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JA SYMPOSIUM

Effect of preoperative carbohydrate loading on the management of blood glucose and body temperature

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Introduction

Enhanced recovery after surgery (ERAS), a program to strengthen postoperative recovery ability, was originally initiated to improve the recovery ability and early discharge of patients who had undergone colon surgery [1]. Since its first publication in 2005, the ERAS program has rapidly become widespread, and it has been applied not only to colectomy but also to various other procedures [2]. This program focuses on reduction of the perioperative fasting period and on achieving early ambulation [1].

As a part of the reduction of the fasting period, preoperative carbohydrate loading may be used. The advantages of this approach are as follows: preoperative thirst, hunger, and anxiety are reduced and insulin resistance is improved [3]. An additional effect is also expected: to decrease the loss of nitrogen and protein and maintain muscle strength after surgery [3]. In particular, it has also been reported that preoperative carbohydrate loading is a component of the recovery protocol that provides a positive influence on postoperative prognosis, along with perioperative fluid therapy [4]. This article provides an outline focusing on preoperative carbohydrate loading, insulin resistance, and temperature management.

Improvement of insulin resistance

Method for measurement of insulin resistance

Insulin resistance, which can be assessed by the homeostasis model assessment-insulin resistance index using fasting insulin and fasting blood glucose values, is widely used in the medical field. However, the hyperinsulinemic normoglycemic clamp can be used to measure insulin resistance more accurately. In this method, at a steady-state blood insulin level of 100 μU/ml, the dose of glucose necessary to maintain a normal blood glucose level (glucose infusion rate, GIR) is used as an index of insulin resistance. In Japan, hyperinsulinemic normoglycemic clamping can be performed easily and accurately with the artificial pancreas STG-22 and the newer model STG-55 (Nikkiso, Tokyo, Japan). When an artificial pancreas is used, a 20 G intravascular catheter is placed into the peripheral vein and connected to the artificial pancreas. As a result, blood glucose levels can be measured in real time. Additionally, a line for insulin and glucose infusion is secured in another vein. After insulin priming is carried out for 10 min, insulin is administered automatically at 1.25 mU/kg/min and the required amount of glucose, which is calculated every minute after administration of

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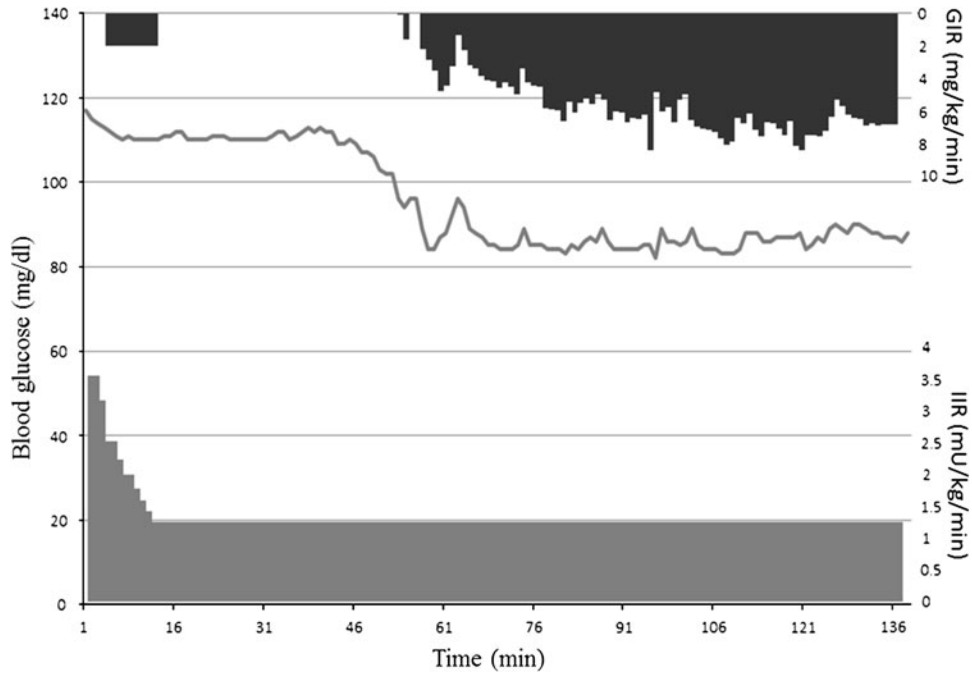

