Anesthesiology
62:294–297, 1985

Effects of Epidural Anesthesia on Catecholamines, Renin Activity, and Vasopressin Changes Induced by Tilt in Elderly Men

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Mean arterial pressure, heart rate, plasma catecholamines, renin activity, and vasopressin changes induced by a 30-degree head-up tilt were studied before and during epidural anesthesia with bupivacaine in eight elderly patients (ages 58–82 yr). The tilt performed before epidural anesthesia did not modify mean arterial pressure, heart rate, plasma catecholamines, renin activity, and vasopressin at 5 and 15 min. During epidural anesthesia, the superior level of analgesia ranged from T4 to T10. Epidural anesthesia induced significant ($P < 0.05$) decreases from control values in mean arterial pressure and plasma norepinephrine (from 85 ± 6 to 67 ± 8 mmHg and from 600 ± 108 to 307 ± 77 pg/ml, respectively, mean ± SEM) without significant changes in heart rate, plasma epinephrine, renin activity, and vasopressin. However 5 and 15 min after tilt, significant decreases from pretilt values were measured in mean arterial pressure (from 67 ± 8 to 57 ± 6 and 55 ± 6 mmHg, respectively) and in heart rate (from 70 ± 8 to 63 ± 7 and 62 ± 7 beats/min). Simultaneously, an increase in plasma vasopressin (from 14.8 ± 5.5 to 36.2 ± 10.3 and 40.0 ± 10.5 pg/ml) was recorded, whereas plasma norepinephrine and epinephrine remained unchanged. Posttilt plasma renin activity values at 5 and 15 min were increased significantly when compared with the preepidural values (2,752 ± 1,168, 2,410 ± 1,214 and 713 ± 190 $pg \cdot ml^{-1} \cdot h^{-1}$, respectively). The authors conclude that during epidural anesthesia in elderly patients 1) the heart rate and the plasma catecholamines responses to hypotension induced by tilt are impaired, even if the level of analgesia is below T4; and 2) vasopressin and, to a lesser degree, the renin–angiotensin system may play important roles in the regulation of arterial pressure. (Key words: Anesthetic techniques: epidural. Blood pressure: hypotension. Hormones: catecholamines; renin–angiotensin; vasopressin.)

IT IS WELL KNOWN that sympathoadrenal and renin–angiotensin systems play important roles in the cardiovascular responses to the decrease in venous return induced by a head-up body tilt[1] or bleeding.[2] Moreover, vasopressin plays an important role in the control of blood pressure and in the response to hypovolemia when the sympathoadrenal system is blocked in dogs.[3,4] Thus, epidural anesthesia, which induces a preganglionic sympathetic block, may interfere with the physiologic response of the sympathoadrenal system to hypovolemia. Indeed, Stanek *et al.*[2] found that the sympathoadrenal response to hypovolemia was altered during epidural anesthesia, whereas the renin–angiotensin system response was not modified. Stanek's work, however, was performed on anesthetized dogs and without measurement of plasma vasopressin. The aim of the present study was to measure heart rate, arterial pressure and plasma catecholamines, renin activity, and vasopressin in response to a head-up body tilt performed before and during epidural anesthesia in elderly men.

Methods

Eight informed consenting male patients, ages 58–82 yr (mean 72 yr), who were scheduled for prostatectomy, were studied after approval by our Institutional Committee. They were free of cardiac, renal, and hepatic disease, had normal sodium intake, and did not take any drugs known to influence the cardiovascular and neuroendocrine systems. They had fasted for 6 h before the procedure. Premedication with diazepam 10 mg and atropine 0.5 mg was administered intramuscularly 1 h before their arrival in a quiet induction room. Throughout the procedure, patients remained in their own bed. Catheters were inserted in the brachial vein, in the radial artery, and in the lumbar epidural space (L3–L4). After a rest period of 20 min, the first control measurements were performed followed by a 30-degree head-up body tilt obtained by raising the patient's bed. The change from supine to tilt position was accomplished within 10 s. Two new sets of measurements were performed 5 and 15 min after tilt. The patients then were tilted down to supine position, rested during a new period of 20 min, and had another set of control measurements, followed by the epidural administration of 14 ml bupivacaine 0.5% without epinephrine. Thirty

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Received from the Department of Anesthesiology of Bicetre Hospital and the laboratory of Renal Physiology of Tenon Hospital. Accepted for publication September 14, 1984. Presented in part at the annual meeting of the American Society of Anesthesiologists, October 1983.

