



Contribución al estudio de la denervación simpática T2-T3: Efecto sobre la vía óculo-simpática y la redistribución del sudor en pacientes con hiperhidrosis primaria

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III. OBJETIVOS

Objetivo general

Con la finalidad de contribuir al estudio de la denervación simpática T2-T3, proponemos el siguiente objetivo:

Evaluar el resultado de la denervación simpática torácica sobre la sudoración corporal y el efecto sobre la función pupilar

Objetivos específicos

Artículo I: “**A. Ureña**, R. Ramos, C. Masuet, I. Macia, F. Rivas, I Escobar, R Villalonga, J Moya. An assessment of plantar hyperhidrosis after endoscopic thoracic sympathectomy. Eur J Cardiothorac Surg 2009; August 36: 360-363”

Objetivo: Registrar las zonas de redistribución anatómica de la sudoración corporal después de la denervación simpática T2-T3.

Artículo II: “R. Ramos, **A. Ureña**, F. Rivas, I. Macia, G. Rosado, S. Pequeño, C. Masuet, M. Badia, M. Miguel, M.A. Delgado, I. Escobar, J Moya. Impact of T3 thoracoscopic sympathectomy on pupillary function: a clinicoanatomic study. Surg Endosc 2012; Apr, 26(4): 1146-52”

Objetivo: Registrar la respuesta simpática del músculo dilatador de la pupila después de la denervación simpática T3.

IV. METODOLOGÍA GENERAL

1. Metodología general

Este trabajo forma parte de una línea de investigación que se inició en el Servicio de Cirugía Torácica del Hospital Universitari de Bellvitge en el año 1995 sobre la cirugía del sistema nervioso simpático, y se divide en dos partes dado que ha dado lugar a dos artículos publicados.

En el primer trabajo se utilizaron los datos de una encuesta prospectiva transversal de carácter observacional y controlada, especialmente diseñada para valorar la localización de la sudoración y el grado de afectación social y laboral, de los pacientes con hiperhidrosis primaria que iban a ser intervenidos, mediante una simpatectomía torácica en el Hospital Universitari de Bellvitge.

En el segundo estudio se valoró la existencia de afectación de la vía óculo-simpática después de la cirugía, por lo que se precisó de la medición pupilar en cada paciente mediante el test de la apraclonidina.

En ambos estudios la inclusión de los pacientes se hizo en la consulta prequirúrgica en la que se obtuvo el consentimiento informado, que explicaba la técnica quirúrgica con sus riesgos, y otro hoja con la metodología del estudio, dándoles la opción de abandonar el estudio en cualquier momento.

Ambos estudios fueron prospectivos y controlados, de seguimiento y analítico limitados a los pacientes intervenidos mediante una simpaticolisis torácica a nivel T2-T3 en el primer estudio y a nivel T3 en el segundo, en nuestro centro.

El seguimiento de los pacientes en ambos estudios se realizó en el momento preoperatorio, postoperatorio inmediato y posteriormente al mes postoperatorio, prolongándose hasta los 12 meses en el primer estudio.

El segundo estudio fue sometido a la aprobación del comité de Ética de nuestra institución dado que en él se realizaba una prueba diagnóstica fuera de la rutina, mediante la técnica de la apraclonidina.

2. Estudio I

“A. Ureña, R. Ramos, C. Masuet, I. Macia, F. Rivas, I Escobar, R Villalonga, J Moya. An assessment of plantar hyperhidrosis after endoscopic thoracic sympathectomy. Eur J Cardiothorac Surg 2009; August 36: 360-363”.

2.1 Metodología y diseño de la encuesta

Se incluyeron 198 pacientes afectados de hiperhidrosis primaria palmar pura, palmo-plantar, y axilar intervenidos mediante la técnica simpaticolisis torácica. Todos los pacientes pasaron un examen preoperatorio completo, y posteriormente completaron un cuestionario específico, 8 semanas antes de la cirugía y 12 meses después de la cirugía.

Se diseñó un cuestionario específico para valorar el grado de sudoración y la repercusión a nivel personal, social y laboral de la hiperhidrosis en estos enfermos.

El *cuestionario preoperatorio* valora las zonas de hiperhidrosis corporal, mediante una gradación de 0, que significa “no sudor”, hasta 3 que significa “suda mucho” (véase hoja cuestionario a continuación).

Dicho cuestionario también valora la afectación personal con la familia, con los amigos y en el trabajo con una gradación de 0 (ningún problema) a 4 (muchísimo malestar), y en él también se registra la sintomatología sistémica acompañante: palpitaciones, temblores, epigastralgia, enrojecimiento facial, cefalea, y el grado de ansiedad que les provocaba el cuadro.

3. Estudio II

“R. Ramos, **A. Ureña**, F. Rivas, I. Macía, G. Rosado, S. Pequeño, C. Masuet, M. Badia, M. Miguel, M.A. Delgado, I. Escobar, J Moya. Impact of T3 thoracoscopic sympathectomy on pupillary function: a clinicoanatomic study. Surg Endosc 2012; Apr, 26(4): 1146-52”

3.1. Metodología y técnica de valoración de la función pupilar

Estudio descriptivo prospectivo sobre 25 pacientes (50 pupilas) entre 18 y 40 años de edad con indicación de simpaticotomía por hiperhidrosis palmar pura y/o palmo-plantar, entre Diciembre de 2009 y Diciembre de 2010.

Se excluyó cualquier paciente con otra localización de hiperhidrosis, cirugía ocular y/o patología ocular o cualquier patología que contraindicase la cirugía de denervación simpática y estudio ocular.

Todos los pacientes fueron valorados preoperatoriamente, a las 24 horas de la intervención y al mes de la denervación simpática mediante la medición de la ratio pupila/iris basal y después de la instilación de un colirio simpaticomimético con apraclonidina 0.5%..

Para obtener la misma imagen en todos los pacientes y evitar así errores de muestra, el paciente se acomoda de una manera confortable en una habitación

con las mismas condiciones luminosas durante 10 minutos, posteriormente acopla la cabeza sobre un instrumento ajustable de tal manera que la distancia ocular queda siempre a la misma distancia. La cámara digital Sony Cyber-Shot con 8 megapíxeles de resolución, se acopla a este quedándose a 15 cm de distancia respecto el globo ocular.



Fig.12. Obtención de la imagen pupilar.

Durante el estudio, se procedió al registro fotográfico ocular (pupila-iris) a nivel preoperatorio, a las 24 horas postintervención y al mes de la intervención. Las valoraciones postoperatorias se realizaron de forma basal y tras la administración de apraclonidina, dejándose 45 min de intervalo entre la instilación del colirio y el registro fotográfico.

Para evitar confusión y errores numéricos por valores absolutos de tamaño pupilar y tamaño iris (en función de la ampliación de la fotografía el tamaño absoluto varía) , y aunque la fotografía se realizó siempre desde la misma distancia, se decidió realizar 3 medidas de cada circunferencia de iris y pupila: horizontal, oblicuo y otro oblicuo, y posteriormente hacer una ratio, para tener un número independiente y fiable para poder comparar a los pacientes.

