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Emotionally Induced Hyperhidrosis

Rachel S. Altman, MD; Robert A. Schwartz, MD, MPH

Hyperhidrosis, a disorder that usually begins in childhood or adolescence, is defined as sweating in excess of what is required for normal thermoregulation. This condition may adversely affect one's quality of life by causing emotional disturbance and social embarrassment. Three forms of hyperhidrosis exist: emotionally induced, localized, and generalized. Hyperhidrosis may be either idiopathic or secondary to other diseases, metabolic disorders, febrile illnesses, or drugs. Diagnosis usually is made based on the patient's history and visible signs of excessive sweating. Various effective treatment options are available.

Epidemiology

Emotionally induced hyperhidrosis most often affects the palms, soles, and axillae. Its prevalence in adolescents and young adults is 0.6% to 1%.[1] Contrary to generalized hyperhidrosis, the onset of localized hyperhidrosis usually occurs in childhood or adolescence.[2] Palmar hyperhidrosis usually begins in childhood (75%), but it also can occur during puberty (25%).[3] In a study of 850 patients with palmar, axillary, or facial hyperhidrosis, the onset was defined as follows: 62% stated that they had the condition as long as they could remember; 33% since puberty; and 5% stated that onset occurred during adulthood. Two studies revealed familial incidence rates of 33%[4] and 55%.[3] Hyperhidrosis has been reported to occur 20 times more frequently in Japanese than in all other ethnic groups.[5,6]

Pathophysiology

Hyperhidrosis is sweating in excess of what is required for temperature homeostasis. Thermoregulation is accomplished in part by eccrine sweat gland secretion of fluid onto the skin, providing an evaporative cooling effect. Individuals with hyperhidrosis have morphologically and functionally normal eccrine glands; however, these glands are hypersensitive to stimuli in the hypothalamic sweat centers.[7] The hypothalamic sweat center that controls the palms and soles is different than that which controls sweat from the rest of the body. Unlike sweating that occurs elsewhere, sweating on the palms and soles is controlled exclusively by the cerebral cortex and is responsive to emotional rather than temperature stimuli.[8] Axillary sweating is induced by both emotional and thermoregulatory stimuli. Therefore, palmoplantar hyperhidrosis does not occur during sleep, whereas generalized hyperhidrosis occurs both during the day and at night. Palmar hyperhidrosis may be caused by a hyperstimulated sympathetic nervous system, specifically the sympathetic nerve fibers that pass through the T2-T3 ganglia.[9]

Differential Diagnosis

Hyperhidrosis may be either primary or secondary to neurologic or neoplastic diseases, metabolic disorders (thyrotoxicosis, diabetes mellitus, hypoglycemia, gout, pheochromocytoma, menopause), febrile illnesses, the use of certain medications (propranolol, physostigmine, pilocarpine, tricyclic antidepressants, venlafaxine),[2] or chronic alcoholism.[10] Nocturnal hyperhidrosis is associated with Hodgkin's disease.[11] Sweating in patients with localized hyperhidrosis may be induced by gustatory stimuli (associated with Frey syndrome, encephalitis, syringomyelia, diabetic neuropathies, herpes zoster parotitis, parotid abscesses) or associated with blue rubber bleb nevus; glomus tumor; POEMS (polyneuropathy, organomegaly, endocrinopathy M protein, skin changes) syndrome; burning feet syndrome, causalgia, pachydermoperiostosis; or pretibial myxedema.[12]

Treatment

Therapy can be challenging, although numerous medical, surgical, and electrical options are now available. Treatment may require visualization of the affected area, which may be accomplished by the iodine starch test (spraying the area with a mixture of 0.5 to 1 gram of iodine crystals and 500 grams of soluble starch). Topical antiperspirants

From Dermatology and Pediatrics, UMDNJ-New Jersey Medical School, Newark, New Jersey.
Reprints: Robert A. Schwartz, MD, MPH, Dermatology, UMDNJ-New Jersey Medical School, 185 South Orange Ave, Newark, NJ 07103-2714 (e-mail: roschwar@umdnj.edu).

containing aluminum chloride or aluminum chloride hexahydrate (20%) dissolved in absolute anhydrous ethyl alcohol (with or without occlusion) are used to treat axillary hyperhidrosis. The patient should use this therapy nightly or until a positive effect is seen at which time frequency may be reduced. This treatment may be irritating if applied to a wet area. To minimize irritation, the patient should induce faster drying by using a hair dryer on the treated axilla, by avoiding the use of antiperspirants during the day, and by applying a topical powder containing baking soda in the morning to neutralize residual aluminum chloride.[8] A possible explanation for the effectiveness of this treatment is that aluminum chloride may mechanically obstruct the eccrine sweat duct orifice and induce atrophy of the secretory cells in eccrine sweat glands, thus decreasing sweat production.[2] Other topical agents such as formaldehyde, boric acid, resorcinol, glutaraldehyde, methenamine, and topical anticholinergics also have been used.[13]

Systemic medications including anticholinergics (probanthine, glycopyrrolate, oxybutynin, benztropine mesylate), diltiazem, clonidine, diazepam, or indomethacin have been tried.[2] Systemic anticholinergics have a poor side-effect profile including dry mouth, blurred vision, mydriasis, tachycardia, and constipation. Benztropine has been found to be especially useful in treating venlafaxine-induced hyperhidrosis.[14] Clonidine has been shown to be an effective treatment for tricyclic antidepressant–induced hyperhidrosis.[15] Sedatives and tranquilizers may be effective for emotionally-induced hyperhidrosis.

