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Original articles

Endoscopic thoracic sympathectomy attenuates reflex tachycardia during head-up tilt in lightly anesthetized patients with essential plamar hyperhidrosis

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Abstract
Purpose. Our purpose was to examine perioperative alterations in hemodynamic changes with head-up tilt (HUT) in patients undergoing endoscopic thoracic sympathectomy (ETS).
Methods. The subjects were 11 patients with essential hyperhidrosis scheduled to undergo ETS (ETS group) and 9 age-matched volunteers undergoing minor surgery (control group). HUT was performed (40°; 5 min) before and after the surgery, under nitrous oxide anesthesia. Orthostatic hypertension and hypotension in response to HUT were defined as changes of 10% or greater in systolic blood pressure.
Results. The increase in heart rate in response to HUT was significantly reduced after surgery in the ETS group (from 34 ± 18 to 14 ± 11 beats·min^{-1}; $P < 0.001$), but not in the control group (from 23 ± 18 to 22 ± 12 beats·min^{-1}; $P = 0.911$). Orthostatic hypertension disappeared completely after ETS (from 5 of 11 to none of 11 patients; $P = 0.035$), whereas the prevalence of orthostatic hypotension increased significantly after ETS (from 3 of 11 to 9 of 11 patients; $P = 0.030$). In the control group, the prevalence of neither orthostatic hypertension nor orthostatic hypotension changed after surgery.
Conclusions. ETS attenuates autonomic circulatory response under nitrous oxide anesthesia.

Key words Endoscopic thoracic sympathectomy · Baroreflex · Essential palmar hyperhidrosis · Head-up tilt · Orthostatic change

Introduction

Endoscopic thoracic sympathectomy (ETS) has become an accepted treatment for essential palmar hyperhidrosis (EPH) [1]. ETS satisfactorily abolishes palmar sweating and is minimally invasive. Recent studies suggest that ETS could also be used to treat other conditions that are resistant to standard therapy, including angina pectoris [2], vascular insufficiency [3], sympathetically maintained pain [4], and social phobia [5]. Because sudomotor fibers to the upper extremities are not selectively ablated in ETS, sympathetic ganglia that are in the pathways of the sympathetic innervation of the heart, the lungs, and the great vessels may be partially destroyed. Therefore, ETS is likely to change the autonomic regulation of the cardiovascular system. In fact, two cases of cardiac arrest of unknown etiology during ETS have been reported [6]. Although the anesthetic implications of ETS have been reviewed [7,8], little is known about the effects of ETS on the autonomic regulation of the cardiovascular system in the perioperative period. Confirmation of the safety of ETS for the treatment of EPH is essential, because EPH is a socially embarrassing, but not life-threatening, disorder. In addition, previous clinical studies have reported contradictory results concerning the effects on baroreflex sensitivity of cardiac sympathectomy induced by cervicothoracic epidural analgesia (CTEA) [9–11]. We are particularly interested in the behavioral differences vesulting from the incomplete or partial sympathetic denervation induced by ETS compared with those resulting from CTEA. The purpose of this study was to obtain basic information about the hemodynamic changes in response to acute central hypovolemia induced by head-up tilt (HUT) before and after ETS.

Methods

The study was approved by the ethics committee of our hospital, and informed consent was obtained from each patient. Patients who were receiving any long-term medications were excluded. Eleven consecutive ASA

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physical status classification I patients who had EPH and were scheduled to undergo ETS were enrolled (ETS group). Nine age-matched status I volunteers scheduled to undergo minor surgical procedures other than ETS were enrolled as control subjects (control group).

No premedication was given before surgery. General anesthesia was induced with propofol (2 mg/kg IV) and tracheal intubation was facilitated with vecuronium bromide (1.5 mg/kg IV). To facilitate surgery, patients undergoing ETS were intubated with an endobronchial tube for differential lung ventilation. After tracheal intubation, vecuronium bromide (approximately 0.15 mg·kg·h[1]) was continuously infused to immobilize the patients and to control ventilation during the study. In all subjects, anesthesia was maintained with sevoflurane and nitrous oxide in oxygen. Acetated Ringer's solution was infused at 5 ml·kg^{-1}·h^{-1}. Heart rate (HR), percutaneous arterial oxygen saturation, end-tidal carbon dioxide tension, and end-tidal sevoflurane concentration were continuously monitored. Blood pressure was measured by the oscillometric method. All variables were measured with a patient monitoring system (model DC-5300; Fukuda Denshi, Tokyo, Japan).

