

Turning the tide: a history and review of hyperhidrosis treatment

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Summary

Hyperhidrosis is a potential cause of severe physical and psychological distress, interfering in activities of daily living. Over the past 100 years, advances have been made regarding the treatment of this debilitating condition with some success. Surgical treatment with sympathectomy was successfully performed for hyperhidrosis in the early part of the 20th century, with various modifications of the technique over the past 100 years. Topical aluminium salt antiperspirants, anticholinergic medications, iontophoresis and botulinum toxin introduced less invasive ways to manage this condition. This historical review will enable dermatologists and non-dermatologists to manage this distressing condition.

Keywords

hyperhidrosis, antimuscarinic, treatment, botulinum toxin, sympathectomy

Introduction

Sweating is a normal physiological response to reduce body temperature but can become a physical and psychological burden for patients when it is perceived to be excessive. Excessive sweating, or hyperhidrosis, causes considerable embarrassment, physical discomfort and affects about 1–3% of the population.^{1,2} It may interfere with activities of daily living and can have a higher impact in patients' quality of life compared with other skin conditions such as atopic eczema, acne, psoriasis or rosacea.² A Victorian perception is characterised by Charles Dickens'³ villain Uriah Heep in *David Copperfield*: 'I found Uriah reading a great fat book, with such demonstrative attention, that his lank forefinger followed up every line as he read, and made clammy tracks along the page (or so I fully believed) like a snail'. The stigmatisation of patients with hyperhidrosis remains a potent source of distress. Various invasive and non-invasive treatment modalities have been developed. This report summarises the development of currently available treatments to help clinicians manage the condition.

Method

We searched MEDLINE and google scholar database from their conception until December 2012. All articles in English language were included. Keywords used included 'hyperhidrosis', 'treatment', 'history', 'sympathectomy', 'antimuscarinic', 'iontophoresis', 'botulinum toxin' and 'topical'. Conference proceedings were not searched. All eligible references were checked and sources obtained. The sources were cross checked.

Surgical treatment

Surgical treatment for hyperhidrosis was developed almost 100 years ago with surgical sympathectomy. The first clinical surgical sympathectomy was performed by Alexander in 1889 as a treatment for epilepsy.⁴ Sympathectomy was initially advocated for idiocy, exophthalmic goitre, glaucoma, angina pectoris, Raynaud's disease and Sudeck's atrophy.¹ Sympathectomy for hyperhidrosis was attempted in 1919 by Kotzareff who demonstrated its efficacy in 1920 for unilateral facial hyperhidrosis.⁵ Adson reported successful treatment for palmar hyperhidrosis with cervical sympathectomy in 1935.⁵ Sympathectomy was initially performed using an open thoracotomy approach but never became popular because of the morbidity. In 1951, Kux⁶ suggested a novel endoscopic approach to the sympathetic chain for duodenal ulcer, angina pectoris, hypertension and diabetes.

It was not until 1975 when the first case series of thoracoscopic sympathectomy for upper extremities hyperhidrosis was published in the German literature.⁷ Video-assisted thoracoscopic sympathectomy was introduced in the 1990s and has become the procedure of choice. The procedure has undergone further modifications including chain resection, transection, cauterisation, and clipping.⁸

Sympathectomy is advocated for debilitating hyperhidrosis of the extremities not responding to less invasive modalities but commonly results in

compensatory increase in sweating elsewhere. Compensatory hyperhidrosis limits the usefulness of the procedure as it can be more troublesome than the original condition.

Excision or curettage of sweat glands from the underside of the axillary skin have also been used for localised axillary hyperhidrosis with good success.⁹ Subaxillary liposuction has also been reported to be successful with significant improvement in patient-reported outcomes measured with the Dermatology Life Quality Index (DLQI).² Subdermal and transcutaneous lasers are newer modalities slowly becoming more popular in recent years with good efficacy.¹⁰ Treatment with electrosurgery using insulated needles was showing promising results but never became very popular.¹¹

Antimuscarinic medications

For more than 50 years, surgery was the only treatment for hyperhidrosis until the introduction of antimuscarinic medications. The use of antimuscarinic medications for hyperhidrosis was first reported in 1950 by Grimson et al.¹² who noticed that patients undergoing treatment with a new antimuscarinic, methantheline (Banthine[®]), for peptic ulcer, commented on dry hands. Grimson et al.¹² treated four female patients with palmar hyperhidrosis with Banthine at a dose of 50–100 mg every 4 h with an excellent response. They concluded that that this new treatment would probably make sympathectomy no longer necessary for hyperhidrosis. A recent randomised double-blind placebo-controlled study using a new commercial preparation of methantheline bromide (Vagantin[®]) 50 mg thrice daily demonstrated significant sweat reduction.¹³ Propantheline (Pro-Banthine[®]), the isopropyl analogue of methantheline, was shown to have approximately five times stronger antimuscarinic activity when compared with methantheline.¹⁴ The duration of action was longer and the relative lack of side effects made propantheline a favourable treatment for hyperhidrosis. Propantheline was shown to work systemically and topically by a Danish group in the early 1960s.¹⁵ It was used successfully when taken systemically for gustatory hyperhidrosis in a patient with thyroidectomy at 15 mg with the clinical effect lasting around 4 h.¹⁶ The usual starting dose is 15 mg thrice daily. It has been tried also as a spray topically on 38 institutionalised, mental subnormal patients with acceptable result.¹⁵

