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Hyperhidrosis in the geriatric population. Etiology, diagnosis, and treatment. A comprehensive review of the literature

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Abstract

Hyperhidrosis (HH) is a dermatologic disorder characterized by sweat production that exceeds the body's thermoregulatory needs. The ailment can occur at any age, including geriatric population. Clinically, HH is diagnosed when excessive sweating causes significant emotional, physical, or social discomfort, leading to a negative impact on the patient's quality of life. Depending on the cause, HH can be divided into the primary and secondary type (triggered by comorbidities, drugs, stress). When diagnosing HH, secondary causes should always be ruled out. Treatment of HH can be complex and long-term. The following article is a review of the available literature and provides a cross-section through the etiology, diagnosis and available treatments. (Gerontol Pol 2024; 32; 92-98) doi: 10.53139/GP.20243212

Keywords: *BTX; aluminum chloride hexahydrate; botulinum neurotoxin; botulinum toxin; compensatory sweating; sympathectomy; hyperhidrosis; iontophoresis; oral anticholinergics*

Introduction

Hyperhidrosis (HH) is a disorder characterized by excessive sweating beyond the body's temperature regulation needs. Approximately 3% of the population is affected by HH [1]. It occurs due to overstimulation of cholinergic receptors on eccrine glands. The condition primarily affects areas such as the axillae, palms, soles, and face. It can cause emotional, psychological, social, and occupational difficulties [2].

HH is classified as primary or secondary. Primary HH typically presents earlier in life and is more localized. Genetic factors are thought to contribute to excessive neural stimulation seen in primary HH, although precise mechanisms involved are not well understood. In contrast, secondary causes of HH include medications (dopamine agonists, SSRIs, antipsychotics, insulin), systemic disorders (diabetes mellitus, hyperthyroidism, Parkinson's disease, neurological disorders), and tumors (pheochromocytoma, lymphoma) [2]. Primary HH is often focal, while secondary HH is usually generalized. It is important to differentiate these two types of disease, because they may need different kinds of treatment. Diagnosis is usually based on clinical evaluation, with grading scales and tests available to assess severity and localization. Laboratory tests may be necessary to rule out underlying causes. Treatment options for HH include topical aluminum chloride and oral anticholinergic medications for mild to moderate cases. More severe or resistant cases may require botulinum toxin A injections, sympathectomy, or local excision. The choice of treatment depends on the individual's response to conservative therapies [3].

An estimated 5% of Americans have HH, more than half of whom have axillary HH. Only one-third of patients reported complaints when talking to their doctor. The prevalence of HH is estimated to be much higher in other countries. We do not have such data for Poland.

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HH can affect individuals of any age, with no specific age restrictions or limitations [2]. There is no significant evidence to suggest that either men or women are at a higher risk for developing HH. The condition can affect individuals of both genders equally.

Primary hyperhidrosis

Primary HH refers to excessive sweating that occurs without any discernible trigger, does not depend on external stimuli and is unpredictable. The exact cause of primary HH is not fully understood, one of them may likely be the result from overactivity of the sympathetic nervous system – a combination of a lowered threshold and exaggerated response to sweating – typically in the upper dorsal ganglia [4]. The ganglia tends to be larger with a higher number of ganglion cells and greater expression of acetylcholine and alpha-7 neuronal nicotinic receptor subunit among patients with primary HH [5].

Several studies have attempted to establish a connection between primary HH and genetic factors. Studies of patients with primary HH who underwent thoracoscopic sympathectomy revealed that 33-56% of these patients had reported positive family history of the condition [6,7]. Greater frequency of positive family history was found in subjects with primary axillary or palmoplantar HH, suggesting a genetic predisposition for these phenotypes – potentially autosomal dominant or recessive [8,9]. Studies have identified specific loci that seem to be associated with primary HH, however the evidence is heterogeneous and limited. Authors of the review of 698 studies suggest a polygenically mode of inheritance of primary HH [10].

As opposed to secondary HH it typically starts in adolescence or childhood with onset around 14-25 years old and persists through adulthood [11]. The occurrence of primary HH tends to be relatively lower among specific age groups – in particular excessive sweating seems to decrease in individuals aged 65+ years – suggesting potential remission of disease [12]. However, data obtained from over 1,300 targeted surveys contradict this finding. Not only did the severity of symptoms not decrease with age but also 89% of the study subjects aged 65+ years reported that symptoms stayed the same over time or have become worse [13].

