Palmoplantar Hyperhidrosis: A Therapeutic Challenge

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Excessive sweating from the palms and soles, known as palmoplantar hyperhidrosis, affects both children and adults. Diagnosis of this potentially embarrassing and socially disabling condition is based on the patient's history and visible signs of sweating. The condition usually is idiopathic. Treatment remains a challenge: options include topical and systemic agents, iontophoresis, and botulinum toxin type A injections, with surgical sympathectomy as a last resort. None of the treatments is without limitations or associated complications. Topical aluminum chloride hexahydrate therapy and iontophoresis are simple, safe, and inexpensive therapies; however, continuous application is required because results are often short-lived, and they may be insufficient. Systemic agents such as anticholinergic drugs are tolerated poorly at the dosages required for efficacy and usually are not an option because of their associated toxicity. While botulinum toxin can be used in treatment-resistant cases, numerous painful injections are required, and effects are limited to a few months. Surgical sympathectomy should be reserved for the most severe cases and should be performed only after all other treatments have failed. Although the safety and reliability of treatments for palmoplantar hyperhidrosis have improved dramatically, side effects and compensatory sweating are still common, potentially severe problems. (Am Fam Physician 2004;69:1117-20,1121.

A patient information handout on sweaty hands and feet, written by the authors of this article, is provided on page 1121.

Palmoplantar hyperhidrosis is a common condition in which the eccrine (sweat) glands of the palms and soles secrete inappropriately large quantities of sweat. The condition may become socially and professionally debilitating. Idiopathic palmoplantar hyperhidrosis begins in childhood and frequently runs in families.[1]

Eccrine glands are distributed over almost all of the body surface but are most dense in the palms and soles. These glands are morphologically and functionally normal in patients with palmoplantar hyperhidrosis.[2,3] Because the hyperhidrosis is stimulated by emotion and stress, it does not occur during sleep or sedation. Conversely, normal sweating is controlled primarily by thermoregulation and, thus, occurs independently of level of consciousness. The primary defect in patients with hyperhidrosis may be hypothalamic hypersensitivity to emotional stimuli from the cerebral cortex.[2,3]

See page 1028 for definitions of strength of recommendation labels.

Patients with hyperhidrosis have normal sweat glands but may have an enhanced response to emotional stimuli.

The clinical diagnosis of palmoplantar hyperhidrosis is obvious because the excess sweating may be readily observed. Various treatment options are available. Some work by interrupting the innervation of sweat glands by sympathetic nerves with acetylcholine as the neurotransmitter, but all have limitations or associated complications. Thus, treatment of palmoplantar hyperhidrosis remains a challenge, and a logical approach must be taken to individualize therapy based on the degree of functional impairment.

Topical Therapy

The most effective topical treatment for palmoplantar hyperhidrosis is 20 percent aluminum chloride hexahydrate in absolute anhydrous ethyl alcohol (Drysol).[3] Less satisfactory results have been achieved with other topical agents, including boric acid, anticholinergic drugs, resorcinol, tannic acid (2 to 5 percent

Because of side effects, systemic anticholinergic agents usually are not used to treat hyperhidrosis.

solutions), potassium permanganate, formaldehyde, methenamine, and glutaraldehyde.

Aluminum chloride is thought to obstruct sweat pores and induce atrophy of secretory cells within the sweat glands. The only contraindication to this treatment is documented hypersensitivity, and aluminum chloride should not be used on irritated, broken, or recently shaven skin.

Patients should apply the agent to dry skin nightly until clinical relief is achieved, at which point maintenance therapy is instituted and frequency of applications can be spread out over time in some patients. The morning after an overnight treatment, patients should wash away residual aluminum chloride and apply topical baking soda to limit skin irritation.

Topical therapy has some drawbacks. Compliance may become an issue because the daily applications necessary for efficacy may be considered too time-consuming for patients.[3,4] Topical therapy also may fail to adequately control hyperhidrosis.

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Systemic Therapy

In the past, systemic anticholinergic drugs have been somewhat successful in the treatment of palmoplantar hyperhidrosis, based on the action of acetylcholine as the periglandular neurotransmitter within the sympathetic innervation of sweat glands. Despite their potential, systemic anticholinergic drugs are impractical treatments for this condition. Long-term therapy is required, and the drugs have numerous side effects, including dry mouth, dry eyes, constipation, blurry vision, mydriasis, and difficulty with urination.[5]

Benzodiazepines can reduce anxiety levels, thereby decreasing the emotional stimuli that trigger hyperhidrosis. However, these agents generally are not used because they may cause dependency and side effects such as lethargy and drowsiness.[6]

IONTOPHORESIS

Iontophoresis, the passage of a direct electrical current onto the skin, is a long-established therapy for hyperhidrosis.[7] Since its introduction in 1952, iontophoresis has proved to be a safe, effective, and relatively inexpensive treatment that is suitable for patients to use at home.[8-10] Side effects usually are minor and related to individual susceptibility, higher amperage, and the length of time that a patient repeatedly uses the treatment. Skin irritation may occur, sometimes with erythema, vesicle formation, slight pain, or paresthesia in the treated areas; in addition, minor burns can occur in previously injured skin.[11]

The underlying mechanism of iontophoresis is not fully understood.[12] According to one hypothesis, iontophoresis may induce hyperkeratosis of the sweat pores and obstruct sweat flow and secretion (although no plugging of the pores has been found).[12] Other proposed mechanisms include impairment of the electrochemical gradient of sweat secretion and a biofeedback mechanism.