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TABLE 1. Effects of Tilt on Arterial Pressure, Heart Rate, and Plasma Catecholamines, Renin Activity, and Vasopression (Mean Values ± SEM) before and during Epidural Anesthesia

	Before Epidural Anesthesia				During Epidural Anesthesia		
	Pretilt Supine	Tilt 5 Min	Tilt 15 Min	Posttilt Supine	Pretilt Supine	Tilt 5 Min	Tilt 15 Min
Mean arterial pressure (mmHg)	84 ± 5	84 ± 6	84 ± 6	85 ± 6	67 ± 8*†	57 ± 7*†‡	55 ± 6*†‡
Heart rate (beats/min)	72 ± 7	73 ± 7	73 ± 7	74 ± 2	70 ± 8	63 ± 7*†‡	62 ± 7*†‡
Plasma norepinephrine (pg/ml)	590 ± 126	590 ± 88	595 ± 73	600 ± 108	301 ± 77*†	209 ± 57*†	345 ± 73*†
Plasma epinephrine (pg/ml)	62 ± 32	73 ± 12	69 ± 24	99 ± 3	133 ± 83	122 ± 57	139 ± 29
Plasma renin activity ($pg \cdot ml^{-1} \cdot h^{-1}$)	714 ± 199	836 ± 311	368 ± 405	713 ± 190	1926 ± 765	2752 ± 1168*†	2410 ± 1214*†
Plasma vasopression (pg/ml)	3.5 ± 1.1	3.2 ± 0.7	3.1 ± 0.8	3.2 ± 1.1	14.8 ± 5.5	36.2 ± 10.37*†‡	40.0 ± 10.5*†‡

* $P < 0.05$ *versus* posttilt supine before epidural anesthesia.
† $P < 0.05$ pretilt and tilt 5 and 15 min *versus* before epidural anesthesia.
‡ $P < 0.05$ *versus* pretilt during epidural anesthesia.

minutes after epidural anesthesia, a new set of measurements was performed with the patients in a supine position. The patients then were tilted again at a 30-degree head-up position, and two new sets of measurements were performed 5 and 15 min after tilt (35 and 45 min after epidural anesthesia). The superior analgesia level was detected by pinprick 20 min after epidural anesthesia and after the last set of measurements. No supplementary anesthetic or vasopressor drugs were administered throughout the study. During the procedure, a volume of 375 ± 105 ml (mean ± SEM) of Ringer's lactate solution was infused in order to avoid a decrease of more than 30 mmHg in systolic arterial pressure. Each set of measurements included 1) heart rate (recorded from the electrocardiogram); 2) mean arterial pressure (measured with a calibrated quartz pressure transducer 1290A Hewlett Packard® kept at the level of the right atrium in both supine and tilt positions); and 3) arterial blood samples collected in dipotassium EDTA for plasma renin activity and vasopressin measurements (20 ml), and in heparin lithium for plasma catecholamines measurements (5 ml). Blood immediately was centrifuged at 4° C for 10 min at 3,000 *g* and plasma stored at 18° C. Plasma epinephrine and norepinephrine were measured by the radioenzymatic method of Da Prada and Zürcker.[5] The sensitivity of this method was ±5 pg/ml for both epinephrine and norepinephrine. Plasma renin activity was measured with a sensitivity of ±125 $pg \cdot ml^{-1} \cdot h^{-1}$ by radioimmunoassay with an antibody prepared in our laboratory.[6] Plasma vasopressin was measured by radioimmunoassay with an antibody from our laboratory.[7] The minimum detectable level of vasopressin was 0.9 pg/ml with this method. Data were analyzed by multifactorial analysis of variance ($P < 0.05$ significant). All values were expressed as mean ± SEM.