In studies attempting to determine the types of localization in primary HH, a similar pattern was observed – in young age the most common affected areas were palms, soles of the feet and axillae whereas patients aged 50+ years had a much higher incidence of facial primary HH [14]. The authors suggested that a higher BMI in this group of patients may be a potential cause for this result. However, attention should be paid to a distinct subtype of primary local HH – postmenopausal craniofacial HH [15]. The onset of HH can occur long before or after the onset of menopause. Patients who experience postmenopausal HH present a distinct group and should not be managed in the same manner as individuals experiencing vasomotor symptoms during menopause. This can be supported by the fact that some women did not benefit from hormone-replacement therapy to control symptoms [15,16].

Secondary hyperhidrosis

Secondary HH can be caused by plenty of factors

Medications

Taking medicine is one of the most common causes of secondary HH. Drugs that can cause HH include antidepressants, cholinergic agonists, hypoglycemics, selective estrogen, receptor modulators, miscellaneous, serotonin reuptake inhibitors, angiotensin II receptor blockers, corticosteroids and thyroid hormone supplements. Patients should be asked about comorbidities and medications taken for them [17].

Alcohol

It was shown that chronic excessive alcohol consumption such as drinking three or more alcoholic drinks during a day was associated with night sweats. Stimulants should be excluded in the diagnosis [18].

Menopause

Women during menopause often struggle with excessive sweating so it is important to take into consideration any menopausal symptoms and hormonal changes like elevations in gonadotropin hormone levels. Men can also experience excessive sweating associated with hypogonadism [19].

Diabetes

Diabetes often occurs with gustatory sweating. It is a form of secondary focal HH activated by food intake. American Diabetes Association (ADA) describes GS as a sudomotor dysfunction with profuse sweating on the face and neck in relation to food intake or smell [20].

Hyperthyroidism

Thyroid hormones potentiate alpha- and beta-adrenergic receptors in multiple tissues throughout the body.

This manifests with generalized sweating but patients also experience tachycardia, increased cardiac output, increased body temperature and warm skin [21].

Infections

HH can also be caused by many infections. It is important to ask if the patient experiences any other symptoms of infection like fever, chills or sweats. HIV infection is an example of the disease, which can occur with excessive sweating. Antiretroviral therapy can be responsible for HH [22]. Symptoms of mononucleosis are mainly generalized sweating, fever, upper respiratory infection and enlarged lymph nodes in the neck. It is usually caused by the Epstein-Barr virus. Heterophile antibodies test is positive in most of the cases while acute phase of mononucleosis. Viral capsid antigen immunoglobulin M antibodies to the Epstein-Barr virus are elevated for up to three months after infection [23].

Physicians should always consider a patient's travel history to assess the possibility of tuberculosis or malaria.

Malignancy

HH disguised as night sweats occurs with many malignancies, but there are usually other presenting symptoms of malignancies so the presence of night sweats alone is diagnostically inconclusive. HH is often the symptom of Leukemia, Lymphoma, Tuberculosis and Pheochromocytoma [22].

Obesity

Overweight and obesity are the most common conditions related to HH. Due to the thick subcutaneous adipose tissue layer, heat loss is constricted and it may cause compensatory excessive sweating. Diet and active lifestyle can be useful with HH treatment [24].

GERD

The connection between night sweats and GERD is rarely described in the literature so it's important to report all cases of HH with GERD. There are no formal trials, however some case reports show diagnose acid reflux as the cause of night sweats [25].

Obstructive sleep apnoea

Half of the patients suffering from obstructive sleep apnoea report nocturnal sweating, localized around the neck and upper body area. One of the published studies of 98 men with OSA showed that 34% of them complained of nocturnal sweating and it was reduced to 12% with PAP treatment [26].

Risk of infections

While HH itself does not directly cause infections, it can potentially increase the risk of infections. The constant wetness can disrupt the natural protective barrier of the skin. Furthermore, prolonged exposure to moisture and increased friction between the skin surfaces, especially in areas where skin-to-skin contact occurs, such as the underarms or between the toes can cause skin maceration, making it more susceptible to infection [27].

A consistently moist environment promotes the growth of pathogens. A case-control study involving 387 patients diagnosed with primary HH found that there was a notable rise in the overall risk of developing site-specific cutaneous infections (OR 3.2; 95% CI 2.2-4.6), which encompassed bacterial – especially pitted keratolysis, fungal – dermatophytosis and viral infections – verruca vulgaris/plantaris, in comparison to controls [28]. A multivariate analysis there reported a 3.5-fold increased risk for patients with athlete's foot to also present with HH [29]. Additionally, the presence of excessive moisture can diminish the efficacy of topical medications. Data show that simultaneous treatment of infection and HH yields better results thereby improving the therapeutic process especially in resistant cases[27].

