients. A starch iodine test is usually recommended for the feet as the entire surface area may not be affected. The technique of injections is the same as for the palms. BTX represents a treatment alternative in patients with plantar hyperhidrosis who have failed topical therapy and iontophoresis. It is, however, often less successful than for axillary or palmar areas.

BTX for facial hyperhidrosis

Facial hyperhidrosis can involve the upper lip, nasolabial folds, and malar regions; however, the most commonly affected area is the forehead. Efficacy of BTX-A for facial hyperhidrosis is largely limited to case reports. Treatment with BTX has resulted in excellent results, with a duration of effect in the range of 5–6 months. The main site of injection is usually a band near the hairline. Frey's syndrome or facial gustatory sweating after parotid surgery or trauma is due to transection of the post-ganglionic sympathetic nerve fibers from the otic ganglion. Treatment with BTX-A has produced clinically significant results and improvements in associated facial flushing, lasting up to 15 months.

Treatment considerations with BTX

The main contraindications to BTX therapy includes neuromuscular disorders such as myasthenia gravis, pregnancy and lactation, organic causes of hyperhidrosis, and medications that may interfere with neuromuscular transmission. Appropriate selection of patients and clinical presentations is essential to ensure a satisfactory treatment response and avoid unnecessary frustrations.

Summary

Hyperhidrosis is a common and extremely distressing condition, with a prevalence of 2.8% of the population. Approximately 50% of patients report feeling depressed. Given that effective treatment, particularly BTX-A injections, can dramatically improve a patient's quality of life underscores the challenge for physicians to diagnose and manage this condition.

Further Reading

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