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REVIEW

Primary hyperhidrosis: an updated review

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Abstract

Background: Hyperhidrosis (HH) is a condition characterized by excessive sweating beyond the physiological needs of thermoregulation. HH can be classified as primary (idiopathic) hyperhidrosis (PHH) or secondary hyperhidrosis (SHH), which is associated with underlying medical conditions, medications or systemic disorders. This narrative review provides an updated overview of PHH, with a focus on epidemiology, aetiopathogenesis, clinical manifestations, diagnostic approaches and current management strategies, particularly highlighting pharmacological and procedural treatment options.

Methods: A literature search was conducted in February 2025 across Ovid Medline, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL) using the key term "hyperhidrosis". The review included observational studies, clinical trials, narrative reviews, guidelines and meta-analyses published in the past 10 years. Additional references were identified through manual searches of relevant bibliographies.

Results: The global prevalence of PHH is estimated to range between 0.072% and 9%, with PHH accounting for 93% of all HH cases. Whilst the precise pathophysiology remains unclear, PHH is believed to result from sympathetic overactivity, whereas SHH is associated with endocrine, neurological, infectious, malignant and medication-induced causes. PHH is diagnosed clinically and distinguishing between primary and secondary forms is essential. Management options vary based on severity, ranging from topical therapies (antiperspirants, anticholinergics), systemic medications (oral anticholinergics, adrenergic modulators), device-based interventions (iontophoresis, microwave thermolysis), injectable therapies (botulinum toxin) and surgical approaches (sympathectomy, excision, liposuction/curettage). Whilst these interventions can significantly improve symptoms and quality of life, long-term efficacy, recurrence and adverse effects remain concerns.

Conclusion: PHH significantly impacts the quality life of patients contributing to both physical discomfort and psychosocial distress. An individualized, multi-modal approach is crucial to optimizing management. Further research is warranted to refine existing therapies and evaluate emerging treatment modalities for improved long-term outcomes.

Keywords: anticholinergics, botulinum toxin, eccrine sweat glands, iontophoresis, primary hyperhidrosis, sympathectomy.

Citation

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Introduction

Hyperhidrosis (HH) is often defined as primary HH (PHH), also known as idiopathic or essential HH, where the cause of the excessive sweating beyond thermoregulation needs is unknown, and secondary HH (SHH), where the cause is due to an underlying medical condition, medication or other systemic affect. HH can further be classified as focal, where it affects a localized area of the body, or generalized, where it affects a large area or the entire body. PHH tends to be more focal, whilst SHH is often more generalized.[1,2] This narrative review aims to provide an overview of HH with the context of highlighting key pharmacological treatments to guide management.

Methods

A search was conducted in February 2025 in Ovid Medline, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) using the key term "hyperhidrosis". The search strategy included all observational studies (including case reports and case series), clinical trials (including open trials, non-randomized controlled trials and randomized controlled trials) and reviews (including narrative reviews, clinical guidelines and meta-analyses) published within the past 10 years. ClinicalKey, DynaMed, Wikipedia and Google were also searched to enrich the review. Additional articles were culled by searching the reference lists. Only papers published in the English literature were included in this review. The information retrieved from the search was used in the compilation of the present article.

Review

Epidemiology

The estimated worldwide prevalence of PHH has been reported to be between 0.072% and 9%.[3–14] HH (both primary and secondary) prevalence in the USA has been estimated at 2.8–4.8% of the population, whereas prevalence in Germany has been estimated at 16.3%.[5,13] PHH is the most common form, representing 93% of all patients with HH.[15,16] Although reported sex differences in PHH prevalence vary across studies — potentially due to differing subtype classifications and healthcare-seeking behaviours — the overall consensus is that, overall, PHH affects both sexes equally.[15–17] Additionally, the prevalence of PHH may be independent of geographical location, however, there may be differences in specific subtypes of PHH depending on sex, ethnicity and age.[17] Further, 30–65% of patients with PHH describe having a positive family history indicating a strong genetic link to the condition.[18]

Aetiopathogenesis

In PHH, patients produce excessive sweating that exceeds the physiological needs for thermoregulation, resulting in a decreased quality of life and burden on patients.[19] The excessive response of PHH is inappropriate and does not match the typical response one would expect based on an emotional or physiological stimulus. The proposed major causes include autonomic nervous system effects, genetics and environmental factors.[19]

There are two main types of sweat glands, eccrine sweat glands and apocrine sweat glands.[19] Whilst eccrine sweat glands are found across the entire body and produce sweat for thermoregulation, apocrine sweat glands are primarily found in hair follicles and contribute towards body odour.[19] Eccrine sweat glands are more common (75% of all sweat glands) and are produced during the embryonic stage of life with none produced after birth. The distribution of these sweat glands parallels the common areas affected in PHH with the highest density of sweat glands in the palmoplantar and axillae regions.[19] Eccrine sweat glands are the culprit in PHH and are innervated by cholinergic fibres of the sympathetic nervous system (SNS) to produce odourless and colourless sweat that consists of mainly water, electrolytes (sodium and chloride), urea and nitrogen metabolites. Apocrine sweat glands, which produce pheromones and develop after puberty, are not involved in PHH. A third type of sweat gland, apoeccrine sweat glands, are only localized to the axillae and are involved in PHH of the axillae.[20] Sweating provides a means of important thermal regulation, allowing for the dissipation and evaporation of water to decrease body heat and temperature.

