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A comparison between sevoflurane and propofol when combined with continuous epidural blockade in adult patients

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Abstract

Purpose. The effects of sevoflurane and propofol, in combination with continuous epidural blockade, on blood pressure control and time of recovery from anesthesia were compared.

Methods. Adult patients were allocated to either a sevoflurane ($n = 54$) or a propofol ($n = 64$) group. Anesthesia was induced with either inhalation of 5% sevoflurane or intravenous administration of 2 mg·kg^{-1} propofol. After an injection of vecuronium, the trachea was intubated and anesthesia was maintained with continuous epidural blockade, air/oxygen, and sevoflurane or propofol. The systolic arterial pressure was maintained within ±30% of that obtained on the ward.

Results. The number of cases requiring a change in the dose of either anesthetics or vasoactive agents was not different between the groups. However, the arterial pressure and heart rate were more stable in the propofol group than in the sevoflurane group ($P < 0.05$). The length of time before tracheal extubation was shorter in the sevoflurane group (10.4 ± 5.2 min, mean ± SD) than the propofol group (15.0 ± 11.2 min, $P < 0.05$).

Conclusion. Propofol anesthesia, in combination with continuous epidural blockade, results in more stable intraoperative hemodynamics than sevoflurane anesthesia, but requries a longer recovery time and results in larger interindividual variability than sevoflurane anesthesia.

Key words: Epidural anesthesia, Sevoflurane, Propofol, Comparative study

Introduction

A new balanced general anesthesia, which combines epidural blockade for analgesia, muscle relaxants, and general anesthetic agents, is widely used in Japan. In selecting a general anesthetic agent, the following factors must be considered. First, this method of anesthesia is based on the assumption that the efficient prevention of nociceptive input into the spinal cord by epidural blockade diminishes stress responses during surgery and provides sufficient postoperative analgesia. However, this assumption is not always reliable. Segawa et al. [1] reported that sensory blockade at least as high as the second cervical level is required to block nociceptive volleys and diminish the rise of blood levels of corticotropin during upper abdominal surgery and that nociceptive volleys may be partially transmitted through the phrenic nerves. Further, there is no reliable monitoring method to identify the level of sensory inhibition by epidural blockade during general anesthesia. Second, epidural anesthesia cannot block either the stimuli caused by tracheal intubation or the stimuli from the upper airway caused by an endotracheal tube and ventilation. This indicates that epidural anesthesia cannot completely block stimuli during anesthesia. Therefore, the anesthetic agent must be able to suppress stimuli-induced responses to supplement the epidural blockade as well as maintain loss of consciousness. Third, epidural anesthesia induces hypotension by its sympathetic blocking actions. A given anesthetic agent may also cause hypotension. If hypotension is treated by decreasing the dose of anesthetic agent too much, consciousness will be regained. Therefore, a certain minimum dose of anesthetic should be maintained and a vasopressor injection used.

Sevoflurane and propofol are candidates for the anesthetic agent used in combination with epidural blockade, because the blood levels of both can be effectively controlled. In the present study, we compared the effects of sevoflurane and propofol as an anesthetic agent combined with continuous epidural blockade in adult patients. Systolic arterial blood pressure was maintained by controlling the dose of anesthetic agents,

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or if this failed, by the administration of vasoactive agents. We compared the frequency of change in the dose of anesthetic agents, the dose of vasoactive agents, and the recovery time from anesthesia.

Materials and methods

After approval by the Institutional Human Study Committee, 123 ASA physical status I and II patients provided informed consent and were admitted to the study. All patients were over 15 years of age and were undergoing elective abdominal or lower limb surgery. Patients were excluded from the study if they had a contraindication to epidural anesthesia, sevoflurane, or propofol. The patients were randomly allocated to the sevoflurane group ($n = 56$) or the propofol group ($n = 67$).

