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Review article

Primary hyperhidrosis. Current status of surgical treatment

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A B S T R A C T

Primary hyperhidrosis-PH is an excessive sweating without known etiology. The PH is more frequent in women and in palms, soles and axillae. Medical treatment is not effective. The objective of the surgery is to remove or to disconnect sympathetic ganglia T2 (craniofacial PH or facial blushing), T3 (palmar PH) and T3-T4 (axillary PH). The surgical techniques are mainly resection/transection, ablation with electrocoagulation, sympathetic block by clipping and radiofrequency. Anhidrosis is achieved in 95% of the patients. The overall rate of complications is less than 5% and these are minor complications. The most important unwanted effect is reflex sweating, presented in 48% of the patients. Reflex sweating is more frequent in back, thorax and abdomen and it appears independently of the surgical technique. Ninety percent of the patients are very satisfied after surgery. Nowadays, thoracic sympathetic surgery is the gold standard for primary hyperhidrosis.

Hiperhidrosis primaria. Situación actual de la cirugía del simpático

Palabras clave:
Hiperhidrosis primaria
Simpaticólisis torácica
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Neuropresión con clip
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R E S U M E N

La hiperhidrosis primaria (HP) es un exceso de sudoración sin causa aparente. La HP es más frecuente en mujeres y en palmas, plantas y axilas. Los tratamientos médicos no son efectivos. La cirugía consiste en eliminar/desconectar los ganglios simpáticos T2 (HP craneofacial y rubor facial), T3 (HP palmar) y T3-T4 (HP axilar). Las técnicas quirúrgicas son la resección/transección, la ablación mediante electrocoagulación, la neuropresión con clip y la radiofrecuencia, fundamentalmente. La anhidrosis se consigue en el 95% de los pacientes. Menos del 5% presenta complicaciones y estas son menores. El efecto secundario más temido es la sudoración refleja, que se presenta en un 48% de los pacientes. La sudoración refleja es más frecuente en espalda, tórax y abdomen y aparece independientemente de la técnica utilizada. Un 90% de los pacientes están muy satisfechos tras la cirugía. Actualmente, la cirugía del simpático torácico es el gold estándar para la HP.

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Introduction

Under normal conditions, an individual's sweat is produced imperceptibly, estimated daily fluid loss due to perspiration being between 8 and 15 $\mu l \times cm^2/min^{-1}$. This loss of water and electrolytes takes place actively through the eccrine sweat glands, which cover the whole body ($1.6–4 \times 10^6$ gl), having a higher density on the skin of the hands, axillae and the soles of the feet (600–700 $gl \times cm^2$).

The sweat glands are activated by multiple, varied stimuli (emotions, physical exercise, heat, fever, and anxiety) which are modulated by the neurovegetative system with the specific participation of the sympathetic nervous system, but through neurotransmitters and cholinergic receptors.

When for some unexplained reason this balance is lost, it can give rise to sweating beyond normal physiological levels, known as primary hyperhidrosis (PH), without any apparent justification. This clinical disorder, which appears in early childhood[1] and continues for the rest of the patient's life, is hereditary with variable penetrance not linked to gender in 49% of cases.[2] It is not possible to attribute the rest of cases to a specific cause, although most authors agree that the mechanism of action involved is neurovegetative hyperactivity mediated by the sympathetic nervous system.[3-5]

Secondary hyperhidrosis also exists and is associated with one of the following types of pathology: hyperthyroidism, phaeochromocytomas, carcinoid tumours, heart diseases, obesity, structural lesions of the autonomous nervous system, brain tumours, peripheral vascular diseases (Raynaud's syndrome, erythromelalgia, acrocyanosis, etc.) ictus or spinal cord diseases. With secondary hyperhidrosis, it must be remembered that the menopause can also be associated with excessive sweating.