The sweat response is regulated by the autonomic nervous system, specifically the SNS via cholinergic neurons. In PHH, this system is thought to be dysregulated due to neurogenic overactivity or hyperexcitability. However, the exact pathophysiology of this remains unclear.[19,20] It is estimated that 30–65% of patients with PHH have a positive family history.[18] Whilst evidence suggests an autosomal dominant inheritance with partial penetrance and variable clinical presentation, it remains unclear whether PHH is purely genetic or multifactorial in origin.[21] Genetic studies have identified several loci potentially associated with primary focal HH, including 14q11.2–q13, 2q31.1, 1q41–1q42.3, 2p14–2p13.3, 2q21.2–2q23.3 and 15q26.3.[22–24] Additionally, mouse model studies have implicated several genes in PHH, such as *AQP5* (encoding aquaporin 5), *ITPR2* (encoding inositol 1,4,5-trisphosphate receptor type 2) and *FoxA1*.[21] Certain environmental factors, such as stress and anxiety, can worsen the sweating in PHH.[25] One characteristic of PHH that may differ from SHH is that sweating only occurs when patients are awake.[26]

When making a diagnosis of PHH, SHH must be ruled out and includes a wide range of potential causes such as endocrine, infectious, neurological, psychiatric, cardiovascular, dermatological, respiratory, gastrointestinal, haematological, musculoskeletal, physiological and autoimmune/autoinflammatory conditions, malignant disease or medications.[27] These categories and corresponding conditions are summarized in Table 1.[15,28–54,55–83]

Histopathology

Eccrine sweat glands in patients with PHH are histopathologically identical to unaffected individuals and there is no increase in the number of glands. However, sympathetic ganglia of patients with PHH may be

Table 1. A list of categories and causes of secondary HH.[15,28–54,55–83]

Category	Conditions
Endocrine	Hyperthyroidism, acromegaly, diabetes, Vitamin D deficiency, obesity, pituitary adenoma, adrenal insufficiency, ovarian insufficiency, hyperpituitarism, polycystic ovary syndrome
Malignancy	Lung cancer, renal cancer, melanoma, carcinoid tumours, pheochromocytomas, histiocytosis, systemic mastocytosis, metastatic chondroblastoma, breast carcinoma, cholangiocarcinoma, pancreatic adenocarcinoma, colorectal adenocarcinoma, prostate adenocarcinoma, hepatocellular carcinoma, Kaposi sarcoma, leiomyosarcoma, non-seminomatous mediastinal germ cell tumour, metastasis of undetermined origin, non-Hodgkin lymphoma, Hodgkin lymphoma, chronic lymphocytic leukaemia, multiple myeloma, myelofibrosis
Infectious	Bacterial endocarditis, pulmonary tuberculosis, pitted keratolysis, non-tuberculous mycobacteria, HIV, CMV, *Helicobacter pylori* gastritis, chronic osteoarticular infection, male urinary tract infection, malaria, pneumonia, postviral syndrome
Medications	Anticholinesterases, selective serotonin reuptake inhibitors, tricyclic antidepressants, antiglaucoma eye drops, bladder stimulants, sialogogues, β-adrenergic receptor agonists, calcineurin inhibitors, TNF inhibitors, antiandrogens, gonadotropin-releasing hormone agonists, aromatase inhibitors, oral contraceptives, ixekizumab, sunitinib, pembrolizumab, dupilumab, alcohol
Neurological	Head trauma, cerebral palsy, spinal cord injury, peripheral neuropathy, hypothalamic lesions, intracranial neoplasms, Frey syndrome, Ross syndrome, stroke, thoracic outlet syndrome, spontaneous episodic hypothermia and hyperhidrosis, postherpetic hyperhidrosis, diabetic neuropathy, dementia, Lewy body dementia, dysautonomia dominant subtype Parkinson disease, sleep apnoea, restless leg syndrome, neuropathic pain, complex regional pain syndrome (reflex sympathetic dystrophy), Arnold–Chiari malformation, burning feet syndrome (Gopalan syndrome), autonomic dysreflexia, syringomyelia, endoscopic thoracic sympathectomy
Psychiatric	Generalized anxiety disorder, depression, social anxiety disorder, schizophrenia, bipolar disorder
Cardiovascular	Myocardial infarction, heart failure, systemic arterial hypertension, vasovagal syncope, shock
Dermatological	Eccrine angiomatous hamartoma, blue rubber bleb nevus, pachyonychia congenita, eccrine nevus, unilateral nevus flammeus, epidermolysis bullosa, congenital ichthyosiform erythroderma, nail–patella syndrome, POEMS syndrome
Respiratory	Chronic obstructive pulmonary disease, asthma
Gastrointestinal	Inflammatory bowel disease, gastro-oesophageal reflux disease
Haematological	Hemochromatosis
Musculoskeletal	Peripheral spondyloarthropathy, fibromyalgia, rheumatoid arthritis, unspecified arthritis, joint pain
Physiological	Physiological gustatory sweating, pregnancy, menopause
Autoimmune/ autoinflammatory	Vasculitis, systemic lupus erythematosus, sarcoidosis, Still disease, morphea, Schnitzler syndrome

larger on histopathological observation, suggesting hyperfunctioning of sweat glands rather than hypertrophy.[19]

