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Hyperhidrosis with a Focus on Primary Axillary Hyperhidrosis

ABSTRACT

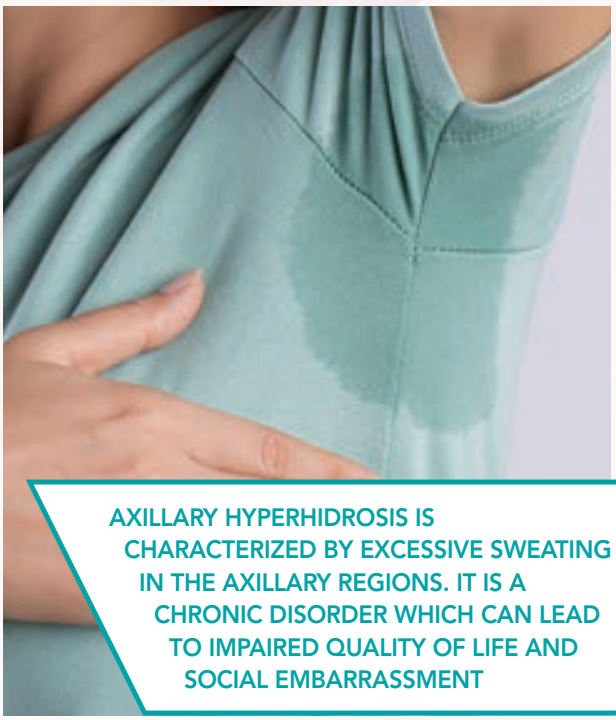
Axillary hyperhidrosis is characterized by excessive sweating in the axillary regions. It is a chronic disorder which can lead to impaired quality of life and social embarrassment. Identifying the condition is important so it can be safely and effectively treated. Evidence shows that Botulinum toxin is a safe and effective method of treatment for focal hyperhidrosis and provides longer-lasting results than topical treatments without the need of invasive surgery.

INTRODUCTION

There are two main types of human sweat glands. The eccrine sweat glands are mainly responsible for thermoregulation over various body surfaces. On the other hand, apocrine sweat glands are restricted to specific areas such as the axillae, anogenital region and areolae, which produce an odourless secretion which then develops malodour through bacterial decomposition.

Sweating is necessary for thermoregulation, however, for 1 – 3% of the population it can cause difficult daily functioning as the body produces more sweat than is needed for normal thermoregulation. When this occurs, it is called hyperhidrosis.[1]

Hyperhidrosis is a condition that causes excessive sweating, usually from the palmar, plantar and axillary surfaces. The underlying mechanism is thought to be a sympathetic overstimulation of the eccrine sweat glands. Hyperhidrosis can be primary or secondary. Primary hyperhidrosis affects around 1% of the general population. It is inherited as an autosomal dominant genetic trait and it usually starts during adolescence and sometimes even before, during childhood. It is bilaterally symmetrical, and commonly affects the axillae, palms, soles or craniofacial regions.[2] Severely affected patients may have secondary microbial infections, as well as other skin changes including maceration. They may be socially stigmatized and it can lead to substantial emotional and physical impairment in a person's occupation and social life. The negative effect on quality of life (QoL) from hyperhidrosis is similar to or greater than that of other dermatologic conditions, including severe acne and psoriasis.[3,4]



AXILLARY HYPERHIDROSIS IS CHARACTERIZED BY EXCESSIVE SWEATING IN THE AXILLARY REGIONS. IT IS A CHRONIC DISORDER WHICH CAN LEAD TO IMPAIRED QUALITY OF LIFE AND SOCIAL EMBARRASSMENT

Secondary hyperhidrosis typically occurs at a later age. It is usually unilateral, asymmetric, generalized and also, present during sleep. It is likely to occur due to an underlying medical condition such as diabetes mellitus, neurological disease, cardiovascular disease, hormonal changes like menopause, malignancy, infection and febrile illness. It can also be caused by a medication adverse effect.[5]

Excessive sweating can not only have an emotional and psychological impact, but it can also lead to physical complications. These include an increased risk of dermatophytosis, keratolysis and it can also be associated with atopic dermatitis.