Material and method

To prepare this review, we have performed an exhaustive search of the literature using the databases accessible online. We used PubMed/Medline (http://www.pubmed.com). On the one hand, we performed a free search entering the words "thoracic sympathectomy", "thoracic sympathicolysis", "primary hyperhidrosis", "compensatory sweating", "compensatory hyperhidrosis", and "reflex sweating". On the other, we used the MeSH database, entering the key words "hyperhidrosis/surgery OR sympathectomy/adverse effects". A search was also carried out using the Cochrane database (The Cochrane Library, http://www.wiley.com/cochrane). In the preparation of the review, we chose the most relevant references and took into consideration our team's experience.

Clinical profile of primary hyperhidrosis

The incidence[6] is 0.6%-4%, this being 20 times higher among the Japanese than Caucasians. PH is more common in women and is usually bilateral and symmetrical.[7] Hyperhidrosis usually affects the palms, soles of the feet and armpits (30%), although it is also common in palms and soles (20%), palms and axillae (15%), and only in the palms (29%). Cranial and facial hyperhidrosis (2.5%) also have to be taken into account.

Apart from the excessive, socially-inconvenient sweating, it is also associated[8] with palpitations, intentional tremor, epigastralgia, facial blushing and headache. This array of symptoms causes varying degrees of anxiety, to the point where it is difficult to confirm if this is a cause or consequence. The disease has negative repercussions on labour and social relations.[7] These negative repercussions drive the patient to seek treatment, eventually opting for surgery.

There is a clinical diagnosis of PH. The usual laboratory tests can help to rule out diseases causing secondary hyperhidrosis.

Medical treatment

As there is no defined cause, symptomatic treatment is given[9]:

Hygiene measures: absorbent powders, cotton or woollen socks and clothes, leather shoes, avoiding rubber and man-made materials, etc.

Topical agents: at first, they are effective, such as aluminium hexachloride 2%, which is effective in 12%-64% of cases, while glutaraldehyde (10%), tannic acid (2%-5%) or potassium permanganate reduce sweating by up to 25%. A disadvantage is that they cause obstruction and even atrophy of the glands, with the consequent skin irritation, browning of the skin, sensitisation and even the rebound effect. Normally, the treatment becomes less effective in the medium term.

Systemic anticholinergic drugs: their efficacy is only temporary and they have many side effects which make their use unadvisable, such as: blurred vision, dry eyes (xerostomia), dry mouth, vaginal dryness and urinary retention.

Iontophoresis: it involves the electrocoagulation of the eccrine glands by direct application of 15-30 mA of galvanic current in 20 min sessions, around 3 times per week. Anticholinergic drugs such as poldine methyl sulphate or glycopyrronium bromide can be added to the water. Although it is an effective procedure, patients develop high levels of dependency and often stop using it.

Botulinum toxin: type A botulinum toxin is a neurotoxin which achieves temporary improvements in hyperhidrosis. The affected area is intradermally injected at several points (1-2 cm apart). The procedure must be repeated every 4-17 months. It has proven to be most effective in the axilla.

Psychotherapy or biofeedback techniques: they have limited effectiveness, have a long duration, require excessive dedication and perseverance, and results are unclear at the moment.

Seventy-eight percent of the patients underwent some form of unsuccessful treatment before surgery. Faced with these awful prospects, patients demanded a solution for their disorder, and thoracic sympathetic surgery met their needs.

Thoracic sympathetic surgery

Thoracic sympathetic surgery is indicated for patients with palmar, craniofacial and axillary hyperhidrosis. This technique is also indicated in vascular disorders such as facial blushing, Raynaud's syndrome, peripheral artery obstruction or Buerger's disease. Sympathetic denervation has also been used successfully in some cardiac rhythm disorders, such as long QT syndrome or polymorphic ventricular tachycardia. This review will focus on the treatment of hyperhidrosis.