Clinical manifestations

As mentioned above, HH can be classified as PHH/essential (idiopathic) or SHH. The terms primary, essential and idiopathic HH are all synonymous.[84] HH can further be classified by distribution, with SHH being generalized and affecting the whole body, and PHH being focal, affecting a specific location of the body. Rzany et al. proposed the terms 'primary focal HH' when only one body site is affected and 'primary multifocal HH' when two or more body sites are affected.[84] PHH is typically focal, with the most common anatomical regions being palms/soles, axillae, face, trunk and genital area.[85] One study found that 80.4% of patients had palmoplantar involvement, 62.7% of patients had axillary involvement, 19.6% had truncal involvement, 17.6% had genital involvement and 16.7% had craniofacial involvement.[86]

PHH is typically focal, most commonly affecting (in descending order) palms/soles (palmoplantar), axillae, trunk, genital area and face/head (craniofacial). PHH is often bilateral/symmetric but can be asymmetric and is

often associated with a family history when presenting in a patient with younger onset.[86] Primary multifocal HH occurs when there are two or more focal areas affected. The most common presentation is of three total body sites affected (45.1% of patients), followed by two (41.2% of patients), four (8.8% of patients) and five (5.9% of patients).[86] Often, sweating will be present for at least 6 months, is absent during sleep, and is associated with increased morbidity and decreased quality of life.[86]

Excessive sweating can cause cold, clammy skin and compromise the skin barrier, leading to maceration and a higher risk of cutaneous infections, including erythrasma, impetigo, pitted keratolysis, dermatophytosis (tinea pedis/cruris, onychomycosis), candidiasis and HPV-related lesions like verruca palmaris and plantaris.[16,87] Sweating may also trigger or worsen eczematous conditions, with PHH linked to irritant contact dermatitis, dyshidrotic eczema and atopic dermatitis.[88,89] Additional complications include bromhidrosis (malodour) and musculoskeletal issues such as poor posture due to attempts to conceal sweating.[90,91]

Diagnosis

There are key clinical features that would aid in diagnosing PHH and a careful and complete history and physical examination is important in making a proper diagnosis. Questions that should be asked include pattern of sweating, age of symptom onset, provocative factors, duration, frequency, amount, time (night sweating) and distribution of sweating, family history of HH, and a review of symptoms related to secondary causes, which should include weight loss, fever and lymphadenopathy.[92,93] Secondary causes must be ruled out and targeted diagnostic testing should be based on clinical suspicions from the history and physical exam.[5,29,94–96] Specific diagnostic criteria for PHH include 6 months of visible, focal and excessive sweating, and at least four of the following: location in sweat gland-rich areas (palms, soles, axillae or craniofacial areas), symmetrical bilateral distribution, disruption of daily activities, occurring at least once or more per week, having an age of onset before 25, positive family history, and absence of nocturnal sweating.[29,94,95,97] Suspicious features of SHH include asymmetric, unilateral or generalized distribution of sweating with the absence of family history, occurring later in life (25 years or older) and an association with night sweats.[28]

Measurements for PHH sweating also exist but are not commonly used clinically. However, they can help determine severity of sweating and are often used to guide treatment and management.[15] Measurement tests include the minor starch-iodine test, which colours affected regions purple;[92,98] the ninhydrin test that reacts with sweat to produce a colour that can be analysed digitally;[93] gravimetric testing, which weighs the sweat with filter paper;[92,99,100] the thermoregulatory sweat test, which measures sweating in a controlled laboratory environment; dynamic quantitative sudometry, which measures sweating over time;[101–103] and the electronic moisture meter, which detects moisture evaporation from the skin.[104] Other more subjective assessment tests based on patient symptom scores include the Hyperhidrosis Disease Severity Scale (HDSS),[5,93,104] the Hyperhidrosis Impact Questionnaire,[87,93,98] the Dermatology Life Quality Index (DLQI) questionnaire,[98,105–107] and the Medical Outcomes Trust Short Form 12 Health Survey.[87,93,108]

The psychological impact of PHH is profound, affecting the quality of life, mental health, self-esteem, social interactions, relationships and career choices.[109] Nearly half (48%) of patients report poor or very poor quality of life,[110] with higher rates of depression and anxiety compared to the general population.[5] The psychological burden of PHH may be comparable to or greater than conditions like psoriasis and acne.[111] Common psychosocial effects include embarrassment (33.3%), shame (25.0%) and discomfort (16.7%).[110] Patients with palmar HH experience a mean productivity loss of 7.24%, resulting in substantial financial impact.[112] Managing PHH is time-consuming, with patients spending 15–60 min daily on symptom control and 50–70% changing clothes more than twice a day.[113] Affected individuals often avoid handshakes, have low self-esteem, withdraw socially and face job restrictions due to issues like rusting metal objects or wet paperwork.[90]

Management

Management of PHH is challenging and often requires patients to trial multiple modalities, with options ranging from lifestyle changes to topical, systemic, device-based therapies, procedures and surgery.[114–119] All treatment modalities discussed in our review are summarized in Table 2 with an overview shown in Box 1.

Lifestyle, behavioural and adjunctive therapies

Lifestyle, behavioural and adjunctive therapies are recommended for all patients with PHH and include crowded areas, tight clothing, spicy foods, alcohol and triggering emotional stimulation.[114] Adjunctive therapies that fall into this category include using moisture-wicking sheets and pyjamas, portable body coolers, pens that can write in wet conditions, shirts with cooling devices, synthetic fabrics, masking sweat with underarm liners, dress shields, leather shoes, absorbent shoe insoles, foot powder and cotton/wool socks.[114,115,200,201] Lifestyle, behavioural and adjunctive therapies are recommended for all patients with PHH regardless of the type, can be initiated at

Table 2. Summary of treatments.