Glycopyrronium bromide (Robinul[®]) was introduced in the early 1960s for gastric ulcer treatment and was thought to have fewer systemic side effects.¹⁷ The effective dose usually varied between 2 mg twice

to thrice daily. It can also be used topically or with iontophoresis. Glycopyrronium used to be manufactured in the UK as an antispasmodic but now can only be imported from the USA at much higher cost to the National Health Service with limited availability.¹⁸ Systemic oxybutynin has been shown to be effective with generalised hyperhidrosis and postmenopausal hyperhidrosis.¹⁹ A recent randomised placebo-controlled study also suggests that oxybutynin may be beneficial to patients with palmar and axillary hyperhidrosis at a dose of 5 mg twice daily.²⁰ The use of antimuscarinic medications is limited by systemic side effects such as dry mouth and constipation.

Topical treatment with aluminium salts

Many topical treatments have been tried over the century, the majority of which were aluminium salts.²¹ In 1916, Stillians first described that 25% aluminium chloride hexahydrate in distilled water applied every 2–3 days improved excessive sweating. Other topical aluminium agents were extensively investigated over the subsequent 85 years, but Stillians' formulation still remains the most effective.²¹ The findings were confirmed in a larger case series of 65 patients of which 64 patients were highly delighted with the treatment with complete control.²² The exact mechanism of action is unknown, but data suggest that it acts only superficially and does not penetrate into the dermis. The usefulness of topical treatment is limited mainly by local irritation which can occur in nearly all patients though this is usually transient.²³ The irritation can be reduced readily by applying 1% hydrocortisone cream on the morning after treatment.

Iontophoresis

Iontophoresis was described in the 18th century as an attempt to introduce heavy metal into the body.²⁴ The use of iontophoresis as a simple alternative treatment of the palms and soles was suggested and confirmed by Levit²⁵ using tap water in 1968. The efficacy of iontophoresis has been confirmed by other authors with the addition of glycopyrronium²⁶ or botulinum toxin²⁷ with good clinical response. Iontophoresis remains an important modality for treatment of hyperhidrosis but requires long-term use to maintain efficacy, necessitating home treatment.

Botulinum toxin A

Botulinum toxin A (Botox[®]) was used in neurology for dystonias before it became more widely utilised

for wrinkle reduction and hyperhidrosis. It reduces sweating by blocking the postganglionic sympathetic cholinergic nerve fibres to the sweat glands. It was first reported in 1994 as a treatment for hyperhidrosis in patients treated for hemifacial spasm.²⁸ The patient treated in this study developed localised anhidrotic patches which lasted for at least three months. It is licensed for use intradermally for severe hyperhidrosis of the axillae unresponsive to topical antiperspirant or other antihidrotic treatment.²⁹ The clinical effect is only temporary lasting between seven and 12 months for axillary hyperhidrosis and four and six months for palmar hyperhidrosis where there is a low reported rate of complications. It has been used for localised facial hyperhidrosis with good response but can cause weakness of muscles of facial expression. In an open-label study with 41 patients with focal hyperhidrosis, all patients reported improvement with quality of life as measured by the DLQI.³⁰ Its use is limited by its relative high cost and the discomfort associated with multiple injection sites.

Conclusion

From open sympathectomy to the introduction of botulinum toxin, dermatology is moving towards safer and more effective methods of treating this debilitating condition. Is the tide finally turning for patients with hyperhidrosis?