Anatomical basis: when the pleural cavity is examined by thoracoscopy, the most apical muscle seen in the posterolateral region is the first intercostal muscle, attached to the second rib. The thoracic sympathetic trunk lies on the heads of the ribs, which are posterior to the parietal pleura; the sympathetic thoracic ganglia which interest us are situated level with the intercostal spaces and not on the costal arch. The sympathetic dermatomes overlap each other and are difficult to systematise. However, we can say that the second sympathetic ganglion (T2) is involved in the sympathetic innervation of the head, neck and upper limb. The third sympathetic ganglion (T3) is involved in the innervation of the upper limb and upper third of the axillae, and the 4th sympathetic ganglion (T4) innervates the lower third of the axillae and the upper limb. There are sympathetic projections from the upper limbs to the cervicothoracic (stellate) ganglion and the middle cervical ganglion. Furthermore, there are sympathetic projections from the upper limbs incorporated in the brachial plexus. This would explain in part some of the secondary effects.[10,11]

Surgical technique: for PH, patients undergo a sequential bilateral procedure using thoracoscopic surgery under general anaesthesia with selective bronchial intubation. Although several technical variants exist, the most common places the patient in supine decubitus, in sitting position or sitting at 25º, with abduction of the upper limbs and slight flexion of the forearms. The operating table is inclined 10º towards the opposite hemithorax being operated on. A portal is placed at the level of the third intercostal space on the medial axillary line to introduce a 5 o 10 mm[7] thoracoscope. If a thoracoscope without a channel for instruments is used, 2 portals are needed. To carry out a sympathectomy, it is sometimes necessary to use 3 ports.

The objective of the method is to totally or partially remove or disconnect the sympathetic thoracic ganglia T2 (craniofacial PH and facial blushing),[12] T3 (palmar PH), T3-T4 (axillary PH),[13] by applying different systems: monopolar electrocoagulation,[14] bipolar electrocoagulation, harmonic scalpel,[15] sympathetic block by clipping[16] or radiofrequency.[17] Disconnecting a ganglion involves acting on the sympathetic trunk at the level of the superior rib, below the intercostal space, where the ganglion is found. In that respect, a sympathectomy is the excision of a fragment of the sympathetic trunk; the transection aims to section the sympathetic nerve or trunk, while sympathicolysis or ablation involves the direct elimination of the sympathetic nerve. For the surgery to be totally effective, it is necessary to remove any accessory sympathetic connections or additional branches communicating with the intercostal nerves (previously called Kuntz's nerves, present in around 10% of patients). Pleural drainage can be left or not, although it is advisable to leave a 10Fr catheter connected to the usual sealing system to completely evacuate the pneumothorax. Once the absence of pneumothorax or pleural effusion has been confirmed, the drainage can be removed a few minutes or hours after the operation. The mean postoperative hospital stay is 17 h, and observation can even be carried out as major outpatient surgery.[7]

Age for surgery: most patients undergo surgery on 20-30 years old. The best age range for surgery is from 18 to 45 years old. For surgery to be indicated in patients under 18 years old the body development is assessed; with patients over 45 years old cases for surgery are chosen carefully, especially with climacteric women or those approaching the menopause.

General results: with the exception of some isolated cases of death,[18] all the series[19-21] reported no mortality, with a morbidity not exceeding 5%. Pneumothorax is the most common complication (2% of patients; of total pneumothorax only 25%-30% requires thoracic drainage), followed by subcutaneous emphysema (1%) and pleural effusion (0.3%-0.5%), which seldom requires drainage.[22] The literature reports isolated cases of complications such as chylothorax, hemopericardium, lesions of the superior intercostal vein, pulmonary oedema, or brachial plexus lesions. The literature shows that sympathicolysis produces less morbidity and better long-term tolerance compared to a sympathectomy.

Eighty percent of patients report pain in the month after surgery, with the rate of work-related disability being 2%. Between the first and second month only 13% have pain, and exceptional cases have been recorded of patients with prolonged neuropathic pain requiring treatment with gabapentin (0.25%).