Category	Treatment	Sites of application	Age group	Efficacy	Common side-effects	Key references
Topical	Aluminium chloride hexahydrate	Axillae, palms, soles, scalp	All ages	94% (axillary), 84% (plantar), 60% (palmar)	Skin irritation, miliaria, dermatitis	114,116,117,120,121
	Glycopyrronium tosylate	Axillae, palms, scalp	≥9 years	60% report symptoms 'much better'	Dry mouth, blurred vision, headache	122–129
	Oxybutynin	Axillae, palms	Children and adults	74% improved (10% gel), 53% (20% lotion)	Pruritus, headache, erythema	130–133
	Sofpironium bromide	Axillae	Adults	Dose-dependent HDSS/DLQI improvement	Dry mouth, blurred vision, dermatitis	134–136
	Umeclidinium	Axillae	Adults	40% HDSS improvement	Pain, bronchitis, systemic absorption	137
Systemic	Oral glycopyrrolate	Generalized	Adults, >11 years	67–79% response	Dry mouth, vision issues, constipation	114,115,138–140
	Oral oxybutynin	Generalized	Adults, children	76.2% symptom relief	Dry mouth, nausea, dizziness	114,115,138,140,141–143
	Methantheline bromide	Generalized	Adults	Improvement in DLQI and HDSS	Not specified	144
	Clonidine	Generalized	Adults	Some efficacy in generalized hyperhidrosis	Dry mouth, dizziness, sedation	145,146
	Benzodiazepines	Generalized (anxiety related)	Adults	Limited evidence	Sedation, dependence	138
Device based	Iontophoresis	Palms, soles, axillae	Adults, some paediatric	~80% improvement	Discomfort, skin irritation	95,147,146,148–151
	Microwave thermolysis	Axillae	Adults	62–90% efficacy	Pain, oedema, numbness	115,152,153
	Ultrasound (VASER)	Axillae	Adults	~80% reduction	Tenderness, numbness	115,154–157
	Fractional microneedle radiofrequency	Axillae	Adults	Improvement at 6–21 weeks	Pain, swelling, hyperpigmentation	158–161
	Laser treatments	Axillae	Adults	Significant improvement at 1–12 months	Pain, sensation loss, scarring	162–166
Procedural	Botulinum toxin injections	Axillae, palms, craniofacial	Adults, off-label paediatric	Axillae: 82–87% Palmar: 80–90% Craniofacial: Up to 92%	Pain, compensatory sweating	114,117,121,167–174
	Local excision, curettage, liposuction	Axillae	Adults	Permanent but relapse possible	Scarring, nerve injury	114,115,118,175–183
Surgical	Sympathectomy (endoscopic thoracic sympathectomy)	Palmar, axillary, craniofacial, plantar	Adults	68–100% efficacy	Pneumothorax, compensatory sweating	114,115,184–199

DLQI, Dermatology Life Quality Index; HDSS, Hyperhidrosis Disease Severity Scale

any time, and are often used in conjunction with another treatment modality to support patients with PHH.

Topical therapies

Topical therapies are first-line treatments for PHH and include topical antiperspirants, topical anticholinergic and topical botulinum toxin (BTX) type A liposomal cream.[115–119,200]

Topical antiperspirants

Topical antiperspirants primarily consist of metal salts, most notably aluminium salts such as aluminium chloride and aluminium zirconium, whilst other metals like vanadium and indium have also been used.[116,202–204] Amongst these, aluminium chloride hexahydrate is the most common and effective, particularly for mild to moderate PHH, and serves as a first-line, affordable option for primary focal HH, especially axillary and palmoplantar types (but including other forms such as craniofacial, which includes the scalp).[29,94,114,116,117,120] Concentrations range from 6% to 40%, delivered in various formulations (solutions, sticks, gels, creams), with over-the-counter products containing up to 12.5% aluminium chloride hexahydrate, whilst prescription formulations commonly include 20% aluminium chloride in ethyl alcohol.[114,116,117,120,121] Application is recommended nightly on dry skin for 6–8 hours, tapering to once weekly as symptoms improve (typically after >1 week).[93,114–118,202] Topical antiperspirants demonstrate high efficacy, with satisfaction rates of 94% for axillary, 84% for primary plantar, and 60% for primary palmar HH and sustained improvement in up to 87% of patients at 5 months.[114,117,202,204] The most common side-effects include skin irritation and itching (reported in 21% of patients), particularly in the axilla and with higher concentrations, as well as miliaria and irritant dermatitis.[93,114,116,147,205–208] These can be mitigated by spacing out applications, using lower concentrations, employing moisturizing agents, or applying triethanolamine or topical corticosteroids (e.g. 2.5% hydrocortisone); however, salicylic acid should be avoided as it is a known irritant.[93,114,116,121,147,205–208] Whilst concerns about links to Alzheimer disease and breast cancer have arisen from animal studies, no such associations have been demonstrated in humans.[114,118]

Topical anticholinergics

Topical anticholinergics work by competitively blocking muscarinic receptors on eccrine sweat glands preventing the binding of acetylcholine and, subsequently, preventing sweating. Topical anticholinergics include topical glycopyrrolate, topical oxybutynin, topical sofpironium bromide and topical umeclidinium.