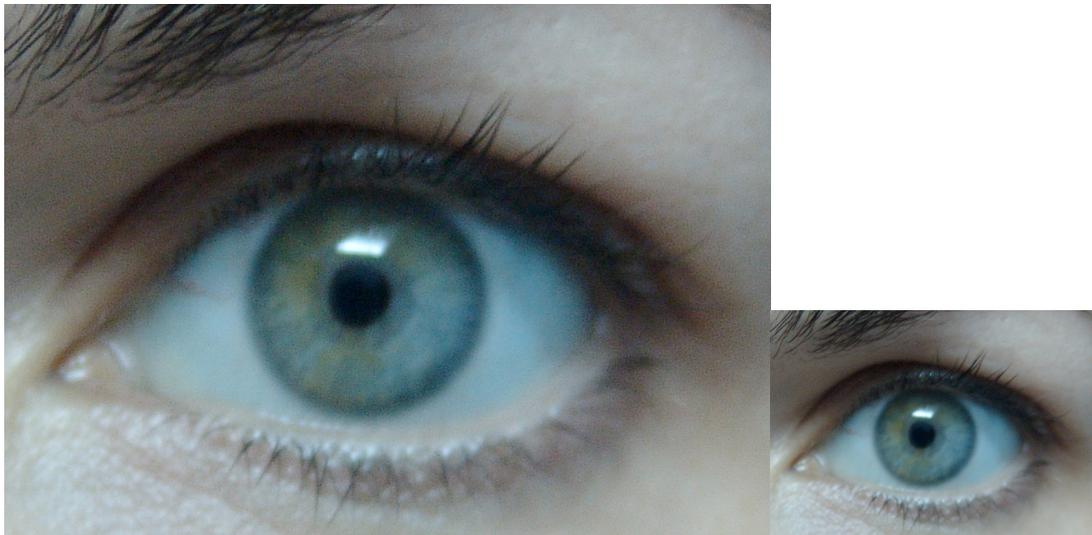


Fig 13. el tamaño numérico del la misma circunferencia varia en función de la ampliación de la fotografía.

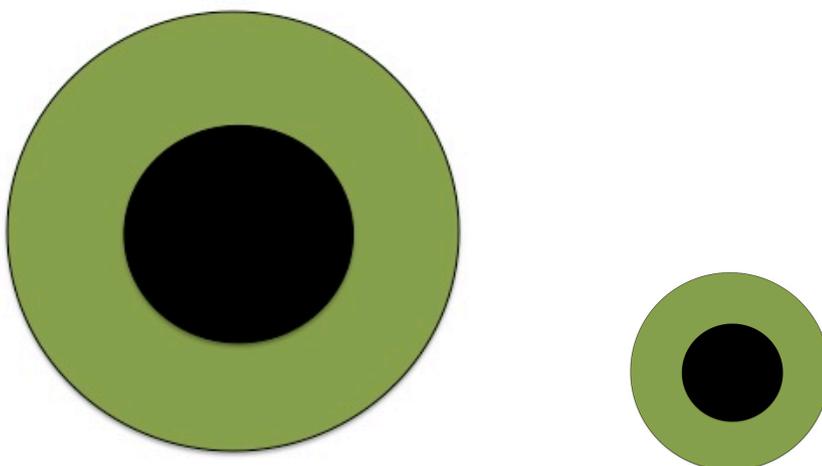


Fig 14. La ampliación es distinta pero se mantienen las proporciones

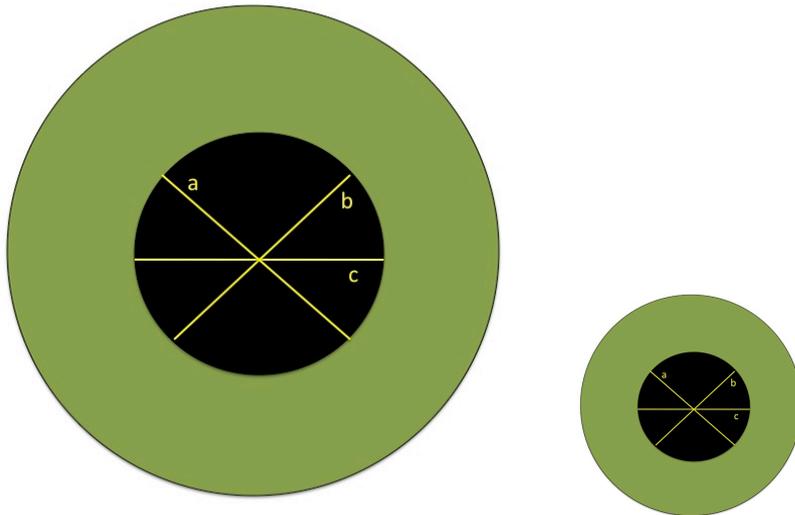


Fig. 15. Diferentes valores para mismo diámetro pupilar y diferente ampliación de la fotografía.

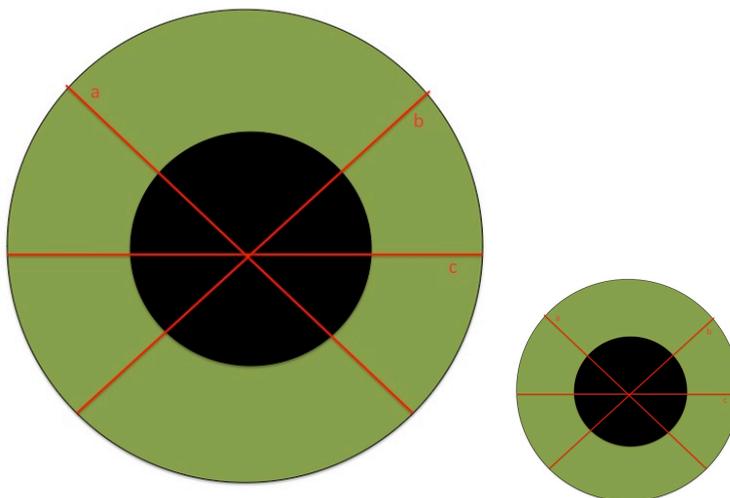


Fig 16. diferentes valores para el mismo iris y diferente ampliación de la fotografía.

$a \neq a$	$b \neq b$	$C \neq c$
$a \neq a$	$b \neq b$	$C \neq c$
$a/a = a/a$	$b/b = b/b$	$c/c = c/c$

Aunque las circunferencias varíen de tamaño, y con ello su diámetro, la proporción entre pupila/iris siempre se mantiene.

Medidas pupila	Media pupila	Medidas iris	Media iris	Proporción media
a		a		
b	P	b	I	P/I
c		c		

Para la recogida de datos se creó una base de datos y un formulario para registrar todas las variables a estudio.

V. RESULTADOS

An assessment of plantar hyperhidrosis after endoscopic thoracic sympathicolysis

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Abstract

Background: Endoscopic bilateral thoracic sympathicolysis (EBTS) is an effective and minimally invasive procedure used for patients with primary hyperhidrosis. The purpose of this study was to examine plantar hyperhidrosis before and after EBTS. **Methods:** A total of 198 patients with primary hyperhidrosis underwent 396 thoracoscopic sympathicolysis of ganglia T2–T3 in a prospective study. All completed a preoperative questionnaire, followed by a second questionnaire 12 months after the operation. The questionnaires evaluated sweating in the different body areas. Only the zones of anhidrosis were considered in delimiting the cutaneous expression of sympathetic ganglia T2–T3. **Results:** Redistribution of perspiration as reported by the patients comprised significant reductions in palmar and axillary hyperhidrosis, and an increase in the zone of the trunk and popliteal region. The incidence of plantar anhidrosis and plantar hypohidrosis was 30.3% and 20.7%, respectively ($p < 0.001$). **Conclusions:** EBTS is followed by redistribution of body perspiration, with, and important, plantar anhidrosis and hypohidrosis. Although EBTS is the standard treatment for palmar primary hyperhidrosis, we must continue studying baseline sympathetic activity in patients affected by primary hyperhidrosis and the neuroanatomy of the sympathetic system to understand the redistribution of sweating and decrease of hyperhidrosis in the zones regulated by mental or emotional stimuli.