Diagnosis

Diagnostic management is usually arranged by a concerned patient seeking help, and should begin with the exclusion of secondary causes of HH [30]. After exclusion of the secondary causes, the patient should be evaluated using established diagnostic criteria. Hornberger et al. [30] have proposed diagnostic criteria for focal primary HH, which include: Focal, visible, and excessive sweating for ≥ 6 months without a known etiology with ≥ 2 of the following:

- bilateral and symmetrical sweating,
- impaired daily activities,
- occurring at least once weekly,
- onset < 25 years of age,
- positive family history,
- cessation while asleep.

A complete physical examination should be performed, and the physician should focus on objective signs and symptoms of HH and on signs of secondary causes of HH [30], which include palpitations, arrhythmia, night sweats, anemia and other abnormalities in morphology result, hypoglycemia and hyperglycemia, nocturia,

waking up at night with shortness of breath, recurrent fever, lymphadenopathy, weight loss, skin lesions, vitamin D deficiency, cough, peripheral edema, abnormalities in neurological examination, blood pressure fluctuations, orthostatic hypotension or other symptoms of autonomic dysfunction, and any concerning signs and symptoms.

Wohlrab et al. [31] have proposed an expert-based scale for assessment of HH. Axillar, palmar, and plantar HH was classified as mild, moderate, or severe based on sweat stains and symptoms (table I.). There are also some objective measurement methods for focal sweat, such as gravimetry, transepidermal water loss (TEWL), Minor's iodine starch test, and the HH Area and Severity Index (HASI) [30].

Hornberger et al. [30] identified several questionnaires for assessing the severity of Hyperhidrosis (HH) and its impact on daily life. These questionnaires include:

- Hyperhidrosis Disease Severity Scale (HDSS): This questionnaire evaluates the tolerability and impact of HH on everyday life.
- Hyperhidrosis Quality of Life Index (HidroQOL©): Specifically designed for clinical and research settings, this questionnaire measures the quality of life in individuals with HH.
- PROM by Kuo et al.: This Patient-Reported Outcome Measure (PROM) assesses the health-related quality of life in patients with HH. It consists of 29 items divided into five domains: functional, psychological, social, affective, and physical.
- Questionnaire by Amir et al.: This questionnaire focuses on assessing the quality of life in individuals with HH. It contains 35 items divided into five domains: functional, social, interpersonal, emotional self, and emotional other.
- Quality of life questionnaire by De Campos et al.: refined and assessed a quality of life questionnaire for individuals with HH. It contains 20 items divided into five domains: functional, social, personal, emotional, and special condition.
- Hyperhidrosis Impact Questionnaire (HHIQ) by Teale et al.: This questionnaire measures the impact of primary HH on daily lives and evaluates the effectiveness of anti-HH treatments. The HHIQ consists of 41 items for baseline assessments and 10 items for follow-up assessments. It is divided into four sections: disease and treatment background, direct impact on medical and non-medical resource utilization, indirect impact on employment and productivity, and intangible impacts on emotional status, limitations in daily living and leisure activities, and treatment satisfaction.

Additionally, Keller et al. developed two questionnaires for self-diagnosing HH and validating them against physical examination and sweat measurements. Cinŕ et al. validated the Illness Intrusiveness Rating Scale (IIRS) to assess the burden of HH and developed 11 new items for this purpose. Other measures include the Hyperhidrosis Disease Severity Measure – Axillary, Axillary Sweating Daily Diary, Swartling Hyperhidrosis Index, and Hyperhidrosis Severity of Quantitative Observation.

Treatment

Treatment of HH can be broadly divided into non-surgical and surgical procedures. Non-surgical procedures are: topical agents, procedural treatment (as tap water iontophoresis or botulinum toxin A injections), systemic treatment and those using energy-based devices (such as microwave devices, diode laser, fractionated microneedle radiofrequency and ultrasound therapy) [32].

Non-surgical methods

Topical agents like aluminum salts antiperspirants are commonly used to treat HH and should be first-line therapy. [33] Aluminum salts form occlusive plugs in the sweat gland ducts, preventing sweating. They can be applied once a day or three times a week without affecting their effectiveness. As eccrine glands follow a circadian cycle (with higher secretion during the day and lower at night) the most products are recommended to apply at night [34]. Aluminum salts may cause skin irritation and itching, but commercial aluminum trichlorohydrate antiperspirants have low irritation potential [34]. Another topical agent, glycopyrronium bromide (GPB), blocks acetylcholine to reduce sweating. It may cause mild to

Table I. Severity of hyperhidrosis by Wohlrab et al.