The patients received 0.5 mg of atropine sulfate i.m. 1–2 h before the induction of anesthesia. An epidural catheter was inserted at an appropriate level for the surgery. Lidocaine, 2 ml of 2% solution, was injected as a test dose. The sensory block levels were assessed with a cold test using diethylether 10 min after administration of the test dose. Induction of anesthesia was performed with 5% sevoflurane in oxygen delivered by a mask in the sevoflurane group or with 2 mg·kg^{-1} propofol i.v. in the propofol group. Following loss of response to verbal command, the inhaled concentration of sevoflurane was maintained above 3% in oxygen, or the dose of propofol was set at 8 mg·kg^{-1}·h^{-1}. The trachea was intubated with the aid of 6–8 mg of vecuronium i.v. Vecuronium was administered as required during surgery. Following tracheal intubation, the inhaled concentration of sevoflurane was set at 1.5% and the dose of propofol was set at 6 mg·kg^{-1}·h^{-1}. The inhaled concentration of oxygen was adjusted by adding compressed air so as to keep the arterial hemoglobin saturation for oxygen over 98%, as monitored with a pulse oximeter (Nellcor, N-200, Hayward, California, USA). Following administration of the appropriate dose of lidocaine into the epidural catheter before skin incision, the volume of 2% lidocaine infused for epidural blockade was set at either 3–5 ml·h^{-1} when the catheter was inserted at the thoracic level, or 4–7 ml·h^{-1} when the catheter was inserted at the lumbar level. The administration of lidocaine was continued until the patient recovered the response to verbal command after surgery. During surgery, the inhaled concentration of sevoflurane and the dose of propofol were adjusted so as to keep the systolic arterial pressure within ±30% of that obtained on the ward, as follows: If the systolic blood pressure rose above 130% of that on the ward or over 180 mmHg, the inhaled concentration of sevoflurane was increased by 0.5% or the dose of propofol was increased by 1 mg·kg^{-1}·h^{-1} following a bolus injection of 10 mg. If the systolic blood pressure decreased below 70% of that on the ward or under 70 mmHg, the inhaled concentration of sevoflurane was reduced by 0.5% or the dose of propofol was reduced by 1 mg·kg^{-1}·h^{-1}. If the dose of sevoflurane or propofol was changed, the systolic blood pressure was measured 2 min later. The range of doses was set at 1%–3% for sevoflurane and 4–8 mg·kg^{-1}·h^{-1} for propofol. If the systolic blood pressure could not be controlled by adjustment of the anesthetic agent within this range of doses, 1 mg of nicardipine or 5 mg of ephedrine was administered i.v. If the heart rate was below 50 min^{-1}, 0.25–0.5 mg of atropine sulfate was administered i.v. If the heart rate continued above 120 min^{-1} for 10 min or above 140 min^{-1} for 5 min, propranolol was administered i.v. The inhaled concentration of sevoflurane was maintained at 1% and propofol was infused at 4 mg·kg^{-1}·h^{-1} for the final 30 min, and the administration of sevoflurane or propofol was discontinued at the time of skin closure after the reversal of muscle relaxation. The patients were extubated after confirmation of sufficient recovery of consciousness and stable circulatory and respiratory states.

The mean arterial pressure and heart rate were recorded on the ward; before induction of anesthesia; just before and after tracheal intubation; before skin incision; 2, 30, and 60 min after skin incision; 10 min before skin closure; at skin closure; and at the time of recovery of response to verbal command. Measurements were made of the times taken before a response to verbal command and before tracheal extubation after discontinuation of anesthetics.

If the patient complained of pain after tracheal extubation or if control of arterial pressure according to the protocol was impossible (such as in massive blood loss), the cases were excluded from the data analysis.

Data are presented as mean ± SD (range). Comparisons of blood pressure, heart rate, time for recovery, and time for extubation between the groups were carried out with the unpaired t-test. The Mann-Whitney U test was used for comparison of the frequency of changes in the dose of anesthetic agents and vasoactive agents, and the chi-squared test for comparison of the number of cases requiring vasoactive agents and for excluded cases. The propofol group was further divided into two subgroups arrording to the time for extubation: less than or more than 20 min. Comparisons between the two subgroups of the duration of surgery, distribution of types of surgery, age, and obesity were made using the unpaired t-test or the chi-squared test. Comparisons of blood pressure and heart rate within groups were made using a repeated-measures analysis of variance with Bonferroni's correction of the paired t-test. Differences yielding critical values corresponding to

$P < 0.05$ were considered statistically significant in each comparison.

