Journal of
Cancer Science & Therapy

Yang et al., J Cancer Sci Ther 2012, 4.5
DOI: 10.4172/1948-5956.1000123

Research Article Open Access

Effects and Safety of Preoperative Oral Carbohydrate in Radical Distal Gastrectomy – A Randomized Clinical Trial

Yu Yang, Zhou Yan-Bing*, Jiao Xue-Long, Chen Dong and Wang Zhi-Hao

Department of General Surgery, Affiliated Hospital, Qingdao University Medical College, Qingdao, China

Abstract

Objective: To investigate the safety of preoperative oral carbohydrate and the impact of preoperative oral carbohydrate on postoperative insulin resistance.

Methods: 60 patients with gastric cancer scheduled were randomly divided into preoperative oral carbohydrate or placebo drink. Preoperative general well-being, 2-3 hours before the induction of anesthesia all patients received either a placebo drink or carbohydrate drink, blood glucose, insulin were measured before and immediately after surgery, Insulin resistance index was calculated using Homeostasis Model Assessment (HOMA), and postoperative complications and length of hospital stay were respectively recorded.

Results: No complications associated with anesthesia were recorded as a result of preoperative fluid consumption. In the two groups, blood glucose, insulin and HOMA-IR immediately postoperative in the preoperative oral carbohydrate group were significantly lower than those in the preoperative oral placebo group. Insulin sensitivity index (ISI) was reduced in both groups; the oral carbohydrate group was higher than oral placebo group. There were no differences between two groups on length of hospital stay.

Conclusion: Preoperative consumption of carbohydrate-containing fluid is safe. Preoperative oral carbohydrate may alleviate the postoperative immediately insulin resistance should be a routine for preoperative preparation.

Keywords: Insulin resistance; Surgery; Carbohydrate

Introduction

Elective surgery is one of the treatments for modern medicine. In the developed countries, about 5% of population will undergo elective operation every year. Traditionally, Elective surgery has been performed in the overnight fasted state. Preoperative fasting has been viewed as the general rule. This means that no intake of solids or fluids is followed from midnight to the time of surgery. The reasonable for preoperative fasting is that it ensures an empty stomach before operation and reduces the risk of pulmonary aspiration of gastric contents during surgery. Since 1848, when a young woman died from pulmonary aspiration, this was the first reported death following general anesthesia [1]. However, the overnight fasting routine depletes liver glycogen store, face to increase metabolic demands of surgery, this fasting state at the beginning of the operation may have a detrimental effect on clinical outcome [2].

Recently, this routine has been questioned, preoperative intake of solids presents a risk at anesthesia, but there was no evidence to suggest that preoperative oral specific beverages were unsafe [3]. Nygren et al. [4] and Ljungqvist et al. [5] have demonstrated that the intravenous infusion of 10-20% glucose and insulin in the preoperative period may improve postoperative glycemic control, attenuate the early postoperative metabolic response, improve insulin resistance and reduce recovery time [2]. Nygren et al. [6] examined that preoperative oral carbohydrate may achieve the same effect as intravenous infusion of glucose and insulin. It has been shown that gastric emptying of an isoosmolar carbohydrate rich drink was complete with 120 min after intake, 2-3h before the induction of anesthesia of oral fluids was shown to be safe.

This study is to prove the safety of preoperative oral carbohydrate and the effects of preoperative oral carbohydrate on postoperative insulin resistance and clinical outcome.

Material and Methods

Patients and methods

The study was granted by the ethics committees of Qing Dao University Medical College Hospital. Before participation, patients knew the details of the treatment procedure. Written informed consent was obtained before study. Patients undergoing radical distal gastrectomy were eligible to participate in this double blind, randomized study. Two days before surgery all patients were instructed to eat regular meals 3 times a day, to sleep at least 6h per night and to avoid any strenuous physical exercise. Exclusion criteria were emergency operation or laparoscopic operation, pre-existing nausea, vomit, pyloric obstruction symptoms or condition known to affect gastric emptying rate, metabolic disease including diabetes mellitus or impaired glucose tolerance, chemotherapy and radiotherapy before surgery, presence of distant metastasis on CT, weight loss greater than 10 percent during the previous 6 months, medication affecting insulin sensitivity, renal or hepatic insufficiency.

Participants receive a placebo drink-the placebo group, or the carbohydrate drink-(CHOD) group. Patients in the CHOD group

***Corresponding author:** Zhou Yan-bing, Department of General Surgery, Affiliated Hospital, Qingdao University Medical College, Qingdao 266003, China, E-mail: zhouyanbing999@yahoo.com.cn

Received April 02, 2012; **Accepted** May 07, 2012; **Published** May 09, 2012

Citation: Yang Y, Yan-Bing Z, Xue-Long J, Dong C, Zhi-Hao W (2012) Effects and Safety of Preoperative Oral Carbohydrate in Radical Distal Gastrectomy – A Randomized Clinical Trial. J Cancer Sci Ther 4: 116-119. doi:10.4172/1948-5956.1000123

consumed 500 ml carbohydrate (10 percent carbohydrate) 2-3h before induction of anesthesia, intake the carbohydrate drink with 20 min. Patients in the placebo group oral the same amount fluid but the fluid is a kind of sweetener could not contain carbohydrate, consumed as in the CHOD group. Before surgery, all patients did not have enteral or parenteral nutritional support, and they have the same preoperative preparation including the same bowel preparation and anesthesia way, done by the same surgeon, intraoperative rehydrate cannot contain glucose and insulin during surgery. Blood samples were collected and the level of blood glucose in plasma by automatic biochemistry analyzer, the serum concentration insulin by automatic chemiluminescence immune assay analyzer before 4 hours surgery and immediately after surgery were measured.