Results

The tilt performed before epidural anesthesia did not modify mean arterial pressure, heart rate, plasma norepinephrine and epinephrine, plasma renin activity, and vasopressin (table 1, figs. 1, 2, and 3). During epidural anesthesia, the superior level of analgesia ranged from T4 to T10. Epidural anesthesia induced a significant decrease from control values in mean arterial pressure and plasma norepinephrine, whereas heart rate, plasma epinephrine, plasma renin activity, and vasopressin did not change significantly (table 1, figs. 1, 2, and 3). Five and 15 min after tilt, a significant decrease from pretilt values in mean arterial pressure and in heart rate and an increase in plasma vasopressin were observed, whereas plasma norepinephrine, epinephrine, and renin activity remained unchanged. However, the posttilt values of plasma norepinephrine were significantly higher than their preepidural values. Both plasma renin activity and vasopressin changes after epidural anesthesia were not correlated to the level of neural block.

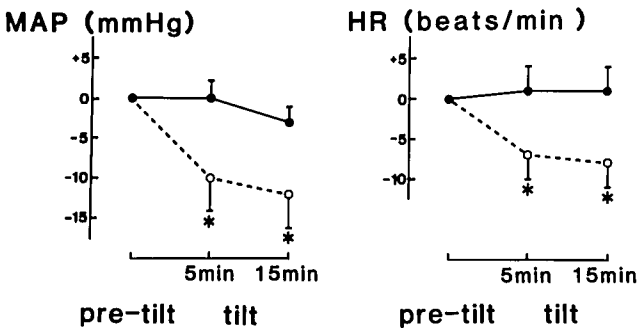

FIG. 1. Changes from pretilt values in mean arterial pressure (MAP) and heart rate (HR) before epidural anesthesia (● —— ●) and during epidural anesthesia (O - - - O). Mean values ± SEM. Significantly different from pretilt value *$P < 0.05$.

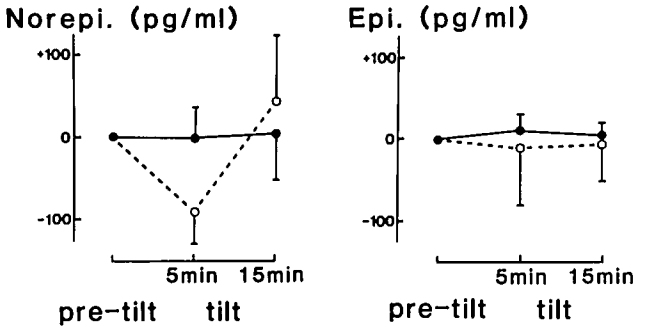

FIG. 2. Changes from pretilt values in plasma norepinephrine (Norepi.) and plasma epinephrine (Epi.) before epidural anesthesia (● —— ●) and during epidural anesthesia (O - - - O). Mean values ± SEM. No significant changes observed.

Discussion

BEFORE EPIDURAL ANESTHESIA

The tilt performed before epidural anesthesia provoked no change in mean arterial pressure and heart rate. This is consistent with previous studies that have shown that mean arterial pressure and heart rate may not change during a 30-degree head-up tilt.[8,9] However, during this same tilt, plasma catecholamines have not varied, while Mancia *et al.* found an increase in norepinephrine and epinephrine during a 60-degree head-up tilt. Since plasma catecholamines may not reflect moderate variations in sympathetic tone activity,[9] we therefore can not presume that the low angle of tilt used in our study did not permit a consistent change in sympathetic activity. The magnitude of the blood pooling and the decrease in venous return to the heart induced by tilt depends on the sympathetic activity of the lower part of the body. It therefore might have been dangerous to perform a more pronounced tilt during epidural anesthesia.

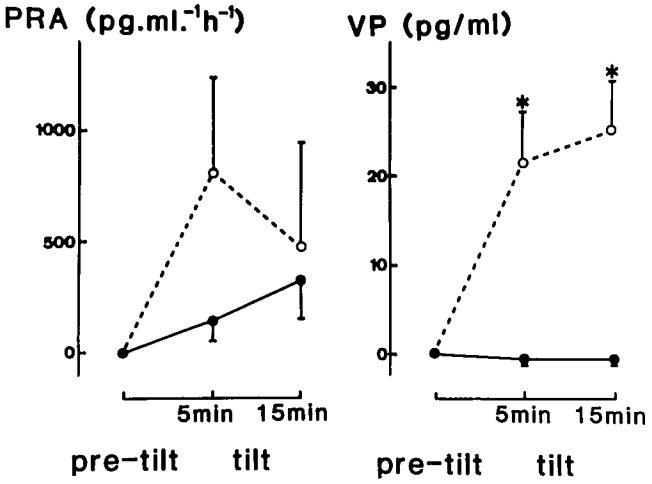

FIG. 3. Changes from pretilt values in plasma renin activity (PRA) and plasma vasopressin (VP) before epidural anesthesia (● —— ●) and during epidural anesthesia (O - - - O). Mean values ± SEM. Significantly different from pretilt value $*P < 0.05$.