DIAGNOSTIC APPROACH FOR PRIMARY HYPERHIDROSIS

Patient History and Examination

Diagnostic criteria for diagnosing focal primary hyperhidrosis have been developed (Table 1). To make a diagnosis in the clinical setting, secondary hyperhidrosis has to be excluded first. Therefore, a detailed clinical history and examination are very important. This includes a detailed medical and surgical history and medication history. One should enquire about neurological and endocrine symptoms like fatigue, weight gain, night sweats, headaches, vision changes, weakness, paresthesia, polyuria, polydipsia and fever. This will help in determining what further tests are needed in case of secondary hyperhidrosis.[5]

Table 1. Diagnostic criteria for focal primary hyperhidrosis.
Source: Hornberger J et al.[5]

Diagnostic criteria
Focal, visible, and excessive sweating for ≥ 6 months without aetiology with two or more of the following: 1. Bilateral and symmetrical sweating 2. Impaired daily activities 3. Occurring at least once weekly 4. Onset < 25 years of age 5. Positive family history 6. Cessation while asleep

On examination, one should observe the pattern of sweating and inspect the sites of the patient-reported hyperhidrosis. The neck should be palpated to check for any lymphadenopathy or thyroid enlargement. The blood pressure should be measured, and baseline laboratory tests carried out if indicated.[6]

The Starch-iodine Test

This is an assessment tool first described by Dr Victor Minor, a Russian neurologist, in 1928. It qualitatively identifies the hyperhidrotic skin areas. After the skin is cleaned and left to dry, it is then covered in 1 – 5% iodine solution. This is allowed to dry and starch powder is brushed on the area. The light brown iodine colour turns to dark purple as an iodine-starch complex forms in the liquid medium as the sweat comes to the surface,[7] determining the area requiring treatment.

Patient-reported Outcome Measures (PROM)

There are several patient-reported outcome measures. The most common one which is used in the clinical setting is the Hyperhidrosis Disease Severity Scale (HDSS). Besides being used to evaluate the presence and severity of axillary sweating for clinical studies, it is also used to evaluate hyperhidrosis for botulinum toxin treatment.[8]

Table 2. Hyperhidrosis Disease Severity Scale (HDSS).
Source: Lowe NJ et al.[8]

Question: How would you rate the severity of your hyperhidrosis?	Score
My underarm sweating is never noticeable and never interferes with my daily activities.	1
My underarm sweating is tolerable but sometimes interferes with my daily activities.	2
My underarm sweating is barely tolerable and frequently interferes with my daily activities.	3
My underarm sweating is intolerable and always interferes with my daily activities.	4

TREATMENT OF HYPERHIDROSIS

Treatment modalities that have shown a rate of reduction of sweat production include:

- Iontophoresis
- Topical application of aluminium chloride
- Administration of anticholinergic agents
- Beta-blockers
- Surgical removal of sweat glands
- Sympathectomy
- Laser or ultrasonography therapy
- Microwave thermolysis
- Intradermal injection of botulinum toxin type A.

TREATMENT WITH BOTULINUM TOXIN A, FOCUSING ON AXILLARY HYPERHIDROSIS

Mode of Action

Botulinum toxin A (Btx-A) works by blocking neuronal acetylcholine release at the neuromuscular junction and in cholinergic autonomic neurons.[9] The mechanism of action of Btx-A in focal hyperhidrosis is still not fully understood, but it is most certainly different than that in muscle spasms.[10]

DIAGNOSTIC CRITERIA FOR FOCAL PRIMARY HYPERHIDROSIS [ARE] FOCAL, VISIBLE, AND EXCESSIVE SWEATING FOR ≥ 6 MONTHS WITHOUT AETIOLOGY, WITH TWO OR MORE OF THE FOLLOWING: BILATERAL AND SYMMETRICAL SWEATING, IMPAIRED DAILY ACTIVITIES, OCCURRING AT LEAST ONCE WEEKLY, ONSET < 25 YEARS OF AGE, POSITIVE FAMILY HISTORY AND CESSATION WHILE ASLEEP

