Recognition, diagnosis, and treatment of primary focal hyperhidrosis

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Primary focal hyperhidrosis is a disorder of excessive, bilateral, and relatively symmetric sweating occurring in the axillae, palms, soles, or craniofacial region. The condition results in occupational, psychological, and physical impairment, and potential social stigmatization.

Hyperhidrosis is not rare; however, data on prevalence may differ depending on how hyperhidrosis is defined. A pilot study of young Israelis reported an incidence of 1%.[1] A recent survey of the US population found a prevalence of 2.8%.[2] Moreover, the survey found that only 38% of affected individuals have discussed hyperhidrosis with a health care professional. Based on referral patterns reported by their patients, clinical experts are concerned that web sites, which direct care to specialized surgical referral centers, are the primary source of published information on hyperhidrosis for many patients.

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From 1.6 to 4 million apocrine and eccrine sweat glands are distributed over the body, with variable density of glands: 64 glands per cm^2 on the back, 181 glands per cm^2 on the forehead, and 700 glands per cm^2 on the palms.[3,4] Thermoregulatory control is regulated through cerebral cortical structures, anterior hypothalamus, and the sympathetic nervous system. The pathophysiology of focal primary hyperhidrosis is poorly understood, but believed to be associated with over-stimulation via an autonomic pathway. Either thermal stimuli or higher cortical stimuli can activate autonomics that affect sweat of the axillae, face, palms, or soles. The pattern of stimulation can be peculiar to an individual's inherited dysfunction of the autonomic system. For example, someone with palmar sweating may suffer episodic sweating with either social stress or high ambient temperature. Many patients report episodic focal sweating with high ambient temperature and without situational stress. Often, it is the unpredictabiliy of the sweating that accounts for some of the social stress and stigma of the condition. In addition, experts believe that hyperhidrosis is not a neuropsychiatric condition. Recent evidence suggests that hyperhidrosis has a familial component, further suggesting a genetic basis for the condition.[1,5-10]

Excessive sweating can be a substantial burden to afflicted individuals, interfering with daily activities and causing social embarrassment.[1,2,11,12] Hyperhidrosis adversely affects one's ability to perform in the workplace, be in public, meet people, and develop personal relationships. Many patients must change their clothing several times per day. One study reported that over one half of patients were moderately or severely affected emotionally.[13] According to standardized and validated quality-of-life surveys, the negative effects of hyperhidrosis are comparable to other conditions, such as severe psoriasis, end-stage renal disease, rheumatoid arthritis, and multiple sclerosis.[14,15]

Clinicians have a number of available treatments for hyperhidrosis that have undergone extensive efficacy and safety evaluation in more than 15 randomized controlled trials. The purpose for the working group was to exhaustively review the clinical literature and develop a consensus statement to guide the recognition, diagnosis, and treatment of primary focal hyperhidrosis.

METHODS

A multidisciplinary task force of internationally recognized experts was convened to review the clinical evidence and develop this consensus statement. The task force employed an evidence-based approach, performing a comprehensive literature search of English language articles.

Table I. Summary of MEDLINE search*

Search limits	Number of citations
Text	1749
English, human	1240
Randomized by patient	1
Randomized by anatomical side	14
Observational/case series	60
Meta-analysis	2
Clinical guidelines	0
Review	59
Editorial	6

*MEDLINE 1966-2002

After searching the literature, we rated each article based on the strength of the evidence presented in the report. We included English-language reports published between 1966 and 2002 that included original research on the recognition, diagnosis, or treatment of primary focal hyperhidrosis, including randomized trials, controlled or concealment studies, observational studies, or single-center case series. We excluded reports that were reviews, single case reports, meta-analyses, or not published. Literature databases included MEDLINE, EMBASE, PUBMED, Cochrane Collaboration, MedScape, and the Agency for Health Research & Quality (AHRQ) web site. We also searched the Internet with the *www.google.com* search engine to assure that other relevant sources of information were not omitted. The search terms included hyperhidrosis, epidemiology, quality of life, and randomized controlled trials. Table I shows a summary of the published literature for the MEDLINE search. Among the 15 controlled trials, only one study was randomized by patient, whereas, the other 14 studies were randomized by anatomical side of treatment administration. There were 60 observational studies or case series. A clinical guideline has not been published on this subject.

