Cardiopulmonary exercise testing following bilateral thoracoscopic sympathicotomy in patients with essential hyperhidrosis

Marc Noppen, Patrick Herregodts, Paul Dendale, Jean D'Haens, Walter Vincken

Abstract

Background – Essential hyperhidrosis is characterised by an overactivity of the sympathetic fibres passing through the upper dorsal sympathetic ganglia D2–D3. Anatomical interruption at the D2–D3 level is a highly effective treatment for essential hyperhidrosis but also causes (partial) cardiac denervation and, after surgical sympathicotomy, important impairment of cardiopulmonary exercise function has been observed. The purpose of this study was to compare the results of cardiopulmonary exercise testing between patients with essential hyperhidrosis and a normal control population, and to examine the effects of thoracoscopic D2–D3 sympathicotomy on cardiopulmonary exercise capacity in patients with essential hyperhidrosis.

Methods – Maximal, symptom limited incremental exercise tests were performed in 26 patients with severe essential hyperhidrosis one week before and one month after D2–D3 thoracoscopic sympathicotomy, and in 14 age and sex matched healthy volunteers. D2–D3 thoracoscopic sympathicotomy was performed using a simplified one stage bilateral procedure.

Results – Palmar hyperhidrosis was relieved in every patient, confirming the D2–D3 denervation. A higher peak heart rate (7%) was seen in the patient group than in the normal subjects, but all other cardiovascular, metabolic, and respiratory parameters were similar. After D2–D3 thoracoscopic sympathicotomy, heart rate at rest (13%) and at peak exercise (7%) were reduced, together with an increase in oxygen pulse. All other parameters remained unchanged.

Conclusions – Sympathetic overactivity relevant to cardiovascular function in essential hyperhidrosis is evident only during sympathetic stimulation. D2–D3 thoracoscopic sympathicotomy causes a small and asymptomatic reduction in maximal and resting heart rate and is not associated with a decrease in exercise capacity, in contrast with the detrimental effects on exercise capacity of open surgical sympathectomy.

(Thorax 1995;50:1097–1100)

Keywords: exercise testing, essential hyperhidrosis, thoracoscopy, sympathicotomy, autonomic function.

Essential hyperhidrosis is characterised by excessive sweating of the palms of the hands and often the soles of the feet and the armpits.^{1–4} The exact cause is unknown, although overactivity of the sympathetic fibres which pass through the dorsal sympathetic ganglia D2 (and D3) has been noted.^{5,6} Interruption of the sympathetic chain at the D2–D3 level (preferably by thoracoscopic intervention) is an effective and safe treatment for essential hyperhidrosis refractory to conventional local, systemic, or other treatment.^{4,7–9} However, the D2 and D3 ganglia are also in the direct pathway of sympathetic innervation of the heart.¹⁰ Interruption of the upper dorsal sympathetic chain has been suggested as treatment for several cardiac disorders – for example, angina pectoris, ventricular tachycardia, and arrhythmias associated with the long QT syndrome.¹¹

Surgical D2–D3 sympathectomy for essential hyperhidrosis induces important cardiopulmonary impairment. After surgical excision of the D2–D3 ganglia via the supraclavicular approach, 30% of patients were unable to perform a maximal exercise test due to dyspnoea, fatigue, or dizziness. In order to study the autonomic (dys)function relative to cardiopulmonary function in patients with essential hyperhidrosis, and to study the effects of upper dorsal thoracoscopic sympathicotomy on cardiopulmonary function during exercise, exercise testing was performed on 26 patients with essential hyperhidrosis before and one month after bilateral D2–D3 thoracoscopic sympathicotomy, and in 14 age and sex matched healthy volunteers.