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Keywords: Hyperhidrosis; Redistribution of sweating; Thoracoscopic sympathicolysis

1. Introduction

Primary hyperhidrosis (PH) is a rare disorder of unknown etiology that is characterized by excessive sweating on the palms of the hands, the soles of the feet, in the armpits (axillary), in the groin area, and/or under the breasts [1]. It is different from secondary hyperhidrosis, which occurs as a consequence of another disorder.

Although the predominant symptom is palmar hyperhidrosis, patients present palmar hyperhidrosis with associated plantar hyperhidrosis or palmar-axillary-plantar hyperhidrosis in more than 70–80% of the cases [2,3].

Endoscopic thoracic bilateral sympathicolysis (ETBS) is currently the standard treatment for primary hyperhidrosis [4–6].

The clinical observation of over 700 patients with hyperhidrosis of the palms and/or soles, subjected to thoracoscopic sympathicolysis of ganglia T2 and T3, suggests that these ganglia present a more extensive dermatome than classically believed [7].

The purpose of this review of a prospectively gathered database was to investigate the effect of T2–T3 sympathicolysis on plantar hyperhidrosis.

2. Patients and methods

A review of a prospectively gathered database was carried out in our department. The sample included 198 patients with primary palmar, axillary, and/or facial hyperhidrosis who underwent ETBS. This study was approved by the ethics committee at our hospital. Information about the technique, results and side effects were provided to patients in a written format during the first consultation. An individual consent was obtained prior to the surgery.

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3. Methods

All patients were subjected to a complete preoperative study, followed by completion of a specific questionnaire 8 weeks before surgery; recording the degree of perspiration in different body regions (*thorax, abdomen, axilla, hand, back, popliteal region and foot*), based on a visual analog scale (VAS) graded between 0 and 4.

Another questionnaire was completed 12 months after surgery; recording the degree of perspiration in the same body regions based on a VAS. All values were incorporated to a customized database for posterior analysis.

Areas without perspiration (i.e., presenting anhydrosis) were defined as those zones yielding a minimum score on the VAS, and were taken to be a direct indication of denervated areas after surgery.

4. Endoscopic thoracic sympathicolysis

The surgical protocol was carried out as following: (a) general anesthesia with double-lumen endotracheal intubation, placing the patient in a 25° sitting position with abduction of the upper extremities and semi-extension of the forearms; (b) lateralization of the table about 10° toward the opposite side of the hemithorax being operated on and creation of a single entry port for the 5 mm Wolf® endoscope (5.5/3.5 mm Ø; Richard Ellis Wolf, University of Leipzig) at the level of the III intercostal space, axillary midline; c) the rib spaces and corresponding segment of the upper thoracic sympathetic chain were then visualized, located 0.5–1 cm laterally from the head of the rib and application of sympathicolysis to the T2–T3 ganglia in palmar hyperhidrosis patients, by means of electrocoagulation with monopolar forceps at 25 W in series of 5–10 applications cutting the chain at the level of the ribs; (d) collateral nervous trunks were coagulated (nerve of Kuntz); (e) hemostasia and evacuation of the pneumothorax by means of air aspiration through the endoscopic working channel, no drain left; and (f) discharge of patients 17 h after the intervention if X-rays were correct.

4.1. Statistical analysis

A descriptive analysis was made of the study parameters. Variable distribution was evaluated with the Kolmogorov–Smirnov test. The results obtained were paired data without a normal distribution; comparisons were thus made with the Wilcoxon signed rank test. The McNemar test was used to analyze the degree of anhydrosis before and after the operation, a value of 0 being indicative of anhydrosis, while a value of 1 corresponded to the presence of perspiration. Statistical significance was considered for $p < 0.05$. The SPSS version 11.0 statistical package was used throughout.

5. Results

The study population comprised of 198 patients. The response rate for the questionnaire was 100%, of which there

were 138 females (69.6%) and 60 males (30.3%), with an average age of 29.3 years (range, 16–53 years).

5.1. Perioperative and postoperative complications

No mortality or perioperative complications were recorded. The overall rate of complications was 2.8% (11/396 procedures) which included 1.5% (6/396) pneumothorax, which required drainage in 1% (4/396) of procedures, and 1.3% (5/396) isolated radiologic subcutaneous emphysema. One patient (1/396 procedures) had unilateral partial Horner syndrome (0.2%) and another patient (1/198) reported gustatory hyperhidrosis (0.5%). Gustatory hyperhidrosis appears on the face, thorax, and back and is associated with eating food.

5.2. Incidence of anhydrosis according to anatomical location

To evaluate the degree of total anhydrosis, we adopted a score of 0 as the sole study variable, grouping the rest of scores as indicative of the presence of perspiration.

Anhydrosis of the hands was achieved in 96% of procedures, with 4% hypohidrosis (the result of the surgery is visible improvement but not completely dry), axillary anhydrosis was 52% and hypohidrosis was 35%; plantar anhydrosis was 30.3% and hypohidrosis was 20.7% (Table 1).

5.3. Compensatory hyperhidrosis according to anatomical region

When the degree of sweating in different body regions was compared according to the preoperative and postoperative questionnaires, the body regions with significant changes in excessive sweating were the trunk and popliteal region (Fig. 1).

6. Discussion

Plantar hyperhidrosis can lead to bromhidrosis, blistering, skin infections, and moisture-related rotting of socks and shoes, and therefore constitutes physical and emotional stress for most people concerned. Various therapy methods are available for the treatment of plantar hyperhidrosis.

Although ETBS over T2–T3 ganglia currently is the standard treatment for primary hyperhidrosis, there is still no consensus in the literature regarding the best resection level for palmar hyperhidrosis: resection at the T2 level, at the T2–T3 level or only T4 level. Some authors directly relate

Table 1
Distribution of the anhidrotic areas before and after surgery.

Anatomical region	Preoperative (n, %)		Postoperative (n, %)		p
	0	1	0	1	
Axilla*	16 (8.1)	182 (91.9)	103 (52)	95 (48)	<0.001
Hand*	2 (1.0)	196 (99.0)	190 (96.0)	8 (4.0)	<0.001
Foot*	7 (3.5)	191 (96.5)	60 (30.3)	138 (69.7)	<0.001

* McNemar test.

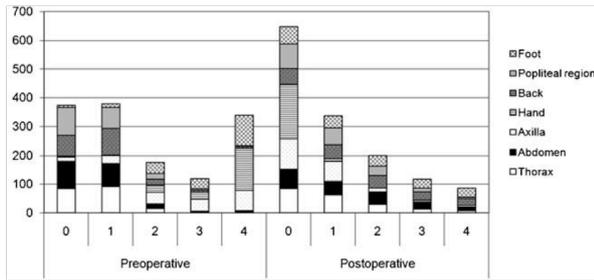


Fig. 1. Distribution of the degree of perspiration before and after surgery in the different body areas. $p < 0.001$; Wilcoxon test for paired data. Preop: preoperative. Postop: postoperative.

compensatory hyperhidrosis to the number of sympathetic ganglia eliminated or the surgical technique [6,8–10].

