Comparison of haemodynamic changes induced by sevoflurane and halothane in paediatric patients

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The purpose of this study is to investigate the haemodynamic effects of 1 MAC and 2 MAC of sevoflurane in children in comparison with halothane. Thirty-eight children (aged from one to six years, average age: 3.6 ± 0.2 yr) were randomly assigned to four groups, depending on the dose and agent (1 and 2 MAC of sevoflurane: S1 and S2; 1 and 2 MAC of halothane: H1 and H2, respectively). After collecting control data during 0.2 MAC of either anaesthetic, end-expired anaesthetics were kept at 1 MAC or 2 MAC for 15 min. Mean blood pressure (mBP) and stroke volume index (SVI), measured by impedance cardiometry, decreased in all groups without differences between groups. Heart rate (HR) increased in groups S1, S2 and H2 but not in group H1. The HR in S2 was higher than that in H2. The cardiac index (CI), a product of SVI and HR, tended to decrease but not significantly in all groups. These results suggested that the haemodynamic depressant effects of sevoflurane in children were similar to those of equipotent halothane concentration except for HR.

Cette étude vise à comparer, avec celles de l'halothane, les répercussions sur l'hémodynamique des enfants du sévoflurane à MAC 1 et 2. Trente-huit enfants (âgés de un à six ans, en moyenne $3,6 \pm 0,2$ ans) sont répartis au hasard en quatre groupes, selon la concentration et l'agent (S1 et S2: sévoflurane MAC 1 et 2; H1 et H2: halothane MAC 1 et 2 respectivement).

Key words

ANAESTHESIA: paediatric;

ANAESTHETICS, VOLATILE: sevoflurane, halothane;

MEASUREMENT TECHNIQUES: cardiac output, impedance cardiometry;

HEART: cardiac output, stroke volume.

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Après le recueil des données de contrôle pendant une anesthésie à MAC 0,2, la concentration téléexpiratoire de l'anesthésique est maintenue à MAC 1 ou 2 pour 15 min. La pression artérielle moyenne (PAM) et l'index systolique (IS), mesuré par la cardiométrie par impédance, diminue dans tous les groupes et sans présenter de différences entre les groupes. La fréquence cardiaque (Fc) augmente dans les groupes S1, S2 et H2 mais pas dans le groupe H1. La Fc dans S2 est plus élevée que dans H2. L'index cardiaque, le produit de IS et de Fc, tend à diminuer mais non significativement dans tous les groupes. Ces résultats suggèrent que les effets déprimeurs sur l'hémodynamique du sévoflurane chez les enfants sont identiques à ceux d'une concentration équivalente d'halothane.

Sevoflurane is used in paediatric anaesthesia^{1,2} because of its small blood-gas partition coefficient (0.63),³ which enables rapid induction of, and rapid emergence from anaesthesia. Paediatric patients have a relatively high minimum alveolar concentration (MAC) of volatile anaesthetics that may cause marked haemodynamic depression, especially in neonates and infants.⁴⁻⁷ In mongrel dogs, sevoflurane decreases cardiac output (CO) and mean blood pressure (mBP) without change in the heart rate (HR).⁸ The MAC of sevoflurane in children is much higher (2.49%)^{2,9} than that in adults (1.71–2.05%).^{10,11} However, there are no reports of haemodynamic effects of sevoflurane in paediatric patients receiving high concentrations of sevoflurane. The purpose of this study was to compare the haemodynamic effects of sevoflurane and halothane in paediatric patients by using impedance cardiometry, a noninvasive method to measure CO and stroke volume (SV).

Methods

After approval by the Ethics Committee of Sapporo Medical University, agreement was obtained from the parents of patients, to whom this study was fully explained. The investigation was carried out in 38 patients (from one to six years old) of ASA class I, who were to undergo

surgery for strabismus or adenotonsilectomy. They were fasted overnight but were allowed free access to clear fluid until three hours before operation. They received premedication with a bromazepam 1.5 to 3 mg suppository. On arrival in the operating room, their sedation was evaluated by a four grade score: (1) sleeping or sleepy, (2) sedated, (3) alert and (4) excited. Patients of grade 4 were excluded from the study. The remaining patients were randomly assigned to four groups, depending on the dose and agent (1.0 and 2.0 MAC of sevoflurane: S1 and S2; 1.0 and 2.0 MAC of halothane: H1 and H2, respectively). In this study, 1 MAC sevoflurane and halothane were defined as 2.49%⁹ and 0.91%,¹² respectively. Anaesthesia was induced with oxygen 2 L · min⁻¹, nitrous oxide 4 L · min⁻¹ and 1 to 2 MAC of sevoflurane or halothane, depending on the group. After an *iv* catheter was placed and vecuronium 0.1 mg · kg⁻¹ was given *iv*, all anaesthetic agents were discontinued and the lungs were manually ventilated with 100% oxygen until the end-expired concentrations of sevoflurane or halothane were reduced to 0.2 MAC. End-expired anaesthetic agent and CO₂ concentrations, sampled from the oral cavity at a rate of 200 ml · min⁻¹, were measured with an anaesthetic gas monitor (5250 RGM, Ohmeda Co. USA). The CO and SV were measured by impedance cardiometry (NCCOM 3, BoMed LTD, USA) and cardiac index (CI) and stroke volume index (SVI) were calculated. The mBP, measured by the oscillometric method, and HR were monitored with a patient monitor (BP308E, Coline Co., Japan). The anaesthetic agent concentrations were then increased to 3% in group S1, 6% in S2, 1.5% in H1 and 2.5% in H2 until the end-expired concentration reached the MAC assigned to the group. Thereafter, the inspiratory concentration was controlled to maintain the assigned end-expired concentrations until the end of the measurement. In the first several cases, measurement was continued for 20 min. However, as no further haemodynamic changes were found after 15 min, the measurement was terminated at 15 min. The end-expired CO₂ was controlled within 35 to 40 mmHg through the measurement.