Methods

PATIENTS

Twenty six patients (22 women) with essential hyperhidrosis of mean (SD) age 27 (8.7) years (range 14–44 years) were studied. All suffered from severe hyperhidrosis of the hands and some the feet (82%) and armpits (65%), which was refractory to local, systemic and/or iontophoretic treatment. Physical examination was otherwise normal, and there was no history of cardiovascular or pulmonary disease. No patient was treated with cardiopulmonary medication. All patients gave informed consent to the study. Patients were studied one week before and one month after sympathicotomy. Fourteen healthy volunteers (11 women) of mean (SD) age 31 (5.8) years (range 22–40)

Respiratory Division
M Noppen
W Vincken

Department of
Cardiology
P Dendale

Department of
Neurosurgery
P Herregodts
J D'Haens

Academic Hospital
AZ-VUB, Free
University of Brussels,
Brussels, Belgium

Reprint requests to:
Dr M Noppen.

Received 15 March 1995
Returned to authors
5 June 1995
Revised version received
15 June 1995
Accepted for publication
11 July 1995

Table 1 Mean (SD) characteristics of controls (*n* = 14) and patients before sympathicolysis (*n* = 26)

	Controls	Patients
M:F	3:11	4:22
Age (years)	31 (5.8)	27 (8.7)
Duration (minutes)	8 (2.6)	7.1 (1.6)
Work of peak exercise (watts)	189.6 (103.6)	186.4 (49.2)
VO ₂ peak (ml/kg/min)	31 (11.8)	30.8 (7)
VE peak (l/min)	78.4 (25.4)	71.2 (18.8)
ΔVd/Vt (Δ%)	17.6 (4.8)	18.9 (7.2)
Vt (ml)	582.9 (172.3)	681.9 (304.4)
Vt peak (ml)	2243.6 (514.8)	2212.9 (593.6)
RR rest (per minute)	16.8 (4.6)	17.5 (3.7)
RR peak (per minute)	35.4 (8.6)	33.5 (5.3)
HR rest (per minute)	81 (8.7)	89.2 (16.1)
HR peak (per minute)	168.3 (15.9)	180.6 (12.9)*
(% pred)	94.4 (7.08)	96.6 (6.4)
Slope HR/VO ₂ /kg (bpm/ml/kg)	3.38 (0.58)	3.41 (0.69)
O ₂ pulse rest (ml/beat)	2.8 (1.2)	2.2 (0.9)
O ₂ pulse peak (ml/beat)	12.2 (5.8)	10.3 (3.0)
SBP rest (mm Hg)	118.1 (14.1)	114.2 (12.7)
SBP peak (mm Hg)	150 (14.8)	155.6 (19.5)
DBP rest (mm Hg)	76.3 (4.8)	73.7 (7.7)
DBP peak (mm Hg)	82.7 (10.1)	81.7 (11.8)

VO₂ peak = oxygen uptake at peak exercise; VE peak = peak ventilation; ΔVd/Vt = change in dead space ventilation; Vt = tidal volume; RR = breathing frequency; HR = heart rate; O₂ pulse = oxygen pulse; SBP/DBP = systolic/diastolic blood pressure.

* *p* < 0.05.

Table 2 Mean (SD) data before and after sympathicolysis in hyperhidrotic patients (*n* = 26)

	Before	After
Duration (min)	7.1 (1.6)	7.3 (1.7)
Work at peak (watts)	186.4 (49.2)	183.7 (48.3)
VO ₂ peak (ml/min)	1888.5 (551.6)	1842.5 (568.3)
VE peak (l/min)	71.2 (18.8)	73.3 (17)
ΔVd/Vt (Δ%)	-18.9 (7.2)	-19.9 (4.8)
Vt at rest (ml)	681.9 (304.2)	595 (138.6)
Vt peak (ml)	2169.9 (583.9)	2119 (533.7)
RR rest (per minute)	17.5 (3.7)	16.4 (2.8)
RR peak (per minute)	33.5 (5.3)	34.9 (5.7)
HR rest (per minute)	89.2 (16.1)	77.4 (12.5)*
HR peak (per minute)	180.6 (12.9)	167.7 (14.1)*
Slope HR/VO ₂ /kg (bpm/ml/kg)	3.41 (0.69)	3.33 (0.85)
O ₂ pulse rest (ml/beat)	2.19 (0.9)	2.3 (0.9)
O ₂ pulse peak (ml/beat)	10.3 (3.0)	10.9 (3.3)*
SBP rest (mm Hg)	114.2 (12.7)	113.4 (18.3)
SBP peak (mm Hg)	155.6 (19.5)	149.6 (16.9)
DBP rest (mm Hg)	73.7 (7.7)	72.6 (5.8)
DBP peak (mm Hg)	81.7 (11.8)	77.2 (9.9)

VO₂ peak = oxygen uptake at peak exercise; VE peak = peak ventilation; ΔVd/Vt = change in dead space ventilation; Vt = tidal volume; RR = breathing frequency; HR = heart rate; O₂ pulse = oxygen pulse; SBP/DBP = systolic/diastolic blood pressure.