Topical glycopyrrolate

Topical glycopyrrolate is the most researched topical anticholinergic medication for PHH and is available in two forms: glycopyrronium bromide and glycopyrronium tosylate. Topical glycopyrrolate has been approved by the FDA for the treatment of primary axillary HH in patients older than 9 years of age. Concentrations and formulations include a 0.5–4% solution, gel, cream, spray or pads. Glycopyrronium tosylate can be delivered as a pre-moistened cloth applied daily with improvement expected after 1 week of use.[122] Randomized control studies (RCTs) and research have indicated that topical glycopyrrolate is a good treatment for axillary HH, palmar HH and craniofacial HH. For example, two RCTs[122,123] and one prospective study[124] utilizing a 4-week course of 2.4% glycopyrronium tosylate and 2% topical glycopyrronium bromide cream for primary axillary HH, resulted in significant reduction in sweating symptoms and improvement in scores on the DLQI and HDSS, with 60% of patients reporting sweating to be "much better" and results maintained at the 44-week follow-up. Another RCT of 497 patients with primary axillary HH showed clinical improvement (50% reduction in sweating and improvement in HDSS and DLQI scores) with 2.4% and 3.75% glycopyrronium tosylate cloths/wipes.[125] For primary palmar HH, 2.4% glycopyrronium tosylate cloth for 30 minutes without occlusion seems to be most effective in treating symptoms.[209] For primary craniofacial (including scalp) HH, two RCTs (39 and 25 patients, respectively)[126,127] showed a decrease in sweating symptoms and slight improvement in HDSS, whilst the other RCT (24 patients) also showed improvement with 2% topical glycopyrronium.[128] In a 44-week RCT of children (ages 9–16 years), the safety and efficacy of topical glycopyrrolate tosylate was maintained for the treatment of primary axillary HH, indicating its effectiveness for use in children older than 9 years of age.[129] Adverse effects associated with topical glycopyrrolate include skin irritation, pruritus, blurred vision, dysuria, headache, dizziness, sore throat, mydriasis, dry mouth, constipation and nasopharyngitis.[122,125,129,210]

Topical oxybutynin

Topical oxybutynin is another topical anticholinergic that is well studied. It is used off-label for PHH. The most common formulations include 1–20% gel or lotion. An RCT of 53 patients showed that 10% topical oxybutynin gel resulted in improvement in DLQI and HDSS scores in 74% of patients after 30 days with primary axillary or palmoplantar HH.[130] Another RCT of 30 patients showed improvement in primary palmar HH with 1% oxybutynin gel and 1% oxybutynin nanoemulgel.[131] The largest phase III RCT (244 patients) with a 20% oxybutynin lotion showed reductions in sweat volume and improvement in symptoms in 53% of patients with primary palmar HH.[132] A pilot study in 10 children found a significant reduction in sweating for axillary HH with 3% topical oxybutynin.[133] Reported adverse events from these studies include side-effects related to headache, pruritus and erythema on the application site.[130]

Topical sofpironium bromide

Topical sofpironium bromide is a recently developed anticholinergic medication that is being used in the treatment of PHH. Its use has been largely studied in primary axillary HH with concentrations of topical sofpironium gel at 5%, 10% and 15%.[134] It is applied daily with improvements seen as fast as 1 week with treatment durations in two separate phase III trials (281 and 185 patients with primary axillary HH, respectively) from 6 weeks to 52 weeks.[134–136] A phase II RCT showed improvement in DLQI scores along with reduced sweating symptoms from the use of topical sofpironium gel for primary axillary HH, with 5%, 10% and 15% showing stepwise improvement with increasing concentration in both DLQI and HDSS scores.[134] Adverse events include dry mouth, blurred vision, dermatitis, erythema and nasopharyngitis.[134–136]

Topical umeclidinium

Only one phase IIa RCT has been conducted on topical umeclidinium at a concentration of 1.85% daily, resulting in a significant reduction of sweating and improvement in HDSS scores in 40% of patients with primary axillary HH after 2 weeks. The only adverse events noted were application site pain, bronchitis, headache and presyncope with evidence of systemic absorption due to measurable plasma levels in 78% of patients.[137]

Topical BTX type A liposomal cream

One RCT in 20 patients with primary axillary HH, showed that daily application of topical BTX type A liposomal cream reduced sweating and resulted in improved HDSS scores at 2 and 8 weeks. No adverse effects were noted.[211] Its use in clinical settings for the treatment of PHH may become more relevant with continued research.

Systemic therapies

Systemic therapies for PHH are primarily in the form of oral anticholinergic drugs.[114–118] These medications are not approved by the FDA and are often reserved for treatment-resistant cases and for the treatment of generalized or multifocal PHH.

Oral anticholinergic medication

Oral anticholinergic medication functions by competitively inhibiting the muscarinic receptor acetylcholine binding site, preventing the production of sweat at eccrine sweat glands.[212] The most common oral systemic anticholinergic medications are glycopyrrolate, oxybutynin and methantheline bromide (used in Europe but not currently available in the USA).