Fig. 1 Typical hyperinsulinemic normoglycemic clamping. *Curved gray line* indicates plasma glucose levels measured by artificial pancreas; *upward gray bar graph* indicates insulin infusion (*IIR*) rate; *downward black bar graph* indicates glucose infusion rate (*GIR*). After the priming infusion (for 10 min), insulin was continuously infused at 1.25 mU/kg/min. Automatic infusion of glucose was carried out for 2 h, until the blood glucose level was steadily maintained at 95 mg/dl. The final stable GIR was recorded

insulin, is administered to keep the blood glucose level within a normal range (approximately 95 mg/dl). The GIR that reaches a stable injected dose after approximately 90–120 min is considered the index of insulin resistance. A typical hyperinsulinemic normoglycemic clamping procedure is shown in Fig. 1. The normal range of GIR remains unclear because few data exist on what is considered a normal range of the GIR [5]. Therefore, in research studies to examine the effects of an intervention, the effect of intervention was assessed based on two clamp results, namely, before and after an intervention [6–8].

Impact of aggravated insulin resistance on perioperative patients

A previous retrospective study had revealed that postoperative hyperglycemia is likely the main cause of surgical site infection [9]. Data from 1,002 general surgery patients showed that the likelihood of developing surgical site infection increased from 3.61 times in patients with a first postoperative glucose level in the 111–140 mg/dl range to 12.13 times in patients with a glucose level higher than 220 mg/dl [9]. Therefore, it is necessary to prevent perioperative hyperglycemia. One of the causes of perioperative hyperglycemia is aggravated insulin resistance [10]. In cardiac surgery, the risk of severe infection became approximately 5 times greater with each increase in GIR by 1 mg/kg/min [11]. Consequently, to lower the risk of surgical site infection or other diseases, it is important to minimize aggravation of insulin resistance during the perioperative period.

Preoperative carbohydrate loading improves insulin resistance

In the ERAS protocol, a 12.6 % carbohydrate beverage is used; how much effect will it be able to provide on insulin resistance? In a crossover study on six healthy volunteers [6], the volunteers underwent four protocols in a crossover-randomized order: administration of carbohydrate beverage both in the evening and morning, only in the evening, only in the morning, and no administration. The amounts of administered carbohydrate beverage in the evening on the day before the test and in the morning of the day of the test were defined as 800 ml (100 g carbohydrate, 400 kcal) and 400 ml (50 g carbohydrate, 200 kcal), respectively. Insulin resistance was measured and evaluated using the hyperinsulinemic normoglycemic clamp. In the no administration and administration only in the evening groups, GIR was 6.1 ± 1.6 and 6.6 ± 1.9 mg/kg/min, respectively. On the other hand, in the administration in the evening and morning and administration only in the morning groups, GIR was significantly higher, that is, insulin resistance was lower (9.3 ± 1.9 and 9.2 ± 1.5 mg/kg/min, respectively) ($P < 0.01$) [6]. These results indicate that intake of carbohydrate beverage in the morning of the test day might alleviate aggravation of insulin resistance as significantly as 3.2 mg/kg/min.

Insulin resistance also improves with an 18 % carbohydrate beverage

In Japan, an 18 % carbohydrate beverage (Arginaid Water; Nestle, Tokyo, Japan) is used for carbohydrate loading.

Will it be able to improve insulin resistance? In a crossover study [7], six healthy volunteers were segregated into two groups: in group A, 375 ml of an 18 % carbohydrate beverage (67.5 g carbohydrate) and 250 ml of an 18 % carbohydrate beverage (45 g carbohydrate) were administered at 21:00–24:00 before the test day and at 06:30 on the morning of the test day. In group B, the subjects consumed only water or tea after 21:00 on the day before the test. In both groups, drinking water was prohibited after 06:30 and hyperinsulinemic normoglycemic clamping was performed using an artificial pancreas after 08:30. GIR was significantly higher in group A (11.5 ± 2.4 mg/kg/min) than in group B (6.2 ± 2.2 mg/kg/min), which indicated that insulin resistance improved with the 18 % carbohydrate beverage compared with fasting ($P = 0.005$) [7]. In addition, we performed a similar examination using a 2.5 % carbohydrate beverage (OS-1; Otsuka Pharmaceutical Factory, Tokushima, Japan) [8]. In the group to receive 500 ml in the evening and 500 ml in the morning, GIR was maintained at 8.6 ± 1.5 mg/kg/min, which indicated that insulin resistance improved with the 2.5 % carbohydrate beverage compared with fasting.

Preoperative carbohydrate loading improve postoperative insulin resistance

In a study that compared postoperative insulin resistance between an adequate blood glucose control group during hepatectomy and a high blood glucose group, it was found that aggravation of postoperative insulin resistance could be alleviated with adequate control of intraoperative blood glucose levels [12]. Preoperative carbohydrate loading improves intraoperative insulin resistance and facilitates intraoperative glycemic control. If intraoperative glycemic control becomes easy, postoperative glycemic control can be achieved appropriately. As a result, surgical site infection would be inhibited and patients could be discharged early from the hospital, leading to a shorter hospitalization stay and possibly a reduction in medical costs.

