High Thoracic Epidural Anesthesia Does Not Inhibit Sympathetic Nerve Activity in the Lower Extremities

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Background: Sympathetic nerve activity was recorded in the leg during high thoracic epidural anesthesia with a segmental sensory blockade of the upper thoracic dermatomes to test the hypothesis that the sympathetic blockade accompanying thoracic epidural anesthesia includes caudal parts of the sympathetic nervous system.

Methods: Experiments were performed on 10 patients scheduled for thoracotomy. An epidural catheter was inserted at the T3–T4 or T4–T5 interspace. In the main protocol (seven patients), blood pressure, heart rate, and skin temperature (big toe, thumb) were continuously monitored, and multunit postganglionic sympathetic nerve activity was recorded with a tungsten microelec-
trode in a muscle-innervating fascicle of the peroneal nerve. After baseline data collection, muscle sympathetic nerve activity was recorded for an additional 45-min period after epidural injection of 4–6 ml bupivacaine, 5 mg/ml. In an additional three patients, the effects of thoracic epidural anesthesia on skin-innervating sympathetic nerve activity were qualitatively assessed.

Results: Activation of thoracic epidural anesthesia caused no significant changes in peroneal sympathetic nerve activity (n = 7), blood pressure, or heart rate. Skin temperature increased significantly in the hand 15 min after activation of the blockade, from 32.7 ± 2.4°C to 34.4 ± 1.5°C (mean ± SD), whereas no changes were observed in foot temperature. The sensory blockade extended from T1 (C4–T2) to T8 (T6–T11).

Conclusions: A high thoracic epidural anesthesia with adequate sensory blockade of upper thoracic dermatomes may be achieved without blockade of caudal parts of the sympathetic nervous system. This finding differs from that of earlier studies that used indirect methods to evaluate changes in sympathetic nerve activity. (Key words: Bupivacaine; microneurography; skin blood flow.)

The degree and extent of sympathetic blockade accompanying epidural and spinal anesthesia have been matters of debate. One reason for this is that most studies have used indirect methods such as skin temperature measurements to monitor sympathetic effector organ function. The assumption that such methods can adequately reflect sympathetic nerve activity is hazardous. Based on the notion that an increase in regional skin temperature in the lower extremities reflects diminished efferent sympathetic nerve activity, experimental and human studies have indicated that the sympathetic blockade associated with segmental high thoracic epidural anesthesia (TEA) extends caudally beyond the area of sensory blockade. However, direct intraneural recording of sympathetic nerve activity in human leg nerves has shown that lumbar epidural and spinal anesthesia with an upper level of sensory blockade above T8 completely eliminates sympathetic outflow to the lower extremities. Because the lower extremities are supplied by sympathetic nerve fibers arising from T9–L1, this also indicates a fairly close correlation between the extent of sensory and sympathetic blockade during regional anesthesia, at least in the lower extremities.

In the present study, we directly recorded sympathetic activity in the peroneal nerve during TEA with a segmental sensory blockade of the upper thoracic dermatomes to test the hypothesis that this blockade can result in a more extensive sympathetic block caudally.

Materials and Methods

Experiments were performed on 10 otherwise healthy patients scheduled for thoracotomy because of tumor or pneu-
mothorax. Written informed consent was obtained from the patients, and the investigation was approved by the Human Ethics Committee at the University of Göteborg.

Nerve Recording
Multunit postganglionic sympathetic nerve activity was recorded with a tungsten microelectrode, with a tip diameter of a few microns, inserted in a muscle- or skin-innervating fascicle of the peroneal nerve at the fibular head. A reference electrode was inserted subcutaneously 1–2 cm away from the recording electrode. When a nerve fascicle was identified, small electrode adjustments were made until a site was found in which sympathetic impulses could be recorded. The criteria for recording muscle and skin sympathetic nerve activity (MSA and SSA, respectively) and evidence for the sympathetic nature of these activities has been described previously. The original nerve signal was amplified with a gain of 50,000 and fed through a bandpass filter with a band width of 700–2,000 Hz and then through an integrating network with a time constant of 0.1 s to obtain a mean voltage display of nerve activity. Recordings of both the filtered and mean voltage neurograms were stored on VHS tape (Racal V-Store; Racal Recorders Ltd., Southampton, England) and on a computer, together with recordings of electrocardiogram (via standard chest leads) and respiratory movement (strain gauge; recorded because of technical reasons). Temperature was measured on the volar aspect of the thumb and the plantar aspect of the big toe, ipsilateral to the nerve recording, using a multichannel thermometer with digital readout (Exacon 2000; Exacon A/S, Roskilde, Denmark).