Declarations

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References

- Parikh D. *Pediatric Thoracic Surgery*. London: Springer, 2009.
- Bechara FG, Gambichler T, Bader A, et al. Assessment of quality of life in patients with primary axillary hyperhidrosis before and after suction-curettage. *J Am Acad Dermatol* 2007; 57: 207–212.
- Dickens C. *David Copperfield* (chapter 16). London: Bradbury and Evans, 1850.
- Hashmonai M and Kopelman D. History of sympathetic surgery. *Clin Auton Res* 2003; 13(Suppl 1): 16–19.
- Greenhalgh RM, Rosengarten DS and Martin P. Role of sympathectomy for hyperhidrosis. *Br Med J* 1971; 1: 332–334.
- Kux E. The endoscopic approach to the vegetative nervous system and its therapeutic possibilities; especially in duodenal ulcer, angina pectoris, hypertension and diabetes. *Dis Chest* 1951; 20: 139–147.
- Fritsch A, Kokoschka R and Mach K. [Results of thoracoscopic sympathectomy in hyperhidrosis of the upper extremities (author's transl)]. *Wiener klinische Wochenschrift* 1975; 87: 548–550.
- Deng B, Tan QY, Jiang YG, et al. Optimization of sympathectomy to treat palmar hyperhidrosis: the systematic review and meta-analysis of studies published during the past decade. *Surg Endosc* 2011; 25: 1893–1901.
- Atkins JL and Butler PE. Hyperhidrosis: a review of current management. *Plast Reconstr Surg* 2002; 110: 222–228.
- Goldman A and Wollina UWE. Subdermal Nd-YAG laser for axillary hyperhidrosis. *Dermatol Surg* 2008; 34: 756–762.
- Kobayashi T. Electrosurgery using insulated needles: treatment of axillary bromhidrosis and hyperhidrosis. *J Dermatol Surg Oncol* 1988; 14: 749–752.
- Grimson KS, Lyons CK, Watkins WT, et al. Successful treatment of hyperhidrosis using bantnine. *J Am Med Assoc* 1950; 143: 1331–1332.
- Müller C, Berensmeier A, Hamm H, et al. Efficacy and safety of methanetheline bromide (Vagantin®) in axillary and palmar hyperhidrosis: results from a multicenter, randomized, placebo-controlled trial. *J Eur Acad Dermatol Venereol* 2013; 27: 1278–1284.
- Johnson EA and Wood DR. A comparison of the peripheral parasympatholytic and autonomic ganglion blocking activities of methanetheline (bantnine) and propantheline (probanthine) with atropine and hexamethonium. *Br J Pharmacol Chemother* 1954; 9: 218–223.
- Frankland JC and Seville RH. The treatment of hyperhidrosis with topical propantheline – a new technique. *Br J Dermatol* 1971; 85: 577–581.
- Cunliffe WJ and Johnson CE. Gustatory hyperhidrosis. A complication of thyroidectomy. *Br J Dermatol* 1967; 79: 519–526.
- Bajaj V and Langtry JA. Use of oral glycopyrronium bromide in hyperhidrosis. *Br J Dermatol* 2007; 157: 118–121.
- Klüber M and Catterall M. Treating hyperhidrosis. Anticholinergic drugs were not mentioned. *BMJ* 2000; 321: 703.
- Tupker RA, Harmsze AM and Deneer VH. Oxybutynin therapy for generalized hyperhidrosis. *Arch Dermatol* 2006; 142: 1065–1066.
- Wolosker N, de Campos JR, Kauffman P, et al. A randomized placebo-controlled trial of oxybutynin for the initial treatment of palmar and axillary hyperhidrosis. *J Vasc Surg* 2012; 55: 1696–1700.
- Shelley WB and Hurley HJ Jr. Studies on topical antiperspirant control of axillary hyperhidrosis. *Acta Derm Venereol* 1975; 55: 241–260.

22. Scholes KT, Crow KD, Ellis JP, et al. Axillary hyperhidrosis treated with alcoholic solution of aluminium chloride hexahydrate. *Br Med J* 1978; 2: 84–85.
23. Ellis H and Scurr JH. Axillary hyperhidrosis – topical treatment with aluminium chloride hexahydrate. *Postgrad Med J* 1979; 55: 868–869.
24. Grice K, Sattar H and Baker H. Treatment of idiopathic hyperhidrosis with iontophoresis of tap water and poldine methosulphate. *Br J Dermatol* 1972; 86: 72–78.
25. Levit F. Simple device for treatment of hyperhidrosis by iontophoresis. *Arch Dermatol* 1968; 98: 505–507.
26. Abell E and Morgan K. The treatment of idiopathic hyperhidrosis by glycopyrronium bromide and tap water iontophoresis. *Br J Dermatol* 1974; 91: 87–91.
27. Kavanagh GM, Oh C and Shams K. Botox delivery by iontophoresis. *Br J Dermatol* 2004; 151: 1093–1095.
28. Bushara KO and Park DM. Botulinum toxin and sweating. *J Neurol Neurosurg Psychiatry* 1994; 57: 1437–1438.
29. Joint Formulary C. *British National Formulary*. UK: British Medical Association and Royal Pharmaceutical Society, 2012.
30. Campanati A, Penna L, Guzzo T, et al. Quality-of-life assessment in patients with hyperhidrosis before and after treatment with botulinum toxin: results of an open-label study. *Clin Ther* 2003; 25: 298–308.