* *p* < 0.05.

agreed to participate as a control population. Patient and control subject characteristics are listed in table 1.

STUDY DESIGN

Cardiopulmonary exercise testing was performed on a Sensor Medics 2900 Metabolic Measurement Cart system coupled to an ergoline cyclo ergometer (Sensor Medics, Bilt-hoven, The Netherlands) using a maximal, symptom limited incremental exercise testing protocol consisting of one minute stages with increments of power of 15–20 watt (women) or 25–30 watt (men) every minute.¹² Before exercise testing baseline spirometric measurements were performed for forced expiratory volume in one second (FEV₁) and vital capacity (VC), and to calculate maximal voluntary ventilation (MVV = 35 × FEV₁ expressed in l/min). Patients breathed through a tight fitting face mask (Survivair Series 7910) equipped with a Rudolph valve (Klaus Rudolph, Kansas City, USA). The 12 lead electrocardiogram (Cardiovit CS-6/12 ECG apparatus, Schiller AG, Baar, Switzerland) and transcutaneous oxygen

saturation (Sensor Medics oximeter) were monitored continuously and stored on-line. Blood pressure was measured every minute before, during, and up to 15 minutes after exercise with a manual sphygmomanometer. Every subject was allowed an adaptation time of about five minutes, as well as an active warm-up (freewheeling) period of 3–4 minutes.

Breath-by-breath gas analysis was performed using a zirconium oxygen analyser and an infrared absorption carbon dioxide analyser which were calibrated daily. Air flows were measured with a thermal conductivity mass flow meter which was calibrated before every test. All data were continuously recorded, stored, and analysed by the 2900 Sensor Medics software package. The parameters measured are given in the results section and shown in the tables.

THORACOSCOPIC SYMPATHICOLYSIS

All interventions were performed under strict aseptic conditions in a fully equipped operating theatre, using general anaesthesia. Intubation was performed with a Hi-Lo jet endotracheal tube (Mallinckrodt) and ventilation was assured using high frequency jet ventilation (Acu-tronic) on both lungs.

After creation of a right pneumothorax a 7 mm trocar was introduced into the pleural cavity through the second intercostal space. The thoracoscope (Richard Wolf, Knitlingen, Germany) was introduced via the trocar, and the dorsal sympathetic chain was identified. An insulated biopsy forceps, connected to a unipolar coagulation unit, was then introduced via a second trocar, under direct vision. The sympathetic trunk was identified and transected at the second and third dorsal rib heads, using 5–15 bursts of 60 watts. After re-expansion of the pneumothorax and skin closure, the same procedure was performed on the other side. Mean duration of this bilateral procedure was about 25 minutes (range 20–40).

STATISTICAL ANALYSIS

Data are expressed as mean (SD) values. Comparisons between healthy controls and patients before sympathicolysis were made using the Mann-Whitney test. Data before and after sympathicolysis in the patients with essential hyperhidrosis were compared using the Wilcoxon rank sum test. The Fisher exact test was used for comparison of sex ratios. *p* values of < 0.05 were considered statistically significant.

Results

In all patients, palmar hyperhidrosis was relieved by the intervention, confirming complete D2–D3 denervation. All control subjects and all patients successfully completed a maximal exercise test before and after sympathicolysis and the results are summarised in tables 1 and 2.

