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ORIGINAL ARTICLE

Preoperative carbohydrate-rich beverage reduces hypothermia during general anesthesia in rats

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Abstract
Purpose Intraoperative hypothermia is associated with several unfavorable events; therefore, it is important to prevent the development of hypothermia. Amino acid consumption and/or infusion have been reported to prevent hypothermia. We hypothesized that preoperative carbohydrate-rich beverage (Arginaid Water^{TM}) loading can reduce intraoperative hypothermia in rats under general anesthesia.
Methods We divided 18 rats into 3 groups (group A, 8 mL/kg of saline; group B, 8 mL/kg of a carbohydrate-rich beverage; and group C, 21 mL/kg of the carbohydrate-rich beverage). The rats were administered each beverage at the abovementioned doses via an oral gastric tube 30 min before the induction of anesthesia. During the 2-h general anesthesia, rectal temperature was measured at 20-min intervals. Serum ketone body concentration was measured at 0 and 120 min.
Results The baseline temperature was not significantly different among the groups. At the end of the experiment, group A showed a significantly greater decrease in temperature from the baseline (5.4 ± 0.8°C) than group B (3.9 ± 0.7°C, $P = 0.01$) and group C (3.8 ± 0.8°C, $P = 0.01$). The temperatures in groups B and C were not significantly different. There was no significant change in the serum ketone body concentration from the baseline at the end of the experiment in group A. However, the serum ketone body concentrations in group B and group C were significantly decreased from the baseline.
Conclusion Preoperative carbohydrate loading reduces hypothermia in rats under general anesthesia.

Keywords Preoperative carbohydrate loading · Enhanced recovery after surgery (ERAS) · Intraoperative hypothermia · General anesthesia

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Introduction

The Enhanced Recovery After Surgery (ERAS) protocol aims to enable patients to recover quickly from major surgery and reduce healthcare costs by reducing the lengths of hospital stays [1]. Previous reports have indicated that the ERAS protocol contributes to rapid recovery after surgery [2–4]. Perioperative oral nutrition is one element of the ERAS protocol [1]. Preoperative carbohydrate loading reduces preoperative thirst, hunger and anxiety, and significantly reduces postoperative insulin resistance [1]. Additional benefits include earlier recovery of gastrointestinal motility and a significantly shorter hospital stay [3, 5].

Avoidance of intraoperative hypothermia is an additional component of the ERAS protocol. Hypothermia increases the extent of bleeding during surgery and also increases the risk of ischemic heart disease and postoperative wound infection. It also induces shivering and delays recovery from anesthesia [6, 7]. The ERAS protocol recommends the use of an infusion of warmed fluid for the management of hypothermia [1]. Selldén et al. [8, 9] used another approach and reported that intravenous amino acid infusion prevents intraoperative hypothermia under general and spinal anesthesia. We also reported that preoperative oral amino acid intake contributes to the prevention of intraoperative hypothermia under general anesthesia in rats [10]. Mizobe et al. [11] reported that preoperative fructose

infusion helped to maintain normothermia by augmenting metabolic heat production and increasing the vasoconstriction threshold.

We hypothesized that preoperative carbohydrate loading can reduce intraoperative hypothermia secondary to general anesthesia as well as amino acids and fructose. Therefore, we investigated the effect of preoperative carbohydrate loading on the development of intraoperative hypothermia under general anesthesia in rats.

Materials and methods

The following experimental protocol was approved by the Ethical Committee of the Animal Care Center of Kochi Medical School. Male Wistar rats (weight 250–270 g; Japan SLC Inc., Hamamatsu, Japan) were maintained under conditions of constant temperature (22 ± 2°C) on a 12:12 h light–dark cycle in an acryl box. The rats were fed a standard diet and water.