All results are expressed as mean ± SEM. Data were analyzed by the Kruskal-Wallis test for patients' characteristics and by repeated-measure ANOVA for haemodynamic variables among groups. Dunnett's *t* test was used to compare haemodynamic variables between control and measurement points. A *P* value of less than 0.05 was considered statistically significant.

Results

There were no demographic differences among the groups (Table I). The end-expired CO₂ and concentrations of anaesthetic agents were maintained within the assigned

TABLE I Demographic data

	<i>n</i>	Age (yr)	Body weight (kg)	Height (cm)	Sedation score
S1	9	4.0 ± 0.3	17.6 ± 1.0	102.8 ± 1.6	2
S2	10	3.6 ± 0.4	16.5 ± 1.2	103.2 ± 3.3	2
H1	9	3.7 ± 0.4	15.6 ± 0.8	96.0 ± 2.7	2
H2	10	3.6 ± 0.6	15.6 ± 1.1	109.9 ± 4.5	2

All results are expressed as mean ± SEM except the sedation score which is presented as the mode. S1; 1 MAC sevoflurane, S2, 2 MAC sevoflurane, H1; 1 MAC halothane, H2, 2 MAC halothane, PETCO₂; end-expired CO₂, mBP; mean blood pressure, HR; heart rate, SVI; stroke volume index, CI; cardiac index.

ranges through the measurement. Control data of haemodynamic variables were shown in Table II.

The mBP decreased at the end of measurement in all groups (*P* < 0.05 in S1 and H1, *P* < 0.01 in S2 and H2). Changes in mBP were not different among the groups (Figure).

The SVI decreased at the end of measurement of all groups except group S1. The SVIs in the 2 MAC groups were lower than those in 1 MAC groups. (S1 vs S2, H1 vs H2, *P* < 0.01) (Figure).

The HR increased in S1, S2 and H2, but not in H1. The HR at the end of measurement was higher in group S2 than in group H2 (135.3 ± 4.2 beats · min⁻¹ in S2 vs. 114.4 ± 4.8 beats · min⁻¹, *P* < 0.01) (Figure).

The CI, the product of SVI and HR, tended to decrease in all groups but not significantly and there were no differences among groups (Figure).

Discussion

The standard method of CO measurement in adults has been thermodilution, which is rarely applied to children without an absolute indication. In haemodynamic studies in children or infants, echocardiography and Doppler ultrasound are widely used.⁴⁻⁶ Although these methods measure CO noninvasively, a skilled hand is necessary to obtain reproducible results because it is critical to avoid changing the position and direction of the probe during measurement. We used impedance cardiometry, which also measures SV and CO noninvasively.^{7,13-15} Two pairs of voltage-sensing electrodes and two pairs of current injection electrodes were attached to the lateral basis of the neck and the lateral thorax at the level of the xiphoid process. In adults, the CO thus obtained has a high correlation with that obtained by thermodilution.¹² Although some bias was reported in measurement of CO and SV in paediatric patients,¹⁴ the control value of SVI in this study were 24.9 to 30.7 ml · m⁻², which corresponds to those obtained by echocardiography in previous reports.⁵ In addition, trends of SVI and CI measured

TABLE II Control values of haemodynamic variables and PETCO₂

	PETCO ₂ (%)	mBP (mmHg)	HR (beat · min ⁻¹)	SVI (ml · m ⁻²)	CI (L · min ⁻¹ · m ⁻²)
S1	38.5 ± 0.8	74.9 ± 0.9	88.1 ± 1.9	29.6 ± 2.0	2.69 ± 0.20
S2	35.3 ± 2.5	73.3 ± 1.7	95.4 ± 4.6	24.9 ± 2.8	2.44 ± 0.20
H1	34.6 ± 1.4	73.1 ± 1.7	87.7 ± 2.5	30.7 ± 2.0	2.63 ± 0.15
H2	37.5 ± 2.8	76.4 ± 2.5	99.7 ± 3.4	27.4 ± 3.0	2.77 ± 0.4

FIGURE Haemodynamic changes with sevoflurane and halothane. All results are presented as mean $\pm$ SEM. Open squares; 1 MAC sevoflurane, closed squares; 2 MAC sevoflurane, open circles; 1 MAC halothane, closed circles; 2 MAC halothane; mBP, mean blood pressure, HR; heart rate, SVI; stroke volume index, CI; cardiac index. *, ** $P < 0.05$, 0.01 vs control, # $P < 0.01$ vs 1 MAC sevoflurane, † $P < 0.01$ vs 1 MAC halothane.

by impedance cardiometry are clinically relevant because technical bias no longer occurs after starting measurement.

