Comparison of the Effects of Etomidate and Propofol on Redistribution Hypothermia during General Anesthesia

Department of Anesthesiology and Pain Medicine, Seoul National University Bundang Hospital, Seongnam;
*Kyung Hee East-West Neo Medical Center; †Seoul National University Hospital, Seoul, Korea

Hee-Young Park, M.D., Jong-Man Kang, M.D.*, Young-Tae Jeon, M.D., In-Yong Choi, M.D.* †, Yong-Seok Oh, M.D., and Jung-won Hwang, M.D.

Background: Redistribution hypothermia can be modified by the effects of induction anesthesia on the systemic vascular resistance. This study compared the effects of etomidate and propofol on redistribution hypothermia during general anesthesia.

Methods: Forty patients were randomly allocated into one of two groups, based on the induction agent used: Group E (n = 20) received 0.2 mg/kg of etomidate and group P (n = 20) received 2.5 mg/kg propofol. After intubation, anesthesia was maintained with sevoflurane and 50% nitrous oxide in oxygen in both groups. The core and peripheral temperatures were measured, and the peripheral temperature gradients (forearm minus fingertip) were used as an index of an arteriovenous shunt.

Results: The patients in both groups demonstrated intense vasoconstriction prior to the induction of anesthesia with similar skin-temperature gradients. After induction, group P showed more rapid and significant vasodilatation than group E (P = 0.02). The difference in vasodilatation between the two groups disappeared after 5 minutes after intubation. The pre-induction core temperatures were similar in both groups. After induction, the core temperatures in group P were consistently lower than those in group E (P < 0.01). The core temperatures during the first hour of anesthesia decreased by 1.5 ± 0.4°C in group P but only by 0.9 ± 0.4°C in group E.

Conclusions: Propofol caused more rapid and aggravated redistribution hypothermia during surgery than etomidate due to the earlier arteriovenous shunt vasodilatation. (Korean J Anesthesiol 2006; 50: S 19–24)

Key Words: etomidate, general anesthesia, propofol, redistribution hypothermia.

INTRODUCTION

Redistribution hypothermia is an internal core-to-peripheral redistribution of body heat during the first hour after the induction of general anesthesia. It is associated with several adverse clinical outcomes, including postoperative shivering, increased blood loss, decreased drug metabolism and clearance, morbid myocardial outcomes, wound infection, and delayed recovery from anesthesia. Redistribution hypothermia results from anesthetic-induced central inhibition of tonic thermoregulatory vasoconstriction in the arteriovenous shunt and anesthetic-induced arterial and venous vasodilation.

Once redistribution of body heat occurred, the heat which had escaped to the peripheral tissues could not be recovered by the core, as heat does not move up a temperature gradient. In the early period of anesthesia, alterations in core temperatures due to difference in systemic vascular resistance (SVR) of induction agents can affect the ultimate severity of redistribution hypothermia occurred during the first hour after the anesthetic induction.

A major difference between etomidate and propofol has been observed in their impact on vasomotor tone. Etomidate results in a minimal degree of reduction in SVR, but propofol induces a severe drop in SVR. Accordingly, we tested the hypothesis that etomidate as an induction agent result in less redistribution hypothermia than propofol.

MATERIALS AND METHODS

Subsequent to approval from the Local Committees and the
acquisition of written informed consent, we studied 40 ASA physical status I-II patients undergoing laparoscopic cholecystectomy under general anesthesia. Obese patients, patients with thyroid or otologic disease, dysautonomia or Raynaud’s syndrome, those receiving vasodilating drugs, those in which the laparoscopic procedure was converted to an open cholecystectomy and those receiving vasoconstrictors during anesthetic induction were excluded from this study.

