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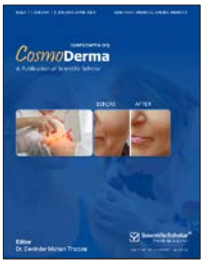

Review Article

Axillary hyperhidrosis: An update

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ABSTRACT

Axillary hyperhidrosis results from excessive sweat production in the armpits. It adversely impacts a patient's quality of life. In this update, we attempt to discuss the basics, pathophysiology, and the management of axillary hyperhidrosis.

Keywords: Hyperhidrosis, Axillary, Review

INTRODUCTION

Hyperhidrosis may be categorized into primary or secondary hyperhidrosis. Primary hyperhidrosis localizes itself over axillae, palms, soles, and face, in a bilaterally symmetrical manner; and the condition is idiopathic. Secondary hyperhidrosis is either focal or generalized, usually associated with an underlying medical condition.[1-5] A comprehensive English language literature search for axillary hyperhidrosis across multiple databases (PubMed, EMBASE, MEDLINE, and Cochrane) for keywords (alone and in combination) and MeSH items as well as non-MeSH terms such as "hyperhidrosis," "axillary hyperhidrosis" AND "pathophysiology," "treatment," and "Management" was undertaken.

PATHOPHYSIOLOGY

This is a clinical condition where a person experiences excessive axillary sweating even in cold temperature or at rest. The activity of the eccrine glands is greater than normal. There is hypertrophy of the eccrine glands, leading to dysregulation involving the sympathetic and parasympathetic systems. There is no difference in the number or distribution of eccrine glands, between the patients and normal individuals. A genetic component present on chromosome 14q is associated with hyperhidrosis. It is believed that there is an increased stimulation or distribution of the local sweat glands. Besides, abnormal innervation of the eccrine glands is also thought to be causative, behind the condition.[6-9]

Primary hyperhidrosis is not caused by any underlying disease and it is considered to be idiopathic. However, secondary hyperhidrosis occurs due to other medical conditions. The sweating may be generalized or focal. The differences between primary and secondary hyperhidrosis have been tabulated [Table 1].

Medical conditions causing secondary hyperhidrosis are acromegaly, anxiety, carcinoid syndrome, ischemic heart disease, overactive thyroid, menopause, Parkinson's, pheochromocytoma, tuberculosis, or other infections.

Table 1: Salient points of difference between primary and secondary hyperhidrosis.

	Primary hyperhidrosis	Secondary hyperhidrosis
Form	Localized/focal form Bilateral	Generalized form Unilateral
Etiology	Idiopathic	Underlying systemic causes (infections, menopause, diabetes, hypothyroid, drug induced)
Pattern	Symmetrical pattern	Asymmetrical pattern
Onset	Adolescence or even before	Any age
Genetics	Autosomal dominant chromosome 14q11.2-q13 Second locus for primary focal hyperhidrosis was identified on chromosome 2q31.1	–

CLINICAL FEATURES

The presentation is during puberty, after the appearance of axillary hairs. The affected area usually extends beyond the hairy region. Factors such as exercise, anxiety, and waking up from sleep worsen the condition. Quality of life is affected, which leads to depression. The diagnostic criteria for hyperhidrosis are mentioned in [Table 2].

It is worth mentioning a few rare presentations such as chromhidrosis, pseudochromhidrosis, and bromhidrosis. Chromhidrosis refers to secretion of colored sweat, resulting from the production of lipofuscin granules within the apocrine glands. Colors include yellow, orange, green, blue, or black depending on the concentration or state of oxidation of lipofuscin granules. Sometimes, bacteria within the eccrine glands produce a pigment, due to metabolism. In pseudochromhidrosis, eccrine glands produce a colorless sweat, which becomes pigmented on coming in contact with skin and dyes or microorganisms such as Corynebacterium. Bromhidrosis refers to sweating with an offensive odor due to bacterial breakdown, which is known to be exacerbated by poor hygiene, diabetes, obesity, etc. All these conditions are notorious and lead to isolation from social gatherings.

INVESTIGATIONS

Starch and iodine test is a simple bedside investigation, for the diagnosis of axillary hyperhidrosis. The armpits are cleaned and dried, following which, application of povidone iodine is done. Thereafter, corn starch is sprinkled. If the area is moist due to sweat, starch and iodine mix with each other, leading to a purplish or bluish discoloration.

Table 2: Diagnostic criteria for hyperhidrosis.

1. Positive family history
2. Impairment of daily life more than once a week
3. Focal occurrence in one or more sites with bilateral symmetry
4. Occurrence of symptoms in childhood or adolescence
5. Absence of night sweats
6. Occurrence of sweat independent of temperature and not consciously controllable

Table 3: Mechanism of the action of therapeutic agents for hyperhidrosis.