A lot of patients referred plantar hyperhidrosis associate to palmar hyperhidrosis. In our series, more than the half of the patients reported that anhidrosis or hypohidrosis plantar after ETBS.

From the anatomical perspective, the cutaneous sympathetic supply for the legs originates in cells of the intermediolateral column from the tenth dorsal to the third lumbar segment. The preganglionic fibers travel through from the 10th dorsal to the third lumbar anterior root, most of them passing caudal within the lumbar and sacral portions of the chain. The postganglionic fibers join the lumbosacral plexus segmentally as gray rami. The typical lumbar sympathectomy consists in resection of the second, third and fourth lumbar ganglia [11,12].

Therefore, Rieger et al. [13] reported that the resection of the sympathetic trunk from the upper edge of the third lumbar vertebral body to the lower edge of the fourth lumbar vertebral body results in an interruption of the entire sympathetic influx to the spinal nerves L4–S3, thereby causing anhidrosis of the feet. Theoretically, the transection of the sympathetic trunk below the lumbar ganglion L2 and/or caudal to the second lumbar vertebral body should be sufficient to accomplish anhidrosis of the feet because no further sympathetic outflow exists from the spinal cord to the sympathetic trunk caudal to L2.

Recently, Wolosker et al. [2], reported good initial improvement in plantar hyperhidrosis after thoracoscopic surgery that reduces to a lower level of improvement after one year. Neumayer et al. [14], on clipping ganglion T4, reported diminished perspiration of the palms, axillae and even soles, though this procedure was not as effective at palm level as T2 sympathectomy, nevertheless, the majority of patients remained unchanged or nearly unchanged. In our series, 51% of soles were completely dry or important diminution after ETBS; similar to results of Hsu et al. who reported that 64% of patients with plantar hyperhidrosis were cured after T2 sympathectomy.

Following the surgical treatment, the level of anxiety and its influence on the daily life showed a statistically significant diminution, after the surgery, coinciding with other reports in the literature, we observed a clear and significant diminution of the anxiety state, which can be explained by the elimination of the generating factor of anxiety [15]. Wolosker et al. [2], reported that after surgery there may be a break in

the negative feedback that might have been leading to plantar sweating.

Although this plantar anhidrosis or hypohidrosis cannot be explained by neuroanatomical or neurophysiologic knowledge, classically, two fundamental types of perspiration have been described according to the type of stimulus involved. Thus, *environmental temperature* induces profuse perspiration of the face, back of the hands, neck, chest and back; with scant response on the part of the palm plantar eccrine glands. In turn, *mental or emotional stimulation* causes massive and profuse perspiration mainly of the palms, soles and/or axillae. The control of emotional perspiration is vehiculated by the promoter regions of the frontal brain cortex, while environmental perspiration is regulated by the hypothalamus [16].

Possibly, the anhidrosis or hypohidrosis of the hands and feet is more closely related to cortical control, and less to the surgical technique employed, though further studies are needed to confirm this.

In conclusion, the results obtained indicate that ETBS is followed by a clear and significant decrease in the zones regulated by mental or emotional stimuli, and an increase in the areas regulated by environmental stimuli, though we are unable to establish the etiology of this redistribution.

Although ETBS is the standard treatment for palmar primary hyperhidrosis and induced important plantar anhidrosis and hypohidrosis, it should not be indicated when there is only plantar hyperhidrosis. In this regard, we believe it would be interesting to study baseline sympathetic activity in patients affected by primary hyperhidrosis and the neuroanatomy of the sympathetic system.

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Impact of T3 thoracoscopic sympathectomy on pupillary function: a cause of partial Horner's syndrome?

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Abstract

Background Thoracoscopic bilateral sympathicotomy of the T3 sympathetic ganglia is an effective treatment for palmar hyperhidrosis, though not without potential complications and consequences such as Horner's syndrome. The objective of our study is to evaluate the repercussion of

T3 sympathetic denervation on pupillary tone in patients with primary hyperhidrosis.

Methods A prospective descriptive study of 25 patients (50 pupils) ranging in age from 18 to 40 years with an indication of T3 sympathectomy for palmar hyperhidrosis or palmar-plantar hyperhidrosis from 1 December 2009 to 31 December 2010 was carried out. We excluded all patients with previous eye surgery or other ocular pathologies and those with pathologies that contraindicate denervation surgery and ocular study. All patients were evaluated before surgery and at 24 h and 1 month after sympathetic denervation. Pupil/iris (P/I) ratio was measured before and after instillation of sympathicomimetic eye drops containing 1% apraclonidine.

Results No statistically significant differences were found when we compared the preoperative P/I ratio of the left eyes versus the right eyes ($P = 0.917$). We found statistically significant differences ($P < 0.001$) between the preoperative P/I ratio [0.40 mm (standard deviation, SD 0.07 mm)] and the postoperative basal ratio [0.33 (SD 0.05)] at 24 h. The P/I ratio at 24 h increased from 0.33 to 0.36 (SD 0.09), a nonsignificant increase ($P = 0.45$), after instillation of medicated eye drops. No differences were observed between the preoperative [0.40 (SD 0.07)] and 1-month basal values [0.38 (SD 0.07)], and instillation of apraclonidine no longer induced a hypersensitivity response.

Conclusions T3 sympathectomy leads to subclinical pupillary dysfunction with a tendency for miosis, even though this impairment is not generally evident on standard physical examination or reported by patients. This subclinical dysfunction may be caused by injury to an undefined group of presympathetic nerve cell axons in caudocranial direction that communicate with the cervical sympathetic ganglia and whose function is mydriatic pupillary innervation.

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Primary hyperhidrosis is a disorder characterized by excessive sweating in all the eccrine glands of the body, especially in areas with greater glandular density—the palms, plantar region, and axillae.

Sympathetic denervation—through endoscopic thoracic sympathectomy or sympathicolysis—is currently the standard treatment that provides the best results with minimal (though not nonexistent) morbidity/mortality [1–3]. If performed by experienced thoracic surgery departments, the complication rate is negligible, with the most common undesirable effect being compensatory sweating [4–12]. One possible complication of sympathectomy that we must be alert to is Horner's syndrome, with an incidence rate ranging from 0 to 4% according to recent reports [13–16].

The objective of the present study is to evaluate the repercussion of T3 sympathetic denervation on pupillary tone in patients with primary hyperhidrosis. Secondly, we also sought to determine whether preganglionic nerve fibers of the oculosympathetic pathway are present at the level of the thoracic ganglia. It was not our intention to quantify pupil size precisely.

Patients and methods

Patients

Patients were selected by the same team of surgeons (two senior thoracic surgeons) who later performed the bilateral endoscopic thoracic sympathicolysis. A total of 25 patients with primary palmar hyperhidrosis, referred by Dermatological or Family Medicine services to the Thoracic Surgery Department of Bellvitge University Hospital, were selected to participate. Pupil/iris (P/I) ratio was measured prior to surgery and postoperatively at 24 h and 1 month; postoperative evaluation included P/I measurements performed before and after instillation of 1% apraclonidine.