Upon patients’ arrivals at the reception room, their tympanic temperatures were taken with Thermoscan Plus Thermometer (Braun, Kronberg, Germany), in which accuracy provided by the manufacturer was ± 0.2°C. Mean value of triple-checked tympanic temperatures was recorded as the initial core temperature baseline measurement. None of the patients who had been enrolled in this study received any premedication. Prior to the induction of anesthesia, mean blood pressure and heart rate were checked and the patients’ peripheral temperatures were measured on the palmar side of the right index finger and lower arm. Skin surface thermometer probes (HP 21078A, Palo Alto, CA, USA), in which accuracy by our measurement were ± 0.1°C, were placed on the fingertip and midway between the wrist and elbow on the radial aspect of the forearm. The room temperature and humidity in the operating room were also measured.

40 patients were randomly assigned to one of two groups based on the induction agent using a sealed envelope method and a random-number table. Group E patients (n = 20) received 0.2 mg/kg of etomidate and Group P patients (n = 20) received 2.5 mg/kg of propofol. After confirming patients’ unconsciousness, an esophageal temperature probe (Deroyal, Powell, TN, USA) was inserted in accordance with the technique described by Kaufman for intraoperative core temperature measurement,10 in which accuracy provided by the manufacturer was ± 0.2°C. Rocuronium (0.6 mg/kg) was used to facilitate endotracheal intubation. The trachea was intubated approximately 4 minutes after induction. After intubation, anesthesia was maintained using 1-4 vol% end-tidal sevoflurane and intermittent injections of alfentanil (5μg/kg). The end-tidal PaCO₂ was maintained at approximately 35 mmHg. Fresh gas flows of oxygen (1 L/min) and N₂O (1 L/min) were administered using a semi-closed circular system without airway heating or humidification. Hartman solution, kept at room temperature, was administrated to both group patients by full dripping from administration of induction agents until tracheal intubation. After that time, administrated fluid volume was adjusted to approximately 4 ml/kg/hr. The patients were covered with a single surgical drape of synthetic cloth except right forearm and hand, which were left exposed throughout the procedure. No active warming systems were employed during the study period. Surgery began at 15-20 minutes after intubation.

In this study, total 3 anesthesiologists were enrolled. At anesthetic induction, propofol or etomidate was administrated to patients by only one anesthesiologist who knew the induction agent. Other two anesthesiologists (data-collecting personnel) without knowledge of the induction agent recorded core and peripheral temperatures in 40 patients equally. The peripheral temperatures were recorded before induction and every minute after induction until inhalation agent or other drug administered. After intubation, the core and peripheral temperatures were measured every 5 minutes for one hour. Heart rate, mean blood pressure and sevoflurane concentrations were monitored every 5 minutes throughout the study.

Skin-surface temperature gradients (forearm minus fingertip temperature gradients) were used as an index of hand arteriovenous shunt perfusion. As in previous studies,17 we considered a gradient below 0°C to indicate vasodilation.

A pilot study of 20 patients revealed that the standard deviation in core temperature taken 15 minutes after intubation was 0.43°C. In order to demonstrate a 0.4°C difference in mean core temperature between two groups as significant at the 0.05 level with a power of > 80%, we calculated that the study required a minimum of 20 patients per group. Results are expressed as means unless otherwise stated. Demographic and anesthetic data were compared using independent T-tests and chi-squared test, as appropriate. Continuous variables including core temperature, skin temperature gradients, heart rate, sevoflurane concentration and mean blood pressure were analyzed with repeated measures of ANOVA. A P value of < 0.05 was considered to be statistically significant.

RESULTS

The demographic data were similar between the two groups, including ambient temperature and humidity in the operating room, as well as the volume of fluid administered throughout the study period (Table 1).

