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Short communications

Intravenous famotidine does not always change core temperature during general anesthesia

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Abstract
It has been reported that oral premedication with the H_2 receptor antagonist famotidine augmented intraoperative hypothermia. We again investigated whether the H_2 receptor antagonist famotidine significantly affected body temperature during open abdominal surgery under general anesthesia. We studied 20 female patients undergoing elective gynecological surgery. Participating patients were assigned randomly to one of two regimens: (1) 10 ml saline given intravenously just before induction of general anesthesia or (2) 20 mg famotidine in 10 ml saline given just before induction of general anesthesia. General anesthesia was induced by 2 mg·kg^{-1} propofol and 0.1 mg·kg^{-1} vecuronium. After tracheal intubation, anesthesia was maintained with sevoflurane (1%–2%) in nitrous oxide (2 l·min^{-1}) and oxygen (1 l·min^{-1}) along with 1–2 μg·kg^{-1} fentanyl as needed. Tympanic temperature (T_{Tym}) was measured as the core temperature, and arteriovenous perfusion of the fingertip was evaluated using the forearm-minus-fingertip skin-surface temperature gradient ($Grad_{a\text{-}f}$). T_{Tym} gradually and significantly decreased in both groups during anesthesia, and no significant differences in these values were observed between the two groups. $Grad_{a\text{-}f}$ did not differ significantly between the two groups during anesthesia. We conclude that intravenous famotidine does not always change the core temperature during general anesthesia.

Key words Famotidine · Core temperature · Thermoregulation

Although intraoperative hypothermia results, in most cases, from anesthetic-induced inhibition of thermoregulatory control [1], many other factors also influence intraoperative temperature. There is a possibility that histamine plays some role in the central thermoregulatory pathways [2], and Hirose et al. [3] reported that oral premedication with the H_2 receptor antagonist famotidine (40 mg) augmented intraoperative hypothermia. However, there is a report that the H_1 receptor, but not the H_2 receptor, has some role in thermoregulatory control [4], and we have no clinical experience of H_2 receptor antagonist-induced hypothermia. We therefore again investigated whether the H_2 receptor antagonist famotidine significantly affected body temperature during general anesthesia.

With the approval of the Committee on Human Research at our institution, we studied 20 female patients (American Society of Anesthesiologists [ASA] physical status I or II, aged 20–60 years) undergoing elective and open abdominal gynecological surgery. Patients with preoperative fever, evidence of current infection, thyroid disease, or dysautonomia were excluded from the study. Participating patients were assigned randomly to one of two regimens: (1) 10 ml saline given intravenously (i.v.) just before induction of general anesthesia (control group) or (2) 20 mg famotidine in 10 ml saline given i.v. just before induction of general anesthesia (famotidine group). General anesthesia was induced by an i.v. injection of propofol (2 mg·kg^{-1}), and muscle paralysis was facilitated with vecuronium (0.1 mg·kg^{-1}). After tracheal intubation, anesthesia was maintained with sevoflurane (1%–2%) in nitrous oxide (2 l·min^{-1}) and oxygen (1 l·min^{-1}) along with 1–2 μg·kg^{-1} fentanyl as needed. Patients were mechanically ventilated to maintain end-tidal CO_2 near 35 mmHg. All i.v. fluids were warmed to 37°C and room temperature was kept near 23°C. Temperatures were monitored at the right tympanic membrane, forearm, and fingertip at 10-min intervals, using Mon-a-therm thermocouples and Model 6500 digital thermometers (Tyco Anesthesiology Products, St. Louis, MO, USA). Tympanic temperature (T_{Tym}) was measured as the core temperature, and arteriovenous perfusion of the fingertip was evaluated using the forearm-minus-fingertip skin-surface temperature gradient ($Grad_{a\text{-}f}$). Elapsed time 0 was defined as the start of anesthetic induction.