Maintenance of intraoperative body temperature

Perioperative hypothermia may cause platelet defects, by impaired clotting system and activation of the fibrinolytic system, which leads to increased bleeding and may increase the need for transfusions [13]. Furthermore, it leads to a high incidence of perioperative cardiovascular events and postoperative tachycardia, which increases the risk of surgical site infection and hospital stay [14, 15]. Thus, maintenance of the appropriate temperature is important for anesthetic management and is recommended by the ERAS protocol [1–3]. Administration of amino acids can prevent intraoperative hypothermia. Energy consumption is increased depending on the dietary intake and nutrient composition during 4–8 h after oral intake, that is, dietary-induced thermogenesis [16]. Although previous studies reported that amino acid and fructose prevent hypothermia, there were no studies about the relationship between preoperative carbohydrate loading and prevention of hypothermia [17, 18]. Therefore, we investigated the effect of preoperative carbohydrate loading on the development of intraoperative hypothermia [19]. Rats were administered 8 ml/kg of an 18 % carbohydrate beverage 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. At the end of the experiment, the control group (saline) showed a significantly greater decrease in temperature from the baseline (5.4 ± 0.8 °C) than the carbohydrate group (3.9 ± 0.7 °C, $P = 0.01$) (Fig. 2). Metabolism in rats is five- to sevenfold that in humans. Therefore, it is necessary to clinically examine the extent of this effect in humans.

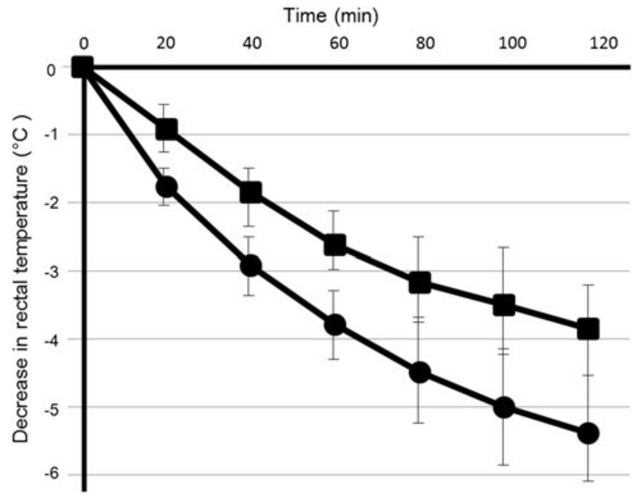

Fig. 2 Alteration of rectal temperature from baseline. From 20 min after the start of anesthesia to the end of the experiment, the decrease in temperature in the carbohydrate group (*squares*) was significantly less pronounced than that in control group (*circles*). At the end of the experiment, decrease in rectal temperature from baseline in the control group (5.4 ± 0.8 °C) was significantly greater than that in the carbohydrate group (3.9 ± 0.7 °C, $P = 0.01$). (Data from Yatabe et al. [19])

Perioperative management to begin with preoperative carbohydrate loading (Fig. 3)

The ERAS protocol is an approach that considers the entire perioperative period including pre-, intra-, and postoperative periods. In this approach, preoperative carbohydrate loading is only one of the factors recommended. However, as already mentioned, it can improve insulin resistance, facilitate perioperative glycemic control, and may contribute to intraoperative temperature management.

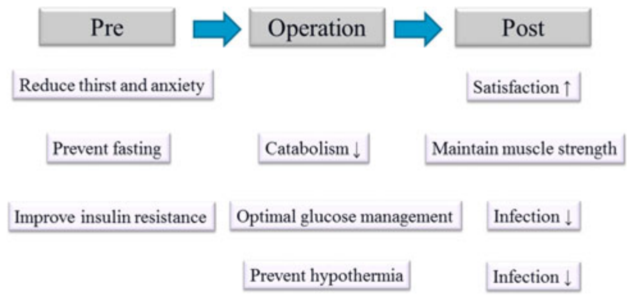

Fig. 3 Role of preoperative carbohydrate loading in perioperative management

Although preoperative carbohydrate loading is only one of the ERAS components, it might contribute more to improvement of patient outcome than the other protocol components.

Conclusion

Preoperative carbohydrate loading is a low-cost, simple, and easy approach for the improvement of insulin resistance and prevention of perioperative hypothermia, which may lead to improved prognosis in perioperative patients. It is expected that much evidence associated with this approach will be provided from Japan in the future.

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