Results

Two cases in the sevoflurane group were excluded from the study because of arrhythmia (atrial fibrillation) and unexpected body movements, and three cases in the propofol group were excluded because of uncontrollable hypertension (two cases) and body movement and blood loss (one case). The number of cases used for analyzing the data was 54 in the sevoflurane group and 64 in the propofol group. The demographic data for the patients in each group are shown in Table 1. There were more female than male patients in both groups, but the proportion of females to males did not differ between the groups. There were no differences between the groups in any of the measured factors.

The changes in mean arterial pressure are shown in Fig. 1. The mean arterial pressure rose after tracheal intubation and skin incision, and at the time of recovery of response to a verbal command in both groups. The sevoflurane group had a higher mean arterial pressure than the propofol group at these points. The changes in heart rate are shown in Fig. 2. The sevoflurane group had a higher heart rate than the propofol group following tracheal intubation, 2 and 60 min after skin incision, and at the time of recovery of response to a verbal command.

The indices of the ability to control blood pressure are shown in Table 2. There were no differences between the groups.

Table 1. Demographic data for patients

Feature	Sevoflurane	Propofol
No. of cases	54	64
Sex (M/F)	20/34	20/44
Age (years)	51 ± 11	53 ± 13
Height (cm)	158 ± 8	156 ± 8
Weight (kg)	57 ± 10	55 ± 9
ASA physical status (I/II)	31/23	34/30
Patients with hypertension	6	6
Patients with diabetes mellitus	2	4
Type of surgery		
General	30	33
Gynecological	21	27
Orthopedic	2	4
Urological	1	0
Blood loss during surgery (g)	330 ± 613	279 ± 283
Fluid loaded (ml)	1537 ± 821	1760 ± 888
Blood transfused (ml)	72 ± 342	26 ± 112
Urine output (ml)	336 ± 297	409 ± 281
Total dose of 2% lidocaine (ml)	19 ± 17	21 ± 19
Duration of anesthesia (min)	166 ± 89	171 ± 75

Values are expressed as means ± SD or number of cases.

The length of time from the discontinuation of anesthetic agents to the recovery of response to a verbal command was 6.5 ± 4.1 (1–21) min in the sevoflurane group and 8.4 ± 7.1 (1–35) min in the propofol group

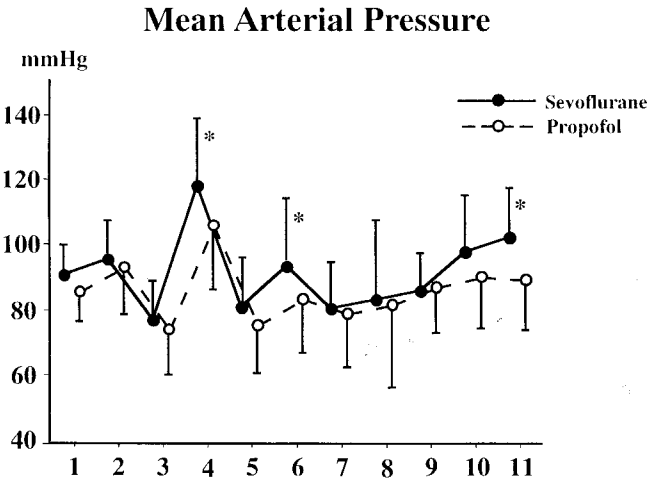

Fig. 1. Changes in mean arterial pressure during sevoflurane or propofol anesthesia in combination with continuous epidural blockade. *1*, Control; *2*, before induction; *3*, before tracheal intubation; *4*, 2 min after intubation; *5*, before skin incision; *6*, 2 min after skin incision; *7*, 30 min after skin incision; *8*, 60 min after skin incision; *9*, 10 min before end of surgery; *10*, end of surgery; *11*, recovery of response to verbal command. Values are means ± SD. $*P < 0.05$ sevoflurane *vs* propofol