Oral glycopyrrolate

Oral glycopyrrolate is another used oral anticholinergic medication in PHH.[138,139] In adults, the most common doses are between 0.5 mg and 3 mg once or twice daily, with children (approved for use in children above 11) typically using 2 mg daily.[115,138,139] Treatment efficacy is often achieved after 1 week and increases in doses may be required.[114] Oral glycopyrrolate has been shown to be an effective treatment in primary focal and multifocal HH with response rates in the range of 67–79% of patients.[140] The most common adverse events include dry mouth, impaired vision, dry eyes, headache, palpitations and urine retention.[140,212] Whilst it may be an effective medication, one-third of patients discontinue the medication due to these side-effects.[139] Absolute and relative contraindications to use include pyloric stenosis, paralytic ileus, myasthenia gravis, gastroesophageal reflux disease, cardiac insufficiency, closed-angle glaucoma and bladder outlet obstruction.[121,139]

Oral oxybutynin

Oral oxybutynin is another anticholinergic medication for PHH. Typical doses in adults include 2.5–5 mg once or twice daily with typical total doses in the range of 5–10 mg a day and maximum doses as high as 20 mg, with improvement seen at 1 week and administered up to at least 6 weeks with ongoing maintenance.[114,138,141,142] Effective doses in children under the age of 14 years range from 2.5 to 10 mg daily.[143] In terms of effectiveness, oral oxybutynin relieved symptoms in 76.2% of patients and improved quality of life in 75.6% of patients.[140] The most commonly reported side-effects include dry mouth in 30–43% of adults and 53% of children as well as nausea, diarrhoea, gastroesophageal reflux, headache, dizziness, flushing, blurred vision, urinary retention, tiredness and constipation.[141–143]

Methantheline bromide

Methantheline bromide is another oral anticholinergic used in PHH. In one RCT of 339 patients, after 4 weeks using a dose of 50 mg three times daily resulted in reduced primary axillary sweating and improved DLQI and HDSS scores.[144]

Other systemic therapies

Other oral therapies used in the literature with limited data include β-blockers, benzodiazepines, α2-adrenergic receptor agonists, prostaglandin E2 inhibitors and calcium channel blockers. Benzodiazepines have been shown to help with anxiety-induced HH.[138] Prostaglandin E2 inhibitors, such as indomethacin, may block prostaglandin E2-induced sweating in vitro.[114,121] Calcium channel blockers may reduce sweating by inhibiting calcium-dependent acetylcholine release.[114] The most widely studied are α2-adrenergic receptor agonists. Clonidine has been used in generalized and paroxysmal localized PHH and works by reducing sympathetic activity on eccrine sweat glands.[145] Dosages that have been used include 0.1 or 0.15 mg twice daily with side-effects

including dry mouth, dizziness, constipation and sedation.[146] The aforementioned medications may be useful in certain cases of patients with PHH but are not widely used and more research is needed to determine their validity.

Device-based therapy

Device-based therapy includes iontophoresis, microwave thermolysis, ultrasound, fractional microneedle radiofrequency and laser treatments.[114–118]

Iontophoresis

Iontophoresis involves immersing the affected skin in tap water or an ionized solution, through which a low-voltage electric current is applied. This current repels hydrogen ions, leading to blockage of the sweat glands by altering the electrochemical gradient, lowering the local pH and potentially inhibiting SNS activity. These changes, including glandular damage, acidification and SNS inhibition, collectively result in obstruction of sweat ducts and a reduction in sweat production.[146,147] Iontophoresis is approved by the FDA as a first-line treatment for primary palmar and plantar HH and used for primary axillary HH by special electrode pads.[146,148] Iontophoresis is not generally used or recommended for craniofacial (including scalp) HH as it can be technically challenging and there may be a high risk of injury. In the USA, iontophoresis machines are only available by prescription (RA Fischer, RA Fischer Co., Northridge, CA, USA; Hidrex, Hidrex USA, LLC, Austin, TX, USA; Drionic, General Medical Co., Los Angeles, CA, USA; and Dermadry, Dermadry Laboratories Inc., Montreal, QC, Canada). Iontophoresis is performed three to four times per week by submerging the affected area (palms, soles or axillae) for 15–40 min at a current of 15–20 mA. Patients see improvement at around 3–4 weeks with transition to maintenance therapy at once per week.[95,146,149] There is higher compliance with at-home devices and iontophoresis is effective in 80% of cases.[147,150,151] Aluminium chloride, anticholinergics and BTX may be added as a medium to the tap water. Topical and/or systemic agents can also be added as combination therapy to improve the effects of iontophoresis.[89,139,214–219] Contraindications to iontophoresis include pregnancy, substantial metal implants, cardiac conditions, epilepsy and implantable electronic devices, including pacemakers.[220–223] Side-effects include discomfort (shock), dryness (mouth and throat), paraesthesias, erythema, transient vesiculations, skin irritation, dermatitis and asteatosis.[220,222,224] Decreasing the frequency and intensity of iontophoresis and application of moisturizers and corticosteroid cream can help reduce these side-effects.[121,225,226]

Microwave thermolysis

Microwave thermolysis is a non-surgical procedure that uses microwave electromagnetic radiation to heat and induce deep dermal fibrosis and cellular thermolysis of eccrine sweat glands, irreversibly destroying them.[152,153] One medical device is approved by the FDA (MiraDry (Miramar Labs, Sunnyvale, CA, USA) for the treatment of primary axillary HH.[153] Microwave thermolysis showed 90% efficacy that persisted for more than 12 months in one study, and 80% efficacy in a statistically significant decrease in sweating severity and symptoms by improvement of HDSS at 1, 6 and 12 months of follow-up in another study.[152,153] The largest RCT evaluating MiraDry in 81 patients showed that 62% of patients who received three treatments achieved 75% efficacy in reduction of gravimetric-measured sweat production.[153] The machine has not been studied in paediatric patients and is approved only for patients 18 years and older.[115] Side-effects were generally mild to moderate, with short-term effects, such as pain, oedema, erythema, rash, dermatitis, ecchymosis, axillary tenderness, numbness and temporary altered sensation resolving within 3 months, whilst long-term effects included compensatory HH, subcutaneous nodules, permanent patchy alopecia and, rarely, brachial plexus injury leading to transient median and ulnar neuropathy.[152,153,224,227–229]