This study, consisting of a series of clinical cases and pre- and postsurgical comparisons, was approved by the hospital ethics board. At initial consultation, all patients received a detailed information sheet describing the technique, expected results, risks of the intervention, and study methodology. Prior to surgery, patients received and signed individual informed consent forms that explicitly stated that patients had the option of abandoning the study at any time, and also described the possible benefits and risks, the voluntary nature of participation, and data confidentiality.

All patients underwent standard preoperative study that included a comprehensive medical history, simple chest X-ray, electrocardiogram (ECG), and complete hemogram including coagulation study and biochemistry.

Methodology

Inclusion and exclusion criteria

We selected 25 patients referred to our service for primary hyperhidrosis (mainly palmar) who presented no previous endocrinal–metabolic, ophthalmologic, or neurological history that would contraindicate the tests to be performed.

We excluded all patients with previous eye surgery or other ocular pathologies and those with pathologies that contraindicate denervation surgery and ocular study.

Data collection and evaluation of P/I ratio

A database and form were created to record all of the study variables. All patients were examined prior to surgery to rule out associated pathologies and family history of primary hyperhidrosis.

Apraclonidine 1% test

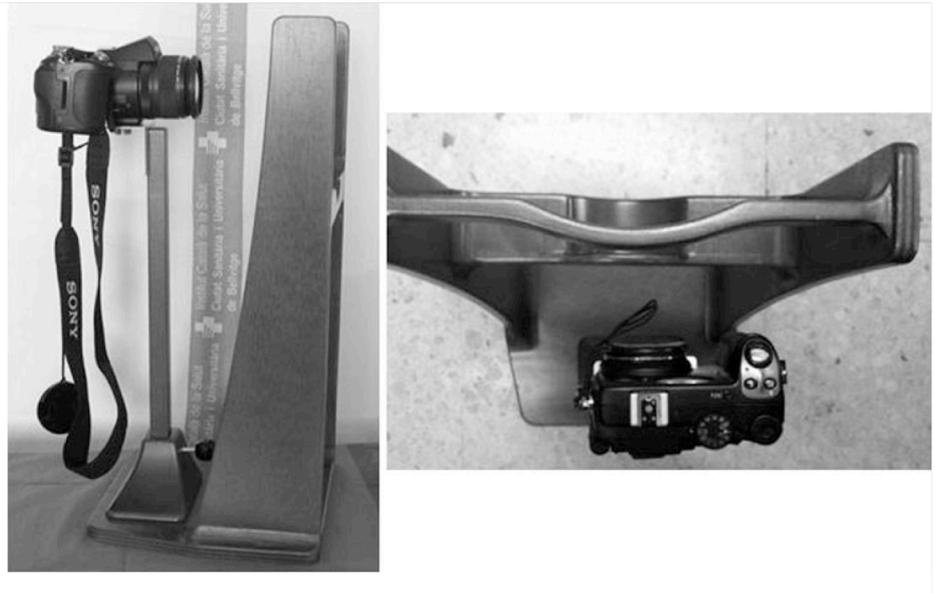
Normal response after application of apraclonidine is a relative miosis. If sympathetic denervation exists, the usual response is mydriasis and ptosis recovery. In terms of mechanism of action, apraclonidine is a weak α -1 agonist and a strong α -2 agonist. In sympathetic lesions, upregulation of α -1 receptors increases sensitivity to apraclonidine. Denervation hypersensitivity results in pupil dilatation and elevation of the eyelid on the abnormal side but without response or slight miosis on the normal side [17, 18].

Assessment of pupillary function

To ensure image consistency and thus avoid sample error, all patients were asked to relax for 10 min in a room with the same lighting conditions. Afterwards, we attached an adjustable instrument to the patient's head to maintain a uniform distance to the eye (Fig. 1). Once the patient was in position, a digital camera (Sony Cyber-Shot) with 8 megapixel resolution and $\times 7$ zoom lens with autofocus capacity of 1 cm (gran angular) to ∞ was attached to the adjustable instrument so that the camera was located at a distance of 15 cm from the eyeball (Fig. 1).

We photographed the eye (P/I) preoperatively, and at 24 h and 1 month following surgery. Postoperative measurements were performed twice: in basal conditions (prior

Fig. 1 Instrument used for positioning the head of the patient to maintain a uniform distance in order to obtain the image with the digital camera mounted on the horizontal metal bar



to apraclonidine administration) and after administration of apraclonidine, with a 45-min interval between eye drop instillation and photography.

Surgical procedure

Although already described in other publications [2, 19], we provide here a brief description of the standard surgical procedure. General anesthesia is administered with selective bronchial intubation, and a single access port for the Wolf® 5/10-mm thoracoscope is prepared at the level of the third intercostal space (midaxillary line). The upper thoracic chain is then located, and bilateral sympathectomy of the T3 ganglia via coagulation is performed. The patient is discharged 24 h after the operation, provided that postoperative X-ray is normal.

Statistical analysis

The SPSS v. 17.0 statistical software package (SPSS Chicago, IL, USA) was used for statistical analysis. First, descriptive univariate analysis was performed. Quantitative variables are expressed as mean (\pm SD) for variables with normal distribution and as median (interquartile range) for variables with nonnormal distribution according to Kolmogorov–Smirnov test. The means of the continuous variables were compared using the Student *T* or Mann–Whitney *U* test depending on normality criteria.

Three measurements of the iris and pupils of the right and left eyes were averaged to produce a single mean, after which we calculated the P/I ratio for each of the time

periods, as established by the study protocol. The Wilcoxon test for nonparametric paired data was used to evaluate the repeated measurements of the P/I ratio. A cutoff of $P < 0.05$ was used to determine statistical significance.

Results

Perioperative and postoperative complications

The study population comprised 25 patients, ten of whom were lost to follow-up, for an overall participation rate of 60%. Of the 15 patients who completed the study, 14 were female and one was male, with average age of 28.4 years (range 17–55 years).

All surgical procedures were performed without incident, and complete anhidrosis was achieved in all patients. Discharge took place 24 h after surgery. No mortality or perioperative complications were recorded. The overall complication rate was 1% (2/50 procedures) due to pneumothorax, which required drainage in one patient. One patient presented unilateral palpebral ptosis (1/15) at 24 h and 1 month following surgery.

Quantification of P/I ratio

After testing for a normal distribution of the variables, we proceeded to compare the P/I ratio of the right eye versus the left eye, with no differences observed ($P = 0.917$). Table 1 presents these ratios. The preoperative P/I ratio was 0.40 ± 0.07 mm.