Severity of disease	Axillar HH	Palmar HH	Axillar, palmar HH
Mild	Sweat stain diameter 5–10 cm	–	Markedly increased skin humidity
Moderate	Sweat stain diameter 10–20 cm	Sweating limited to palms and soles	Formation of sweat pearls
Severe	Sweat stain diameter > 20 cm	Sweating also on the dorsal side of the fingers and toes and on the side of hands and feet	Sweat dripping off

moderate side effects like constipation, dryness, and local skin irritation [35]. If they appear ineffective, can be changed to another non-surgical treatment or combined with different therapeutic options [32].

Botulinum toxin (BTX) type A injections block acetylcholine release, preventing local sweating in HH resistant to topical agents. Caution is needed when administering BTX to individuals on oral anticoagulants due to increased risk of subcutaneous hematomas. Effects last approximately 6 to 9 months [36].

Iontophoresis uses direct or alternating current to introduce ions, closing eccrine gland ducts and inhibiting nerve conduction to limit sweat gland activity. Contraindications include implantable electronic devices, metal implants near the treatment site, cardiac arrhythmia, epilepsy, and pregnancy. It is a second-line treatment for palmoplantar HH but less effective and more side effects in axillary HH [37].

Systemic treatment is a second-line therapy for HH when topical agents fail, but it comes with significant systemic side effects [2]. Anticholinergics like oxybutynin and glycopyrronium are commonly used, with low doses recommended to minimize side effects. Oxybutynin is effective for postmenopausal sweating when hormone replacement therapy is ineffective. Adverse events of systemic treatment include dry mouth, constipation, blurred vision, and drowsiness. Oral anticholinergics are contraindicated in certain conditions like pyloric stenosis and myasthenia gravis. They are relatively contraindicated in conditions like gastroesophageal reflux disease and glaucoma [2].

Propranolol, a non-selective beta-blocker, is used for HH accompanied by anxiety and stress. Other mentioned oral drugs include clonidine, benzodiazepines, and calcium channel blockers [38].

Surgical procedures

Surgical methods for treating HH include sympathectomy, sympathectomy, topical sweat gland removal, and subcutaneous axillary liposuction-curettage [32]. Sympathectomy is commonly performed and effective, especially among elderly patients, with potential occurrence of compensatory hyperhidrosis (CH). Endoscopic sympathectomy is preferred due to shorter operation time and less scarring, but CH is a significant adverse effect. Leiderman DBD et al. examined the effects of sympathectomy on hyperhidrosis in older patients. It was found that older patients experienced improved sweating in the main site of hyperhidrosis. Furthermore, the outcomes of sympathectomy in older patients were similar to those observed in younger patients in terms of the improvement in quality of life and the occurrence of compensatory hyperhidrosis (CH) [39]. Removal of sweat glands can be done through excision or subcutaneous curettage with open techniques or superficial liposuction. These procedures have milder adverse effects compared to thoracic sympathectomy but can still lead to issues like wound healing problems or infections.

Food and non-pharmacological behaviors

HH can be exacerbated by stimulant-containing foods, especially those containing caffeine and theobromine. In milder cases, restricting the intake of coffee, tea, caffeinated soft drinks and chocolate can help to alleviate the symptoms. Restricting these items in one's diet may contribute to an improvement in HH. Additionally, wearing sweat-absorbing clothes and weight reduction can also be beneficial in managing the symptoms of HH [32].

Effect on quality of life

The quality of life of patients with severe HHis poor. Approximately 48% of patients with HH report a poor or very poor quality of life (QoL) [40]. It is due to the impact on daily activities, social functioning and occupational functions. It is estimated that the quality of life of people with HH is comparable to patients diagnosed with severe psoriasis, end-stage of renal disease, multiple sclerosis, rheumatoid arthritis [2].

Patients with HH commonly report a significant level of psychological strain, with an increased association of HH with both anxiety and depression. In social situations, stress can trigger sweat production, resulting in even higher stress levels. This creates a vicious cycle that has an exponentially negative effect on the quality of life (QoL) of patients with HH [40].

Conclusions

HH is a frequently reported ailment in elderly patients in daily medical practice. HH causes feelings of embarrassment, and many times is a concealed ailment for a long time. HH can affect poor quality of life, impairing functioning. In the diagnosis of HH, it is important to remember to exclude secondary causes, and then propose the optimal form of therapy taking into account the type, severity of symptoms and expectations of the patient. It is recommended to initiate therapy with topical agents as the first-line treatment. If satisfactory results are not achieved, the next step would involve the introduction of

systemic therapy or outpatient procedures. Surgical management should only be considered as a last resort in the treatment process.

Conflict of interest
None

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