After anesthesia had been induced and an indwelling Foley catheter had been placed, the inhalation of sevoflurane was discontinued. The patients were placed in the horizontal supine position and mechanically ventilated with 66% nitrous oxide in oxygen. The respiratory rate was fixed at 10 breaths·min^{-1}. Tidal volume was adjusted to maintain end-tidal carbon dioxide tension at approximately 35 mmHg. Rectal temperature was maintained at more than 36°C with a fluid warmer and a warming mattress. After the end-tidal sevoflurane concentration (less than 0.2%) was confirmed and hemodynamic stability was obtained, HR and arterial blood pressure were recorded at 1-min intervals for 10 min or more. Patients were then tilted to a 40° upright position (transit time, approximately 15 s) for 5 min by means of a motorized operating table with a foot board support. After 5 min of HUT, sevoflurane was administered again and ETS was performed in the following manner. The patient was placed in a half-sitting position. A small punch incision was made in the second or third intercostal space, and carbon dioxide was insufflated to obtain a surgical view. The bilateral second and third thoracic sympathetic ganglia (T2 and T3) were ablated with a modified transurethral electroresectoscope. In patients with axillary hyperhidrosis, the fourth ganglia (T4) were also bilaterally ablated. For surgical procedures, a small amount (less than 2 ml) of 1% lidocaine with epinephrine (1 : 100 000) was injected into each incisional site. After ETS had been completed, the hemodynamic measurements associated with HUT were carried out in the same way as before HUT.

The mean values of three consecutive measurements immediately before HUT were defined as the pre-HUT values. The maximum change in HR was used to represent intra-HUT values. Orthostatic hypertension and hypotension in response to HUT were defined as an increase and a decrease, respectively, in systolic blood pressure (SBP) by 10% or greater from the pre-HUT values. Data values were compared by means of Student's paired and unpaired *t*-tests and Fisher's exact test. Differences with a P value of less than 0.05 were considered statistically significant.

Results

The ETS and control groups were similar in respect to age, sex, body weight, and height. The duration of surgery and anesthesia did not differ significantly between the groups (Table 1). In the ETS group, 5 of 11 patients underwent ETS of T2 and T3 only, and 6 patients underwent ETS of T2, T3, and T4. Patients in the control group underwent minimally invasive procedures, mainly on the body surface (plastic, orthopedic, or otorhinolaryngological procedures and a mediastinoscopic biopsy). Intraoperative bleeding in the ETS group was insignificant, whereas that in the control group did not exceed 135 ml. In both groups, presurgical HUT was performed more than 30 min after the administration of propofol.

Pre-HUT HR and SBP before surgery did not differ significantly between the groups (Table 1). However, the pre-HUT SBP after ETS was significantly lower

Table 1. Patient characteristics and pre-HUT values in the two groups

	ETS group (n = 11)	Control group (n = 9)
Sex (male/female; n)	7/4	5/4
Age (years)	24 ± 4	24 ± 3
Weight (kg)	59 ± 10	59 ± 14
Height (cm)	167 ± 9	167 ± 11
Surgery time (min)	72 ± 18	104 ± 67
Anesthesia time (min)	190 ± 17	236 ± 76
Heart rate (beat·min^{-1})		
Before surgery	59 ± 7	54 ± 6
After surgery	59 ± 8	61 ± 14
Systolic blood pressure (mmHg)		
Before surgery	112 ± 6	114 ± 11
After surgery	111 ± 9*	123 ± 8

* $P < 0.05$ vs control group; Student's unpaired *t*-test. No significant difference was detected between before and after surgery

