

Management of Primary Focal Hyperhidrosis

Dr. L. Y. Chan and Dr. Y. M. Tang

Social Hygiene Service (Dermatology), Department of Health, Hong Kong

ABSTRACT

Primary focal hyperhidrosis is a common problem that can be socially embarrassing and occupationally disabling. Aluminium chloride hexahydrate is widely used as a first line treatment which is cheap and effective for mild cases. Tap water iontophoresis can be effective when patients fail or are intolerant to topical antiperspirant. Recently, botulinum toxin has been used successfully for patients with severe hyperhidrosis not responsive to conservative treatments. Improved techniques in cervical sympathectomy have made the procedure relatively simple and safe. Excision of axillary skin bearing sweat glands is a definitive treatment for axillary hyperhidrosis and/or bromhidrosis but the risks of haemorrhage, infection and contractural scarring preclude its wide use. The removal of axillary fat that contains the sweat glands by tumescent liposuction has therefore evolved into an effective and safe alternative treatment without the disadvantage associated with axillary skin excision. The various treatment modalities for primary focal hyperhidrosis are reviewed.

Keywords: hyperhidrosis, iontophoresis, botulinum toxin, sympathectomy

INTRODUCTION

There are two to three million eccrine sweat glands all over the body with uneven distribution. The palms and soles have a maximum density of 600-700 glands/cm², the forearms 108 glands/cm² and the back 64 glands/cm². The main function of sweating is to regulate a rising body temperature. However, when sweating exceeds what is required to cool the body, hyperhidrosis results. This may render the patient socially embarrassed and incapacitated to work and activities. While febrile diseases, neoplasia, drugs, metabolic and endocrine disturbances could account for generalized hyperhidrosis, majority of patients with palmoplantar and axillary hyperhidrosis do not have obvious causes. This is referred to as primary or idiopathic

hyperhidrosis. This condition has a prevalence of 0.6% to 1.0% among the general population. It usually begins in adolescence and is worsened by emotional stimuli and heat. It is known that eccrine sweat glands are innervated by sympathetic post-ganglionic fibres with acetylcholine as the neurotransmitter. A central influence is exerted by a sweat control centre in the preoptic area and anterior hypothalamus. This centre is influenced by changes in internal temperature and cerebral cortical events such as emotional change and anxiety which in turn affect the sympathetic sudomotor fibre activities. An increased sympathetic outflow could be demonstrated in patients with primary focal hyperhidrosis and a history affecting family members is often found.

The various treatment modalities of primary focal hyperhidrosis is summarised in the table:

1. Pharmacological	Topical antiperspirant Systemic agents Botulinum A toxin
2. Physical	Iontophoresis
3. Surgical	Sympathectomy Axillary skin excision Axillary liposuction

Correspondence address:
Dr. L. Y. Chan
Tuen Mun Social Hygiene Clinic
5/F Tuen Mun Polyclinic
4 Tuen Lee Street
Tuen Mun
New Territories

1. Pharmacological

Topical antiperspirant

Topical antiperspirant is the first line treatment in primary focal hyperhidrosis. Aluminium chloride hexahydrate solution is most commonly used and often effective for mild hyperhidrosis. It combines with keratin in the sweat ducts, resulting in ductal occlusion. Emphasis on correct use improves success rate. The skin should be dried thoroughly before application for better drug penetration. Presence of moisture may also cause skin irritation due to the formation of hydrochloric acid. Treatment should be started with once nocte application and then less frequently when response occurs. Occlusion with plastic wrap for two to three nights a week can be tried for the less responsive patients. Topical antiperspirant treatment should be supplemented with general measures such as use of absorptive powder to reduce sweat, continual drying of the palms, and keeping a good hygiene with frequent changing of socks. Side-effects of topical antiperspirant include irritation, dryness and fissures, which can be reduced by emollient and topical steroid such as hydrocortisone cream. Apart from aluminium chloride, zirconium chloride, boric acid, resorcinol, formaldehyde and glutaraldehyde have also been used but sensitization may occur with them and glutaraldehyde may stain skin. Topical antiperspirants are cheap and easily available. For patients with axillary hyperhidrosis and severe palmoplantar hyperhidrosis, topical antiperspirant may not be effective.

Systemic agents

Systemic anticholinergic agents such as probantheline bromide and glycopyrrolate can be used in generalized and localized hyperhidrosis. However, the clinical effect achieved by a high dose is offset by many side-effects including blurred vision, dry mouth, constipation and urinary retention. Tranquilizers such as diazepam can be used for combating anxiety-producing events which might aggravate or precipitate an hyperhidrotic episode. In general, long term use of systemic drugs for hyperhidrosis is not advisable.