Sweating results: in the long term[7,23] anhidrosis is achieved in 92%-98% of patients, hypohidrosis in 2.4%-7%, with a failure rate for the technique of 0.2%-2% (3.4%-5% using sympathetic block by clipping). The best sympathectomy and sympathicolysis results have been obtained for palmar hyperhidrosis, followed by axillary, and finally, craniofacial hyperhidrosis.

Relapse of hyperhidrosis after surgery has been reported in 1%-2% of patients, most commonly in axillary hyperhidrosis. Good results have been seen for reoperation for persistent palmar hyperhidrosis or relapse.[24]

Paradoxically, 30.3% of patients have reported anhidrosis and 20.7%[25] hypohidrosis of the soles of their feet after sympathicolysis.

Consequences: the most common and worrying consequence is reflex or compensatory sweating (Table 1), suffered by around 48% of patients,[7,26] affecting, above all, the back, abdomen and the anterior thorax.[7,24,27-36] This sweating is not related to situations of stress or anxiety, as in PH, but rather to environmental temperature or physical activity. It appears a short time after surgery and is mild in 61% of patients, moderate in 31%, and severe in 8%.[27]

The analysis of the literature reveals the lack of homogeneity of the surgical techniques used and the levels

Table 1 – Reflex sweating according to ganglion disconnected/removed and technique used

Author	Year	Type of study	No. of patients	Mean age	Technique	Reflex sweating			
						Ganglion disconnected			
						T2	T3	T4	T5
Gossot[27]	2003	CCS	125	28	Sympathectomy	[	86%	]	
Freeman[24]	2009	CCS	321	21	Sympathectomy		31%		
Freeman[24]	2009	CCS	40	27	Sympathectomy		53%		
Moya[7]	2006	CCS	325	27	Sympaticolysis	[	48%	]	
Li[28]	2008	ER	117	21	Transection		21%		
Li[28]	2008	ER	115	22	Transection	[	29%	]	
Liu[29]	2009	ER	141	27	Transection		77%	56%	
Miller[30]	2009	CCS	179	23	Transection	13%			
Miller[30]	2009	CCS	103	24	Transection	[	34%	]	
Weksler[31]	2009	CCS	112	29	Transection	[	74%	]	
Weksler[31]	2009	CCS	88	28	Transection	[	84%	]	
Lin[32]	2004	CCS	102	24	Clip	84%			
Sugimura[34]	2009	CCS	672	27	Clip	15%	[	8%	]
Sugimura[34]	2009	CCS	55	27	Clip	[	24%	]	
Chou[35]	2006	CCS	25	?	Sympaticolysis			0%	
Chou[35]	2006	CCS	439	?	Clip	43%	27%	0%	0%
Inan[36]	2008	ER	20	21	Sympatectomy	[	15%	]	
Inan[36]	2008	ER	20	22	Sympaticolysis	[	25%	]	
Inan[36]	2008	ER	20	22	Transection and sympaticolysis	[	15%	]	
Inan[36]	2008	ER	20	23	Clip	25%			

CCS indicates observational study of series of clinical cases; ER, randomised analytical experimental study

disconnected. At times, different results are obtained regarding reflex sweating, making it difficult to draw conclusions. Nevertheless, the onset of reflex sweating seems to be independent of the technique used for sympathetic trunk interruption (Table 1). Different studies support the use of sympathetic trunk interruption with clips as a method for stopping hyperhidrosis. The theoretical advantage of this method is that it is reversible. Removing the clips in a second operation acts to reduce reflex sweating if this is severe and badly tolerated. This second operation is performed using the same ports as before.

Series of patients who have had the clips removed show a reduction in reflex sweating in around 60% of the patients[35,37] (Table 2). However, the series involve few cases where the clips have been removed (no more than 20 cases) and the follow-up has been short to date. The series do not concur about the time to remove the clip, and there are differences regarding the moment at which the sweating reflex improves. The level of experimental evidence is low, with nerve regeneration occurring after sympathectomy in 41% of cases and not before 180 days,[38] which does not correlate with the clinical results presented by some authors who defend the clipping technique.

