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Sevoflurane anesthesia maintains reflex tachycardia on position change from supine recumbent to head-up tilt

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Abstract: This study evaluated the effects of inhalational anesthetics on hemodynamic changes in response to head-up tilt in humans. Twenty-four patients were randomly divided into three groups that received either halothane, isoflurane, or sevoflurane. Changes in heart rate, blood pressure, and plasma norepinephrine concentrations were determined before and during head-up tilt position in the awake and anesthetized state. Head-up tilt caused a significant increase in the heart rate, concomitantly with a decrease or no significant changes in systolic blood pressure in the awake state. However, under 2 minimum alveolar concentrations (MAC) of halothane and isoflurane anesthesia, the heart rate did not significantly change during head-up tilt in spite of significant decreases in systolic blood pressure. In contrast, under 2 MAC of sevoflurane anesthesia, the heart rate significantly increased during head-up tilt. Plasma norepinephrine did not significantly alter during head-up tilt in the awake as well as the anesthetized state. These results suggest that sevoflurane maintains an increase in heart rate in response to head-up tilt, whereas halothane and isoflurane attenuate the response.

Key words: Halothane, Isoflurane, Sevoflurane, Baroreflex, Head-up tilt

Introduction

Volatile anesthetics used clinically have a potent influence on the circulatory system. Especially halothane and isoflurane have been reported to depress the sympathetic nervous system and provoke failure of baroreflex control of blood pressure [1,2]. Recently, sevoflurane has been widely used in clinical anesthesia. Sevoflurane has been reported to depress circulation, as do other modern volatile anesthetics [3]. The degree of circulatory depression by sevoflurane is weaker than that induced by halothane, and the nature of the depression is similar to that caused by isoflurane [4,5]. However, there have been few reports that analyzed the effect of sevoflurane on the baroreflex control of circulation. In the present study, we compared the effects of halothane, isoflurane, and sevoflurane on baroreflex-mediated heart rate response during the head-up tilt position in humans.

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Materials and methods

Twenty-four patients who were classified ASA physical status I were selected in the present study. There were no signs of abnormalities in the autonomic nervous system in any patient. Patients were randomly divided into three groups consisting of the halothane group ($n = 8$), isoflurane group ($n = 8$), and sevoflurane group ($n = 8$) after informed consent was obtained. The patients had fasted after 9 P.M. the day before anesthesia and received no preanesthetic medication. They were positioned horizontally recumbent on a table in the operating theater. Teflon catheters (20-guage) were introduced into the cubital vein and the radial artery under local anesthesia. An arterial catheter was connected to a pressure transducer, a waveform was displayed on a cathode ray tube, and blood pressure was recorded on a polygraph (Life Scope 11, Nihon Koden Kogyo, Tokyo, Japan). A venous catheter was used for fluid infusion. A manchette was attached to the other side of the upper arm to measure arterial blood pressure by the automated oscillometric method (BP-103i Nihon Colin, Nagoya, Japan). Electrodes were attached to the chest wall, and the electrocardiogram from a standard II lead was displayed on a CRT and recorded on a polygraph. After 15 min of bed rest, a 10° head-up tilt was performed within 10 s in the awake state. Systolic and diastolic blood pressure, and heart rate were measured and