The results clearly showed that SVI was depressed with both sevoflurane and halothane in a dose-dependent fashion. The magnitude of the decrease in SVI with 1 MAC halothane corresponded to that in a previous report.⁵ Although myocardial depression with halothane or isoflurane in infants and children has been investigated,³⁻⁷ the effects of sevoflurane on myocardial function has only been reported in adults and animal experiments. Kazama and Ikeda⁸ reported that left ventricular dp/dt max de-

creased as the sevoflurane concentration increased in mongrel dogs. Kikura and Ikeda¹⁶ also reported that sevoflurane/nitrous oxide depressed myocardial contractility in adults. Although preload changes were not evaluated, these results suggest that myocardial depression is predominant for the sevoflurane-induced decrease in SVI observed in this study.

The HR increased in all groups except H1 in a dose-dependent fashion. The difference in HR between groups S2 and H2 was significant, while mBP decreased to a similar extent in both groups. Changes in HR with halothane were consistent with previous reports.^{4,5} Lerman *et al.*² reported that 1 MAC sevoflurane increased HR moderately in children older than three years. Heart rate is influenced by many factors, such as preoperative condition, premedication and the induction method. There was no difference in the level of preoperative sedation among the groups (Table I). Bromazepam, used for premedication, is a benzodiazepine,¹⁷ which has little haemodynamic effect in the suppository dose of 1.5 to 3.0 mg. The baroreflex, which is one of the mechanisms for increasing HR when BP is decreased, is attenuated by halothane.^{18,19} This may explain why HR increased only moderately despite decreases in mBP in the halothane groups. There are no reports of the effects of sevoflurane on the baroreflex. Thus, baroreflex preservation during sevoflurane anaesthesia may increase the HR in response to decreasing blood pressure. Another possible mechanism increasing HR with sevoflurane is airway irritation. Among volatile anaesthetics, isoflurane and desflurane are reported to activate the sympathetic nervous system and consequently increase HR.^{21,21} Airway irritation is considered to be one of the mechanisms causing tachycardia. Although sevoflurane is less irritant,² the high concentration used in this study may have increased HR through a mechanism similar to that of isoflurane or desflurane.

In the haemodynamic comparison of sevoflurane and halothane, HR was the only variable different between the groups. In the experiment with mongrel dogs, mBP, CI, systemic vascular resistance and dp/dt max decreased similarly in both agents up to 2 MAC. Halothane has little effects on vascular resistance in adults.²² Such an effect, however, was not confirmed in infants or children.

It is difficult to evaluate directly changes in preload with both impedance and echocardiography.⁵ More precise investigation is necessary to clarify the difference in preload or vascular resistance among groups, if any.

The conditions under which control data are obtained are important in paediatric research. Although control data were often obtained before induction of anaesthesia,^{2,4-6} setting up the measurement equipment often makes children apprehensive and they become excited or cry. Thus, we measured control data during light anaesthesia. This could have resulted in underestimating the mBP, SVI and CI changes. We did, however, observe changes in mBP and SVI. In contrast, changes in HR might be emphasized in comparison with previous reports.^{2,5} A recent report suggested that the MAC awake of sevoflurane is 0.3 in children,²³ which is slightly higher than the MAC during our control data collection. However, no children complained of unpleasant experiences or remembered events during data collection.

In this study, we maintained a constant end-expired concentration for 15 min, which allows sevoflurane to equilibrate in the brain.⁹ In addition, we observed that haemodynamic variables in some cases had already reached a stable state 15 min after induction even in the halothane groups. Thus, the results in this study were not different from those observed after long-term equilibration.

End-expired gas was sampled from the oral cavity to reduce entrained inspired gas. The lungs were manually ventilated at a slow rate (≤ 20 breaths $\cdot$ min⁻¹) with a relatively large tidal volume.²⁴ This manoeuvre prevented contamination by inspiratory gases, in which the agent concentrations were higher than in expired gas. Although sampling from a tracheal tube is more accurate, the trachea was not intubated to avoid haemodynamic changes during measurement.

In summary, the haemodynamic effects of 1 MAC and 2 MAC of sevoflurane and halothane were investigated in 38 children. Both volatile anaesthetics decreased mBP, SVI and increased HR in a dose-dependent fashion. The CI tended to decrease, but not significantly, in all groups. There were no differences in haemodynamic variables between the sevoflurane and halothane groups except in HR. The increase in HR in the 2 MAC sevoflurane groups was higher than that in the 2 MAC halothane group, resulting in attenuation of the decreased CI.

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