Looking to minimise the percentage of patients with severe sweating reflex, Miller et al[39] propose a temporary anaesthetic block (bupivicaine, Marcaine®) of the sympathetic ganglion or ganglia to be disconnected, so that the patients can assess the results on their hyperhidrosis and the possible reflex sweating. If they are satisfied with the result, a second, definitive operation can be carried out.

Table 2 – State of reflex sweating after clip removal

Series	Year	No. of clips removed*	%	Improvement in sweating
Lin[16]	1998	5/326	1.5	80
Lin[32]	2004	2/102	2	100
Reisfeld[33]	2006	31/1274	2.4	81
Chou[35]	2006	13/439	2.9	85
Kang[37]	2008	15/116	13	64
Sugimura[34]	2009	34/727	4.7	48

*Patients with clips removed over total number of patients.

Another aspect analysed with regard to the surgical technique is the onset of reflex sweating in relation to the ganglion or ganglia disconnected. Some authors describe lower percentages of reflex sweating if surgery is performed on the inferior ganglia (T3-T4[29,33-35]). The analysis of the literature does not clarify whether eliminating a greater number of ganglia is related to more reflex sweating, but the most recent studies show that there is less reflex sweating if one single sympathetic ganglion is disconnected.[28,30,31]

There are some studies showing a reduced intensity of reflex sweating in the year following surgery, which is associated with the patient acceptance. Other studies only report an improvement in reflex sweating in a few patients, the condition remaining stable in most cases. Anatomical

experimental evidence indicates that it is the disruption, to a greater or less degree, of the preganglionic fibres that conditions the reflex sweating response, since the cell bodies of the neurons of these preganglionic fibres are located at levels from C8 to T7 of the spinal cord. Consequently, the more cranial the transection is, the higher the number of preganglionic fibres disrupted, with a greater response of the sweating reflex.[10,11]

The different treatments used for the sweating reflex, such as topical agents, anxiolytics, antidepressants, oral anticholinergics, or botulinum toxin have not been successful to date. Doubt has been placed on the success of attempts to reconstruct the injured sympathetic trunk using intercostal or sural nerve. They are isolated cases with high rates of morbidity.

Other side effects, such as excessive dryness of the hands, ptosis or partial Horner's syndrome, and gustatory sweating, do not usually reach 1% of cases.

Finally, thoracic sympathectomies/sympathicolysis lead to a small reduction in maximum expiratory volume in 1 second and in carbon monoxide diffusion capacity, as well as a slight increase in airway resistance. Regarding cardiac function, it causes slight bradycardia and a small decrease in ejection fraction, neither having clinical repercussions.[40]

Degree of satisfaction: regarding the degree of satisfaction, measured with specific questionnaires, the series show that 89% of patients are very satisfied, 9% are not very satisfied and 2% are unsatisfied.[7,22,26] The quality of life scores recorded using validated, dermatological surveys are very high, with substantial decreases in anxiety levels and perception of disability.[41]

In summary, based on all the aforementioned results, as well as those obtained for quality of life and degree of satisfaction, this procedure can be said to be the gold standard for PH. Regarding reflex sweating, methods are needed which make it possible to easily deduce and measure the quantity and severity of sweating in patients. This would make it possible to homogenise the results and get more precise knowledge about reflex sweating. Furthermore, randomised studies with a large number of patients are needed to enable the latest advances in surgical technique to be validated. It is necessary to continue studying the sympathetic nervous system, as well as it would be of interest to study the basal sympathetic activity of patients with PH to differentiate subgroups, making it possible to predict the effect of surgery and offer each patient the most suitable technique.

Conflict of interests

The authors affirm that they have no conflicts of interests.

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