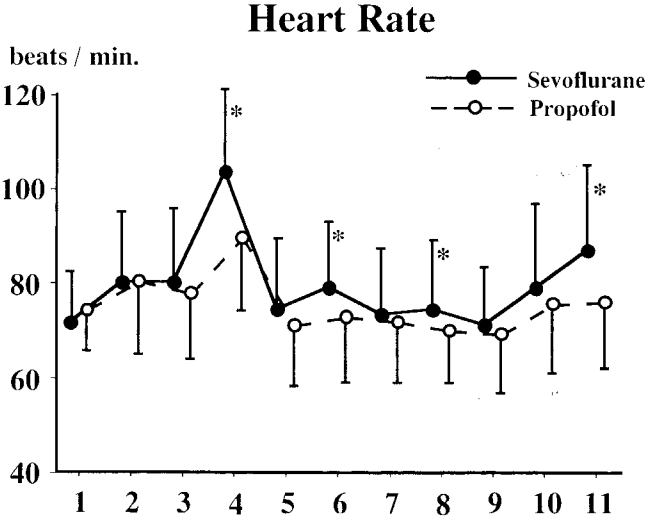

Fig. 2. Changes in heart rate during sevoflurane or propofol anesthesia in combination with continuous epidural blockade *1*, Control; *2*, before induction; *3*, before tracheal intubation; *4*, 2 min after intubation; *5*, before skin incision; *6*, 2 min after skin incision; *7*, 30 min after skin incision; *8*, 60 min after skin incision; *9*, 10 min before end of surgery; *10*, end of surgery; *11*, recovery of response to verbal command. Values are means ± SD. $*P < 0.05$ sevoflurane *vs* propofol

Table 2. Indices of ability to control blood pressure

Index	Sevoflurane (n = 54)	Propofol (n = 64)
Cases requiring a change in dose	35	40
Increase	24	31
Decrease	33	28
Frequency of change in dose	3.0 ± 2.3 (1 ~ 10)	2.9 ± 12.1 (1 ~ 10)
Cases requiring use of vasoactive agents	20	24
Cases in which ephedrine was used	19	17
Frequency of using ephedrine in each case	1.7 ± 0.9 (1 ~ 4)	1.5 ± 0.9 (1 ~ 3)
Cases in which nicardipine was used	4	9
Frequency of using nicardipine in each case	1.5 ± 1.0 (1 ~ 3)	2.1 ± 1.3 (1 ~ 4)
Cases in which atropine was used	4	5

Values are means ± SD or number of cases.

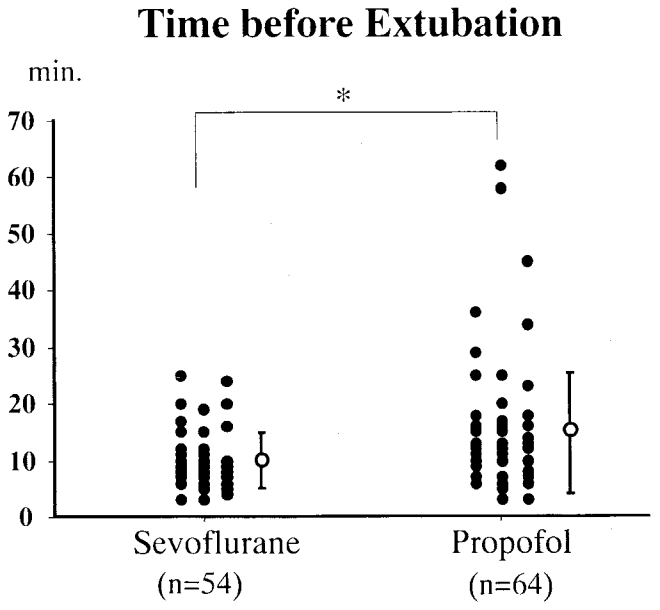

Fig. 3. Length of time before extubation from sevoflurane or propofol anesthesia. Each *dot* indicates length of time before extubation. Bars indicate means ± SD. *$P < 0.05$ sevoflurane *vs* propofol

(difference not significant). The length of time before tracheal extubation in the sevoflurane group (10.4 ± 5.2 min, 3–25 min) was shorter than that in the propofol group (15.0 ± 11.2 min, 3–62 min, $P < 0.05$). In both of these assessments, the time of recovery from anesthesia in the propofol group showed large interindividual variations (Fig. 3). The factors that might influence the time for recovery from propofol anesthesia (duration of surgery, type of surgery, age, and obesity) were not different in the cases requiring less than 20 min and those requring more than 20 min before extubation in the propofol group (data not shown).