Various agents have been used in conjunction with iontophoresis, including tap water, salt water, and anticholinergic drugs.[13] Iontophoresis with saline is less effective than tap-water iontophoresis. A galvanic current of 0.2 milliamperes (mA) per cm^2 on intact skin has no adverse side effects, and a rate of up to 20 to 25 mA per surface generally is tolerable.[14]

Successful induction of hypohidrosis by tap-water iontophoresis requires the application of 15 to 20 mA to each palm or sole for 30 minutes per session for 10 consecutive days, followed by one or two maintenance sessions per week. Initially, many patients experience an aggravation of their

symptoms, but this problem resolves after three to five treatments. Without maintenance therapy, symptoms recur in one to two weeks.[11] No side effects have been reported from the use of 20-mA iontophoresis in pregnant women or patients with pacemakers.

Use of the anticholinergic drug atropine during tap-water iontophoresis sometimes is helpful, but extreme caution is necessary to avoid toxicity from atropine overdose. No more than 1 mg of atropine should be added to 30 mL of tap water. The solution is poured over thin gauze placed on a stainless steel anodal plate. Atropine–tap-water iontophoresis should be used only by physicians well trained in this method.

Use of combined aluminum chloride, an anticholinergic drug, and tap-water iontophoresis for one hour each day resulted in the remission of symptoms for 20 days, compared with 3.5 days for the use of iontophoresis alone; this combination also was more effective in reducing the severity of symptoms.[15] Employing a device for home use makes this treatment relatively affordable and accessible.

Botulinum Toxin Type A

Injections of botulinum toxin type A (Botox) are safe and effective, and often improve quality of life in patients with hyperhidrosis.[16] The toxin inhibits the release of acetylcholine at the neuromuscular junction and affects the postganglionic sympathetic innervation of the sweat glands.[17]

An area about 1.2 cm in diameter is made anhidrotic around each injection site; therefore, multiple injections spaced 1 to 2.5 cm apart are necessary over the hyperhidrotic areas. Efficacy can be observed within one week. Anhidrosis induced by botulinum toxin injections persists for four to 13 months.[18,19] For successful long-term therapy, injections must be repeated regularly.

Intracutaneous injections are recommended rather than subepidermal injections, which are too close to nerve endings.[20] Botulinum toxin injections are painful and require the use of an anesthetic. Ulnar and median nerve blocks or intravenous regional anesthesia is more effective in preventing pain than is topical application of a local anesthetic.[21]

Potential side effects of botulinum toxin injections include transient, slight weakness in the muscles of the hand and the formation of small hematomas at the injection sites.[22] Cost also should be considered. It may take 100 units (acquisition cost: approximately $426) for each hand. Many physicians charge $1,400 to $1,600 for both palms, and the injections have to be repeated every four to six months.

Tap-water iontophoresis is a more effective treatment for hyperhidrosis than saline iontophoresis.

Surgical Treatment

Sympathectomy has been performed since 1920 in patients with disabling, recalcitrant hyperhidrosis. Although the procedure is generally quite effective, it is permanent and therefore should be considered only after all other therapeutic options have been exhausted. Sympathectomy involves the surgical destruction of the second and third thoracic sympathetic ganglia for the palms. The risk of permanent sexual dysfunction limits the usefulness of lumbar sympathectomy for the treatment of plantar hyperhidrosis.[3]

In recent years, open surgery has been replaced by a minimally invasive endoscopic approach that has fewer complications, requires less operating time, and results in less scarring. There still can be complications, including recurrence of the hyperhidrosis, gustatory sweating, compensatory sweating in previously unaffected areas of the body (in up to 60 percent of patients), pneumothorax, Horner's syndrome, neuralgia, atelectasis, pneumonia, and hemothorax.[23,24] In some patients, compensatory sweating can be treated effectively with intradermal botulinum toxin injections.[25]

Cauterization and clamping methods for endoscopic thoracic sympathectomy have been compared in a study of 1,312 patients with hyperhidrosis.[26] All but one patient with palmar hyperhidrosis were cured. Within the two cauterization groups, the satisfaction rate was 94.3 percent for early treatment and 95.1 percent for late treatment; the satisfaction rate was 98 percent in the clamping group. Fewer than 6 percent of patients had severe compensatory hidrosis, and the recurrence rate was 3 percent. Clamping was shown to be at least as effective and safe as electrocautery and had the advantage of being potentially reversible.

Dorsal percutaneous stereotactic thermocoagulation in T2 ganglionectomy and sympathectomy is a newer alternative procedure. It involves the insertion of a thermocoagulation probe through the skin of the back after the application of a local anesthetic and the administration of a mild systemic analgesic. The procedure can be performed on an outpatient basis. One study of 1,688 patients with palmoplantar hyperhidrosis reported a 99.5 percent success rate after initial treatment, with a 7.8 percent relapse

rate after an average of 39 months; all of the patients who relapsed were retreated successfully, resulting in a final success rate of 99.9 percent.[27] This study did not address compensatory hyperhidrosis but did report pneumothorax in 0.2 percent of patients and partial Horner's syndrome in 0.15 percent of patients.

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Strength of Recommendation

Key clinical recommendation	*Strength of recommendation*	*Reference*
Injections of botulinum toxin type A (Botox) are safe and effective, and often improve quality of life in patients with hyperhidrosis.	B	16