recorded before tilting and at 2.5 and 5.0 min after tilting. Blood specimens were withdrawn through the radial artery before and 5.0 min after tilting and used for analysis of norepinephrine. Blood norepinephrine was analyzed by the high-performance liquid chromatography (HPLC) technique. After the first procedure, the operating table was returned to the horizontal position. One of the volatile anesthetics was given to the patients through a face mask at a concentration of between 2 and 3 minimum alvedar concentrations (MAC). After induction of anesthesia, vecuronium ($0.1\,mg \cdot kg^{-1}$) was injected for muscle relaxation to facilitate placement of an endotracheal tube. Respiration was controlled by a mechanical ventilator. Respiratory rates and tidal volume were determined to maintain the end-tidal carbon dioxide concentration at between 35 and 40 mmHg. The concentration of inhaled anesthetics was maintained at 2 MAC by monitoring inhalational concentration using an anesthetic gas analyzer (Capnomac Ultima, Datex, Helsinki, Finland). Thirty minutes after the start of anesthetic inhalation at 2 MAC when hemodynamic parameters were stabilized, a 10° head-up tilt was performed again. Hemodynamic parameters and blood specimens for norepinephrine were obtained in the same way as in the awake state. One MAC concentration for each anesthetic was determined as 0.75% for halothane, 1.15% for isoflurane, and 1.71% for sevoflurane. The numerical data obtained were represented by mean (X) ± standard deviation (SD). Differences among the three anesthetics were tested by one-way factorial analysis of variance (ANOVA) followed by Fisher's PLSD method for multiple comparisons. Differences between data obtained before and after head-up tilt were analyzed by paired *t*-test. A probability below 0.05 was considered significant.

Results

Demographic characteristics of the patients are presented in Table 1. There were no significant differences in age, height, or body weight. Changes in heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and serum norepinephrine (NE) concentration are presented in Table 2. SBP declined significantly at 5 min after head-up tilt in the halothane and isoflurane groups in the awake state. There was no significant difference between the three groups throughout the study. Blood pressure fell significantly in all three groups at 2.5 and 5.0 min after the change in position in the anesthetized state (Fig. 1); no difference was observed among the three groups. DBP was maintained in the awake state in all three groups throughout the study. Under anesthesia, DBP declined significantly at 2.5 min in the halothane and isoflurane groups and at 5.0 min in all three groups. There was no difference among the three groups. Significant elevations of HR were observed in all three groups in the awake state. HR recovered quickly to control values 5 min after changing positions. However, these changes were inhibited in the halothane and isoflurane groups, and no elevation of HR was noted at 2.5 min after the head-up tilt position. On the contrary, HR increased from 68.6 to 72.9 at 2.5 min and 73.5 at 5.0 min after the change in position in the sevoflurane group (Fig. 2). Plasma NE levels showed no change in any of the three groups in the awake and anesthetized state by the head-up tilt position change.

Discussion

Systemic circulation is maintained by two main factors: cardiac pump function and peripheral vascular resis-

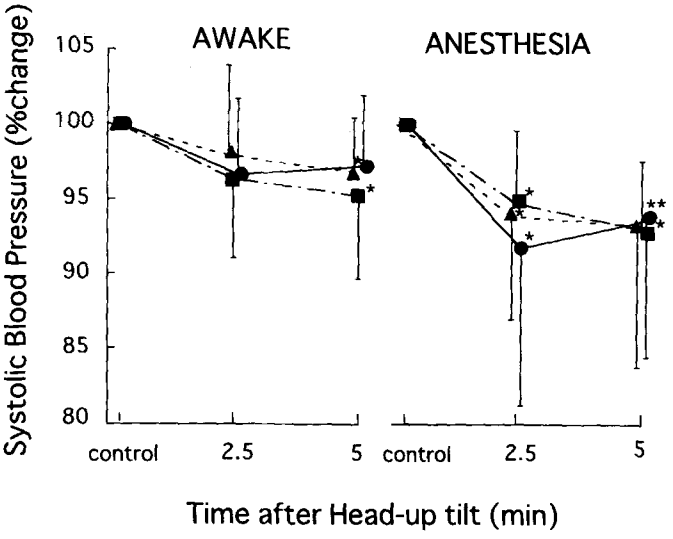

Fig. 1. Mean percent changes in systolic blood pressure (SBP) in awake patients and under 2 minimum alveolar concentrations (MAC) anesthesia with halothane (*squares*), isoflurane (*triangles*), or sevoflurane (*circles*). $^{*}P < 0.05$ within group (*vs* control). After head-up tilt, signficant increases in SBP were found at 5 min in the halothane an isoflurane groups in the awake state and at 2.5 and 5 min in all three groups in the anesthetized state

Table 1. Patient data

	Halothane group ($n = 8$)	Isoflurane group ($n = 8$)	Sevoflurane group ($n = 8$)
Age (years)	34 ± 8	34 ± 9	38 ± 14
Weight (kg)	51.4 ± 6.3	51.0 ± 9.2	57.3 ± 8.6
Height (cm)	157.7 ± 5.8	160.1 ± 8.2	157.9 ± 9.3

Values are expressed as mean ± SD.

