

Effect of preoperative amino acid infusion on thermoregulatory response during spinal anaesthesia

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Background. Intravenous amino acid infusion during general anaesthesia prevents decreases in core temperature resulting from increased energy expenditure and heat accumulation.

Methods. We investigated whether such stimulation also occurs during spinal anaesthesia, which blocks sympathetic nervous activity. We examined the effect of i.v. amino acid infusion on changes in core temperature during spinal anaesthesia. Thirty-five patients were divided into two groups: an i.v. amino acid infusion group (4 kJ kg⁻¹ h⁻¹ starting 2 h before surgery); and a saline infusion group. Tympanic membrane core temperature, forearm–fingertip temperature gradient (an index of peripheral vasoconstriction) and mean skin temperature were measured for 90 min after the onset of spinal anaesthesia.

Results. Changes in mean arterial pressure and heart rate did not differ significantly between the groups during the study period. Mean final core temperature 90 min after induction of spinal anaesthesia was 35.8 (SEM 0.1)°C in the saline group and 36.6 (0.1)°C in the amino acid group ($P<0.05$). The increased level of oxygen consumption in the amino acid group compared with the saline group was preserved even after the onset of spinal anaesthesia. The thermal vasoconstriction threshold, defined as the tympanic membrane temperature that triggered a rapid increase in forearm–fingertip temperature gradient, was increased in the amino acid group [36.8 (0.1)°C] compared with the saline group [36.5 (0.1)°C] ($P<0.05$).

Conclusions. Preoperative infusion of amino acids effectively prevents spinal anaesthesia-induced hypothermia by maintaining a higher metabolic rate and increasing the threshold core temperature for thermal vasoconstriction.

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The administration of amino acids stimulates resting energy expenditure and increases the metabolic rate to levels above the basal state, which subsequently exceeds the theoretical expected metabolic cost for nutrient processing.^{1,2} For many years, it has been proposed that the mechanisms by which nutrients stimulate energy expenditure require central activation of the sympatho-adrenal system, which is known to stimulate the metabolic rate in peripheral tissue, such as skeletal muscles.^{3–5} It is still unclear whether the increase in the central stimulation of sympathetic activity is quantitatively important for the thermal effect of amino acids.

Hypothermia is common, and may be severe during neuraxial and general anaesthesia. The core temperature typically decreases by about 0.5–1.0°C shortly after induction of anaesthesia.⁶ Core hypothermia during general anaesthesia is associated with adverse outcomes, including increased incidence of myocardial ischaemia, wound infections, and coagulopathy.^{7–9} There are no reports suggesting that regional anaesthesia is advantageous compared with general anaesthesia as a measure against these hypothermia-

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Table 1 Patient characteristics and preinduction values. Mean (SEM or range). No statistically significant differences between groups

	Saline infusion	Amino acid infusion
Age (yr)	55 (20–65)	59 (23–65)
Weight (kg)	64 (3)	62 (1)
Height (cm)	166 (3)	163 (2)
Gender (M/F)	13/4	14/4
Tympanic (core) temperature (°C)	36.5 (0.1)	36.6 (0.1)
Mean skin temperature (°C)	32.2 (0.1)	32.3 (0.1)
Oxygen consumption (ml min ⁻¹)	201 (10)	205 (112)
Mean arterial pressure (mm Hg)	90 (2)	92 (5)
Heart rate (beats min ⁻¹)	88 (4)	85 (3)

related complications. Therefore, limiting core hypothermia during spinal anaesthesia may improve patient outcome.

Preoperative amino acid infusion is known to prevent perioperative hypothermia during general anaesthesia as a result of increased thermogenesis.^{10–11} Accordingly, this study was undertaken in order to test the hypothesis that i.v. amino acid infusion would also cause thermogenic stimulation under partially blocked sympathetic nervous activity induced by spinal anaesthesia, and that it might also counteract core hypothermia during surgery.