Eighteen rats were divided into 3 groups ($n = 6$). Rats in group A received 8 mL/kg of saline, those in group B received 8 mL/kg of a carbohydrate-rich beverage (Arginaid Water™, Nestle Nutrition, Tokyo, Japan) which included 18% carbohydrate and 2% arginine, and those in group C received 21 mL/kg of the carbohydrate-rich beverage. The energy contents in the loading doses for groups B and C were 26.8 and 70.6 kJ/kg, respectively. In the present study, we calculated the caloric intake of group B rats in accordance with the recommendations of the ERAS protocol, which specifies the administration of 400 mL of a clear carbohydrate-rich beverage 2–3 h before surgery [1]. This dose was equivalent to 8 mL/kg in a patient weighing 50 kg. Hence, we administered 8 mL/kg, which corresponded to an energy content of 26.8 kJ/kg, to the rats in group B and 8 mL/kg of saline solution to the rats in group A. However, rats in group C received 21 mL/kg of the carbohydrate-rich beverage, which corresponded to an energy content of 70.6 kJ/kg. In a previous study, we administered 70.6 kJ/kg of amino acid to rats and observed that this dose prevented hypothermia [10]. Although this dose seems much larger than the doses appropriate for humans, it should be considered that the rat metabolism is 5–7 times higher than that of humans, and that protein consumption by weight in rats is approximately 7 times that in humans [10].

Before anesthesia, all rats were fasted for 12 h with free access to water. Thirty minutes before the induction of anesthesia, the rats were sedated in an acryl box by administering 5% sevoflurane for 1 min through inhalation and the abovementioned dose of saline or carbohydrate-rich beverage via an oral gastric tube. After removing this tube, the rats were kept in the cage for 30 min until the induction of anesthesia. Anesthesia was induced by introducing 5% sevoflurane into the acryl box for 1.5 min. Room temperature was kept constant at 24°C. After inducing anesthesia, the rats were placed on a paper pad on a table. The skin on the right side of the neck was incised, and a catheter was inserted into the right internal jugular vein while the rats were under anesthesia with 2–3% sevoflurane. After inserting the catheter, anesthesia was maintained by the continuous infusion of 1% propofol at a rate of 1.5 mL/h for the first hour and 0.7 mL/h for the second hour. The warm pad was not used in this study. At the end of the experiment, arterial blood samples were taken from the aorta.

Rectal temperature was measured using a digital thermometer (BDT-100; Bioresearch Inc., Tokyo, Japan) at 20-min intervals for 2 h after inducing anesthesia. Serum ketone body concentration, electrolyte concentrations (Na^+, K^+, Ca^{2+} and Cl^-), blood glucose concentration, and serum insulin level were determined by a clinical laboratory testing company (SRL Inc., Tokyo, Japan). Blood glucose concentration was measured using a hexokinase method. The serum insulin level was measured by the chemiluminescent enzyme immunoassay (CLEIA) technique, and the serum ketone body concentration was measured using an enzyme cycling method. In addition, baseline samples were taken from the pretreated control group just after inducing anesthesia with sevoflurane. The results for the blood analyses, blood glucose concentrations and serum insulin levels were compared between the three groups and with those for the baseline.

Data are presented as mean ± standard deviation (SD). Statistical analyses were performed using a statistical software package (JMP 9; SAS Institute Japan, Tokyo, Japan). Alterations in the rectal temperature among groups and the blood chemical analyses among groups were analyzed by factorial ANOVA with post hoc testing (Tukey–Kramer method). P values <0.05 were considered to be statistically significant.

Results

The baseline temperatures were 36.6 ± 0.3°C in group A ($n = 6$), 36.6 ± 0.2°C in group B ($n = 6$), and 36.7 ± 0.2°C in group C ($n = 6$). In all groups, rectal temperature gradually decreased during anesthesia (Table 1). From 20 min after the start of anesthesia to the end of the experiment, the decreases in temperature in groups B and C were significantly less pronounced than that in group A. At the end of the experiment, the decrease in the rectal temperature from the baseline in group A (5.4 ± 0.8°C) was significantly larger than those in group B (3.9 ± 0.7°C, $P = 0.01$) and group C (3.8 ± 0.8°C, $P = 0.01$); there was no significant difference between the values for group B and group C (Fig. 1).