Main Protocol: MSA
For quantitative evaluation of sympathetic nerve discharge after TEA, MSA was recorded in seven patients. Because it is remarkably stable over time, MSA is suitable for quantification. For comparison with previous TEA studies, skin temperature was also monitored in these experiments (six patients; data from one patient was lost because of technical reasons). Temperature was measured on the volar aspect of the thumb and the plantar aspect of the big toe, ipsilateral to the nerve recording. After a baseline recording of all parameters for 15 min, 20–30 mg (4–6 ml) bupivacaine was injected through the epidural catheter. The recordings of MSA and other variables were continued for an additional 45 min. The last two 5-min periods before epidural injection were taken as control periods, with the mean of them defined as 100%. The activity after injection was calculated in 5-min periods before reported time at 5, 10, 15, 20, and 45 min. MSA bursts were identified by visual inspection of the mean voltage neurogram, aided by a computer software developed in our laboratory. MSA was expressed as burst frequency (bursts/min) and total or integrated MSA (total area under bursts/min). The area of sensory blockade was determined by loss of cold sensation (ice cube) 15 min after injection of bupivacaine.

Qualitative Assessment of SSA
Skin sympathetic nerve activity is highly variable over time and was therefore considered less suitable for a quantitative evaluation of the effects of TEA. However, a qualitative assessment of SSA during TEA was performed in three patients. To allow an evaluation of both vasomotor and sudomotor components of SSA, specific cutaneous effector organ function was registered instead of skin temperature in these experiments. Skin perfusion was monitored with laser Doppler flowmetry (Periflux 4000; Perimed AB, Stockholm, Sweden), with probes placed on glabrous skin of the big toe of the leg used for nerve recording and on the ipsilateral thumb. Calibrations for...

Anesthesiology, V 91, No 5, Nov 1999
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Baseline | 20 min TEA | 45 min TEA
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ECG | | |
MSA | | |

Fig. 1. Records of muscle sympathetic activity (MSA) and electrocardiogram (ECG) from two subjects at baseline and 20 and 45 min after thoracic epidural anesthesia (TEA).

zero perfusion were made in all recordings by aiming the probe toward a white reflecting background. The analog output of the flowmeter gives no absolute value but shows relative changes in the flux of red blood cells.9-11 Sudomotor function was monitored by recording skin electrical resistance (galvanic skin response) with a modified van Gogh GSR module (built in our laboratory), using Ag/AgCl electrodes (Medicotest A/S, Olstykke, Denmark) placed on the volar and plantar aspects of the hand and foot ipsilateral to the nerve recording. The measuring current was 12 μA, and filter settings were 0.7-100 Hz.

Because the SSA recordings contain both sudomotor and vasomotor bursts with highly variable shape and duration, the number of bursts per time does not provide a good measure of SSA. Instead, the area under the neurogram to an added baseline was calculated with a computer program, and SSA was expressed as the average area for 5-min periods.12 Apart from evaluation of SSA at rest, the effects of short arousing stimuli (sudden noises) performed repeatedly before and after activation of TEA and mental stress (serial subtraction of 17 from 1,000 as fast as possible) performed 30 min after activation of TEA were studied.

Duration of SSA protocol and determination of sensory blockade was similar to the main protocol.

**Statistical Analysis**

Quantitative data are presented as means ± SD. Changes in sympathetic activity, blood pressure, and skin temperature were evaluated with one-way analysis of variance for repeated measures followed by single degree-of-freedom contrast analyses. \( P < 0.05 \) was considered statistically significant.

**Results**

The sensory blockade elicited by TEA extended from T1 (range, C4-T2) to T8 (range, T6-T11).

**Effects of TEA on MSA, Heart Rate, Blood Pressure, and Skin Temperature**

Lower limb MSA (n = 7), blood pressure (n = 10), and heart rate (n = 10) were not significantly altered during the 45 min after TEA (figs. 1 and 2). Skin temperature (n = 6) increased significantly in the hand, from 32.7 ± 2.4°C to 34.4 ± 1.5°C, whereas foot skin temperature remained unaffected (fig. 3).

**Effects of TEA on SSA, Skin Perfusion, and Galvanic Skin Response**

After activation of TEA, SSA decreased at rest in all three subjects (to 5%, 12%, and 35% of control level, respectively). However, short arousing stimuli consistently evoked vigorous bursts of SSA throughout the experimental sessions, of similar amplitude before and after TEA (fig. 4). A 1-min period of mental stress 30 min after activation of TEA increased the level of SSA above
control level in all three subjects (to 34%, 43%, and 44% above control, respectively). In all three subjects, skin perfusion on the big toe was stable, and galvanic skin response remained in the foot throughout the experiment, whereas skin perfusion increased substantially on the thumb, and galvanic skin response was abolished in the hand (within the sensory anesthetic area; fig. 4).

**Discussion**

This study shows that TEA with bupivacaine (5 mg/ml) resulting in a segmental sensory blockade restricted to the upper thoracic dermatomes is not associated with any signs of a pharmacologic blockade of sympathetic nerve activity to the legs.

Sympathetic nerve activity is highly differentiated, with distinctly different discharge patterns in sympathetic fibers innervating the muscle vascular bed (MSA) and cutaneous vessels and sweat glands (SSA), respectively.\(^8\)\(^6\) MSA consists of baroreceptor reflex-controlled pulse synchronous bursts of activity that are largely unaffected by transient environmental stressors, and resting MSA is remarkably constant over time, making it well suited for quantitative assessments. The present finding of unaltered peroneal MSA after TEA argues strongly against a significant blockade of sympathetic nerve outflow to the legs after high thoracic segmental blockade. The nonsignificant tendency toward increased MSA should be considered in the light of a recent study by Taniguchi et al., who evaluated compensatory sympathetic excitation of unblocked segments during epidural anesthesia (1% lidocaine) in pentobarbital-anesthetized cats.\(^14\) TEA (C8-T6) induced a decrease in heart rate.