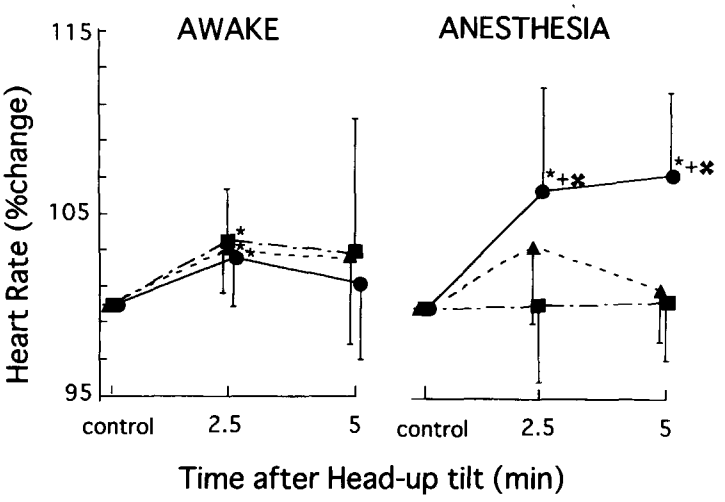

Fig. 2. Mean percent changes in heart rate (HR) in awake patients and under 2 MAC anesthesia with halothane (*squares*), isoflurane (*triangles*), or sevoflurane (*circles*). *Asterisk*, $P < 0.05$ within group (*vs* control); *plus sign*, $P < 0.05$ between sevoflurane and isoflurane groups; *Maltese cross*, $P < 0.05$ between sevoflurane and halothane groups. After head-up tilt, significant increases in HR were found at 2.5 min in all three groups in the awake state, and at 2.5 and 5 min only in the sevoflurane group in the anesthetized state

Table 2. Effect of anesthetics on SBP, DBP, HR, and serum NE during head-up tilt

	Awake			Anesthesia		
	Control →	2.5 min	5 min	Control →	2.5 min	5 min
Halothane group (n = 8)						
SBP (mmHg)	110.0 ± 6.3	105.8 ± 6.7	104.6 ± 6.6*	91.4 ± 10.1	86.5 ± 10.1*	84.9 ± 8.9*
DBP (mmHg)	59.9 ± 4.4	61.8 ± 3.9	60.3 ± 5.9	52.5 ± 10.2	48.0 ± 6.6	48.0 ± 3.8
HR (bpm)	62.6 ± 10.6	64.6 ± 10.7*	63.9 ± 8.6	59.0 ± 6.5	59.1 ± 7.3	59.2 ± 7.4
NE (pg·ml^{-1})	121.9 ± 71.4		123.4 ± 53.9	297.6 ± 175.3		292.5 ± 153.2
Isoflurane group (n = 8)						
SBP (mmHg)	117.5 ± 11.6	114.9 ± 10.7	113.6 ± 11.8*	96.1 ± 18.8	90.8 ± 21.6*	90.0 ± 21.0*
DBP (mmHg)	64.8 ± 9.8	66.0 ± 7.4	63.6 ± 8.4	52.5 ± 10.2	48.0 ± 6.6*	48.0 ± 3.8*
HR (bpm)	68.5 ± 12.5	70.4 ± 12.1*	70.1 ± 12.8	79.1 ± 10.8	82.1 ± 13.8	80.0 ± 11.7
NE (pg·ml^{-1})	159.9 ± 80.3		137.4 ± 66.9	289.3 ± 48.4		289.8 ± 51.0
Sevoflurane group (n = 8)						
SBP (mmHg)	119.3 ± 14.6	114.9 ± 10.9	115.6 ± 11.6	97.5 ± 10.6	89.6 ± 15.1*	91.1 ± 12.5*
DBP (mmHg)	66.5 ± 8.8	67.5 ± 9.7	67.9 ± 10.3	52.6 ± 12.8	49.6 ± 13.9	48.8 ± 13.9*
HR (bpm)	65.1 ± 5.8	66.8 ± 5.7*	65.8 ± 4.6	68.6 ± 7.9	72.9 ± 7.4*	73.5 ± 7.8*
NE (pg·ml^{-1})	148.8 ± 81.8		170.3 ± 100.8	210.4 ± 76.5		221.6 ± 64.2

