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Clinical Observation of Preoperative Oral-Carbohydrate Combined with Individualized Medication in Patients with Type 2 Diabetes Mellitus

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Abstract: To observe the clinical effect of preoperative oral carbohydrate(POC) combined with individualized medication (oral hypoglycemic agents or/and insulin) that has been used steadily in patients with type 2 diabetes mellitus. Patients undergoing elective laparoscopic non-gastrointestinal surgery were studied. Thirty type 2 diabetic patients with good glycemic control were selected as diabetic group (Group D) and 31 non-diabetic patients were recruited as control group(Group C). In both groups, 400mL carbohydrate drink was taken orally 2 hours before anesthesia. Anti-diabetes medication was given individually in the diabetic group(Group D) according to their daily use. Blood glucose was detected and recorded at the time of fasting (T_0), 1 hour after POC (T_1), before anesthesia(T_2), 15min after pneumoperitoneum(T_3), 30min after pneumoperitoneum (T_4), and in recovery room (T_5) for both groups. Ultrasound of gastric antrum was assessed and semi-quantification of gastric contents(Perlas A scale) was performed. Perioperative hunger, nausea, vomiting and postoperative exhaust time were also recorded. There was no statistically significant difference between two groups above in blood glucose at T_0 and T_5(P> 0.05);at T_1,T_2,T_3 and T_4, compared with Group C, patients in Group D had significantly higher blood glucose (P<0.05), but within 250mg/dl(13.9mmol/L). No additional hypoglycemic intervention implemented; no symptoms of discomfort was reported as well. For gastric antrum Perlas A grading before general anesthesia, there was no statistically significant difference in the scores between the two groups (P> 0.05), and no reflux aspiration was observed in both groups. There was no statistically significant difference in perioperative hunger, nausea and vomiting, and postoperative exhaust time between the two groups (P> 0.05). Preoperative oral carbohydrate (POC) can be applied to well glucose-controlled type 2 diabetic patients.

1. Introduction

With the implementation of the concept of enhanced recovery after surgery (ERAS) at home and abroad, the traditional concept that longer fasting is safer has been gradually denied [1]. The ERAS guidelines at home and abroad advocate that the no-drinking period should be extended to 2 hours before the operation and clear fluid beverage can be taken orally. Currently, oral carbohydrate-containing drinks are recommended, but not routinely recommended for diabetic patients[2]. In diabetic patients, fasting and drinking for a long time are likely to lead to severe hypoglycemia [2], but their insufficient insulin secretion, insulin resistance and surgical stress, and they are also prone to severe conditions such as hyperglycemia, hypoglycemia, ketosis and even acid-base imbalance[3]. The purpose of this study was to explore the preoperative oral carbohydrate combined with stable individual medication (oral hypoglycemic agents or/and insulin) in type 2 diabetes patients with good blood glucose control, to observe perioperative blood glucose fluctuations, preoperative aspiration risk assessment, perioperative comfort level and other conditions compared with non-diabetic patients, so as to provide research basis for clinical practice.

2. Material and Methods

2.1 General Information

This study was approved by the Ethics Committee of Wenzhou central hospital (Ethics approval number: 202303160135000460392), and all patients signed informed consent. Sixty-one patients aged 35 to 65 years old who received elective laparoscopic non-digestive tract surgery in our hospital from August 2021 to August 2022 were selected, with ASA grade I to III, of which 30 were type 2 diabetes patients (Diabetes group D) and 31 were non-diabetes patients (Control group C). Group D was diagnosed with type 2 diabetes mellitus and stably used for more than 1 year, including various oral hypoglycemic agents and subcutaneous insulin injection. Glycosylated hemoglobin (Hb A1c) < 8%; There were no complications such as severe liver or kidney function injury. The operation time of all patients was between 11:00 and 14:00, and the operation duration was within 150 minutes. Exclusion criteria: changes in surgical methods (Such as switching to open surgery during the operation), high-risk patients with reflux aspiration (Delayed or obstructed gastric emptance, digestive tract obstruction, etc.), and previous history of gastrointestinal surgery; Morbid obesity 40), a history of mental illness. Types of laparoscopic surgery include hernia repair, cholecystectomy, and gynecological surgery. There were no significant differences in gender, age, BMI, operation time and other general data between the two groups ($P > 0.05$), as shown in Table 1.

Table 1: Comparison of General Conditions between the Two Groups

Group	Event	Sex Ratio(Male/ Female)	Age	BMI (kg/m^2)	Case			Operation time
					Hernia repair	Cholecystectomy	Gynecological operation	
Group D	30	11/19	48.8 ±14.6	23.2 ±4.7	9	10	11	107.8 ±35.2
Group C	31	13/18	49.2 ±13.3	24.8 ±3.5	8	11	12	110.3 ±32.6

2.2 Methods

Two hours before general anesthesia, patients in both groups were given 400 mL of carbohydrate drink (Sugan, maltodextrin fructose drink, Jiangsu Zhengda Fenghai Pharmaceutical Co., LTD.) orally, and drank it within 10 minutes. Patients in group D were self-administered according to their usual medication (oral hypoglycemic agents or/and insulin). Perioperative blood glucose in both groups was closely monitored, if the blood glucose was too high [>250mg/dl(13.9mmol/L)] or too low [<70mg/dl(3.9mmol/L)][2,4], blood glucose control plan was made: glucose infusion or insulin was further regulated, and blood glucose was monitored again every half hour.