Injection of botulinum toxin type A into the affected areas can minimize sweating by inhibiting the release of acetylcholine, the mediator of sympathetic neurotransmission in the sweat glands. In a study of 145 patients with unexplainable axillary hyperhidrosis, subjects were treated with intradermal botulinum toxin type A (200 units divided into 10 injections per axilla) on one axilla and placebo on the other. The quantitative difference in sweat reduction between the 2 groups at 2-weeks postinjections was 111 mg of sweat production per minute (measured gravimetrically). No major adverse side effects were noted from this study, with 98% of patients stating they would recommend the procedure to others.[16] These injections must be repeated at varying intervals to maintain long-term results. In a similar study, 4 female patients with severe palmar hyperhidrosis since childhood were treated with 50 subepidermal injections of 2 units of botulinum toxin type A in each palm, resulting in a 12-month period of anhidrosis in one patient, a 7-month period in 2 patients, and a 4-month period in the fourth patient.[17] The injections were preceded with regional median and ulnar nerve blocks. Each injection produced an anhidrotic region of 1.2 cm in diameter. The only side effect noted was mild thumb weakness in one patient that resolved 3 weeks after treatment.

Iontophoresis consists of passing an ionized substance through intact skin by applying a direct electric current.[2] Although Shelley et al[18] proposed the mechanism of action to be poral plugging via poral hyperkeratosis serving as a barrier to the flow of sweat, the exact mechanism of action of iontophoresis is unknown. Sweat secretion may have been inhibited by keratinization and plugging of the sweat duct via epidermal injury induced by iontophoresis;[19] however, Hill et al[20] found no such change. Numerous substances have been used in the past for iontophoresis, including tap water and anticholinergic agents. Iontophoresis is a useful therapy for palmar and plantar hyperhidrosis but may be difficult to implement for axillary hyperhidrosis. Some patients had increased sweating following initial treatment, which subsided after 3 to 5 treatments.[21] Marked improvement in sweat production was noted with daily treatments for 12 days for palmar hyperhidrosis and 10 days for plantar hyperhidrosis followed by 1 to 2 maintenance treatments per week.[21] Other studies incorporated the use of anticholinergics, which were more effective than tap water but resulted in mild systemic side effects, such as dry mouth, problems with visual accommodation, abdominal discomfort, and micturition problems.[22] A study by Shen et al[23] incorporated both anticholinergics and aluminum chloride for one hour daily to diminish sweat secretion (via anticholinergic) and cause structural changes of the sweat gland (via aluminum chloride). This combination iontophoresis treatment compared to tap water iontophoresis resulted in a remission period of 20 days versus 3.5 days and a reduction in severity of symptoms of -3.1 versus -1.5.[23] Any device that can provide at least 20 mA of direct current should be effective, and for palmar hyperhidrosis, daily treatments with tap water iontophoresis for 30 minutes at 15 or 20 mA usually induces hypohidrosis within a week.[8] Intact skin can tolerate up to 0.2 mA/cm^2 of galvanic current without causing burning, and up to 20 to 25 mA per palm can be tolerated.[12]

Thoracic sympathectomy has been documented as a permanent treatment for hyperhidrosis as early as 1920.[24] It deinnervates the eccrine sweat glands, thereby prohibiting sweat production. Recently, an endoscopic approach has been utilized, which minimizes complications and scars previously

encountered with the open approach. Regardless of which approach is taken, certain sympathetic ganglia must be destroyed based on the source of excessive sweating. The second and third thoracic ganglia are responsible for palmar hyperhidrosis whereas the fourth thoracic ganglion is responsible for axillary hyperhidrosis. Facial sweating is controlled by the first ganglion. Endoscopic transthoracic sympathectomy has been shown to be an effective treatment for hyperhidrosis, with immediate positive results in 832 of 850 patients. After a 31-month average follow-up, recurrent symptoms appeared in 17 of the patients.[4] The same study showed that endoscopic transthoracic sympathectomy is a minimally invasive procedure with few complications. A common complication is compensatory sweating in previously unaffected areas. Of the 850 patients who underwent endoscopic transthoracic sympathectomy, 55% had compensatory sweating (mostly on the trunk) and 36% had gustatory sweating.[4] In a similar study of 72 patients who underwent transthoracic endoscopic sympathectomy (T2 or T2+3) for palmar hyperhidrosis, a success rate of 93.1% was found, with compensatory sweating in 98.6% of patients within one month postsurgery and gustatory sweating in 16.7%.[3] Other less commonly encountered complications included Horner's syndrome, intercostal neuralgia, and pneumothorax. The possible cause of this compensatory sweating may be thermoregulation via sweat redistribution.[3]

Surgical excision is another alternative treatment for emotionally induced hyperhidrosis. After identifying the source of excessive sweat (using the starch-iodine test), patients previously treated unsuccessfully with topical agents may undergo surgical excision of the affected area to remove the offending sweat glands. This method is particularly useful for axillary hyperhidrosis.