In basal resting conditions there were no significant differences between controls and patients before treatment, although heart rate and oxygen pulse tended to be lower in the

patients (table 1). Peak exercise heart rate was significantly higher in the patients before treatment than in the controls: 180.6 (12.9) versus 168.3 (15.9) bpm ($p < 0.05$), although this difference did not reach statistical significance when expressed as percentage predicted. There were no differences in cardiovascular (blood pressure), ventilatory or metabolic parameters, nor in the subjective reasons for cessation of exercise.

Pairwise data analysis in the patients before and after sympathicotomy showed a significant decrease in resting and maximal heart rate, and an increase in oxygen pulse. These post-operative values are not statistically different from the data obtained in normal volunteers. All other parameters, including the subjective reasons for cessation of exercise, remained unchanged after sympathicotomy.

Discussion

We have compared cardiopulmonary exercise testing in healthy controls and hyperhidrotic patients, and in these patients before and after thorascopic D2–D3 sympathicotomy. Thorascopic sympathicotomy had no influence on exercise capacity nor on the ventilatory response to exercise, and only minimal effects on the cardiac response to exercise.

Essential hyperhidrosis is probably caused by increased activity of the sympathetic fibres which pass through the D2 and D3 dorsal sympathetic ganglia. It causes autonomic dysfunction with less reflex bradycardia in response to the Valsalva manoeuvre or facial immersion, a higher degree of cutaneous vasoconstriction in response to finger (or cold) immersion,⁵ and a reduction in cholinergic-induced hypothermia.⁶

Our results suggest that the overactivity of the sympathetic nervous system in the patients has a very small effect only on the integrated cardiorespiratory metabolic function at rest, and a moderate effect at maximal exercise. This is in agreement with the fact that, in the resting state (when the stress on the cardiovascular system is minimal), heart rate is mainly under vagal restraint,¹³ whereas during exercise an increase in heart rate occurs through a simultaneous decrease in vagal activity and an increase in sympathetic activity.^{13–15} The sympathetic overactivity in patients with essential hyperhidrosis therefore seems to exert its effect mainly in conditions of sympathetic activation.

After sympathicotomy the heart rate at rest was significantly reduced, confirming that in these patients resting heart rate is (at least partially) also under sympathetic control. More important changes have been reported by Papa *et al.*¹⁶ who observed a decrease of 16% in resting heart rate and 18% in maximal heart rate after bilateral surgical (supraclavicular approach) D2 and D3 sympathectomy. Furthermore, about 30% of their patients were unable to complete the postoperative exercise test because of weakness, dyspnoea, dizziness, or general fatigue at submaximal levels of work. These dramatic changes were not seen in our patients, probably because thorascopic sym-

pathicotomy offers a far more accurate and precise interruption of the sympathetic chain⁴ and because the procedure causes less effect on lung volumes and airflow rates than conventional surgery.^{17,18}

Our findings are comparable with the effects of sympathectomy performed in patients with various cardiovascular disorders – for example, paroxysmal atrial tachycardia, angina, and hypertension. Bilateral D2–D5 sympathectomy decreasing the heart rate from 8% to 28.9% at rest and from 21.8% to 31.9% during exercise have been observed.^{16,19} Similarly, after medical β receptor blockade only small decreases in heart rate occur at rest, but greater reductions occur at maximal exercise.^{15,19,20} After β receptor blockade cardiac output is maintained by a parallel increase in stroke volume through the Frank-Starling mechanism²¹ which may explain the increase in oxygen pulse seen in our patients after sympathicotomy. Finally, similar findings have been observed after acute epidural sympathetic denervation by a sensory block of C4–D7: mean resting heart rate significantly dropped from 66 to 58 beats per minute.²²

D2–D3 sympathicotomy in patients with essential hyperhidrosis had no effect on ventilatory and metabolic parameters, in contrast to the effects of β blockade in normal subjects in whom measured oxygen uptake is slightly reduced by about 5%, and the anaerobic threshold is lowered by about 20%.²⁰

The authors would like to thank the nursing staff of the Respiratory Division (Karine Michiels, Anne Ringoir, Brigitte Terryn, Bea Van Elewijck, Sonja Van Poyer, Daniel Schuermans) for their enthusiasm and competence and Hilde De Smedt for the preparation of the manuscript.