We divided the articles into two groups according to whether the study and/or the research question were related to diagnosis or to treatment. The criteria for rating studies on diagnosis are: (1) it is a good diagnostic test, (2) there are good diagnostic criteria, (3) the test and criteria are reproducible, (4) there is proper patient selection, and (5) there are at least 50 cases and 50 controls.[16] Studies rated level 1 (meeting all 5 criteria) or level 2 (meeting 4 of the 5 criteria) are considered strong evidence. Studies rated level 3 meet 3 of the 5 criteria and are considered moderate evidence. Studies that meet fewer than 3 criteria, level 4 (2 criteria) or level 5 (one criterion), are considered limited or weak evidence.

Clinical recommendations were rated level 1 if they utilize several randomized controlled trials (RCTs) that demonstrate a significant difference, level 2 if there is an RCT that demonstrates a significant difference, and level 3 if there is an RCT showing some difference. Levels 1, 2, and 3 are considered strong evidence. We rated nonrandomized controlled trial or subgroup analysis of an RCT level 4 and comparison studies with some kind of control/comparison level 5. Levels 4 and 5 are considered moderate evidence. Case series without controls are rated level 6, and case reports with fewer than 10 patients are rated level 7. Levels 6 and 7 are considered limited or weak published evidence, based primarily on expert opinion.[17]

The task force met for 2 days to extensively review the evidence reports and relevant articles. Recommendations were drafted and discussed, followed by a vote of all members.

SCOPE

This recommendation and consensus statement addresses the management of patients with excessive sweating localized to the armpits, palms, soles, or face that cannot be identified as secondary to another underlying disease process. Dermatological and neurological experts who specialize in the management of focal primary hyperhidrosis report that patients often have been misdiagnosed or mismanaged in their initial physician encounters. Experts generally perceive that they see only a small fraction of the patients with primary focal hyperhidrosis.

Primary care physicians and pediatricians should be well-informed of the clinical presentation and available treatment options concerning hyperhidrosis so that they can make appropriate diagnoses and referrals. The recommendations address the distinctions between primary focal hyperhidrosis, and its differential diagnosis—such as generalized hyperhidrosis or hyperhidrosis secondary to known underlying medical conditions—but focuses only on the treatment of primary focal hyperhidrosis.

RECOGNITION

Recommendation

When performing a medical evaluation, the review of systems should include questions regarding problematic excessive sweating.

Discussion

Physicians and patients frequently fail to recognize that primary focal hyperhidrosis is a relatively common and treatable medical condition. Aside from a pilot study of young Israelis that reported an incidence of 1%, the frequency of this condition in the general population is not well documented.[1] A recent survey of the US population found a prevalence of 2.8%. Only 38% of affected individuals have discussed the condition with a health care professional.[2] A large proportion of patients report a positive family history.[1,5-10]

Most cases involve the axillae, palms, soles, face, or a combination of these anatomic sites. Hyperhidrosis can occur at any age, but the mean age at time of onset varies depending on the anatomic site involved. Palmar hyperhidrosis typically presents during childhood or adolescence, and axillary disease during adolescence.[2,8,18] Many patients, especially children and adolescents, are embarrassed or reluctant to raise the issue or discuss in detail their excessive sweating and the impact it has on their lives.

DIAGNOSIS OF PRIMARY FOCAL HYPERHIDROSIS

Recommendation

Primary focal hyperhidrosis is defined as excessive, bilateral, and relatively symmetric sweating occurring in at least one of the following sites: the axillae, palms, soles, or craniofacial region. Primary focal hyperhidrosis frequently results in occupational, psychological, and physical impairment, and can result in social stigmatization. The following criteria are recommended for establishing the diagnosis of primary focal hyperhidrosis:

Focal, visible, excessive sweating of at least 6 months duration without apparent cause with at least two of the following characteristics:

- Bilateral and relatively symmetric
- 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

Discussion

The diagnosis of primary focal hyperhidrosis should be made only after excluding secondary causes of excessive sweating (Table II).[18-21] In the presence of unilateral or asymmetric presentation, particular care must be taken to rule out a neurological lesion or malignancy.[3]

EVALUATION

Recommendations

1. The history should include questions about the following items:
   a) pattern of sweating (duration of symptoms, frequency, volume, areas involved, symmetry, specific triggers, presence of sweating during sleep);