Ultrasound

Ultrasound therapy is a device-based therapy that is not commonly used in clinical practice but has been used as an off-label treatment for primary axillary sweating. It involves the use of low levels of focused thermal injury resulting in collagen remodelling in sweat glands.[114,154] Specifically, an ultrasound system (VASER, SoltaMedical, Inc., Hayward, CA, USA) approved by the FDA for body contouring and soft tissue emulsification showed an 80% reduction in sweating and 90% satisfaction in one study.[155,156] Whilst minimally invasive, it has not been tested in the paediatric patient population.[115] Adverse events related to side-effects include temporary tenderness, redness, numbness and bruising.[115,157]

Fractional microneedle radiofrequency

Fractional microneedle radiofrequency involves the insertion of microneedles into the skin, particularly eccrine sweat glands, with subsequent emission of bipolar thermal energy causing destruction of the sweat gland.[118,158,159] Whilst not routinely used clinically, the literature indicates that patients with primary axillary HH showed improvements in HDSS scores and reduction of sweating at 6 weeks, 9 weeks and 21 weeks.[159] Adverse events included transient erythema, pain, swelling, desquamation, burning sensation, post-inflammatory hyperpigmentation as well as mild pain, swelling and redness.[160,161]

Laser treatments

Laser treatments for PHH are not routinely used in a clinical setting but have shown some success in the literature.[114] These include the 1064 and 1320 nm

neodymium-doped yttrium aluminium garnet (Nd:YAG) laser and diode lasers (800, 924 and 975 nm).[162–166] In an RCT of 100 patients, a diode-powered laser with a wavelength of 975 nm with 20 W alone and wavelengths of 924 and 975 nm simultaneously, both showed improvement in HDSS scores and reduced sweating at 1 and 12 months for primary axillary HH.[165] An RCT of six patients using the Nd:YAG laser demonstrated that the 1064-nm wavelength reduced axillary sweating after 1–3 months.[166] Adverse events related to side-effects include local pain, sensation loss, hair reduction, hematoma, oedema, burns, skin erosion and compensatory HH.[162–166]

Small procedures

Small procedures are non-device-based local procedures that are potential treatment modalities for PHH. These include BTX injections, excision, curettage, liposuction or a combination of these treatments. All procedures have a risk of compensatory sweating resulting in worse symptoms.[114–119]

BTX injections

BTX injections, specifically BTX-A and BTX-B are the two most commonly used for PHH, and the FDA has approved onabotulinum toxin A for severe primary axillary HH treatment.[121] BTX is a protein produced by gram-positive bacteria *Clostridium botulinum* and works by temporarily blocking the release of neuronal acetylcholine from the presynaptic junction (through preventing exocytosis of vesicles) of the SNS, preventing the action of sweating.[117,118,121] In the USA, there are three BTX-A formulations available, namely onabotulinum (Botox; Allergan, Irvine, CA, USA), incobotulinum (Xeomin; Merz Pharmaceuticals, Greensboro, NC, USA) and abobotulinum (Dysport; Galderama Laboratories, Fort Worth, TX, USA), and one BTX-B formulation available for PHH (rimabotulinum, Myobloc; Solstice Neurosciences, Louisville, KY, USA).[230] BTX injections have been studied in primary axillary (FDA approved in 2004), palmoplantar and craniofacial (including scalp) HH in adults, with off-label use in paediatric patients.[114,119] One double-blind, placebo-controlled trial with 320 patients[167] showed a response rate of 94% with 50 units of onabotulinum toxin A per axilla, whilst other studies[167–169] showed improved outcomes with 100–200 units per axilla, with improvement seen within 2–4 days after treatment and sustained for 3–9 months, with patients often requiring 1–2 onabotulinum toxin A injections annually.[114,117] Different doses may be required, with higher doses for primary palmoplantar HH compared to primary craniofacial (including scalp) HH. For example, one study indicated that injections for primary palmar HH required 50–100 units of onabotulinum toxin A or 100–240 units of abobotulinum toxin A per hand injected 1–1.5 cm apart.[230] BTX is usually placed at the dermal-subcutaneous junction, 2.5 mm below the skin with 10–20 injections administered 1–2 cm apart.[114] One study of paediatric patients with primary axillary HH found that two treatment cycles with BTX-A spaced 2–8 weeks apart found a 2-point improvement in HDSS scores and significantly reduced sweating symptoms.[170] Treatment of primary axillary HH shows 82–87% efficacy and up to 98% satisfaction rates, followed by primary plantar HH with 80–90% efficacy reported in various studies, and primary craniofacial (including scalp) HH showing efficacy rates of up to 92% and satisfaction rates of 87% but may have the highest potential for side-effects with many reporting craniofacial defects.[167–174] BTX-B has a quicker response time but has a reduced period of action, a broader side-effect profile and is more painful to administer.[121,231–233] The most common complaint with treatment is pain, particularly in the palmar and plantar regions, with discomfort lasting an average of 2.4 days but potentially extending up to 10 days. Techniques to reduce these side-effects during injections include needle-free anaesthesia, cryoanalgesia, vibration analgesia, pocketed microneedles, topical anaesthetics, dilution with lidocaine, sedation, intravenous regional anaesthesia and nerve blocks. For palmar and plantar botulinum injections, topical anaesthetic agents or ice can provide relief, whilst ulnar, median and radial nerve blocks or a modified Bier block are effective

Box 1. Treatment options for hyperhidrosis.