Values are expressed as means ± SD, except for numbers of males and females

HUT, Head-up tilt; ETS, endoscopic thoracic sympathectomy

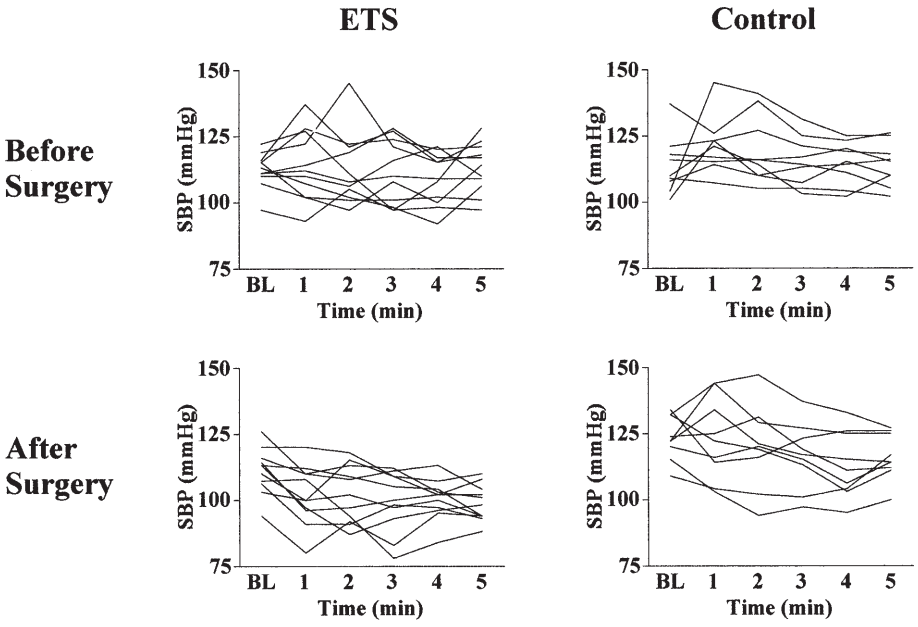

Fig. 1. Individual time courses of systolic blood pressure changes during head-up tilt before and after surgery in the endoscopic thoracic sympathectomy (*ETS*) and the control (minor surgery) groups. Subjects were tilted to an upright position at 40° for 5 min while under nitrous oxide anesthesia. *BL*, Baseline; SBP, systolic blood pressure

than that after the control surgeries (Table 1). The increase in HR in response to HUT was significantly reduced after surgery in the ETS group (from 34 ± 18 to 14 ± 11 beats·min^{-1}; $P < 0.001$), but not in the control group (from 23 ± 18 to 22 ± 12 beats·min^{-1}; $P = 0.911$). In contrast, SBP during the 5 min of HUT fluctuated without an apparent trend (Fig. 1). Orthostatic hypertension completely disappeared after ETS (from 5 of 11 to none of 11 patients; $P = 0.035$), but orthostatic hypotension was significantly more prevalent after ETS (from 3 of 11 to 9 of 11 patients; $P = 0.030$). After the minor surgeries, the prevalence of neither orthostatic hypertension (from 3 of 9 to 2 of 9 patients; $P > 0.999$) nor orthostatic hypotension (from 2 of 9 to 5 of 9 patients; $P = 0.335$) increased significantly in the control group. Hypotension/hypertension or bradycardia/tachycardia requiring treatment did not occur during HUT. However, in 1 patient in the ETS group, frequent ventricular and atrial premature beats with moderately increased blood pressure (from 119 to 145 mmHg, SBP) were observed during presurgical HUT.

Discussion

We found that ETS of the bilateral T2 to T3 ganglia, with or without T4 ganglia, attenuated the tachycardic response during HUT. Despite the lack of a standardized protocol, HUT has been used for several decades to detect the autonomic dysfunction seen in disorders such as orthostatic dysregulation, diabetic neuropathy, and Parkinsonism. Passive postural change to an upright position reduces venous return to the heart, and the body is able to compensate quickly for acute central hypovolemia by increasing HR, cardiac output, and vascular tone. HUT may provoke the activation of arterial and cardiopulmonary baroreceptor reflexes and may initiate the aforementioned compensation. On the other hand, the Bainbridge reflex, the existence of which remains controversial in humans, possibly results in a decrease in HR in response to acute central hypovolemia as a counterbalance to the baroreceptor reflex [12]. Among the mechanisms of blood pressure control that respond to central hypovolemia, the arterial baroreceptor reflex plays a major role, especially for instantaneous regulation.

Our method of HUT differed from more commonly used methods in several ways. First, our tests were performed with the subjects under controlled mechanical ventilation with muscle relaxation. Second, the subjects were lightly anesthetized with nitrous oxide and received a minimal concentration of sevoflurane. Third, the results of postsurgical HUT could have been affected by noxious stimuli of varying degree from the preceding surgery. Fourth, the trachea may have been stimulated by the tracheal (or endobronchial) tube accompanied by the tilting movement.

Mechanical lung inflation can alter afferent dicharges from slowly adapting pulmonary stretch receptors and can thus modify baroreflex function [13]. Positive intrathoracic pressure may reduce venous return to the right side of the heart. Skeletal muscle relaxation, especially in the lower part of the body, can impair the "muscle pump" that assists cardiac filling from the gravity pool [14]. Although volatile anesthetics in general, including sevoflurane, have been reported to depress

baroreflex sensitivity [15–20], nitrous oxide has minimal effects in this regard [15–17,21]. Furthermore, reflex tachycardia in response to HUT has recently been reported to be better preserved with sevoflurane than with isoflurane or halothane [22]. Therefore, we believe that the minimum concentration of sevoflurane combined with nitrous oxide that we used has no significant effects on the baroreflex control of HR. On the other hand, the sympathomimetic action of nitrous oxide is well established [21,23]. Accordingly, the baseline sympathetic tone in the subjects was, presumably, augmented and possibly affected the results of HUT.