Table II. Strength of recommendation and level of evidence

Recommendations	Strength of recommendation*	Level of evidence†	Reference Nos.
Recognition			
Include questions regarding problematic excessive sweating in ROS	Unanimous working group opinion	L7	
Evaluation			
Direct the history towards severity of sweating and possible secondary causes of sweating	Unanimous working group opinion	L7	
Focus the physical examination on visible sweating and signs of secondary causes of sweating	Unanimous working group opinion	L7	
Additional laboratory testing is not required if characteristic presentation	Unanimous working group opinion	L7	
Quantification of sweat production and mapping are not routinely performed	Unanimous working group opinion	L7	
Treatment of axillary hyperhidrosis			
Educate the patient on appropriate use of OTC antiperspirants	Unanimous working group opinion		
Initiate therapy with topical AlCl	Unanimous working group opinion and moderate evidence	L4/5	27-30
Botulinum toxin if patient fails topical therapy	Unanimous working group opinion and strong evidence	L1	22, 24, 31-43, 102, 103
If the patient fails to respond, may refer for surgical procedure, such as removal of the overactive sweat glands using subcutaneous curettage, tumescent liposuction, limited local incision with removal of the underlying apoeccrine glands, or endoscopic transthoracic sympathectomy	Majority working group opinion and limited evidence	L6	6, 25, 44-49

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ETS, Electrical transcranial stimulation; *OTC*, over the counter; *ROS*, review of systems.

*Recommendations are based on the following: unanimous working group opinion supported by strong to moderate levels of evidence, majority working group opinion supported by strong to moderate levels of evidence, unanimous working group opinion supported by limited or weak scientific evidence, majority working group opinion supported by limited or weak scientific evidence, unanimous working group opinion only, and majority working group opinion only.

†The criteria for rating the level of evidence of a particular article is dependent on whether the study and/or the research question relates to diagnosis or treatment.

The rating criteria for studies on diagnosis are (1) it is a good diagnostic test, (2) there are good diagnostic criteria, (3) the test and criteria are reproducible, (4) there is proper patient selection, and (5) there are at least 50 cases and 50 controls.[16] Studies that meet at least 4 of these 5 criteria are rated level 1 (all 5 criteria) or level 2 (4 of the 5 criteria) and are considered strong evidence. Studies that meet 3 of the 5 criteria are rated level 3 and are considered moderate evidence. Studies that meet fewer than 3 criteria are rated level 4 (2 criteria) or level 5 (one criterion) and are considered limited or weak evidence.

Studies on treatment are rated level 1 if there are several randomized controlled trials (RCTs) that demonstrate a signicant difference, level 2 if there is an RCT that demonstrates a significant difference, and level 3 if there is an RCT showing some difference. Levels 1, 2, and 3 are considered strong evidence. A nonrandomized controlled trial or subgroup analysis of an RCT is rated level 4 and a comparison study with some kind of control/comparison is rated level 5. Levels 4 and 5 are considered moderate evidence. Case series without controls are rated level 6, and case reports with fewer than 10 patients are rated level 7. Levels 6 and 7 are considered limited or weak evidence.[17]

Table II. Cont'd

Recommendations	Strength of recommendation*	Level of evidence†	Reference Nos.
Treatment of axillary hyperhidrosis (cont'd)			
Before surgery, patient should be evaluated by surgeon and by a dermatologist, and be well informed and willing to accept the surgical risks, such as compensatory hyperhidrosis	Majority working group opinion and limited evidence	L6	
Iontophoresis or systemic anticholinergic drugs may be tried before surgery in selected cases	Majority working group opinion	L7	18, 50-52, 55, 104
Treatment of palmar hyperhidrosis			
Initiate therapy with topical AlCl	Unanimous working group opinion and limited evidence	L6	30, 54
Tap water iontophoresis is an alternative first-line treatment	Unanimous working group opinion and strong evidence	L2	55-57
Offer botulinum toxin if patient fails topical therapy and iontopheresis. Patients must be informed that they may experience transient mild weakness of the intrinsic hand muscles.	Unanimous working group opinion and strong evidence	L1/2	13, 25, 33, 59, 61-63, 65, 66, 105, 106
Despite lack of evidence, systemic anticholinergic drugs or other medications may be tried before surgery in selected patients	Majority working group opinion		7, 18, 75, 104
Offer ETS to patients with severe disease who fail other treatments and are well informed of the risks/benefits	Majority working group opinion and limited evidence	L7	6, 8-10, 49, 72-79, 81-84, 86
Before surgery, patient should be evaluated by surgeon and by a dermatologist, and be well informed and willing to accept the surgical risks, such as compensatory hyperhidrosis	Majority working group opinion and limited evidence	L6	
Treatment of plantar hyperhidrosis			
Educate the patient regarding frequent changing of socks, use of absorbent powder, and alternating shoes	Unanimous working group opinion	L7	
Initiate therapy with AlCl	Unanimous working group opinion and limited evidence	L6	30, 100
Tap water iontophoresis is an alternative first-line treatment	Unanimous working group opinion and limited evidence	L6	50-52, 87, 88
Offer botulinum toxin A if patient fails topical therapy and iontophoresis	Unanimous working group opinion and limited evidence	L7	37, 107
Treatment of craniofacial hyperhidrosis			
Educate the patient to recognize and avoid triggers of sweating	Unanimous working group opinion	L7	
Trial of topical AlCl, taking care to avoid the eyes	Majority working group opinion	L7	
Botulinum toxin is an alternative first line treatment	Majority working group opinion and limited evidence	L6	36, 43, 93, 95-99