Botulinum toxin

Botulinum toxin (BTX), one of the most poisonous substance known to mankind, is produced by the obligate anaerobic bacterium, *Clostridium botulinum*. So far, seven types of *C. botulinum* are recognised (types

A - G), each produces a distinct neurotoxin. Types A, B, and E cause most human epidemics of botulism, a potentially fatal disease consequent to widespread inhibition of pre-synaptic release of acetylcholine. Due to the unique property of BTX, it has been successfully used for treating various neurological or neuromuscular diseases such as blepharospasm, strabismus, wrinkles, and focal dystonia. Recently, BTX type A has been used with great success for treating severe focal hyperhidrosis. Two commercial preparations of BTX type A are now available: Botox and Dysport. One unit of Botox roughly corresponds to 3-5 units of Dysport. Shelley et al reported four patients with severe palmar hyperhidrosis treated with subepidermal injections of 100 units of Botox over 50 sites in each palm.¹ Anaesthesia was achieved by regional nerve block of the median and ulnar nerves. Therapeutic effect soon occurred in all patients and anhidrosis lasted for 12 months in one patient, 7 months in two patients, and 4 months in one patient. Treatment related adverse effects included pain on injection and one patient also developed mild reversible weakness of the thumb. In a randomized, double-blind study, Schnider et al used 120 mU (mouse units) of Dysport injected over 6 different sites on one palm of 11 patients.² The other palm which served as a control was injected with sterile saline. A statistically significant reduction of sweat production was noted in the treated palm and lasted over a follow up period of 13 weeks.

The authors have the experience of using Botox to treat four patients with severe palmar hyperhidrosis who failed to improve with aluminium chloride and tap water iontophoresis (unpublished data). Each received a dose of 48-52 units of Botox, given intracutaneously to the left hand after a washout period of two months. The right hand was not injected and served as a control. Ten sites was injected: five on palm and five on fingers. There was a similar sweat reduction on both the treated and control palms over a six weeks' follow up period but it could be accounted for by a decrease of ambient temperature. Three patients experienced reversible, mildly reduced gripping power. The low efficacy of Botox seen in our study may be due to poor dispersion consequent to only five palmar injections.

We foresee that BTX will become a popular and powerful treatment tool for severe hyperhidrosis of palms, soles and axillae; but the exact dosage, and number of injection sites will need to be determined. Moreover, the drug is very costly. Treatment involves

deep dermal/subcutaneous injections which are painful, and inadvertent injection or diffusion of the toxin into adjacent muscles may produce muscle weakness, though reversible. The drug is contraindicated in patients with known hypersensitivity to any ingredient in the product and is relatively contraindicated in pregnancy. It can also unmask subclinical neuromuscular diseases and is contraindicated in myasthenia gravis. Experience of treating strabismus and blepharospasm has shown that repeated frequent toxin injections in large doses may lead to antibody formation, thus reducing efficacy. The chance can be reduced by keeping the dose below 200U in a month period.

2. Physical

Iontophoresis

Iontophoresis is the use of an electromotive force to enhance percutaneous absorption of a drug or chemical. Tap water iontophoresis (TWI) is an established treatment modality for palmar, plantar, and axillary hyperhidrosis. The mechanism of action is unknown but induction of hyperkeratinization and subsequent obstruction of the eccrine sweat duct units was thought to occur.³ Bouman et al reported an improvement in 90% of their 113 patients with palmoplantar hyperhidrosis.⁴ Similar efficacy was also demonstrated in other studies.^{5,6,7}

Using TWI delivered by a pulsed current with adjustable current density, the authors have treated nine adult patients (mean age 30.4 years, range: 16-47 years) who failed to respond to topical aluminium chloride solution.⁸ The treatment was carried out for 20 minutes, three times a week for six consecutive weeks. Sweat output was measured by the net weight gain of a diaper after exercise. The mean objective sweat output reduction was 49% and 51% after three and six weeks respectively. Side-effects were mild and transient. However, the beneficial effects gradually weaned off upon cessation of treatment, thus continuing or intermittent use of TWI is necessary to maintain an hypohidrotic state. This problem can be overcome by home therapy using portable iontophoretic unit. In 1987, Akins studied 22 patients with 27 sites using home iontophoretic unit for treating hyperhidrosis.⁹ The treatment was carried out for 30 minutes twice a day for 5 days and then 30 minutes daily. Within 14 days, 80% of the hands, 33% of the soles, and 37.5%

of the axillae showed at least 50% improvement. Side-effects including discomfort during treatment, vesicles, erythematous papules and scaling were mild. A portable iontophoretic unit (hands/feet pair and underarms pair) is now available locally. It was claimed that sweating can be inhibited for up to six weeks after cessation of treatment. Apart from using tap water, glycopyrrolate can be used which might be more effective but systemic anticholinergic side-effects may occur.