Biochemical analysis

Before 4 hours surgery and immediately after surgery, the blood samples were collected and plasma insulin and glucose concentration were measured. Glucose was measured by using a standard enzymatic principle. Blood samples were sent into water bath for 10 min, and then all samples were centrifuged at 2000rmp for 10min, Blood glucose concentration was measured by automatic biochemistry analyzer. Insulin was measured by automatic chemiluminescence immune assay analyzer.

Homoeostasis model assessment

Homeostasis model assessment(HOMA) was applied to assess the status of insulin resistance (HOMA-IR), basic function of pancreatic β cell (HOMA-βcell) and Insulin Sensitivity Index (ISI), the homoeostasis model assessment was used according to the formula: HOMA-IR = (blood glucose (mmol/L) × blood insulin (μunits/ml)/22.5. HOMA-β = (20× (blood insulin (μunits/ml)/blood glucose (mmol/L)-3.5. ISI = 1/(lg(blood glucose (mmol/L)) + lg (blood insulin (μunits/ml))) [7,8].

Length of stay and complication

All patients were infused with 120-150g exogenous glucose and 30-40ml⁄kg liquid during operation day, and postoperative period patient were fed with parenteral or enteral nutrient solution, including 20-25 non-protein kcal⁄kg. Postoperative complications and length of hospital stay were respectively recorded.

Statistical analysis

Data were analyzed by using SPSS. All data are given as mean ± SEM, The Student's *t*-test were used for comparisons of means. Length of hospital stay was analyzed by using the Mann-Whitney U test. The 5% level was taken as the level of significance.

Results

Patient demographics and surgical characteristics

Sixty patients underwent radical distal gastrectomy were recruited in this study. Of these 60 patients. Eight of these patients did not complete the study; two patients underwent radical subtotal gastrectomy; in addition distal metastasis was found in the other two patients during surgery. The gender, age, nutritional status, anthropometric and surgical procedure of patients in two groups was list in Table 1.

Biochemistry

Preoperative blood glucose and insulin did not differ significantly between the two groups. Postoperative the level of blood glucose

Data	CHOD (n = 24)	Placebo (n = 24)	Statistic	P
Sex ratio (M:F)	17/7	17/7	X^2 = 0.000	1.000
Age (years)	63.38 ± 9.07	62.58 ± 10.22	t = 0.516	0.476
Height (cm)	165.29 ± 8.77	166.25 ± 8.14	t = 0.127	0.723
Weight (kg)	64.6 ± 10.4	63.8 ± 10.3	t = 0.051	0.823
Body mass index (kg/m^2)	23.64 ± 2.80	2.91 ± 3.19	t = 0.858	0.359
NRS grade			X^2 = 0.820	0.574
1~2	17	14		
3~4	7	10		
5~6	0	0		
ASA classification			X^2 = 0.202	0.904
I	8	9		
II	12	12		
III	4	3		
> III	0	0		
Liver function Child state			X^2 = 0.762	0.666
A	20	22		
B	4	2		
C	0	0		
Duration of surgery (min)	165.38 ± 33.31	151.83 ± 34.29	t = 0.023	0.881
Intraoperative blood loss (ml)	248.75 ± 76.0	225.83 ± 87.52	t = 0.516	0.476
Intraoperative fluid transfusion (ml)	1495.83 ± 295.59	514.58 ± 344.99	t = 0.442	0.510

NRS: Nutritional Risk Screening; ASA: The United States before surgery anesthesiologist association risk classification

Table 1: Patient demographics and surgical characteristics.

and insulin were higher than before surgery, but the level of blood glucose and insulin is significantly lower in CHOD group than that in the placebo group, while median level of HOMA-IR in two groups increased significantly by the end of surgery. In the CHOD group HOMA-IR was significantly lower than that in the placebo group (Table 2), and ISI in the CHOD group was significantly higher compared with that in the placebo group at the end of surgery (Table 2). There were no differences in HOMA-β between two groups after surgery.

Length of stay and complication

Median postoperative length of hospital stay was 10.2 ± 3.7 days in the placebo group and 9.7 ± 2.8 days in the CHOD group, which was not significantly different (P = 0.439). Clinical complication was recorded in 5 placebo group and 5 CHOD group (Table 3).