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Table 1. Patient characteristics and intraoperative data

	Control group (n = 10)	Famotidine group (n = 10)
Age (years)	44 ± 11	44 ± 15
Height (cm)	157 ± 6	160 ± 7
Weight (kg)	56 ± 6	62 ± 9
BSA (m^2)	1.6 ± 0.1	1.7 ± 0.1
Duration of anesthesia (min)	149 ± 14	141 ± 11
Duration of operation (min)	117 ± 8	116 ± 11
Amount of bleeding (g)	229 ± 162	207 ± 143
Urinary volume (ml)	280 ± 110	256 ± 123
Volume of fluid transfusion (ml)	1680 ± 420	1610 ± 316

Data values are expressed as means ± SD. There were no significant differences between the groups
BSA, body surface area

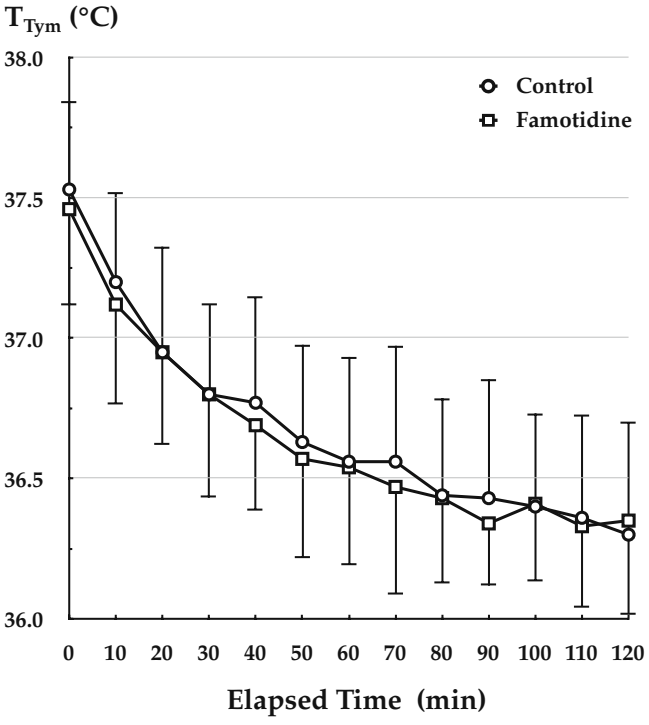

Fig. 1. Changes in tympanic temperature (T_{Tym}) during general anesthesia. Data values are expressed as means ± SD; n = 10 in each group. *Elapsed time 0*, The start of anesthetic induction. T_{Tym} was significantly decreased by anesthetic induction, and there were no significant difference in these values between the groups at the same elapsed times