**Fig. 2.** (Left) Muscle sympathetic activity (MSA) at baseline and at intervals after activation of thoracic epidural anesthesia (TEA; n = 7). No inhibition of MSA to the legs was observed; tot MSA% = total MSA as % of control; c = control. (Right) Systolic and diastolic blood pressure (SBP and DBP, respectively) and heart rate (HR) during baseline and at intervals after activation of thoracic epidural anesthesia (n = 10). No significant changes were observed.

**Fig. 3.** Skin temperature in the hand and the foot at baseline and at intervals after activation of thoracic epidural anesthesia (TEA; n = 6). Skin temperature increased significantly in the hand 15 min after activation of the blockade, whereas no changes were observed in the foot.
mean arterial blood pressure, and cardiac sympathetic nerve activity, which, in turn, was accompanied by a baroreflex-mediated increase in renal sympathetic nerve activity. In the present study, high segmental TEA induced no significant change in resting heart rate or blood pressure, despite the fact that this procedure has been shown (with cardiac norepinephrine spillover technique) to completely inhibit cardiac sympathetic activity. This discrepancy could be explained by the fact that resting human heart rate is mainly controlled by efferent vagal tone, under the influence of arterial baroreceptors. However, despite an unchanged arterial blood pressure in our patients, an altered activity from central blood volume receptors could theoretically explain the tendency toward increased MSA. These studies strongly suggest that the sympathetic blockade associated with high segmental TEA does not extend beyond the area of sensory blockade, but, rather, that unblocked sympathetic segments are still under the influence of baroreflexes and central sympatho-excitatory drive.

Hopf et al. demonstrated increased foot skin temperature in patients who received TEA compared with those in a control group who received saline, and they interpreted this as an inhibition of sympathetic outflow to the leg. Two possible mechanisms for such an effect of TEA are: (1) a significant proportion of sympathetic preganglionic fibers supplying the leg were within the thoracic segments blocked by the TEA; or (2) TEA may intraspinally block the bulbospinal pathways mediating the central sympatho-excitatory drive, which is necessary for peripheral sympathetic fibers to be active. Because our previous studies on lumbar epidural anesthesia, as well as studies of patients with spinal cord injury, have demonstrated that sympathetic outflow to the legs occurs below T8, the first explanation seems less likely. With regard to the second explanation, epidural anesthesia is considered to act mainly through a paravertebral blockade and a spinal root blockade, and our present findings support this notion, showing no evidence of inhibition of central sympathetic drive. In this context, however, the different concentrations of bupivacaine used by Hopf et al. (7.5 mg/ml, 31.5 mg) and in our study (5 mg/ml, 20–30 mg) may be of importance. It is conceivable that more concentrated solutions of local anesthetics may reach concentrations in the peripheral areas of the spinal cord sufficient to block nerve con-
duction in descending bulbospinal pathways or their transfer to sympathetic preganglionic neurons in the intermediolateral column. If so, a reduced central sympatho-excitatory drive could theoretically explain the relative increase in foot skin temperature after TEA in the study by Hopf et al.5

Skin sympathetic nerve activity is mainly controlled by thermoregulation but is also profoundly affected by degree of environmental stress. The well-known large variability of SSA induced by environmental stimuli1 prompted us to avoid its use in the quantitative assessment. It was also the basis for our interpretation that the decrease in SSA after TEA was primarily a result of the diminished environmental stress after the initial experimental procedures. This was in contrast to the complete abolition of lower-limb SSA and cutaneous effectors in the foot but not the hand, maintained highly responsive to short-lasting arousal stimuli as well as mental stress throughout the experiments. This is also the basis for central sympathetic inhibition18 and thus argue for relaxation/sedation rather than a peripheral blockade of sympathetic outflow to the leg. The lack of a time-vehicle control may be considered a limitation of these studies, but the well-established stability of MSA over time6,13 and our present finding of unchanged MSA after TEA lead us to consider such a control less important in our qualitative MSA protocol. With regard to our qualitative SSA experiments, a time-vehicle control would clearly be necessary to prove that the SSA reduction at rest is exclusively caused by relaxation. However, given the large variability of SSA, a very large number of time-vehicle-controlled experiments would be needed to argue this point. This consideration, and the fact that MSA (influencing resistance in the large muscle vascular bed) is far more important for hemodynamic control, made us decide against time-vehicle control studies.

In conclusion, the present study shows that TEA using bupivacaine (5 mg/ml) is not associated with any inhibition of resting sympathetic nerve activity to the legs. This argues against spinal inhibition of central sympathetic drive and may explain the clinical experience of hemodynamic stability observed with TEA in conscious patients.19,20

References