Table 1 Rectal temperature

	Baseline	20 min	40 min	60 min	80 min	100 min	120 mim
Group A (°C)	36.6 (0.3)	34.8 (0.4)	33.7 (0.5)	32.8 (0.6)	32.1 (0.8)	31.6 (0.9)	31.2 (0.8)
Group B (°C)	36.6 (0.2)	35.6 (0.3)*	34.7 (0.3)*	33.9 (0.4)*	33.3 (0.5)*	33.1 (0.7)*	32.7 (0.7)*
Group C (°C)	36.7 (0.2)	35.7 (0.4)*	35.0 (0.3)*	34.1 (0.5)*	33.5 (0.7)*	33.2 (0.8)*	32.9 (0.8)*

Data are mean (standard deviation)

* $P < 0.05$ for difference from group A

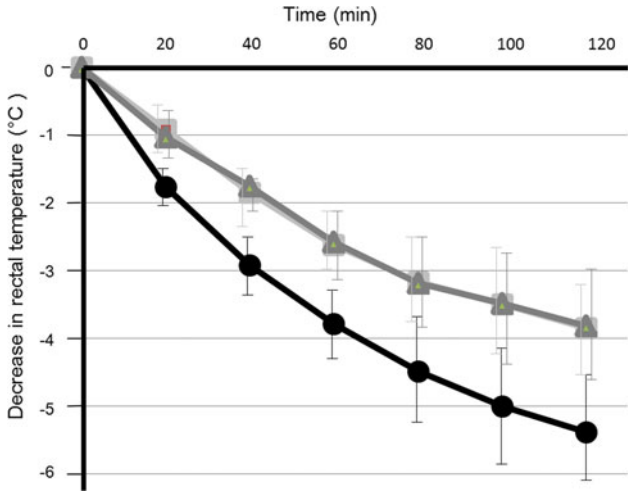

Fig. 1 Alteration of rectal temperature from the baseline. From 20 min after the start of anesthesia to the end of the experiment, the decreases in temperature in groups B (*squares*) and C (*triangles*) were significantly less pronounced than that in group A (*circles*). At the end of the experiment, the decrease in rectal temperature from the baseline in group A (5.4 ± 0.8°C) was significantly larger than those in group B (3.9 ± 0.7°C, $P = 0.01$) and group C (3.8 ± 0.8°C, $P = 0.01$); there was no significant difference between the values for group B and group C

The serum ketone body concentrations measured at the end of the study were significantly higher in group A than in group B ($P < 0.001$) and group C ($P < 0.001$), and those in group B were significantly higher than those in group C ($P = 0.02$) (Table 2). There were no significant changes in the value of the serum ketone body concentrations from the baseline at the end of experiment in group A. However, the values of the serum ketone body concentrations in group B and group C were decreased significantly compared with the baseline. The insulin levels and electrolyte concentrations of the 3 groups were not significantly different (Table 2). The blood glucose level in group C was significantly higher than those in groups A and B, but was not significantly different from the baseline value.

Discussion

Our data showed that preoperative carbohydrate-rich beverage loading attenuates the development of hypothermia during general anesthesia in rats. Furthermore, carbohydrate-rich beverage loading inhibits the production of ketone bodies. These results indicate that preoperative carbohydrate loading is beneficial for the prevention of hypothermia and provides nutritional benefits such as suppression of catabolism.

In the present study, we confirmed that carbohydrate loading before general anesthesia attenuates the marked decrease in rectal temperature during anesthesia. This result is similar to the results of our previous study on treatment with amino acids [10], so we consider that the effect of the carbohydrate-rich beverage on the reduction of hypothermia can be attributed to nutrient-induced thermogenesis (NIT). It is well recognized that the body core temperature increases after food ingestion. This phenomenon is referred to as NIT. NIT constitutes 10% of the daily energy expenditure, but there are wide variations among individuals. Moreover, there is a large difference in the effects of the 3 macronutrients on NIT. The percentages of the carbohydrate-, fat-, and protein-derived energy intakes that are spent in NIT are 8, 2, and 20–30%, respectively [12]. This thermic effect is generally attributed to the metabolic costs of peptide-bond synthesis, ureogenesis, and gluconeogenesis [13]. In particular, the metabolic cost of glycogen synthesis and lipogenesis is believed to account for 55–65% of the thermic effect of carbohydrate ingestion [13].