Discussion

Hyperinsulinaemic euglycaemic clamp technique is viewed as gold standard in quantifying insulin sensitivity [18], but this technique needs frequent blood in patient for a short time, the bulk of patients cannot bear it, so the hyperinsulinaemic euglycaemic clamp technique is limited in clinical practice. The HOMA-IR model is a kind of non-invasive and convenient way to estimate insulin sensitivity and β-cell function from glucose blood and plasma insulin concentration [7,8], there is a good correlation between HOMA and hyperinsulinaemic euglycaemic clamp technique for estimating of insulin resistance, and HOMA is viewed as a reliable indicator of insulin resistance [7,9] and previous studies show that HOMA-IR model can be utilized as a reliable indicator and marker of postoperative insulin resistance in surgical patients [10].

This study illustrated two main aspects, one point that the preoperative carbohydrate beverage and non-energy water were well tolerated and no obvious complications associated with preoperative oral loading were noted during surgery, the other point was that patients who receive carbohydrate fluid before radical distal gastrectomy had reduced postoperative insulin resistance, display less impaired postoperative insulin sensitivity as compared to patients in placebo group.

Insulin resistance is a key factor of the postoperative metabolic response to surgical injury [11]. The main feature of IR was a hyperglycemia state, due to increasing glucose and reducing insulin-stimulated glucose uptake in liver and peripheral (mainly skeletal muscle and fat tissue) [12,13], Hyperglycemia due to insulin resistance has been shown to increase morbidity and infection rate. Furthermore, insulin resistance has been shown to be an independent factor affecting postoperative length of hospital stay [14].

Although preoperative loading with carbohydrates has been documented beneficial effects and has been used in clinical practice in many centuries, the mechanisms behind the reduction in postoperative insulin resistance are not fully understood. Preoperative fasting or oral non-energy fluid made liver glycogen storage virtually depleted and is possible to add to the detrimental effects of the increased catabolic state. This kind of state was viewed as fasting stress. When this fasting stress combined with the increased metabolic demand of surgery injury, may result in a worse clinical outcome [2]. However, preoperative oral carbohydrate could change metabolism from the fasted state to the fed state. Compared with fasted state, patient in a fed state were in a less stressful response to the surgical trauma. Insulin, known anabolic hormone, was likely to be one of the keys in this metabolic from the fasted to the fed state. Insulin is a hormone central to regulating carbohydrate and fat metabolism in the body. Insulin causes cells in the liver, muscle, and fat tissue to take up glucose from the blood,

	4 hours before surgery	After surgery	t	P
FBGmmol⁄L				
Placebo group	4.93 ± 0.59	9.32 ± 1.31	13.624	0.000
CHOD group	5.08 ± 0.50	7.64 ± 0.78	13.918	0.000
t	0.746	5.294		
P	0.392	0.026		
FINSU				
Placebo group	8.25 ± 1.62	30.72 ± 6.66	15.781	0.000
CHOD group	8.54 ± 1.89	16.72 ± 3.88	10.011	0.000
t	0.612	4.797		
P	0.438	0.034		
HOMA-IR				
Placebo group	1.82 ± 0.45	12.68 ± 3.13	16.318	0.000
CHOD group	1.90 ± 0.36	5.67 ± 1.40	14.190	0.000
t	0.698	9.646		
P	0.408	0.003		
ISI				
Placebo group	0.63 ± 0.41	0.41 ± 0.19	23.000	0.000
CHOD group	0.62 ± 0.31	0.48 ± 0.26	22.561	0.000
t	0.829	5.112		
P	0.367	0.029		

Table 2: Biochemical index.

Complications	CHOD	Placebo
Anastomotic leak	1	1
Surgical Site Infection	0	1
Drug reaction	1	0
Nausea and vomiting	2	2
Postoperative hyperpyrexia	1	1

Table 3: Clinical complications.

storing it as glycogen in the liver and muscle. Excluding decreasing blood glucose, Insulin also has some other functions, including anti-inflammatory, immunoregulation, reduced oxidative stress, prevented endothelial injury and so on [14,15]. However, the concentration of carbohydrates is too low (less than 8%) to cause an insulin response. So a carbohydrate beverage was developed containing 10% carbohydrate. Preoperative oral carbohydrate was equivalent to that seen after a normal meal [6]. The present study has shown that preoperative oral carbohydrate could improve PIR, although the exact mechanisms had been elusive, it was strongly suggested that IR lied at insulin signaling [16,17]. Previous studies on potential mechanisms of insulin resistance in animal models of burn injury [18]. Preoperative oral carbohydrate could promote insulin release, intensive insulin sensitivity and insulin pathways result in increasing the GLUT-4 protein expression, which lead to improve postoperative insulin resistance.

The present study showed that there was no difference in two groups on the length of stay and expense. Preoperative oral carbohydrate could not shorten the length of stay, and decrease the hospitalization expense. With the fast tract developing, clinical outcomes have been improved obviously, enhance recovery after surgery need a comprehensive program [19]. These measure included bowel preparation, routine nasogastric decompression, preoperative or postoperative fasting, routine prophylactic drainage, fluid management, postoperative analgesia. But this does not mean preoperative oral carbohydrate is waste. In the study preoperative oral carbohydrate improve postoperative insulin resistance and this treatment is a safe, efficient, noninvasive mean, contribute to fast tract, improve the patients postoperative, preoperative oral carbohydrate should be a routine for preoperative preparation.

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