Subcutaneous liposuction (removal of the eccrine sweat glands) has been documented as an effective treatment for axillary hyperhidrosis. Liposuction may eliminate the eccrine sweat glands in the axillae without causing major disruption to the overlying skin, resulting in small surgical scars and a smaller area of hair loss.[13]

REFERENCES

1. Adar R, Kurchin A, Zweig A, et al. Palmar hyperhidrosis and its surgical treatment: a report of 100 cases. *Ann Surg*. 1977;186:34-41.
2. Stolman LP. Treatment of hyperhidrosis. *Dermatol Clin*. 1998;16:863-867.
3. Lai YT, Yang LH, Chio CC, et al. Complications in patients with palmar hyperhidrosis treated with transthoracic endoscopic sympathectomy. *Neurosurgery*. 1997;41:110-113.
4. Drott C, Gothberg G, Claes G. Endoscopic transthoracic sympathectomy: an efficient and safe method for the treatment of hyperhidrosis. *J Am Acad Dermatol*. 1995;33:78-81.
5. Cloward RB. Treatment of hyperhidrosis palmaris (sweaty hands): a familial disease in Japanese. *Hawaii Med J*. 1957;16:381-389.
6. Cloward RB. Hyperhidrosis. *J Neurosurg*. 1969;30:545-551.
7. Wenzel FG, Horn TD. Nonneoplastic disorders of the eccrine glands. *J Am Acad Dermatol*. 1998;38:1-17.
8. Sato K, Kang WH, Saga K, et al. Biology of sweat glands and their disorders, II: disorders of sweat gland function. *J Am Acad Dermatol*. 1989;20:713-726.
9. Shih CJ, Wu JJ, Lin MT. Autonomic dysfunction in palmar hyperhidrosis. *J Auton Nerv Syst*. 1983;8:33-43.
10. Tugnoli V, Eleopra R, DeGrandis D. Hyperhidrosis and sympathetic skin response in chronic alcoholic patients. *Clin Autonom Res*. 1999;9:17-22.
11. Gobbi PG, Pieresca C, Ricciardi L, et al. Night sweats in Hodgkin's disease: a manifestation of preceding minor febrile pulses. *Cancer*. 1990;65:2074-2077.
12. Sato K, Ohysuyama M, Samman G. Eccrine sweat gland disorders. *J Am Acad Dermatol*. 1991;24:1010-1014.
13. Lillis PJ, Coleman III WP. Liposuction for treatment of axillary hyperhidrosis. *Dermatol Clin*. 1990;8:479-482.
14. Garber A, Gregory R. Benztropine in the treatment of venlafaxine-induced sweating. *J Clin Psychiatry*. 1997;58:176-177.
15. Feder R. Clonidine treatment of excessive sweating. *J Clin Psychiatry*. 1995;56:35.
16. Heckmann M, Ceballos-Baumann AO, Plewig G. Botulinum toxin A for axillary hyperhidrosis (excessive sweating). *N Engl J Med*. 2001;344:488-493.
17. Shelley WB, Talanin NY, Shelley ED. Botulinum toxin therapy for palmar hyperhidrosis. *J Am Acad Dermatol*. 1998;38:227-229.
18. Shelley W, Horvath P, Weidman F, et al. Experimental miliaria in man, I: production of sweat retention anhidrosis and vesicles by means of iontophoresis. *J Invest Dermatol*. 1948;11:275-291.
19. Gordon BI, Maibach HI. Eccrine anhidrosis due to glutaraldehyde, formaldehyde, and iontophoresis. *J Invest Dermatol*. 1969;53:436-439.
20. Hill AC, Baker GF, Jansen GT. Mechanism of action of iontophoresis in the treatment of palmar hyperhidrosis. *Cutis*. 1981;28:69-70,72.
21. Holze E, Alberti N. Long-term efficacy and side effects of tap water iontophoresis of palmoplantar hyperhidrosis: the usefulness of home therapy. *Dermatologica*. 1987;175:126-135.
22. Abell E, Morgan K. The treatment of idiopathic hyperhidrosis by glycopyrronium bromide and tap water iontophoresis. *Br J Dermatol*. 1974;91:87-91.
23. Shen JL, Lin GS, Li WM. A new strategy of iontophoresis for hyperhidrosis. *J Am Acad Dermatol*. 1990;22:239-241.
24. Kotzareff A. Resection partielle de trone sympathetique cervical droit pour hyperhidrose unilaterale. *Rev Med Suisse Romande*. 1920;40:111-113.