b) age of onset;
c) impact on daily activities/quality of life;
d) family history;
e) review of systems to exclude secondary causes;
f) symptoms that suggest systemic disease (eg, constitutional symptoms of fever, weight loss, anorexia, palpitations), signs and symptoms of thyroid and neurological disease.

2. The focus of the physical examination should be on (1) visible evidence of excessive sweating in the characteristic focal locations, (2) detection of signs that suggest a secondary cause of hyperhidrosis.
3. Additional laboratory tests are not needed if the presentation is characteristic of primary focal hyperhidrosis:
   a) bilateral and relatively symmetric involving focal axillae, palms, soles, or face;
   b) typical age of onset;
   c) no evidence of secondary causes by history and physical examination.
4. Tests quantifying sweat production are not practically or routinely performed in clinical practice. However, they may be helpful in making the diagnosis or directing therapy in selected patients, and are used in clinical research.

Table III. Causes of secondary hyperhidrosis[3,18-21]

Generalized	drugs, substance abuse, cardiovascular disorders, respiratory failure, infections, malignancies, endocrine/metabolic disorders (thyrotoxicosis, hypoglycemia, pheochromocytoma, acromegaly, carcinoid tumor), neurologic (Parkinson's disease)
Regional	stroke, peripheral nerve damage, central or peripheral nervous system lesions that cause localized anhidrosis can cause compensatory sweating in other areas (stroke, spinal cord lesion, neuropathy, Ross syndrome)
Focal	Frey syndrome, gustatory sweating, eccrine nevus, social anxiety disorder, unilateral focal hyperhidrosis (eg, neurological disorder or tumor)

Discussion

There are no controlled studies on the sensitivity and specificity of history, physical examination, or laboratory testing in accurately diagnosing primary focal hyperhidrosis or in characterizing its severity. However, one study suggests that focal sweating of more than 50-100 mg/5 minutes per axillae as measured gravimetrically supports the diagnosis of focal axillary hyperhidrosis.[22] Diagnosis requires both a typical clinical presentation and a lack of evidence for any underlying pathology that may cause sweating as a secondary manifestation (see Table III). Additional laboratory tests should be performed for generalized hyperhidrosis and atypical focal hyperhidrosis, as indicated by the specific clinical presentation.[19]

Tests quantifying sweat production or that map the area of sweating are often used in clinical trials to assess treatment response, but are not generally required in routine clinical practice. Gravimetric testing of sweat collected on absorbent paper under controlled conditions may be helpful in selected patients when the diagnosis is in question.[22] One study showed a nearly five-fold increase in axillary sweat production among hyperhidrosis patients when compared to controls.[23] Minor's iodine starch test is useful in mapping areas of excessive sweating prior to injection with botulinum toxin or local surgery, but does not provide accurate information on the quantity of sweat produced.[22,24-26]

TREATMENT OF AXILLARY HYPERHIDROSIS

Recommendations (Fig 1)

1. Ensure that the patient has appropriately used an over-the-counter antiperspirant. If necessary, educate the patient about the difference between antiperspirants and deodorants.
2. Initiate topical therapy with AlCl hexahydrate after educating the patient on proper use.
   a) Most patients benefit from a trial of topical AlCl hexahydrate in absolute alcohol or in a salicylic acid gel. Although a 25% solution may be required to achieve euhidrosis, an initial concentration of 10%-12% may be tried to minimize irritation. It may be reasonable to try a 35% solution; however, many patients will experience unacceptable skin irritation.
   b) To minimize irritation, AlCl should be applied to the dry underarm at bedtime and washed off after 6 to 8 hours. Typically, AlCl is applied every 24 to 48 hours, and sometimes more often, until euhidrosis is achieved. Maintenance therapy is normally required once every 1 to 3 weeks.
   c) Skin irritation can be treated by reducing the frequency of treatment and applying 1% hydrocortisone cream to the affected area twice daily for less than 2 weeks. Persistent irritation is an indication for a dermatology referral.