The thermic effect of nutrients in awake subjects is small. However, the thermic effect in subjects under general anesthesia was found to be fivefold higher than that in awake individuals [14]. Mizobe et al. [11] reported that the metabolic rate is increased by approximately 20% during anesthesia due to the administration of fructose. However, the mechanism underlying this increase has not been elucidated. Since the carbohydrate-rich beverage used in the present study includes sucrose and dextrin, which are similar to fructose, it is possible that the thermic effect of this beverage might be augmented by general anesthesia.

Our data showed that the carbohydrate-rich beverage did not have a capacitative effect on the reduction of hypothermia. However, the production of serum ketone bodies in group C was significantly lower than that in group B. Therefore, the additional carbohydrate provided to group C rats was certainly absorbed and used as an energy source. Although we could not ascertain the reasons for this

Table 2 Laboratory data

	Ketone (μmol/L)	Glucose (mg/dL)	Insulin (μIU/mL)	Na^+ (mmol/L)	K^+ (mmol/L)	Cl^- (mmol/L)	Ca^{2+} (mmol/L)
Baseline	1505 (290)	140 (12)	0.4 (0.5)	140 (0.5)	3.8 (0.3)	104 (1)	1.37 (0.02)
Group A	1695 (203)	104 (15)$^+$	1.5 (1.6)	140 (1.4)	3.8 (0.1)	103 (1)	1.48 (0.01)
Group B	737 (258)*,$^+$	122 (8)$^+$	1.4 (1.2)	138 (1.0)	3.9 (0.1)	101 (1)	1.43 (0.03)
Group C	289 (87)*,$^+$	129 (4)*	1.7 (0.9)$^+$	137 (1.5)	3.9 (0.3)	104 (2)	1.43 (0.03)

Data are mean (standard deviation)

* $P < 0.05$ difference from group A, $^+P < 0.05$ difference from the baseline

finding, this may be due to the ceiling effect of carbohydrate-induced thermogenesis under general anesthesia. It appears that 8 mL/kg of carbohydrate-rich beverage is enough to reduce hypothermia during general anesthesia, and 21 mL/kg of this drink is better than 8 mL/kg from the point of view of suppressing catabolism.

The effect of carbohydrate-rich beverage loading on the prevention of hypothermia in group B in the present study was similar to that of amino acid treatment in our previous study. One possible explanation is that the thermic effects of different types of carbohydrates are different [15]. In particular, the thermic effect of sucrose is larger than that of glucose [15]. These differences in thermic responses can be attributed to the energy released from the hydrolysis of sucrose to glucose and fructose [15]. Since sucrose was included in the beverage used in the present study, we consider that the fructose produced from the hydrolysis of sucrose plays an important role in NIT. Furthermore, the 2% arginine included in the beverage may have aided the process of thermogenesis.

Since the amino acid solutions prepared for intravenous infusion have low electrolyte concentrations, the infusion of a large amount of amino acid solution is a risk factor for hyponatremia [10]. In contrast, the preoperative intake of a carbohydrate-rich beverage is recommended in the ERAS protocol [1]. In the present study, this drink did not cause electrolyte abnormality, with normoglycemia and a reduction of ketone body production noted.

The present study has some limitations. First, this beverage is not pure carbohydrate; it contains an amino acid as well. This makes it difficult to attribute the difference in effect solely to carbohydrates. In our country, this beverage is popular as a preoperative drink, but nobody uses a carbohydrate-only preoperative drink. Therefore, our results may be worth using in routine clinical practice. Second, although these rats were fed 30 min before the induction of anesthesia, the patients could not be fed at that time. However, we thought that this was tolerable because the rat metabolism is 5–7 times higher than that in humans [10]. Third, we did not perform any surgical procedure. Hence, we could not clarify the effects of surgery when applying the results in clinical practice. In addition, although the present study was performed under general anesthesia with sevoflurane induction and propofol maintenance, differences in anesthetic agents may also affect the thermogenesis. Fourth, we measured rectal temperature in the same manner as in our previous study [10]. However, the rectal temperature lags behind the temperatures measured at core sites such as the pulmonary artery and the distal part of the esophagus [16].