Methods

This study was approved by the Review Board on Human Experiments, Kyoto Prefectural University of Medicine. Written informed consent was obtained from patients before participation in the study. Thirty-five patients (ASA physical status I or II), aged 20–65 yr, who were scheduled to undergo peripheral surgery under spinal anaesthesia, were enrolled in this prospective, randomized, double-blinded study. None of the subjects was obese, febrile, receiving vasodilators or medications likely to alter thermoregulation, or had a history of thyroid disease or dysautonomia.

Patients were assigned randomly into two groups: an amino acid infusion group ($n=18$) and a saline infusion group ($n=17$). In the group infused with amino acids (Teruamino, a mixture of 18 amino acids, 18 g N litre⁻¹; Terumo, Tokyo, Japan), infusions were given at a rate of 2 ml kg⁻¹ h⁻¹, corresponding to 4 kJ kg⁻¹ h⁻¹, for 2 h before induction of spinal anaesthesia. Results were compared with those from a control group receiving the same amount of nutrient-free standard saline solution.

All patients fasted for more than 8 h before surgery. All operations were performed between 08:00 and 12:00. No premedication was given before surgery. Ambient operating room temperature was maintained near 23°C. Spinal anaesthesia was induced using tetracaine 10 mg dissolved in saline solution. After the onset of spinal anaesthesia, both groups received Ringer's solution 12–15 ml kg⁻¹ h⁻¹ lactated maintained at ambient temperature. The patients were covered with a sheet, but were allowed to cool passively.

Blood pressure, heart rate and oxygen saturation were recorded at 5-min intervals during surgery. Final body

sensory block levels were evaluated after surgery by response to cold sensation and pin-prick test. Core temperature was measured at the tympanic membrane using Mon-a-Therm[®] thermocouples (Mallinckrodt Anesthesiology Products, St Louis, MO, USA) before amino acid or saline infusion and during surgery. The aural probes were inserted by the subjects until they felt the thermocouple touch the tympanic membrane; appropriate placement was confirmed when the subjects easily detected a gentle rubbing of the attached wire. The auditory canal was occluded with cotton and taped in place. Skin temperatures were measured with Mon-a-Therm[®] thermocouples at the index fingertip (opposite the nail bed), the forearm (halfway between the elbow and the wrist), the anterior part of the chest and the lateral area of the mid-thigh. Index fingertip and forearm skin temperatures were measured on the non-infused arm. Mean skin temperature was calculated using a method described previously.¹²

Oxygen consumption was measured before amino acid or saline infusion and during surgery using a Deltatrac (Datex Instrumentarium, Helsinki, Finland) in 10 patients from each group, because not all patients consented to this measurement. This monitor measures the oxygen concentration in exhaust gas drawn at a constant flow of 40 litre min⁻¹ through a clear plastic canopy placed over the patient's head. Oxygen uptake is determined from the difference in oxygen content between the mixed exhaust gas and the inspired ambient air. Measurements were averaged over 1-min intervals.

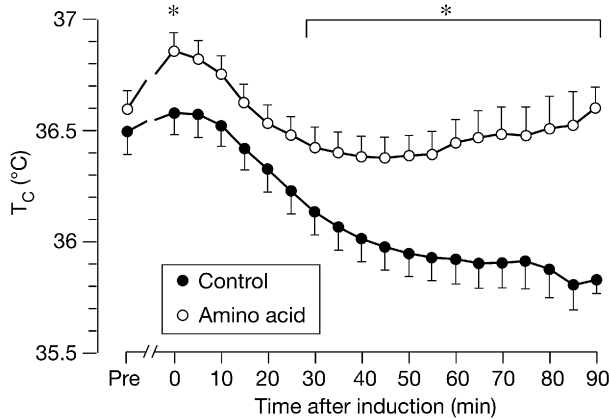
As in previous studies, we defined the vasoconstriction threshold as the tympanic membrane temperature that triggered a rapid increase in the forearm–fingertip skin temperature gradient.^{13–14} The threshold was determined individually for each patient by an investigator blinded to treatment. Once the threshold was reached, thermal responsiveness (gain) was defined by the slope of the regression between the skin temperature gradient and core temperature. Thermal responsiveness (gain) and core temperature threshold data for vasoconstriction were analysed with general linear regression models for one-way analysis of variance (ANOVA) (one between factor), followed by a multiple comparison test with Fisher's least significant difference test. The effects of amino acid infusion and time on the cardiovascular and thermogenic responses were analysed with general linear regression model procedures for two-way ANOVA with repeated measures (one between factor, one within factor), followed by a multiple comparison test with Fisher's least significant difference test. Results are presented as mean (SEM) and $P<0.05$ was considered statistically significant.