Discussion

The present study shows that propofol is preferable to sevoflurane for achieving more stable hemodynamics during anesthesia, but that a more rapid recovery from anesthesia is achieved with sevoflurane anesthesia.

For a comparison between a volatile anesthetic and an intravenous anesthetic, we selected the most commonly used doses for maintaining anesthesia in combination with continuous epidural blockade: 1.5% for sevoflurane and 6 mg·kg^{-1}·h^{-1} for propofol. Although we did not assess the level of epidural blockade postoperatively, the dose of 2% lidocaine did not differ between the groups, and no patient complained of pain on emergence from anesthesia.

Following the induction of anesthesia, there was no significant difference in either arterial pressure or heart rate between the groups. This indicates that the basal depression of hemodynamics by anesthetics alone was similar. Smith et al. [2] reported that propofol had a greater suppressive effect than sevoflurane on the hemodynamics during induction of anesthesia. However, they did not report the dose of each agent, and nitrous oxide was added in the sevoflurane group, so we cannot compare their results with those of our study. The rise in arterial pressure and heart rate following tracheal intubation and skin incision was greater in the sevoflurane group than in the propofol group. Sevoflurane has weaker suppressive effects on the hemodynamic responses to tracheal intubation and skin incision than halothane [3]. We have also reported previously that the rise in blood levels of catecholamines during surgery was less in propofol anesthesia than in sevoflurane anesthesia when fentanyl was coadministered [4]. The mean arterial pressure during surgery did not show significant changes in propofol anesthesia, but it rose after skin incision in sevoflurane anesthesia. This shows that epidural anesthesia did not completely block the surgical stimuli in the present

study, and that propofol had greater suppressive effects on the hemodynamic response than sevoflurane at the doses used in this study.

The ability to control anesthesia was assessed by the frequency of change in dose of the anesthetic agent and by the requirement for vasoactive agents. These indices were comparable between the groups. Administration of ephedrine was required in about a third of the cases in both of the groups. This indicates that a combination of epidural blockade and sevoflurane or propofol commonly requires an aggressive treatment for hypotension. However, the mean frequency of injection of ephedrine was less than two, showing that ephedrine is effective for treating hypotension in both of the groups.

The time of recovery from anesthesia was short in both of the groups. Although the time required before recovery of response to a verbal command was similar in the two groups, that for tracheal extubation in the propofol group was significantly longer than in the sevoflurane group. Previous investigators reported that the recovery time from sevoflurane anesthesia was similar to [5] or shorter than [6,7] that from propofol anesthesia. The cause for the delay in tracheal extubation in the propofol group was mainly a delay in the recovery of stable respiration. Propofol has been reported to induce a longer period of apnea than thiopental when these anesthetics are used for induction of anesthesia [8]. The greater suppression of the respiratory center by propofol should be investigated in future studies. The present study showed a large interindividual variation in the length of time before tracheal extubation in the propofol group. Although the recovery time and the decrease in brain concentration are dependent on ventilation in the case of sevoflurane anesthesia, they are mainly dependent on liver metabolism and redistribution to other tissues in propofol anesthesia [9]. The possible factors expected to influence recovery time and cause such interindividual variability in propofol anesthesia are the duration of surgery, the type of surgery, age, and obesity. However, we were unable to identify the factors, possibly because of the small number of cases.

We conclude that propofol, in combination with continuous epidural blockade, achieves more stable hemodynamics but requires a longer recovery time and results in greater inter-individual variability than sevoflurane.

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