DURING EPIDURAL ANESTHESIA

Heart Rate and Arterial Pressure. During epidural anesthesia, the hypotension induced by tilt was associated with a decrease in heart rate. This suggests that baroreceptor reflexes were impaired. Two assumptions may explain such an impairment: 1) The advanced age may explain partly the absence of tachycardia despite hypotension. However, age causes only a relative impairment of baroreceptor reflexes but not their absolute absence.[10] 2) Enhanced vagal tone due to a low-pressure receptor reflex may be invoked. It has been demonstrated that hemorrhage produces a pronounced bradycardia in the animal. This response is found to be mediated through a vasovagal reflex arch.[11] Atropine, given at a dose of 0.5 mg intramuscularly an hour before our experimental procedure and 2.5 h before epidural anesthesia measurements, probably does not play a role nor constitute an argument against enhanced vagal tone. A decrease in heart rate, despite a decrease in arterial pressure, has been observed in dogs receiving spinal anesthesia with a low sensory level (T8–T10).[12] This work was performed, however, on dogs anesthetized with enflurane, which may have interacted with the effect of spinal anesthesia. In our study, three factors that decrease venous return may have stimulated the low-pressure receptor reflex: 1) peripheral vascular blood pooling caused by sympathetic blockade, which is more significant than the pooling obtained with a tilt without epidural anesthesia; 2) low volume of Ringer's lactate solution infused; 3) head-up tilt. Another cause can be the blockade of the efferent limb of the baroreceptor reflex. It generally is admitted that during epidural anesthesia the superior level of analgesia is similar to the superior level of the sympathetic blockade.[13] Thus, cardioaccelerator fibers that are higher than T4 theoretically were not reached in our patients, and a possible blockade of sympathetic innervation of the heart can be eliminated.

Plasma Catecholamines, Renin Activity, and Vasopressin. In the present study, we observed a decrease in plasma norepinephrine during epidural anesthesia and no increase after tilt. This confirms previous studies on anesthetized animals[2] and is an argument in favor of an important loss in peripheral sympathetic tone that is not counterbalanced by a compensatory increase in norepinephrine release from unblocked upper regions. No significant increase in plasma epinephrine was observed, despite the decrease in arterial pressure. In spite of a significant decrease of mean arterial pressure after the tilt during epidural anesthesia, both norepinephrine and epinephrine secretion responses are impaired, as has been demonstrated in dogs with epidural anesthesia.[2] Since aging produces a wide spectrum of alteration in

the physiology of the endocrine systems,[14] the wide variation in vasopressin and plasma renin values observed after epidural anesthesia may be due to the age of the elderly patients studied. After tilt, plasma renin activity did not increase from its pretilt value but had significantly increased from the preepidural value. Renal sympathetic afferents (T6–L2) are considered to be necessary for the normal release of renin during a head-up tilt.[1] Renin release during epidural anesthesia may have been due to two factors: 1) the decrease in renal arterial perfusion pressure may induce a direct stimulating effect on renin secretion[15]; and 2) the decrease in plasma norepinephrine also may have a direct stimulating effect on renin secretion.[16] Vasopressin, which is known to be stimulated by hypotension and hypovolemia,[17] increased after tilt during epidural anesthesia, a result that can be expected, since the vagal afferents are not blocked during epidural anesthesia. Indeed, it appears that both low-pressure (left atrial) and high-pressure (carotid and aortic) receptors via the parasympathetic pathways provide the major nonosmotic pathway for vasopressin release.[18] It was not the purpose of this article to study the exact role played by the renin–angiotensin system and vasopressin on the regulation of arterial pressure during epidural anesthesia. We know that increased renin activity generates additional angiotensin, which is a known potent vasoconstrictor,[19] and that vasopressin plays a major role in the regulation of arterial pressure in ganglionic blocked dogs.[3] However, our finding in elderly men cannot be extrapolated to younger patients. Indeed, since plasma catecholamines are higher in elderly than in younger patients,[20] their blockade by epidural anesthesia may have had more significant consequences than for younger patients.