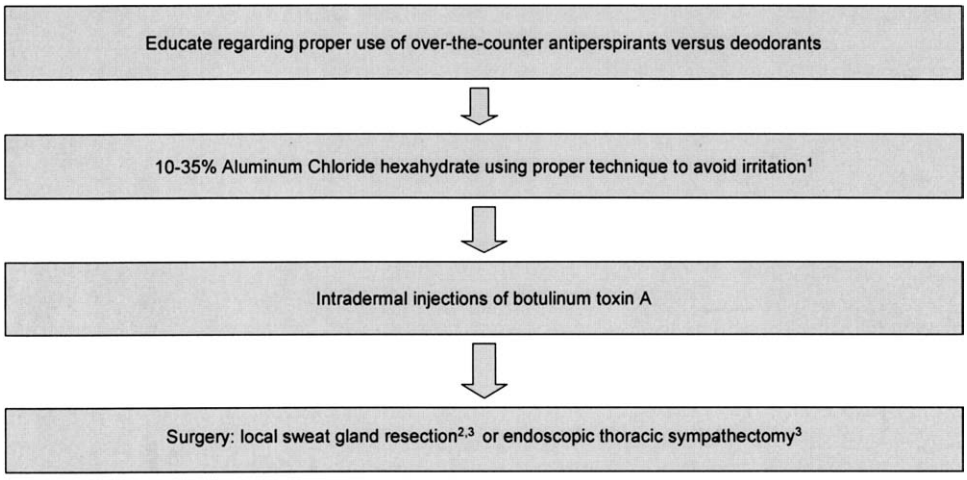

Fig 1. Treatment algorithm for axillary hyperhidrosis.

3. If the patient fails to respond to topical therapy, intradermal injection of botulinum toxin may be administered to the areas of excessive sweating.
4. Failure to respond or intolerance to other treatments may be an indication for referral for a surgical procedure. Options include removal of the overactive sweat glands using subcutaneous curettage, tumescent liposuction, limited local incision with removal of the underlying apoeccrine glands, or endoscopic thoracic sympathectomy.
   a) The patient should be seen by the surgeon and a dermatologist prior to surgery.
   b) Patients must be well informed and willing to accept the surgical risks, such as compensatory hyperhidrosis.
5. Convincing evidence is lacking for the effectiveness of both iontophoresis and systemic anticholinergic drugs for axillary hyperhidrosis. Iontopheresis is difficult to administer and frequently causes irritation. At the doses needed to alleviate symptoms of hyperhidrosis, systemic anticholinergic drugs also may cause adverse effects, such as dry eyes, dry mouth, and problems with urinary voiding, including retention. Iontophoresis or systemic anticholinergic drugs may be tried before surgery in selected cases.

Discussion

Two small controlled studies and two larger observational studies have demonstrated the efficacy of topical AlCl hexahydrate in the treatment of axillary hyperhidrosis.[27-30] Treatment response was assessed using patient self-reported severity of sweating and/or gravimetry. Topical AlCl was generally well tolerated. The most frequent side effect was local skin irritation, often responding to a reduction in concentration or frequency of application or to topical 1% hydrocortisone cream.[29]

Fourteen prospective, observational, or placebo-controlled studies, totaling more than 700 patients, have assessed the safety and efficacy of botulinum toxin type-A for axillary hyperhidrosis.[24,31-42] This neurotoxin inhibits the release of acetylcholine from the presynaptic nerve endings. Intradermal injection blocks the sympathetic cholinergic autonomic fibers innervating the sweat glands.[24] All studies showed a significant treatment response by patient self-report or by sweat quantification tests.

In the largest of the studies, 320 patients were randomized to receive either botulinum toxin A or placebo in both axillae. Patients were followed for 16 weeks. Patients achieving greater than a 50% reduction in sweat production by gravimetry were defined as treatment responders. Ninety-four percent of patients were treatment responders with an average reduction in sweat production of 83%. Side effects were minimal.[24] Quality of life improved substantially including a marked improvement in the ability to perform current work activities.[13,24] An open label continuation study allowed 207 patients to receive up to 3 further botulinum A injections over the ensuing 12 months. This study showed