Pre-induction core temperatures were similar in the two groups. After induction, there was significant difference in core temperature between groups (P < 0.01, Fig. 1). Core temperatures in the patients receiving propofol were signifi-
Table 1. Demographic and Anesthetic Data

<table>
<thead>
<tr>
<th></th>
<th>Group E (n = 20)</th>
<th>Group P (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>52 ± 7</td>
<td>50 ± 8</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>10/10</td>
<td>9/11</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>162 ± 7</td>
<td>161 ± 8</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>63 ± 7</td>
<td>60 ± 8</td>
</tr>
<tr>
<td>Ambient temperature in operation room (°C)</td>
<td>21.8 ± 0.6</td>
<td>21.9 ± 0.5</td>
</tr>
<tr>
<td>Humidity in operation room (%)</td>
<td>57 ± 1</td>
<td>57 ± 2</td>
</tr>
<tr>
<td>Operation time (min)</td>
<td>78 ± 20</td>
<td>76 ± 18</td>
</tr>
<tr>
<td>Total intravenous fluid (ml)</td>
<td>455 ± 146</td>
<td>478 ± 153</td>
</tr>
<tr>
<td>Total number of patients received alfentanil/total dose of alfentanil used (µg)</td>
<td>3/1000</td>
<td>2/600</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD. There are no differences in demographic and anesthetic data between groups. Group E: received etomidate 0.2 mg/kg as induction agent, Group P: received propofol 2.5 mg/kg as induction agent. Total intravenous fluid represents total volume of fluid administrated during one hour of anesthesia.

![](image1.png)

Fig. 1. Time course of core temperature. There is significant difference in temperature between groups (P < 0.01). Core temperature decreases more rapidly and severely in group P than in group E. ⁺: P < 0.01 vs value at baseline in each group. Group E: received etomidate 0.2 mg/kg as an induction agent, Group P: received propofol 2.5 mg/kg as an induction agent. Base: baseline, Intu: intubation.

Fig. 2. The change of forearm-fingertip temperature gradients after induction but before administration of sevoflurane or alfentanil. A gradient value below 0°C indicates vasodilation. There is significant difference in decrease of temperature gradients between groups (P = 0.02). ⁺: P < 0.05 vs before induction in each group. Group E: received etomidate 0.2 mg/kg as an induction agent, Group P: received propofol 2.5 mg/kg as an induction agent.

Significantly lower than those in the patients receiving etomidate (P < 0.01). One hour after intubation, core temperatures decreased from baseline by 1.5 ± 0.4°C in group P but only 0.9 ± 0.4°C in group E. After intubation, core temperatures were significantly different from baseline values in group P, whereas 10 minutes after intubation, core temperatures were significantly different in group E (P < 0.01).

The patients in both groups demonstrated intense vasoconstriction before induction of anesthesia with similar skin-temperature gradients (forearm minus fingertip). The gradients decreased quickly more after propofol administration than after etomidate (P < 0.05, Fig. 2). The patients receiving propofol already showed vasodilation 2 minutes after injection. In contrast, the patients receiving etomidate remained vasoconstricted 4 minutes after injection. The patients in both groups kept similarly vasodilated from 5 minutes after intubation and thereafter (Fig. 3).

There was no significant difference in mean blood pressure, heart rates and sevoflurane concentration between two groups (Fig. 4).

**DISCUSSION**

This study show that core temperature decreased significantly
more after induction with propofol than with etomidate and that hypothermia persisted for the duration of surgery.

The most likely explanation for the rapid and exaggerated hypothermia observed in group P, compared to group E, is that the drug induced a brief period of systemic vasodilation which facilitated the core-to-peripheral redistribution of body heat in early period of anesthesia, such as anesthetic induction. Once redistribution occurred, the heat which had escaped to the peripheral tissues could not be recovered by the core, as the transfer of heat is normally from a high temperature part (core of body) to a lower temperature part (periphery of body). Moreover, because anesthesia after intubation was maintained with sevoflurane and nitrous oxide in all patients and there were no significant differences in sevoflurane concentrations and total dose of alfentanil used between the groups, the observed temperature differences presumably result exclusively from the choice of induction drug applied.

This study demonstrates that immediately after intubation (approximately 4 minutes after induction but before inhaled sevoflurane administration), core temperature remarkably decreased from preinduction value by 0.5°C in group P and that the core temperature in group P was significantly lower than that in group E at that time. Because of difference in time intervals measured, such finding has not been reported in

![Graph](image)

**Fig. 3.** Time course of forearm-fingertip temperature gradients during operation. A gradient value below 0°C indicates vasodilation. After intubation, there is no difference in temperature gradients between groups. Group E: received etomidate 0.2 mg/kg as an induction agent, Group P: received propofol 2.5 mg/kg as an induction agent, Intu: intubation.