In conclusion, during epidural anesthesia in elderly patients, heart rate and plasma catecholamines response to hypotension induced by a head-up tilt are impaired, even if the level of analgesia is below T4. Vasopressin and, to a lesser degree, the renin–angiotensin system therefore may play major roles in the regulation of arterial pressure in such circumstances.

The authors thank Drs. M. Stanton-Hicks and A. Berdeaux for their valuable assistance in writing the manuscript, M. Horiot and E. Comoy for technical assistance, and G. Rosine for secretarial assistance.

References

1. Dampney RAL, Stella A, Golin R, Zanchetti A: Vagal and sinoartic reflexes in postural control of circulation and renin release. Am J Physiol 237:H146–H152, 1979
2. Stanek B, Schwarz M, Zimpfer M, Raberger G: Plasma concentrations of noradrenaline and adrenaline and plasma renin activity during extradural blockade in dogs. Br J Anaesth 25:305–311, 1980
3. Houck PC, Fiksen-Olsen MJ, Britton SC, Romero JC: Role of angiotensin and vasopressin on blood pressure of ganglionic blocked dogs. Am J Physiol 244:H115–H120, 1983
4. Gavras H, Hatzinikolaou P, North WG, Bresnahan M, Gavras I: Interaction of the sympathetic nervous system with vasopressin and renin in the maintenance of blood pressure. Hypertension 4:400–405, 1982
5. Da Prada M, Zurcher G: Simultaneous radioenzymatic determination of plasma and tissue adrenaline, noradrenaline and dopamine within the femtomola range. Life Sci 19:1161–1174, 1976
6. Fyrquist F, Soveri P, Puutula L, Stenman UH: Radioimmunoassay of plasma renin activity. Clin Chem 22:250–256, 1976
7. Caillens M, Paillard F, Rousselet F: Etude et réalisation d'un système radioimmunologique de dosage de l'hormone antidiurétique sensible à 10^{-12}. Ann Pharm Fr 40:113–123, 1982
8. Tuckman J, Schillinglord J: Effect of different degrees of tilt on cardiac output, heart rate, and blood pressure in normal man. Br Heart J 28:32–39, 1966
9. Mancia G, Ferrari A, Gregorini L, Leonetti G, Parati G, Picotti GB, Ravazzani C, Zanchetti A: Plasma catecholamines do not invariably reflect sympathetically induced changes in blood pressure in man. Clin Sci 65:227–235, 1983
10. Duke PC, Wade JG, Hickey RF, Larson CP: The effects of age on baroreceptor reflex function in man. Can Anaesth Soc J 23:111–124, 1976
11. Oberg B, White S: The role of vagal cardiac nerves and arterial baroreceptors in the circulatory adjustments to hemorrhage in the cat. Acta Physiol Scand 80:395–403, 1970
12. Balasarawathi K, Kumar P, Glisson SN: Epinephrine, norepinephrine and hemodynamic change during subarachnoïde block (abstract). ANESTHESIOLOGY 53:S222, 1980
13. Bromage PR: Physiology and pharmacology of epidural anesthesia ANESTHESIOLOGY 28:592–608, 1967
14. Gregerman RI, Bierman EL: Aging and hormones, Textbook of Endocrinology. Edited by Williams RH. Philadelphia, WB Saunders, 1982, pp 1192–1212
15. Laragh JH, Sealey JE: Handbook of physiology, Renal Physiology. Edited by Orloff J, Berlinger RW, Geiger SR. Baltimore, Williams and Wilkins, 1973, pp 873–875
16. Carvalho JS: Inhibitory effect of circulation norepinephrine on epinephrine induced renin secretion. J Cardiovasc Pharmacol 5:72–76, 1983
17. Share L: Vascular volume and blood level of antidiuretic hormone. Am J Physiol 202:791–974, 1962
18. Schrier RW, Berl T, Anderson RJ: Osmotic and nonosmotic control of vasopressin release. Am J Physiol 236:F321–332, 1979
19. Heyndrickx GR, Boettcher DH, Vatner SF: Effects of angiotensin vasopressin and methoxamine on cardiac function and blood flow distribution in conscious dogs. Am J Physiol 231:1579–1587, 1976
20. Ziegler MG, Lake CR, Kopin IJ: Plasma noradrenaline increases with age. Nature 261:333–335, 1976