Results

Patients in the two groups were comparable with respect to gender, age, weight and height. Core temperature and cardiovascular parameters before amino acid infusion were

Table 2 Anaesthetic management during surgery. Mean (SEM). No statistically significant differences between groups

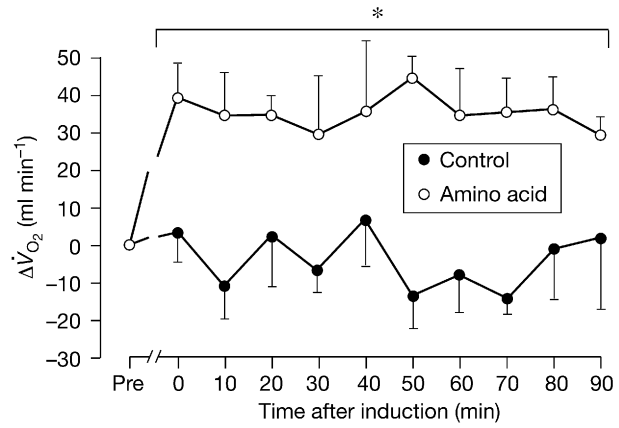
	Saline infusion	Amino acid infusion
Ambient temperature (°C)	23.6 (0.4)	23.9 (0.4)
Blood loss at 90 min (ml)	17 (5)	22 (5)
Fluid replacement at 90 min (ml)	1280 (180)	1160 (165)
Final sensory block (median, range)	T10, T7–T12	T10, T8–T12

**Fig 1** Change in tympanic membrane core temperature (T_c) during the study. Mean (SEM). T_c values at 0 min and after 30 min were significantly higher in the amino acid infusion group than in the saline group. 'Pre' indicates the period before amino acid infusion. *Statistically significant difference between groups ($P<0.05$).

also similar between the groups (Table 1). Furthermore, anaesthetic management did not differ significantly between the two groups (Table 2). During the study, mean arterial pressure decreased by 7 (3) mm Hg in the saline infusion group and 5 (3) mm Hg in the amino acid infusion group. Heart rate also decreased by 5 (3) beats min^{-1} in the saline infusion group and 7 (3) beats min^{-1} in the amino acid infusion group (no significant differences).

Amino acid infusion caused an increase in core temperature, and the core temperature values after 30 min of amino acid infusion were significantly higher than those in the control group ($P<0.05$; Fig. 1, Table 3). Patients in both groups began to vasoconstrict within 10 min after the onset of spinal anaesthesia, and patients assigned to the amino acid infusion group vasoconstricted at higher body core temperatures than the control group ($P<0.05$; Table 3). The gain in vasoconstriction (slope of the forearm–fingertip temperature gradient/core temperature relationship below the threshold) was 9.8 (3.5) in the saline group, 10.8 (4.1) in the amino acid group (no significant difference). No significant differences were found in mean skin temperature between the two groups during the study.

Oxygen consumption increased by 39 (9) ml min^{-1} in the amino acid infusion group. The increased level was maintained after the onset of spinal anaesthesia, and was significantly higher than that in the saline infusion group during the study ($P<0.05$; Fig. 2).