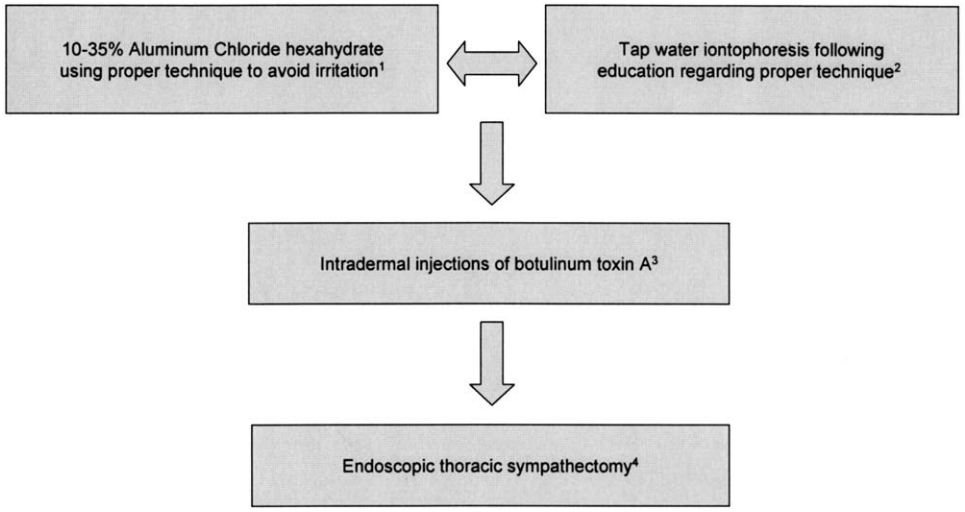

Fig 2. Treatment algorithm for palmar hyperhidrosis.

a sustained response of 7 months on average, although a substantial proportion of patients had a benefit of up to 16 months following only a single treatment session.[43]

In another randomized trial, 145 patients were assigned to receive botulinum toxin A in one axillae and placebo in the other.[31] After 2 weeks, the patients underwent gravimetry and could opt for botulinum A injection in the axillae that had received placebo. Patients were then followed for 24 additional weeks. Gravimetry showed a marked and significant diminution in sweat production at both 2 and 24 weeks following treatment with botulinum toxin A. Side effects were minimal and 92% of patients were satisfied or completely satisfied at 4 weeks. Mean sweat production at 24 weeks was still below 50% of initial sweat rates measured by gravimetry.

Results of case series of surgical interventions have been reported. In early anecdotal reports of sweat gland resection, the procedure consisted of en bloc resection of skin and underlying sweat glands. This procedure produced suboptimal results secondary to wound infection or contracture scars. Subsequent anecdotal reports suggested that using a smaller Z- or W-shaped incision reduced this complication.[44-46] Others report that tumescent liposuction may also be used to treat axillary hyperhidrosis.[47,48] One moderately strong study supports subcutaneous curettage in the treatment of axillary hyperhidrosis. Gravimetry was performed on 77 patients after an average of 28 months. Sweat production was reduced to 46% of baseline and 84% of patients were satisfied with the treatment.[25] Two studies of endoscopic thoracic sympathectomy for axillary hyperhidrosis followed a total of 80 patients for approximately 15 years. Twenty percent of patients reported that they were dissatisfied with their treatment.[6,49]

Data on the clinical utility of iontophoresis for axillary hyperhidrosis are limited. Three studies, enrolling a total of 12 patients, using either tap water or anticholinergic solutions, showed conflicting results.[50-52] Iontophoresis is difficult to apply to the axillae and tends to produce skin irritation. No studies assess the effect of systemic anticholinergic medications on axillary hyperhidrosis. Anecdotal reports and clinical experience indicate that the anticholinergic systemic side effects are generally intolerable.[18,19,53]

TREATMENT OF PALMAR HYPERHIDROSIS

Recommendations (Fig 2)

1. Initiate topical therapy with AlCl hexahydrate after educating the patient on proper use.
   a) Some patients will benefit from a trial of topical AlCl hexahydrate in absolute alcohol or in a salicylic acid gel. An initial concentration of 10%-12% may be tried to minimize irritation, although a 25% solution is required to achieve euhidrosis in the majority of patients. Some patients tolerate a 35% solution, although this significantly increases the risk of intolerable skin irritation.