A. Lifestyle, behavioural and adjunctive therapies
1. Avoidance of triggering and exacerbating factors
2. Use of moisture-wicking fabrics and cooling/absorbent devices

B. Topical therapies
1. Topical antiperspirants (e.g. aluminium chloride formulations)
2. Topical anticholinergics (e.g. glycopyrrolate, oxybutynin, sofpironium bromide, umeclidinium)
3. Topical botulinum toxin type A liposomal cream

C. Systemic therapies
1. Oral anticholinergic medications (e.g. glycopyrrolate, oxybutynin, methantheline bromide)
2. Other systemic agents (e.g. β-blockers, benzodiazepines, α2 agonists)

D. Device-based therapies
1. Iontophoresis
2. Microwave thermolysis
3. Ultrasound, fractional microneedle radiofrequency and laser treatments

E. Procedural and surgical interventions
1. Botulinum toxin injections
2. Excision, curettage and/or liposuction
3. Sympathectomy

for the palms, and posterior tibial and sural nerve blocks may be used for the plantar region.[117,121,234–247] Complications are rare and generally mild but include headaches, myalgia, itching and, more rarely, compensatory sweating in previously unaffected areas.[100,121,167,168,248–250]

Local excision, curettage or liposuction

Local excision for PHH may be warranted when conservative treatments have failed.[251] Side-effects include scarring and restriction in arm movement.[175,176,184,251,252] No studies in paediatric patients have been conducted on excisional procedures.

Excisions with either a curette, liposuction cannula or both can be performed for permanent removal of axillary eccrine and apocrine sweat glands when medical management has failed.[114,118] Excision with curettage is slightly more effective than liposuction but has an increased risk of scarring and morbidity.[175] Patient satisfaction is high due to permanent removal of sweat glands. However, relapses are possible, outcomes are dependent on the skill of the surgeon, and there are several side-effects. No studies have been conducted in paediatric patients.[115] Curettage reduces the risk of scarring compared to other procedural methods but carries a risk of complications, including bleeding, pain, bruising, skin erosion, infection, ecchymosis, hyperpigmentation, seroma, damage to the brachial plexus, dysaesthesia, hair loss, recurrence of HH and compensatory sweating, along with other potential side-effects common to skin injuries such as scarring, hyperpigmentation and dysaesthesia.[175–183]

Surgical interventions

Surgical interventions include sympathectomy, sympathicolysis and video-assisted thoracoscopic sympathectomy, including endoscopic thoracic sympathectomy. These procedures remove tissue through bilateral sympathectomy or ganglionectomy via transecting, resecting, cutting, ablating or clipping the sympathetic trunk at the T1–T5 level.[114–119,185,186] This results in denervation of sweat glands and subsequent decrease in sweating.[187] Sympathectomy is often a last resort treatment for PHH, with its effectiveness seen best in upper extremity PHH, specifically primary palmar HH.[115] Sympathectomy has better results in patients with early-onset PHH (before age 25 years), a body mass index of <28 kg/m^2 and in the absence of nocturnal sweating, serious comorbidities and bradycardia.[187] Sympathectomy is effective in 68–100% of cases, though satisfaction rates tend to decline over time, with patients with primary palmar HH reporting the highest satisfaction.[188–190] When ETS is used for primary palmar HH, it targets the T2 and T3 ganglia, whilst craniofacial (including the scalp) ETS is done above the T3 level, axillary at the T3/4 level, and plantar at L3/L4.[114,191] Postoperative complications may include pneumothorax, haemothorax, subcutaneous emphysema, intrathoracic bleeding, hematoma, paraesthesia, upper limb neurological impairment, stellate ganglion injury leading to Horner syndrome (ptosis, miosis and anhidrosis), hyperthermia, phrenic nerve injury, bradycardia, sensory and/or motor limb changes, and scarring. Additionally, postoperative pain, compensatory sweating and recurrent HH are potential concerns.[184,185,190–197] Recurrent primary focal HH and compensatory sweating of the abdomen, back, legs and gluteal region are also common long-term effects.[187,198,199] Sympathectomy has not been studied in the paediatric population, and given the risks involved with anaesthesia, the procedure itself, and its irreversibility, its use requires caution and consideration in only the most severe cases of refractory PHH.[115]

Conclusion

It is important for clinicians to recognize HH and to differentiate primary from secondary forms to ensure that patients receive an appropriate diagnostic evaluation and tailored management. Given that HH can significantly impact both physical comfort and psychological well-being, early identification is essential to minimize unnecessary investigations and to implement effective treatment strategies.

For patients with mild HH, conservative measures, such as lifestyle modifications and the use of topical antiperspirants (e.g. aluminium chloride formulations), can provide adequate symptom relief. In contrast, patients with moderate to severe or refractory HH may benefit from additional modalities, including topical anticholinergics, device-based therapies (such as iontophoresis, microwave thermolysis and laser treatments), systemic anticholinergic agents and BTX injections. Although surgical interventions like sympathectomy are generally reserved for cases that do not respond to less invasive treatments, its use remains somewhat controversial.

Ultimately, a multidisciplinary and individualized approach is essential to optimizing both the physical and psychosocial outcomes of patients with HH. Further well-designed studies are warranted to refine these therapeutic strategies and to better define the long-term safety and efficacy of emerging treatment modalities.

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