In conclusion, preoperative carbohydrate-rich beverage loading reduces hypothermia and catabolism without causing electrolyte abnormalities in rats under general anesthesia.

References

1. Fearon KC, Ljungqvist O, Von Meyenfeldt M, Revhaug A, Dejong CH, Lassen K, Nygren J, Hausel J, Soop M, Andersen J, Kehlet H. Enhanced recovery after surgery: a consensus review of clinical care for patients undergoing colonic resection. Clin Nutr. 2005;24:466–77.
2. Mohn AC, Bernardshaw SV, Ristesund SM, Hovde Hansen PE, Røkke O. Enhanced recovery after colorectal surgery. Results from a prospective observational two-centre study. Scand J Surg. 2009;98:155–9.
3. Teeuwen PH, Bleichrodt RP, Strik C, Groenewoud JJ, Brinkert W, van Laarhoven CJ, van Goor H, Bremers AJ. Enhanced recovery after surgery (ERAS) versus conventional postoperative care in colorectal surgery. J Gastrointest Surg. 2010;14:88–95.
4. Stoot JH, van Dam RM, Busch OR, van Hillegersberg R, de Boer M, Olde Damink SW, Bemelmans MH, Dejong CH. The effect of a multimodal fast-track programme on outcomes in laparoscopic liver surgery: a multicentre pilot study. HPB (Oxford). 2009;11:140–4.
5. Noblett SE, Watson DS, Huong H, Davison B, Hainsworth PJ, Horgan AF. Pre-operative oral carbohydrate loading in colorectal surgery: a randomized controlled trial. Colorectal Dis. 2006;8:563–9.
6. Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. N Engl J Med. 1996;334:1209–15.
7. Schmied H, Kurz A, Sessler DI, Kozek S, Reiter A. Mild hypothermia increases blood loss and transfusion requirements during total hip arthroplasty. Lancet. 1996;347:289–92.
8. Selldén E, Bränström R, Brundin T. Preoperative infusion of amino acids prevents postoperative hypothermia. Br J Anaesth. 1996;76:227–34.
9. Widman J, Hammarqvist F, Selldén E. Amino acid infusion induces thermogenesis and reduces blood loss during hip arthroplasty under spinal anesthesia. Anesth Analg. 2002;95:1757–62.

10. Imoto A, Yokoyama T, Suwa K, Yamasaki F, Yatabe T, Yokoyama R, Yamashita K, Selldén E. Bolus oral or continuous intestinal amino acids reduce hypothermia during anesthesia in rats. J Nutr Sci Vitaminol (Tokyo). 2010;56:104–8.
11. Mizobe T, Nakajima Y, Ueno H, Sessler DI. Fructose administration increases intraoperative core temperature by augmenting both metabolic rate and the vasoconstriction threshold. Anesthesiology. 2006;104:1124–30.
12. Rasmussen LG, Larsen TM, Mortensen PK, Due A, Astrup A. Effect on 24-h energy expenditure of a moderate-fat diet high in monounsaturated fatty acids compared with that of a low-fat, carbohydrate-rich diet: a 6-mo controlled dietary intervention trial. Am J Clin Nutr. 2007;85:1014–22.
13. Johnston CS, Day CS, Swan PD. Postprandial thermogenesis is increased 100% on a high-protein, low-fat diet versus a high-carbohydrate, low-fat diet in healthy, young women. J Am Coll Nutr. 2002;21:55–61.
14. Selldén E, Lindahl SG. Amino acid-induced thermogenesis reduces hypothermia during anesthesia and shortens hospital stay. Anesth Analg. 1999;89:1551–6.
15. Sharief NN, Macdonald I. Differences in dietary-induced thermogenesis with various carbohydrates in normal and overweight men. Am J Clin Nutr. 1982;35:267–72.
16. Sessler IS. Temperature regulation and monitoring. In: Miller RD, editor. Miller's anesthesia. 7th ed. Philadelphia: Elsevier; 2010. p. 1533–56.