![Graph](image)

**Fig. 4.** Time course of heart rate, mean blood pressure and sevoflurane concentration used. There are no differences in heart rate, mean blood pressure and sevoflurane concentration used between groups. Group E: received etomidate 0.2 mg/kg as an induction agent, Group P: received propofol 2.5 mg/kg as an induction agent. Base: baseline, Ind: induction, Intu: intubation.
previous similar studies in which core temperature in patients receiving propofol as induction agent was different from core temperature in those receiving ketamine or inhaled sevoflurane at least 15 minutes after induction. As a result, we insist that the decrease in core temperature in the patients receiving propofol can occur earlier than 15 minutes after induction and thereby, difference in core temperature between group P and group E can occur earlier than the time reported in previous studies. This study also demonstrates that forearm minus fingertip temperature gradients decreased from preinduction value one minute after propofol injection in group P, but 3 minutes after etomidate injection in group E. In addition, vasodilation occurred two minutes after injection in group P, but 5 minutes after intubation (approximately 9 minutes after etomidate injection) in group E. In other words, group P showed immediate vasodilation after injection, whereas group E showed relatively slow-onset vasodilation. Based on our result, we think that such difference in arteriovenous vaso- motor status between propofol and etomidate has great influence on the extent of alterations in core temperatures in the early period of anesthesia.

In clinical setting, additive administration of opioid and/or vasodilator with induction agent is often used to prevent increased hemodynamic response due to intubation. We also think that such drug having a vasodilating characteristic can aggravate redistribution hypothermia in the early period of anesthesia. But, further data collection should be needed to verify it.

Caution is warranted in the interpretation of the decreases in core temperatures and forearm-fingertip temperature gradients by induction agents in this study. Temperatures can be affected by noxious stimulus such as endotracheal intubation which may augment shunt tone because painful stimulation slightly increases the vasoconstriction threshold. In addition, Temperatures also can be modified by the vasodilatory effects of alfentanil, sevoflurane and nitrous oxide used to maintain anesthesia.

This study had some limitations. We directly measured neither extremity perfusion, nor core-to-periphery flow of heat. Our results indicate only that etomidate and propofol exert markedly different effects on arteriovenous shunt. Skin-temperature gradients are relatively specific measures of the arteriovenous shunt vasomotor status. However, skin-temperature gradients cannot be considered as an index for systemic vasomotor status. We indirectly determined the effects of propofol and etomidate on systemic vasomotor status by observing changes in mean blood pressure. We regarded that although statistically not significant, the decrease in mean blood pressure in group P, compared to group E, in the early period of anesthesia reflects greater systemic vasodilation in group P. We used two different sources ( tympanic membrane and esophagus) for core temperature in this study because we did not measure esophageal temperature as baseline value in awake patient due to ethical concern. Two different sources for core temperature were used in a previous study. Al- though tympanic temperature is about 0.1°C lower than esophageal temperature, these two temperatures can be used inter-changeably in the clinical setting. Fluid temperature and the administered amount can affect body temperature. It is ideal to use fluid in which its temperature is the same as body temperature. In this study, fluid kept at room temperature was excessively administrated to all patients during anesthetic induction. However, in clinical setting, excessive fluid administration is necessary to avoid hypotension during anesthetic induction. Moreover, warmed fluid is not routinely used.

This study demonstrates that even a brief period of propofol-induced vasodilation immediately after anesthetic induction can induce substantial redistribution hypothermia, which persists more than one hour. In conclusion, etomidate is a more useful induction agent for decreasing intraoperative redistribution hypothermia compared to propofol.

REFERENCES

6. Lenhardt R, Marker E, Goll V, Tschemich H, Kurz A, Sessler DI,