Table 1 P/I ratio of the 30 patients in the study

	Eye	Pre intervention		Post intervention		
		Baseline	Baseline	Apraclonidine	Baseline	Apraclonidine
1	RE	0.38	0.34	0.34	0.44	0.44
2	LE	0.34	0.31	0.26	0.41	0.37
3	RE	0.49	0.42	0.39	0.47	0.42
4	LE	0.49	0.43	0.39	0.44	0.40
5	RE	0.50	0.38	0.38	0.48	0.41
6	LE	0.50	0.37	0.35	0.35	0.40
7	RE	0.43	0.28	0.30	0.50	0.44
8	LE	0.47	0.30	0.30	0.47	0.45
9	RE	0.30	0.33	0.29	0.31	0.30
10	LE	0.33	0.31	0.30	0.32	0.26
11	RE	0.37	0.33	0.27	0.33	0.30
12	LE	0.31	0.29	0.41	0.30	0.27
13	RE	0.36	0.49	0.47	0.48	0.49
14	LE	0.35	0.39	0.45	0.38	0.45
15	RE	0.45	0.32	0.35	0.43	0.37
16	LE	0.50	0.29	0.32	0.44	0.35
17	RE	0.40	0.28	0.43	0.46	0.30
18	LE	0.44	0.30	0.64	0.30	0.49
19	RE	0.29	0.29	0.30	0.30	0.32
20	LE	0.30	0.27	0.28	0.34	0.36
21	RE	0.46	0.34	0.37	0.42	0.39
22	LE	0.46	0.33	0.33	0.44	0.38
23	RE	0.30	0.28	0.31	0.32	0.33
24	LE	0.30	0.31	0.28	0.29	0.30
25	RE	0.44	0.35	0.35	0.38	0.30
26	LE	0.41	0.33	0.24	0.28	0.30
27	RE	0.46	0.31	0.35	0.35	0.40
28	LE	0.38	0.48	0.31	0.32	0.33
29	RE	0.46	0.36	0.46	0.40	0.33
30	LE	0.43	0.27	0.59	0.39	0.38

RE right eye; LE left eye

At 24 h post intervention, the P/I ratio was measured before (0.33 ± 0.05) and after apraclonidine administration (0.36 ± 0.09 mm). Comparison of the preoperative and postoperative basal measurements showed a significant change ($P < 0.001$), with notable postsurgical miosis. Due to denervation hypersensitivity, administration of the sympathicomimetic eye drops produced a nonsignificant ($P = 0.045$) increase in P/I ratio.

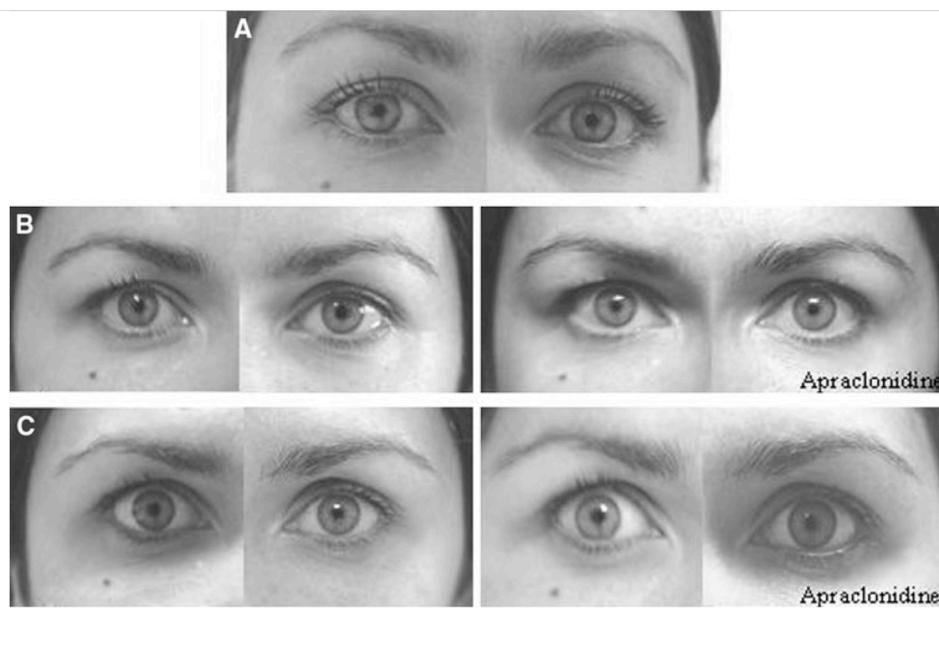
No significant differences were observed between the preoperative [0.40 (SD 0.07)] and 1-month [0.38 (SD 0.07)] baseline P/I ratios. Moreover, installation of apraclonidine not only ceased to induce a hypersensitivity response but actually caused a decrease (0.36 ± 0.06 , $P = 0.04$), a common effect in complete oculosympathetic pathway blockage (Fig. 2).

Discussion

Bilateral thoroscopic sympathectomy/sympathicolysis remains the technique of choice to treat primary hyperhidrosis of the palms [1–3]. Nevertheless, the level at which thoracic ganglia dissection should be performed is still unclear; good results have been reported at the T2, T2–T3, and T3 levels, and even at lower levels (with less anhidrosis but also decreased compensatory sweating). We perform T3 sympathectomy based on our clinical observation of over 1,000 patients with hyperhidrosis and lower risk of compensatory hyperhidrosis [4, 10, 20–23].

The most common undesired side-effect is compensatory hyperhidrosis, which is well tolerated by most patients, although it can be debilitating in some cases.

Fig. 2 Preoperative examination (A) and at 24 h (B) and 1 month (C) following surgery (basal condition and apraclonidine administration)



Other undesired effects or less common complications include gustatory hyperhidrosis, excessive hand dryness, and Horner's syndrome, which can be total or partial without evidence of miosis.

Horner's syndrome is an uncommon complication, with incidence rate ranging from 0 to 4% [13–16]. Some possible causes that have been suggested are diffusion of the monopolar current, excessive traction on the sympathetic chain during exeresis, and incorrect localization of the ribs [24].

Anatomically, the efferent sympathetic pathway starts at the diencephalic level, in the posterolateral hypothalamic region, and descends along the encephalic trunk to the intermediolateral horn cells of the thoracic spinal cord. Axons arising from the first three thoracic levels or even up to the fifth level [25] communicate with the stellate ganglion and the upper cervical ganglion, from which the fibers responsible for pupil dilation arise posteriorly towards the pupillary dilator muscle, winding around the internal carotid artery to the ophthalmic branch of the trigeminal nerve. Following the nasociliary branch, these nerve fibers connect to the muscle fiber of the iris [26].

None of our patients experienced miosis, and only one exhibited ptosis, which was slight. Overall, we observed a significant decrease in pupillary function following surgery, which indicates that the T3 ganglia contain a number of preganglionic neurons that communicate with pupillary-dilating muscle fibers. If the oculosympathetic pathway is injured, the pupil will respond to apraclonidine by increasing in size, a result that is indicative of the drug's effect [27], thus confirming possible injury to this pathway.

This leads us to believe that the group of oculosympathetic nerve cells located at the T3 level must be minimal, as standard physical examination shows no evidence of injury, and the subclinical effects are reversible 1 month after surgery. This lesion is not visible on conventional physical examination but is evident on photographic study and through basic pharmacological studies used to diagnose Horner's syndrome [28].

The effectiveness of sympathectomy on craniofacial hyperhidrosis is well known, although to achieve clear reduction in hyperhidrosis the T2 ganglia must be dissected, because a large number of preganglionic neurons are distributed throughout the external carotid plexus and posteriorly to the craniofacial sweat glands [25, 29]. Undoubtedly, if we measured the P/I ratio in patients with T2 sympathectomy, we would find increased pupillary dysfunction, because the number of neurons increases as we approach the stellate ganglia. Poole et al. [30] described the presence of Horner's syndrome in a patient with herpes zoster at T3–T4, a fact that also confirms the presence of oculosympathetic pathway neurons at the level of the T3 ganglia.