   b) To minimize irritation, AlCl should be applied to the dry palm at bedtime and washed off after 6 to 8 hours. AlCl is applied every 24 to 48 hours until euhidrosis is achieved. Maintenance therapy is typically required once every 1 to 3 weeks.
   c) Skin irritation can be treated by reducing the frequency of treatment and applying 1% hydrocortisone cream to the affected area twice daily for less than 2 weeks. Persistent irritation is an indication for a dermatology referral.
2. Tap water iontophoresis is an effective and safe treatment for palmar hyperhidrosis and is preferred by some physicians as a first line treatment. It is contraindicated in patients who are pregnant or who have a pacemaker or metal implant. Patient education regarding proper technique is essential for optimal effect. Outcomes may vary substantially depending on the performance of commercially available devices.
   a) Patients undergo 3 to 4 treatments per week for 20 to 30 minutes using a device that provides direct current at 15 to 20 mA. The current direction is switched halfway through the treatment since the anode may be more effective.
   b) Euhidrosis is typically achieved after 6 to 10 treatments. Frequency of maintenance treatments is titrated to the individual response, typically required at 1- to 4- week intervals.
   c) Skin dryness or irritation can be treated by decreasing the frequency of treatments and with emollients. For more significant irritation, 1% hydrocortisone cream can be applied twice daily, but should be used for less than 2 weeks. Persistent irritation requires a dermatology referral. Apply petrolatum to open wounds to prevent a burning sensation during iontopheresis.
3. Intradermal botulinum toxin injections may be offered to patients who fail to achieve a satisfactory response with AlCl or iontophoresis. The pain in the hand of botulinum toxin injections may be especially bothersome for some patients. Consequently, local or regional anesthesia is frequently indicated to manage the pain of palmar injection. Patients must be informed that they may experience transient mild weakness of the intrinsic hand muscles.
4. Endoscopic thoracic sympathectomy is an option for selected patients who are unable to tolerate other therapies and for whom the burden of hyperhidrosis is severe.
   (a) Patients should be referred to a dermatologist and informed of the risk-benefits of various options before undergoing surgery.
   (b) Patients should be informed of the local results of endoscopic thoracic sympathectomy, including primary success rate, adverse event rate, and rate of compensatory hyperhidrosis.
5. Convincing evidence is lacking for the effectiveness of systemic anticholinergic drugs and other systemic drugs in the treatment of palmar hyperhidrosis. Although these treatments may be poorly tolerated, a trial may be indicated before surgical treatments in selected cases.

Discussion

Two observational studies support the use of topical AlCl hexahydrate in treating palmar hyperhidrosis, but there are no controlled trials.[30,54] Although expert consensus based on clinical experience suggests that for some patients topical AlCl is less effective for palmar than for axillary disease, experts typically recommend a trial of AlCl.

Three small controlled studies using galvanic units have demonstrated the efficacy of tap water iontophoresis in reducing palmar sweating.[55-57] Patients must be adequately trained in the use of the equipment and instructed regarding the need for ongoing maintenance therapy.

When iontophoresis was performed using anticholinergic agents in solution, the euhidrosis effect lasted longer but patients frequently experienced anticholinergic side effects including dry mouth and mydriasis.[51,52,58]

Four controlled studies, enrolling a total of 61 subjects, and 6 observational studies, enrolling 168 patients, were performed to assess the efficacy, tolerability, and safety of botulinum toxin injections for palmar hyperhidrosis.[33,59-66] The response rates exceeded 90% and the duration of euhidrosis generally exceeded the length of the trial. The only notable side effect was mild and transient weakness of the intrinsic hand muscles.[33,36,60-62,65,67] This complication was well tolerated, but patients must be informed that fine motor control of the hand may be compromised. The chief problem with this treatment is the intense pain associated with injections into the densely innervated skin of the palm. Loco-regional pain management is recommended. The topical anesthetic agent EMLA was less effective than other methods including application of ice immediately before injection, nerve blocks, and intravenous regional anesthesia (Bier's block).[68-71] Potential side effects of anesthesia such as damaging peripheral

nerves or vessels (wrist block or plexus block) have to be discussed with the patients.

There are over 20 published case series evaluating endoscopic thoracic sympathectomy in palmar hyperhidrosis, involving more than 14,000 patients.[6,8-10,49,72-86] These series lack uniformity in patient inclusion criteria, particularly in how severity of disease was assessed. Reported surgical technique varied widely among the series with the sympathetic trunk or ganglion sometimes divided with scissors, excised, ablated, clipped, or cauterized. The upper end of the sympathetic chain was everted in some series to prevent nerve re-growth and relapse of symptoms. The preferred method in one series was selective cutting of the rami communicantes. The level of the procedure also varied among the series with surgeons choosing to interrupt the sympathetic chain at T2 only, T2-T3, T2-T4, or lower T1-T4.