Sweat glands have a different nerve supply (sympathetic sudomotor C fibres instead of cholinergic α-motor neurons). The inhibitory action of Btx-A is not limited to the neuromuscular junction. The toxin also blocks the autonomic cholinergic fibres, including the sympathetic fibres to sweat glands. The effect of Btx-A on focal hyperhidrosis lasts longer (8-9 months) than on muscle spasm disorders (3-4 months).

In a study by Swartling et al.[10] palmar skin biopsies were performed on 26 hyperhidrotic patients before Btx-A treatment, and also on 11 controls. The aim was to study the effect of Btx-A on the size and innervation of sweat glands in patients with palmar hyperhidrosis. Biopsies were taken again one to six months after the injections. The sweat gland morphology was similar in patients and controls before the treatment.

After the treatment, the tubular dimensions remained the same, however, the lumen of the sweat gland appeared smaller. Also, staining showed that functional nerve growth diminished and therefore Btx-A therapy induces long-lasting functional denervation of the sweat glands.[10]

Safety and Efficacy

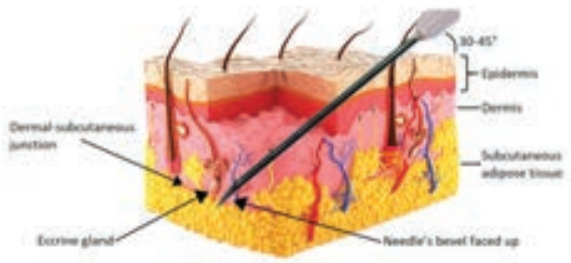
A 52-week multicenter double-blind, randomized, placebo-controlled study of efficacy and safety on 322 patients by Lowe et al. (2007) showed that Btx-A treatment effectively reduces the symptoms of primary axillary hyperhidrosis. It is well tolerated and has a safety profile similar to that of a placebo.[8]

Therapeutic Approach

The sweat glands are targeted when Btx-A is injected intradermally at the dermal-subcutaneous junction, around 2mm deep in the axilla. A hypodermic needle is oriented at 30° to 45° to the skin surface with the bevel facing up.[2]

At least a total of 50 units of Btx-A per axilla are needed to treat hyperhidrosis. The injections are done in 10 to 20 sites in each axilla, 1.5 to 2.5cm apart. After the treatment, the effect is commonly observed within 7 to 10 days. It lasts for about 6 to 10 months.[11]

Figure 1. The proper technique for injecting botulinum toxin for the treatment of primary hyperhidrosis.
Source: Nawrocki S et al.[2]



Adverse effects observed when treating axillary hyperhidrosis with BTX-A include pain, hematomas, bruises, headaches, muscle soreness, local pruritis which is mild, and also, compensatory sweating in 5% of patients.[12]

When treating palmar and plantar hyperhidrosis, higher doses of BTx-A are required i.e. 75 to 100 units per hand/foot are commonly used. These are uniformly distributed into 5 to 50 sites spaced 1 to 1.5cm apart. The digits usually require 2 to 3 injections each.[13,14] Of note is the fact that BTx-A treatment for palmar hyperhidrosis is very painful.

Contraindications

BTX-A should not be used in pregnant or breastfeeding women. It should also not be used if the patient has a known hypersensitivity to any of the formulation components, if the area of injection is infected, in patients suffering from secondary hyperhidrosis, patients who have undergone surgical removal of sweat glands, and patients with blood-clotting disorders.[11]

CONCLUSION

In conclusion, treatment with botulinum toxin produces a significant reduction in the severity of primary axillary hyperhidrosis and evidence shows that this treatment has a high safety and efficacy profile.

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