**Fig 2** Change in oxygen consumption ($\dot{V}O_2$) during the study. Mean and SEM ($n=10$). All $\dot{V}O_2$ values after amino acid infusion in the amino acid group were significantly higher than in the saline infusion group. *Statistically significant difference between groups ($P<0.05$).**Table 3** Thermoregulatory responses. Mean (SEM). * $P<0.05$ compared with saline infusion group

	Saline infusion	Amino acid infusion
Vasoconstriction threshold (°C)	36.5 (0.1)	36.8 (0.1)*
Vasoconstriction gain	9.8 (3.5)	10.8 (4.1)
Core temperature at 90 min (°C)	35.8 (0.1)	36.6 (0.1)*

Discussion

Recently, there has been increased awareness of the fact that amino acid infusion prevents perioperative hypothermia during general anaesthesia and is subsequently advantageous in shortening the stay in hospital.^{10 11 15} However, no previous study has shown the effects of amino acid infusion on thermoregulation during spinal anaesthesia. Our study documented clinical improvement and showed that pre-operative amino acid infusion prevents decreases in core body temperature during spinal anaesthesia. The mechanisms that underlie these findings are possibly related to the augmented level of energy expenditure in spite of spinal block. An increased threshold core body temperature for thermoregulatory vasoconstriction during surgery might also contribute partly to the maintenance of body core temperature.

Amino acid infusion increased energy expenditure by about 20%. Thereafter this increased level was maintained in spite of the induction of spinal anaesthesia, which indicates that sympathetic nervous activity does not affect any increase in metabolic rate due to amino acid infusion. The thermic effect of nutrition is divided into an obligatory component, which represents the theoretical metabolic costs for processing and storing ingested nutrients, and a facultative component, which represents a general stimulation of whole-body energy expenditure, which is reportedly attributable to increased central activation of the

sympathoadrenal system.¹⁻⁵ Aksnes and colleagues¹⁶ reported that i.v. administration of amino acid solution in tetraplegic patients, in whom the pathways connecting the brain with the peripheral sympathetic nerves are severed and who show low peripheral sympathetic nervous activity, caused the same or a greater increase in the metabolic rate compared with healthy volunteers.

The level of sympathetic nervous system block in the present study was sufficient for us to examine the possible role of the sympathetic nervous system in the increase in metabolic rate. Brundin and Wahren¹ reported that the splanchnic tissues account for approximately one-half of amino acid-induced whole-body thermogenesis, whereas extra-splanchnic tissues are responsible for the remaining half. Although they also stated that the site of the extra-splanchnic increase in energy expenditure remains to be elucidated, our experimental conditions fully blocked the sympathetic nervous activity controlling the splanchnic tissues.

Amino acid infusion increased the threshold core temperature for thermoregulatory vasoconstriction by 0.3°C. Brundin and Wahren¹ reported that amino acid administration allows a considerable increase in heat accumulation, resulting in an increase in core temperature, an effect different from that of other nutrients. They also speculated that this phenomenon mimics the pyrogenic effect on the thermoregulatory centre, whereby the core temperature threshold for thermoregulatory response during heating and cooling is known to shift upward generally. Our findings indicate that amino acid infusion causes an increase in the core temperature threshold for thermoregulatory vasoconstriction.

A significant increase in oxygen consumption as the result of amino acid infusion is not observed until 1 h after infusion. Therefore, amino acid infusion starting at the onset of spinal anaesthesia would be less effective than amino acid infusion 1 or 2 h before the onset of anaesthesia.¹ A recent paper reported that preoperative amino acid infusion is more effective than intraoperative infusion during general anaesthesia, because it increases the patient's pre-anaesthesia temperature and prevents, to some extent, the initial redistribution of heat from the body core to the peripheral tissues.¹¹ Our previous study showed that a rapid decrease in core temperature, resulting mostly from the redistribution of heat from the body core to the peripheral tissues, occurs within the first hour after epidural anaesthesia,¹⁷ and this theory might also hold true in the present study.

A limitation of this study is that age and gender are known to influence thermoregulation, and we did not control for this.⁶ However, there were no significant differences in age and gender between the two groups in our study.

In summary, we evaluated the efficacy of preoperative amino acid infusion on the change in core temperature during spinal anaesthesia. Our findings indicate that core

temperature was maintained during spinal anaesthesia as a result of an increased level of energy expenditure and an upward shift in the threshold for thermal vasoconstriction.

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