Based on our results, we believe that the three hypotheses proposed to account for Horner's syndrome: (1) excessive traction, (2) diffusion of electric current, or (3) improper identification of the sympathetic chain, while possible, are actually associated with the surgical elimination of oculosympathetic pathway neurons. Depending on the number of neurons eliminated during denervation surgery, the effect of these factors may be more or less pronounced. Nevertheless, we believe that traction or

excessive electrocoagulation of the sympathetic chain is likely only a contributory factor to the existing subclinical lesion.

In conclusion, although the number of patients in our study was small, mainly due to the restrictive inclusion criteria and the fact that it was easy for patients to abandon this experimental clinical study at any time, our study confirms the classical anatomical basis of the oculosympathetic pathway. We can confirm that endoscopic T3 sympathectomy leads to significant but transitory subclinical pupillary dysfunction. Consequently, we have an obligation to inform patients of the risks of pupillary dysfunction in this type of surgery. These risks may vary according to the distribution of preganglionic neurons at the level of the sympathetic ganglia eliminated, but we must assume that pupillary dysfunction will occur even when denervation is performed at the T3 level.

Disclosures Authors Ramos, Ureña, Rivas, Macia, Rosado, Pequeño, Masuet, Badia, Miguel, Delgado, Escobar, and Moya have no conflicts of interest or financial ties to disclose.

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VI. DISCUSIÓN

La hiperhidrosis palmo-plantar es una enfermedad invalidante que impide a los pacientes realizar las actividades de la vida diaria a nivel personal y laboral, pudiendo acentuar problemas de ansiedad, incluso en forma de fobia social.

El efecto secundario más frecuente e importante para los pacientes es la sudación compensatoria, que en la mayoría de los casos es bien tolerada pero puede ser invalidante. Por el momento no existe ninguna técnica ni estudio que nos permita saber quién presentará sudación compensatoria, en qué lugar y con qué intensidad.

Entre otros efectos secundarios, menos frecuentes, podemos encontrar: la sudación gustatoria; la sequedad excesiva de manos, o el Sd de Horner total o parcial, con una incidencia (el Sd de Horner) entre el 0 y el 4% según últimas series^{6, 66, 67}.

La hiperhidrosis puede conllevar humedad importante que después desintegra la ropa, en el caso de la hiperhidrosis plantar se desintegran los calcetines y zapatos. Estos pacientes pueden presentar clínica de bromhidrosis, así como, sintomatología dermatológica asociada a la hiperhidrosis pudiéndose formar ampollas, enrojecimiento de la piel con fragilidad, dolor, incluso úlceras en la zona más afectada con sobreinfecciones.

La simpaticolisis torácica bilateral endoscópica sigue siendo la técnica Gold Standard para el tratamiento de la hiperhidrosis primaria palmar, pero por el momento no existe un consenso entre expertos que permita indicar dicha cirugía para la hiperhidrosis plantar. Algunos autores⁶⁶ describen una disminución de la

sudoración plantar en el 51 y el 64% de los casos después de la cirugía a nivel torácico, que coincide con nuestras series.

En la mayoría de los casos la hiperhidrosis plantar se presenta de manera conjunta con la hiperhidrosis palmar. En nuestra serie, más de la mitad de los pacientes intervenidos refiere anhidrosis o hipohidrosis plantar después de la cirugía.

Después del tratamiento quirúrgico, en nuestra serie, hemos observado que el nivel de ansiedad baja de manera significativa, y eso puede ser explicado porque se elimina el factor causante de dicha ansiedad: el sudor. Asimismo, se elimina el factor de retroalimentación negativa que tiene la ansiedad sobre la sudoración palmo-plantar, pudiendo ser una explicación de la disminución de la sudoración plantar.

Desde la perspectiva anatómica la inervación simpática para las extremidades inferiores se origina en el haz intermedio-lateral ventral de la columna del décimo segmento dorsal hasta el tercer segmento lumbar. Las fibras preganglionares viajan a través de la décima dorsal a la tercera raíz lumbar anterior, la mayoría de ellas pasa en dirección caudal dentro de las porciones lumbar y sacra de la cadena. Las fibras postganglionares se unen al plexo lumbosacro en forma de ramas grises. La simpatectomía lumbar típica consiste en la resección del segundo, tercer y cuarto ganglios lumbares^{69, 45}.

Por lo tanto, la resección del tronco simpático desde el borde superior de la tercera vértebra lumbar al borde inferior de la cuarta vértebra lumbar se traduce en una interrupción completa de la afluencia simpática de los nervios espinales L4-S3, causando con ello anhidrosis de los pies.

Teóricamente, la sección transversal del tronco simpático por debajo del ganglio simpático lumbar L2 y/o caudal de la segunda vértebra lumbar debería ser suficiente para conseguir anhidrosis de los pies debido a que no existe más flujo de salida de información simpática desde la médula espinal hasta el tronco simpático caudal a L2, pero ello conlleva efectos secundarios poco tolerables⁵¹.

Por el momento, esta disminución de la sudoración plantar después de la cirugía toracoscópica por hiperhidrosis palmar no puede explicarse de manera neuroanatómica, ya que las zonas anuladas no se corresponden con los dermatomas simpáticos ya descritos⁴⁵.

Existen zonas de sudoración controladas por la temperatura ambiental (cara, espalda, cuello, pecho, espalda, ingles y zona poplítea) y otras zonas de sudoración en relación a la estimulación mental o emocional (cara, axilas, palmas y plantas).

El control de la sudoración emocional está bajo las zonas del córtex frontal cerebral, y regulada por el Hipotálamo³. Esta afirmación podría explicar el control de la sudoración plantar por parte del sistema nervioso central que se produciría posterior a una regulación de la sudoración postquirúrgica de las otras zonas de sudoración emocional (palmas).

El Síndrome de Horner es una complicación postquirúrgica poco frecuente, con una tasa de incidencia oscila entre 0 y 4%^{6, 11, 66, 67}. Algunas de las causas posibles que se han sugerido son la difusión de la corriente monopolar, la tracción excesiva en la cadena simpática durante la exéresis, y la localización incorrecta de los nervios⁷⁰.

Anatómicamente, la vía eferente simpática desciende desde el hipotálamo posterolateral por el tronco encefálico por el haz intermedio-lateral ventral de la médula espinal. Los axones que se dirigen a la vía óculo-simpática llegan hasta tercer o incluso quinto nivel torácico⁵⁴ y, posteriormente, ascienden hacia el ganglio cervical, desde donde llegarán al músculo dilatador de la pupila envolviendo en su trayecto a la arteria carótida interna hasta la rama oftálmica del nervio trigémino. A raíz de la rama nasociliar, estas fibras nerviosas se conectan a las fibras musculares del iris⁵⁷.

Esta descripción podría hacer pensar que todos los pacientes intervenidos, a los cuales se les ha realizado una denervación quirúrgica entre los niveles T2 y T5, tendrían que presentar clínica ocular posterior a la cirugía. Con nuestro estudio pretendimos demostrar que, al menos, cierto porcentaje de fibras sí descienden hasta nivel T3.

Ninguno de nuestros pacientes presentó una miosis postquirúrgica evidente, uno presentó ptosis palpebral leve. En general, se observó una disminución significativa en la función pupilar después de la cirugía, lo que indica que los ganglios T3 contienen un número de neuronas preganglionares que comunican con el plexo que envuelve la carótida interna y las posteriormente a fibras musculares que afectan a la vía pupilar-dilatación⁶⁵.