Values are expressed as mean ± SD.
SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; NE, serum norepinephrine.
*$P < 0.05$ *vs* control.

tance. The former is composed of preload, afterload, and cardiac contractility. When patients are brought to the head-up tilt position, preload declines abruptly due to a reduction in the cardiac return of venous blood [6]. The baroreflex plays an important role in restoring blood pressure. In the present study, the degree of head-up tilt was limited to 10°.

In this study, the degree of SBP change was larger in the anesthetized state than in the awake state, especially at 2.5 min after tilting. Heart rate increased significantly at 2.5 min after patients were placed in the head-up tilt position in the awake state, showing an active response of the baroreflex. These findings agree with those of a previous study in that in the awake state, blood pressure did not change as remarkably as in the anesthetized state, and it remained almost constant during the tilting test. Osumi et al. mentioned that this rapid regulation of arterial pressure may be induced directly by the higher central nervous system [7].

In anesthetized patients in the supine recumbent position, systolic blood pressure decreased significantly. No difference was observed among the three groups. The results indicated that all three anesthetics depressed the circulatory system. The systolic blood pressure declined significantly at 2.5 and 5.0 min after head-up tilt in all three groups. The heart rates remained unchanged in the halothane and isoflurane groups. However, the sevoflurane group showed signifi-

cant elevations of the heart rate at 2.5 and 5.0 min after head-up tilt position.

The baroreflex consists of the receptor function, afferent nerve pathway, central nervous system, efferent nerve pathway, and effector organs. Under halothane anesthesia, the baroreceptor itself is more sensitive, but other components of the reflex arc (the central nervous system, efferent nerve pathway, and cardiac chronotropic function) are depressed, and the net effect is inhibition of the baroreflex [8–10]. Kimura et al. reported that halothane markedly depresses sympathetic cardiac activity and arterial baroreflex control of heart rate in a dose-dependent manner [11]. Palmisano et al. reported, in an animal study, that 1 MAC and 1.5 MAC halothane reduced baroreflex sensitivity by approximately 80%–90% of conscious values [10]. Kotrly et al. reported, in a human study, that 1 MAC isoflurane diminished baroreflex sensitivity to about 70% of conscious values and 1.5 MAC isoflurane, to 42% of conscious values, while 1.25 MAC halothane nearly abolished baroreflex sensitivity [2]. Attenuation of the baroreflex by isoflurane was reported to be weaker than that induced by halothane. This was in part attributed to the increased heart rate caused by isoflurane [12].

The present study showed a reduction of systolic blood pressure with 2 MAC of sevoflurane before the change in position, and reflex tachycardia after the change to the head-up tilt position. The results suggested a possible restoration of the baroreflex. The effects of sevoflurane on the baroreflex are remains unknown. But Nagayama reported that the baroreceptor system had a strong influence on renal sympathetic nerve activity even under 2 MAC sevoflurane in rats [13]. This report indicates that sevoflurane may have a weaker influence on the baroreflex. Our results confirmed those of other findings that halothane and isoflurane depressed baroreflex control of the heart rate while sevoflurane did not affect it as much under 2 MAC anesthesia.

In conclusion, sevoflurane anesthesia induced reflex tachycardia when the patient's position was changed from the supine recumbent to the head-up tilt position, suggesting a possible maintenance of baroreflex control of the heart rate.

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