- Cloward R. Hyperhidrosis. *J Neurosurg* 1969;30:545–51.
- Harris JD, Jepson RP. Essential hyperhidrosis. *Med J Aust* 1971;2:135–8.
- Adar R, Kurchin A, Zweig A, Mozes M. Palmar hyperhidrosis and its surgical treatment. A report of 100 cases. *Ann Surg* 1977;186:34–41.
- Noppen M, Herregodts P, D'Haens J, Vincken W. Thorascopic sympathicotomy for essential hyperhidrosis: results in 35 patients and review of the literature. *Chest* (submitted).
- Shih CJ, Wu JJ, Lin MT. Autonomic dysfunction in palmar hyperhidrosis. *J Autonomic Nerv Syst* 1983;8:33–43.
- Shih CJ, Lin MT. Effects of cholinergic drugs on sudomotor, metabolic, respiratory, vasomotor, and temperature response in palmar hyperhidrosis. *J Neurosurg* 1980;53:684–9.
- Byrne J, Walsch TN, Hederman WP. Endoscopic trans-thoracic electrocautery of the sympathetic chain for palmar and axillary hyperhidrosis. *Br J Surg* 1990;77:1046–9.
- Claes G, Göthberg C. Endoscopic trans-thoracic electrocautery of the sympathetic chain for palmar and axillary hyperhidrosis. *Br J Surg* 1991;78:760.
- Lin CC. Extended thorascopic T2-sympathectomy in treatment of hyperhidrosis: experience with 130 consecutive cases. *J Laparosc Surg* 1992;2:1–6.
- Firestone L. Autonomic influences on cardiac function: lessons from the transplanted (denervated) heart. *Int Anaesthesiol Clin* 1989;27:283–91.
- Kadowaki MH, Levitt JM. Sympathectomy in the treatment of angina and arrhythmias. *Ann Thorac Surg* 1986;41:572–8.
- Zabellos RJ, Weisman IM. Behind the scenes of cardiopulmonary exercise testing. *Clin Chest Med* 1994;15:193–213.
- Shepherd JT. Circulatory response to beta-adrenergic blockade at rest and during exercise. *Am J Cardiol* 1985;55:87D–94D.
- Savin WM, Davidson DM, Haskell WL. Autonomic contribution to heart rate recovery from exercise in humans. *J Appl Physiol* 1982;53:1572–5.
- Epstein SE, Robinson BF, Kahler RL, Braunwald E. Effects of beta-adrenergic blockade on the cardiac response to maximal and submaximal exercise in man. *J Clin Invest* 1965;44:1745–53.
- Papa MZ, Schneiderman J, Tucker E, Bass A, Drori Y, Adar R. Cardiovascular changes after bilateral upper dorsal sympathectomy. *Ann Surg* 1986;204:715–8.
- Molho M, Kurchin A, Ohry A, Adar R. Pulmonary function

- abnormality after upper dorsal sympathectomy. *Am Rev Respir Dis* 1977;116:879-83.
- 18 Molho M, Shemesh E, Gordon D, Adar R. Pulmonary functional abnormality after upper dorsal sympathectomy: a comparison between the supraclavicular and transaxillary approach. *Chest* 1980;77:651-5.
 - 19 Swithwick RH, Chapman EM, Kinsey D, Whitelaw GP. The human heart rate: some observations and deductions based upon the effect of removing portions of the sympathetic nervous system in man. *Surgery* 1949;26:727-34.
 - 20 Petersen ES, Whipp BJ, Davis JA, Huntsman DJ, Brown HV, Wasserman K. Effects of beta-adrenergic blockade on ventilation and gas exchange during exercise in humans. *J Appl Physiol* 1983;54:1306-13.
 - 21 Anderson K, Vik-Mo H. Role of the Frank-Starling mechanism during maximal semisupine exercise after oral atenolol. *Br Heart J* 1982;48:149-55.
 - 22 Takeshima S, Dohi S. Circulatory responses to baroreflexes, valsalva manoeuvre, coughing, swallowing and nasal stimulation during acute cardiac sympathectomy by epidural blockade in awake humans. *Anesthesiology* 1985;63:500-8.