El grupo de células nerviosas ubicadas en oculosimpática el nivel de T3 debe ser mínima, ya que el examen físico normal no muestra evidencia de lesión y los efectos subclínicos son reversibles un mes después de la cirugía.

Anatómicamente⁵⁴, las neuronas preganglionares que se originan a nivel de T3-T5 en la médula espinal ascienden a través de los ganglios simpáticos T3-T4-T5, y así se eliminan cuando la simpatectomía T3 se lleva a cabo. Esta lesión no es

visible en un examen físico convencional, pero es evidente en el estudio fotográfico y a través de los estudios básicos farmacológicos utilizados para diagnosticar el síndrome de Horner⁷¹.

Se escogió la apraclonidina entre otros posibles fármacos para realizar el test porque es el que presenta menos efectos secundarios, y una sensibilidad y especificidad, como mínimo, igual que el test de la cocaína⁵⁵⁻⁶⁵.

La eficacia de la simpatectomía en hiperhidrosis craneofacial es bien conocida, aunque para lograr una reducción clara en la hiperhidrosis, los ganglios T2 deben ser disecados porque un gran número de neuronas preganglionares se distribuyen por todo el exterior del plexo carotídeo y posteriormente inervan a las glándulas sudoríparas craneofaciales^{54, 72}. Sin lugar a dudas, si se mide la relación P/I en pacientes con simpatectomía T2, nos encontraríamos con aumento de la disfunción pupilar, porque aumenta el número de neuronas a medida que nos acercamos al ganglio estrellado.

Dado que la lesión se presentó de manera subclínica en todos nuestros casos, esto nos hace pensar que el conjunto de neuronas de la vía óculo-simpática que descienden a nivel torácico T3 son una pequeña proporción de todas las fibras que forman la cadena, y que, los pacientes que presentan clínica de miosis es debido a una lesión más extensa de las fibras producida bien por una mayor presencia de fibras descendientes, bien por una mala localización de la cadena simpática o, bien por lesión de la cadena por difusión de la corriente del bisturí.

En base a nuestros resultados, creemos que las 3 hipótesis propuestas para explicar el síndrome de Horner: 1) una tracción excesiva en el momento de la electrocoagulación de la cadena; 2) la difusión de la corriente eléctrica durante la cirugía o 3) la identificación incorrecta de la cadena simpática.

Dependiendo del número de neuronas eliminadas durante la cirugía de denervación, el efecto de estos factores puede ser más o menos pronunciada. Sin embargo, creemos que la tracción excesiva o electrocoagulación de la cadena simpática es probable que sólo sea un factor que contribuye a la lesión subclínica existente.

VII. CONCLUSIONES

1. La simpaticolisis torácica bilateral endoscópica es el Gold standard para el tratamiento de la hiperhidrosis primaria.
2. La STBE está aceptada como el tratamiento estándar de la hiperhidrosis palmar pura, palmo-plantar, y palmo-axilar. Hemos objetivado que produce una disminución significativa de la sudoración plantar, aún así, no debería indicarse para el tratamiento aislado de la hiperhidrosis plantar. Al disminuir el nivel de ansiedad de los pacientes intervenidos por HP palmar se elimina el efecto de retroalimentación negativa que ejerce dicha ansiedad sobre la hiperhidrosis plantar, disminuyendo en un 51% de los pacientes intervenidos a niveles torácicos.
3. Nuestro estudio confirma las bases anatómicas de la vía óculo-simpática: Un porcentaje de fibras nerviosas preganglionares de la vía óculo-simpática desciende hasta niveles torácicos, al menos hasta el nivel T3. Podemos confirmar que la simpatectomía a nivel de T3 conlleva a una disfunción pupilar subclínica de manera significativa, y por ello, debemos informar a los pacientes de dicho riesgo. Estos riesgos, pueden variar de acuerdo a la distribución de las neuronas preganglionares a nivel de los ganglios simpáticos eliminados, pero debemos suponer que la disfunción pupilar se produce incluso cuando la denervación se realiza en el nivel de T3.

La ptosis, asociada con el músculo de Müller, es un problema menos común, que nos lleva a creer que el grupo de los nervios que inervan los músculos palpebrales, deben estar situados más cerca del cráneo que los responsables de la función pupilar.

VIII. BIBLIOGRAFÍA

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VIII. ANEXOS

NaCl	Cloruro sódico
K	Potasio
HCO ₃	Bicarbonato
Gl	Glándula
T2, T3, T4, T5, T10, T12	Niveles torácicos del sistema nervioso simpático a nivel de la 2 ^a , 3 ^a , 4 ^a , 5 ^a , 10 ^a , y 12 ^a costillas, respectivamente.
STAI	Cuestionario ansiedad Estado-Rasgo
HP	Hiperhidrosis primaria
Cm	Centímetros
W	Vatio (unidad que representa potencia eléctrica)
Ach	Acetilcolina
SNC	Sistema nervioso central
SNA	Sistema nervioso autónomo
SNV	Sistema nervioso vegetativo
NA	Noradrenalina
A	Adrenalina
m.suprarrenal	Médula suprarrenal
m.esquelético	Músculo esquelético
m.liso	Músculo liso
C1	Nivel cervical del sistema nervioso simpático, a nivel de la 1 ^a costilla
L1, L2,L3, L4, L5	Nivel lumbar del sistema nervioso simpático, a nivel de la 1 ^a , 2 ^a , 3 ^a , 4 ^a , y 5 ^a vértebra lumbar.

S3	Nivel sacro del sistema nervioso simpático, a nivel de la 3ª raíz medular.
mm	Milímetros
n. trigémino	Nervio trigémino
a. carótida int.	Artéria carótida interna
Sd.	Síndrome

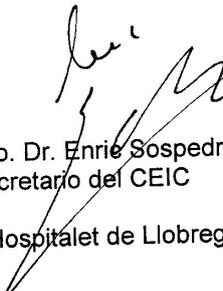
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**INFORME DEL COMITÉ ÉTICO DE INVESTIGACIÓN CLÍNICA
SOBRE PROYECTOS DE INVESTIGACIÓN**

El Comité Ético de Investigación Clínica del Hospital Universitari de Bellvitge, en su reunión de fecha 25 de septiembre de 2008, tras examinar toda la documentación presentada sobre el proyecto de investigación nuestra ref. **PR 146/08**, titulado:

"CONTRIBUCIÓN AL ESTUDIO DE LA DENERVACIÓN SIMPÁTICA T2-T3 SOBRE LA REGIÓN CRANEOFACIAL EN PACIENTES CON HIPERHIDROSIS PRIMARIA", que incluye hoja de información al paciente y consentimiento informado versión de fecha 20/08/08,

presentado por el Dr. Ricard Ramos del Servicio de Cirugía Torácica del Hospital Universitari de Bellvitge, como investigador principal, ha considerado que no existe inconveniente ético para su realización y ha acordado dar su APROBACIÓN DEFINITIVA al mencionado proyecto.


 **Bellvitge**
Hospital
 Comitè Ètic d'Investigació
Clínica

Fdo. Dr. Enrie Sospedra Martínez
Secretario del CEIC

L'Hospitalet de Llobregat, 25 de septiembre de 2008