The reported primary success rate for endoscopic thoracic sympathectomy exceeds 95%, but reported follow-ups were usually short term. Relapse rates vary between 0% and 16%. Acute complications including pneumothorax, hemothorax, bleeding from intercostals vessels, atelectasis, pneumonia, wound infection, and persistent intercostal pain occurred in less than 2% of cases. Although no operative deaths were reported in these series, members of the expert panel are aware of a small number of patient deaths. The reported rates of long term complications including Horner's syndrome, compensatory hyperhidrosis, and gustatory hyperhidrosis vary widely (up to 90% in some series), perhaps because of a lack of standardized follow-up methods. Some patients may prefer surgery because of its potential to permanently alleviate the condition. It may be appropriate for such a patient to undergo surgery if the patient has been fully informed by both a surgeon and a dermatologist of the risks and benefits of all treatments options.

There are no studies assessing the effect of systemic anticholinergic medications on palmar hyperhidrosis. Anecdotal reports indicate that the anticholinergic systemic side effects are generally intolerable.[18,19,53]

TREATMENT OF PLANTAR HYPERHIDROSIS

Recommendations

1. Educate the patient regarding local hygiene measures including changing the socks at least twice daily, using an absorbent foot powder twice daily, and alternating pairs of shoes on a daily basis to allow full drying before wearing. Avoid boots or sports shoes, which may have an occlusive effect.
2. Initiate therapy with topical AlCl hexahydrate in a regimen similar to that for palmar hyperhidrosis.
3. Tap water iontophoresis is a reasonable first-line treatment for plantar hyperhidrosis. Proper technique is essential and similar to that described for palmar iontophoresis.
4. Intradermal botulinum toxin injections may be offered to patients who fail to achieve a satisfactory response with AlCl or iontophoresis. The pain of botulinum toxin injections of the foot is worse than for the axillary. Consequently, local or regional anesthesia may be required to manage the pain of plantar injection.
5. Lumbar sympathectomy is not recommended because of associated sexual dysfunction.

Discussion

Far fewer studies have been conducted that addressed the treatment of plantar hyperhidrosis, perhaps because plantar hyperhidrosis is less common or perceived as less problematic than axillary or palmar disease. One large observational study supports the use of topical AlCl hexahydrate.[30] Of 139 patients enrolled, 84% had a good or excellent response to 30-40% AlCl in a salicylic acid gel. In a study of 11 patients, 10 patients achieved euhidrosis using 25% AlCl in absolute ethanol.[54] In 5 observational studies of tap water iontophoresis, response rates were between 90% and 100%.[50-52,87,88]

Although there are no published controlled studies of botulinum toxin in plantar hyperhidrosis, the expert panel consensus is that the response rate is slightly lower than in palmar disease, largely because the thickened stratum corneum makes intradermal injection more challenging. Approximately 50% of patients with palmoplantar hyperhidrosis who undergo endoscopic thoracic sympathectomy for excessive palmar sweating also have a reduction in plantar hyperhidrosis.[9,86]

TREATMENT OF CRANIOFACIAL HYPERHIDROSIS

Recommendations

1. Educate the patient to recognize and avoid food triggers and other stimulating factors.
2. Although evidence is lacking, topical AlCl may be tried, taking particular care to avoid the eyes.

3. Intradermal injection of botulinum toxin is a reasonable option.

Discussion

The treatments for primary craniofacial hyperhidrosis are similar to those for craniofacial hyperhidrosis secondary to Frey syndrome or diabetic neuropathy. Despite the lack of published studies, a majority of the expert panel felt that a trial of topical AlCl was warranted in many cases. Topical glycopyrrolate has been used with success in patients with gustatory hyperhidrosis secondary to Frey syndrome or diabetic neuropathy and may have a similar effect in primary craniofacial hyperhidrosis.[89-92]

In two small series evaluating botulinum toxin A for frontal hyperhidrosis, all patients achieved euhidrosis lasting longer than 5 months.[36,93] In 6 observational series of botulinum toxin A for gustatory hyperhidrosis, 163 of 165 patients responded with a duration of 5-17 months.[94-99] Data on the efficacy and safety of endoscopic thoracic sympathectomy for craniofacial hyperhidrosis are extremely limited.[73,77,100,101] This option should be restricted to selected patients who are unable to tolerate other therapies and for whom the burden of hyperhidrosis is severe. Patients should be informed of the local results of this procedure including primary success rate, adverse event rate, and rate of compensatory hyperhidrosis.

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