In addition, previous clinical studies have reported that baroreflex control is affected by abnormal arterial blood gas levels [24], aging [25,26], sex [26,27], level of consciousness [28], mental state [29], and noxious stimuli [29]. However, we enrolled healthy young adults matched for age and sex as control subjects, and our experimental protocol provided adequate ventilation and allowed little or no variation in the subjects' mental state.

Kohno and Taneyama [30] have recently shown that depression of the baroreflex control of HR by surgical stimuli differs markedly depending on the location of surgery. They found that upper abdominal surgery significantly depressed baroreflex function, but that surgery of the lower abdomen, extremities, or chest wall had no effect on this function. Of the noxious stimuli produced by the preceding surgery, therefore, we believe that there were nonsignificant differences in the backgrounds for baroreflex control of HR between the chest wall punch incision resulting from ETS and the minor surgeries. Thus, various co-existing factors which may influence hemodynamic regulation are unlikely to have significantly affected the major findings of the present study. However, as the trachea and bronchi are mechanosensitive, it is possible that a tilting movement could have provoked a pressor response although the subjects were fully paralyzed. If this had been so in the present study, both pressor and depressor responses may have been elicited by HUT.

The increased prevalence of orthostatic hypotension after ETS appears to be caused by sympathetic denervation. However, because our criterion for orthostatic change was rather modest, we do not beleive that this increase indicates that ETS is associated with an increased risk of clinically significant orthostatic hypotension. However, severe orthostatic hypotension has been reported in a patient with EPH who underwent an extensive thoracic sympathectomy that affected splanchnic innervation [31]. Further study is needed to establish the incidence of such possible sequelae.

Unlike orthostatic hypotension, orthostatic hypertension is uncommon. In general, orthostatic hypertension most often occurs because of sympathetic overcompensation with an excessive release of catecholamines or because of nephroptosis with orthostatic activation of the renin-angiotensin system [32]. In our experimental setting, underlying sympathomimesis caused by nitrous oxide and the stress response to tracheal stimulation may have contributed to the increase in blood pressure and HR during HUT. Orthostatic hypertension with frequent premature beats occurred in one of our patients with EPH, but did not occur after ETS. We speculate that this event was, possibly, caused by transient, excessive catecholamine release, although we did not examine the possible involvement of humoral factors, and hemodynamic variables were not measured on a beat-by-beat basis. The disappearance of orthostatic hypertension after ETS was probably a result of sympathetic denervation and the subsequent decrease in the release of catecholamines.

Noppen et al. [33] found that ETS reduced plasma concentrations of norepinephrine, but not epinephrine, in patients with EPH. Their results indirectly support our findings, in that the postsurgical, pre-HUT SBP in the ETS group was significantly lower than that in the control group, whereas postsurgical, pre-HUT HRs were similar in both groups.

On the basis of our observations, we speculate that the hemodynamic response to acute central hypovolemia would be blunted in patients after ETS. A sufficient and instantaneous compensatory response by the remaining innervated fibers to the cardiovascular system may not always occur. Accordingly, we should be alert to the reduction in tachycardic response and the severe hypotension that could be caused by possible postoperative complications, such as hemothorax [8].

Takeshima and Dohi [10] reported that baroreflex sensitivity, as calculated with the depressor test (baroreflex slope calculated with R-R interval change per decrease in systolic pressure change), was unchanged in a patient with cardiac sympathectomy induced by epidural anesthesia in whom sensory analgesia developed from C4 to T7. However, Goertz et al. [11] reported that epidural anesthesia producing analgesia above T1 reduced baroreflex sensitivity, as calculated with the depressor test. The major differences between the two studies were that, in the study of Takeshima and Dohi [10], CTEA was performed with lidocaine, with the patient conscious, whereas, in the study of Goertz et al. [11], CTEA was induced with bupivacaine during nitrous oxide-fentanyl anesthesia. Our present findings are in contrast to those of Takeshima and Dohi [10], but are quite similar to those of Goertz et al. [11], although the scope of our study probably encompassed factors other than the depressor response. Therefore, we speculate that consciousness may help to preserve the tachycardic response evoked by acute central hypovolemia after the partial or incomplete denervation of cardiofugal sympathetic fibers.

In conclusion, we found that the tachycardic response during HUT was reduced by ETS, but not by various types of minor surgery. Because of the safety concerns, physiologic implications, and increasing popularity of ETS, further studies are needed to evaluate its perioperative and long-term effects on the autonomic cardiovascular system, with and without underlying anesthesia.

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