3. Surgical

Sympathectomy

Sympathectomy is an effective means in reducing the sympathetic tone of sweat glands and achieving hypo/anhidrosis, and has been practised for years. Lumbar sympathectomy for plantar hyperhidrosis is less often done because of the risk of sexual dysfunction. The use of endoscopic transthoracic sympathectomy improves safety and allows a smaller scale operation. Horner's syndrome, pneumothorax, haemothorax, surgical emphysema and brachial plexus injuries are possible risks of sympathectomy. Since up to 40% of the sweat gland function is lost after bilateral cervical sympathectomy, sprouting of sympathetic nerve fibres in distant sites to achieve an overall constant and effective thermoregulation may lead to compensatory hyperhidrosis. Video-assisted thoracoscopy (VAT) is the current choice for upper thoracic sympathectomy. It enables a superior view so that anatomy can be clearly visualized, thus avoiding complications associated with the conventional approach. Several reports have demonstrated a greater than 95% success rate with sympathectomy performed under VAT for palmar hyperhidrosis.^{10,11}

A recent local study by Tai et al on 29 VAT sympathectomies done under general anaesthesia involving 10 women and 5 men (age 17-31 years; mean = 22 years) with severe palmar hyperhidrosis reported a 100% success rate.¹² The sympathetic chains with T2 and T3 ganglia were excised by an endoscopic diathermy hook. T4 ganglion was also excised if there was simultaneous axillary hyperhidrosis. Anhidrosis was achieved in all patients during a follow up period of 5-35 months (mean = 15.6 months). There was no Horner's syndrome or lung injury, and only three patients experienced mild compensatory sweating in other areas.

Surgical Removal of Axillary Eccrine Sweat Glands

Surgical Excision

While sympathectomy is effective for palmoplantar hyperhidrosis, extirpation of eccrine sweat glands remains the definitive surgical treatment for patients with axillary hyperhidrosis who fail to respond to conservative treatments. The conventional method entails excision of eccrine sweat gland bearing skin in the axillary vault. The area of maximum glandular density correlates approximately with the hairy portion of the axilla, and the use of starch-iodine test can facilitate precise localization. Mere excision of the skin at apex of the axilla is the simplest and effective method because this part gives the greatest sweat production.¹³ The excision should be deep enough to reach the subcutaneous layer to include the secretory portion of the eccrine apparatus. If the treatment aims to eradicate axillary bromhidrosis, a common condition affecting Orientals, the depth of excision may even be deeper to include deeper situated apocrine glands. For very severe hyperhidrosis, a wide excision to include the peripheral part of the axilla is also required.¹⁴ In this case, post-operative morbidity such as wound dehiscence, haemorrhage, wound infection and contractural scarring that limit shoulder movement necessitating skin grafting would be a definite risk. Hence wide excision of axillary skin should not be undertaken lightly. Various modifications in the excision technique that bear different names have been proposed by different investigators to reduce operative morbidity and complications and to study their different merits.

Liposuction

Since most axillary eccrine and apocrine glands are situated deep within the subcutaneous fat layer, removal of this compartment by liposuction for axillary hyperhidrosis^{15,16} is therefore an effective alternative to direct surgical excision. Suction can be carried out by a liposuction cannula through a small incision in the anterior axillary fold. The dermal and subcutaneous portions are 'vacuumed' in all directions with multiple strokes to remove the dermal and subcutaneous fat tissue. Liposuction can be carried out under general or local anaesthesia. In recent years, liposuction performed under tumescent anaesthesia has revolutionised traditional liposuction technique. This refers to liposuction performed under a method of regional anaesthesia whereby a very dilute solution of lignocaine,

epinephrine ($\leq 1\text{mg/L}$), saline and sodium bicarbonate (10mEq/L) is directly infiltrated into the target fat compartment. Upon infiltration, this compartment swells and becomes firm, permitting an increased ease and accuracy in liposuction using microcannulae. In addition, the epinephrine-induced vasoconstriction minimizes blood loss, bruising and postoperative soreness; postsurgical irregularities or rippling of the skin is also minimized. Moreover, the risk of lignocaine toxicity has been reportedly low despite a large quantity of lignocaine which if given in the conventional manner would be hazardous. Despite all these advantages, care must be exercised and the procedure should be backed up with stand-by resuscitation equipment since deaths, though rare, have been reported after tumescent liposuction.¹⁷

Learning points:

Tap water iontophoresis is a good alternative to topical antiperspirant before considering botulinum toxin or sympathectomy.

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