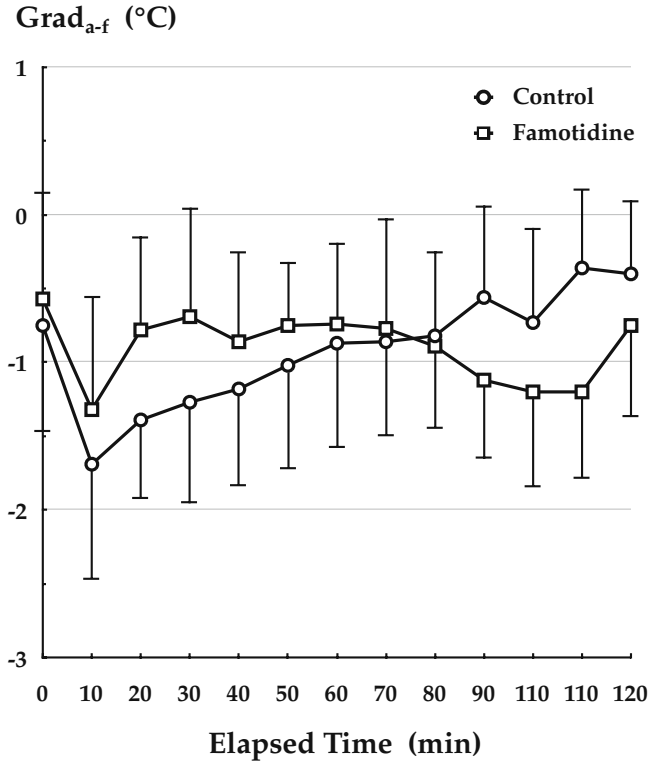

Fig. 2. Changes in forearm-minus-fingertip skin temperature gradient ($Grad_{a-f}$) during general anesthesia. Data values are expressed as means ± SD; n = 10 in each group. *Elapsed time 0*, The start of anesthetic induction. $Grad_{a-f}$ did not differ significantly between the groups during general anesthesia

Demographic and morphometric characteristics were compared using the unpaired t-test. Temperatures were compared with repeated-measures analysis of variance (ANOVA) and Scheffé's F-test. Data values are presented as means ± SD, and $P < 0.05$ was considered statistically significant.

The groups were similar with regard to morphometric and intraoperative data (age, height, weight, body surface area, duration of anesthesia, duration of surgery, amount of bleeding, urinary volume, and volume of fluid transfusion; Table 1). As shown in Fig. 1, the core temperature (T_{Tym}) gradually and significantly decreased in both groups during anesthesia, and no significant differences in these values were observed between the two groups. The $Grad_{a-f}$ did not differ significantly between the two groups during anesthesia (Fig. 2).

As has also been reported previously [1, 5], the core temperature in the present study was significantly decreased by the induction of general anesthesia, mainly

due to redistribution of body heat and imbalance of heat production and heat loss. However, changes in core temperature in the famotidine-premedicated group were not different from those in the unpremedicated group. It could be considered that a $Grad_{a\text{-}f}$ value of 0°C indicates significant thermoregulatory vasoconstriction [6]; however, $Grad_{a\text{-}f}$ was below 0°C and there were no significant differences in these values between the groups throughout the study period. Hirose et al. [3] worked on the same issue and reported that oral premedication with the H_2 receptor antagonist famotidine augmented intraoperative hypothermia; this finding differs from the conclusion in the present study. The difference might be explained mainly by the difference in the anesthetics used, which alter the vasoconstriction threshold variably. It is well known that general anesthetics impair the thermoregulatory response [5]. Anesthesia was maintained with 0.4%–0.6% isoflurane in 66% N_2O in the study of Hirose et al. [3] and the vasoconstriction threshold was estimated at approximately 36.0°C for the anesthesia. Famotidine significantly reduced the thermoregulatory threshold for vasoconstriction in the leg (35.0°C) compared to that in the placebo group (36.4°C) in their study. On the other hand, in the present study, anesthesia was maintained with sevoflurane (1%–2%) in nitrous oxide ($2\ l \cdot min^{-1}$) and oxygen ($1\ l \cdot min^{-1}$) along with 1–2 $\mu g \cdot kg^{-1}$ fentanyl as needed. The threshold for vasoconstriction was estimated as 35.1°C in patients given 2% sevoflurane [7]. N_2O [7–9], fentanyl [8], and propofol [9] are also known to alter the vasoconstriction threshold. These facts therefore suggest that the vasoconstriction threshold in the present study would have been under 36.0°C. But the core body temperature was maintained at more than 36.0°C in our study indicating that famotidine did not target thermoregulatory response. The $Grad_{a\text{-}f}$ value in the control group (below 0°C) supports this point of view. This value of $Grad_{a\text{-}f}$ would explain the difference between the results of these studies, ours and Hirose's [3]: the findings obtained in our present study indicate that intravenous famotidine does not always change core and peripheral temperatures during general anesthesia.

In conclusion, intravenous famotidine does not always change the core temperature during general anesthesia, especially when the core temperature is maintained at more than 36.0°C.

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