Treatment modality	Mechanism of action
Aluminum salts	Occlusion of the ductal opening
Anticholinergics	Reduced production of sweat
Botulinum toxin	Reduced production of sweat
Cryosurgery	Duct blockage
Microwave thermolysis	Destruction of the eccrine and apocrine gland via heat waves
LASER	Reduction in the number of eccrine and apocrine glands
Microfocused ultrasound	Reduction in the number of eccrine and apocrine glands
Iontophoresis	Reduction in the number of eccrine and apocrine glands
Aspiratory curettage	Destruction of the eccrine and apocrine gland
Endoscopic thoracic sympathectomy	Destruction of the eccrine and apocrine gland

TREATMENT

Therapy revolves around general measures to reduce sweating (wearing loose fitting cotton clothing and avoiding friction), topical and systemic agents, and surgeries [Table 3] in refractory cases.[10,11]

Topical

Aluminum salts (12.5–30%) constitute the first line of treatment. There is occlusion of the distal ducts, and prolonged blockage of the glands leads to acinar degeneration and reduced sweat. Aluminum ions precipitate with mucopolysaccharides and damage the epithelial cells along the ductal lumina and block sweat secretion. The formulation should be applied on dry skin at night. Side effects include miliaria, irritation, and burning. Low-potency corticosteroid creams may reduce the irritation.[12]

A novel topical foam has been developed (Versafoam), which contains 20% aluminum sesquichlorohydrate. It reduces the amount of sweating by 50%–60%. Side effects have not been reported.[13,14]

Topical glycopyrrolate 2% used twice daily, is a good agent. Conflicting results have been noted in different studies. Overall, the evidence seems to be lacking. Besides, anticholinergic gels of different concentrations, oxybutynin and umeclidinium, are being investigated. Topical sofpironium bromide has also been tried.[15-18]

Botulinum toxin Type A has demonstrated significant reduction in the production of sweat. No serious adverse events were noted. It should be remembered that misuse may lead to ptosis and facial asymmetry. Newer topical formulations for botulinum toxin are being investigated.

Systemic

Anticholinergic drugs such as glycopyrrolate, oxybutynin, and bornaprine are useful. However, the side effects such as dry mouth, blurring of vision, dryness of eyes, and urinary retention limit the use of these agents. Other medications including beta-blockers and clonidine (0.5 mg BD) are also used.[19-22]

Injectables

Botulinum toxin is an inhibitor of acetylcholine release. Two types of botulinum toxin were extensively tested for axillary hyperhidrosis: Onabotulinumtoxin A and abobotulinumtoxin A. Prior to initiating treatment with botulinum toxin, patient history should be taken in details. The primary underlying disease should be treated, patient should be well educated about the potential adverse effects, contraindications, and alternative treatments. The need for reinjection after 6–9 months should be explained to the patient. Pregnancy and lactation periods are highly contraindicated. Patients with pre-existing comorbidities such as myasthenia gravis, Eaton-Lambert syndrome, or amyotrophic lateral sclerosis are not fit for the therapy. Use of 50–100 U is recommended in each axilla. Anesthetic creams and application of ice packs and vibration reduce pain. The procedure requires multiple injections, with 1–2 cm distance between them. The toxin vial is diluted in 2 mL of 0.9% saline solution and 2 U injected per point. The median duration of the effect of the toxin is 7.6 months. After dilution, it must be stored in a refrigerator at 2–8°C and must be used within 4 h of reconstitution. A 30 gauge or insulin syringe is used at an angle of 45 approximately 2 mm into the dermis. The minimum dose for each injection is from 2.0 to 2.5 U depending on the colorimetric response generated by minor starch test. As the diffusion capacity of botulinum toxin injection is 1.0–1.5 cm in diameter, the injected points should be this distance apart. The literature reveals that the botulinum toxin A has a reported effectiveness of higher than 90% for hyperhidrosis and has greater improvements within the first 22 weeks of treatment, and the effect lasts for 4–9 months only.[23-26]

Iontophoresis

A small electric current is made to pass through the electrodes for 20–30 min. However, the treatment is not very effective. The combined use of anticholinergic agents, such as poldine methylsulfate and glycopyrronium bromide, can increase the effectiveness of iontophoresis.[27-31]

Cryotherapy

It is used on the sites of nerve block injections combined with or without iontophoresis (2% lignocaine for 15 min). Major adverse effect is the formation of blisters.[32]

Newer therapies

Microwave thermolysis has been successfully used in treating hyperhidrosis.[33-35] MiraDry® is a US FDA-approved device for this. Here, heat waves destroy the eccrine and apocrine glands. Before the start of the procedure, an injectable local anesthetic is given to decrease the pain. Two applications are performed at 3 months interval. Side effects include pain, ecchymosis, edema and erythema, and rarely brachial plexus damage. In some cases, sensitization is required that lasts for 5 weeks. Here, there is reduction in sweating that lasts for about 2 years after treatment. Besides, microneedling has also been tried.[36]

Lasers

Nd:YAG 1064 nm and other lasers show significant reduction in hyperhidrosis when associated with surgical excision of the glands.[37-42]

Microfocused ultrasound

The ultrasound energy is applied to 4.5 mm of the skin surface 2 times, over an interval of 30 days resulting in significant improvement.[43,44]

Surgery

Aspiratory curettage provides long-lasting results in hyperhidrosis. This therapy is preferred as it does not need periodic repetition, less expensive and it has minimum risks. Endoscopic thoracic sympathectomy may be done in recalcitrant cases.[45-57]

CONCLUSION

Axillary hyperhidrosis is one of the common dermatological conditions, impairing the quality of life of patients. It is unfortunate that the therapeutic modalities which can be offered to the patient are limited in a resource poor setting. Therefore, counseling and utilization of the common drugs form the mainstay of therapy. Nothing except physical

measures (devices or surgery) provide permanent solution, and most of the therapies are associated with their own set of adverse events limiting the scope of utility of the topical and systemic agents.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

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