Before anesthesia, antrum ultrasound scanning and semi-quantitative evaluation of gastric contents (Perlas scale grading) [5] were performed to rapidly screen high-risk patients with reflux aspiration according to the score: two-dimensional portable ultrasound instrument (TE7; Mindray, China) low-frequency probe (curved array 60 mm, frequency 2-6 MHz) was used to scan the antrum of the patient in the supine position and the right decubitus position. The evaluation grade of the antrum was 0, and no fluid was detected in either position. Level 1: Liquid was present in the right decubitus position, but not detected in the supine position. Level 2: Fluid is present in both positions or solid or viscous particles are found in either position. If grade 2 antrum is present, delay surgery or change to intubation general anesthesia, considering the high risk of reflux aspiration.

All patients received laryngeal mask and intravenous anesthesia. Anesthesia induction: Sufentanil 0.25μg/kg, etomidate 0.2mg/kg, cisatracurium 0.2mg/kg. After the muscle relaxant took effect, the laryngeal mask was implanted. During the operation, propofol was continuously pumped 4 to 5mg/ (kg ħ), remifentanil was continuously administered and sufentanil was intermittently administered for analgesia. Noninvasive blood pressure, heart rate (HR), electrocardiogram (ECG), pulse oxygen saturation (SpO_2), and end-breath carbon dioxide ($EtCO_2$) were closely monitored during the operation. The changes in blood pressure and heart rate were maintained within 30% of those before anesthesia induction, $P_{ET}CO_2$ was maintained at 35-45mmHg, and BIS was between 40 and 60. Toanisetron was administered 0.2mg/kg before the end of surgery.

2.3 Observation Indicators

Blood glucose levels in fasting (T0), 1 hour after oral carbohydrate intake (T1), before anesthesia (T2), 15min(T3), 30min(T4) and recovery room (T5) were recorded in both groups. The gastric antrum and gastric evaluation grade were recorded. Perioperative hunger, nausea and vomiting and postoperative exhaust time were recorded.

2.4 Statistical Analysis

SPSS22.0 statistical software was adopted. The measurement data were expressed as mean ± standard deviation ($\bar{x} \pm s$), the comparison between the two groups was performed by t-test, and the comparison of count data was performed by $\chi 2$ test. Means at multiple time points were compared by repeated measure analysis of variance, and *P*-value was corrected by Bonferroni method for pairwise comparison. $P < 0.05$ was considered statistically significant.

3. Result

3.1 Comparison of Perioperative Blood Sugar between the Two Groups

There was no significant difference in fasting blood glucose (T0) and recovery room (T5) blood glucose levels between the two groups ($P > 0.05$). At T1, T2, T3 and T4, blood glucose in group D

increased more significantly, and the difference was statistically significant (P <0.05), see Table 2 for details. Perioperative blood glucose fluctuations in both groups ranged from 70 to 250 mg/dl(3.9 to 13.9 mmol/L), and none of the patients received additional insulin or glucose solution.

Table 2: Comparison of Blood Glucose Level between the two groups at different time periods (mmol/L)

V	T_0	T_1	T_2	T_3	T_4	T_5
Group D	6.0±0.9	9.3±1.9*	9.6±2.0*	9.5±2.0*	9.4±2.0*	7.2±1.3
Group C	5.3±0.8	8.6±1.2	8.3±1.2	7.8±1.1	7.7±1.2	6.6±1.1
F	0.084	5.643	3.002	4.154	4.006	1.929
P	0.773	0.021	0.002	0.001	<0.001	0.414

A. Fasting (T0), 1 hour after oral carbohydrate intake (T1), before anesthesia (T2), 15min pneumoperitoneum (T3), 30min pneumoperitoneum (T4), and recovery room (T5) blood glucose levels

B. *Compared with Group C. Note: A. Fasting (T0), 1 hour after oral carbohydrate administration (T1), before anesthesia (T2), 15min pneumoperitoneum (T3), 30min pneumoperitoneum (T4), and recovery room (T5) blood glucose levels

B. * Compared with Group C. 0.05, there was statistical difference

3.2 Comparison of Semi-Quantitative Evaluation of Gastric Contents

There was no significant difference between the two groups in the Perlas A Scale before general anesthesia (P<0.05), see Table 3 for details. No patients with grade 2 scores were found in the two groups, that is, no patients at high risk of aspiration.

Table 3: Comparison of Perlas a Grade Evaluation of Gastric Contents before general anesthesia between the two groups

Perlas A Grade	0	1	2
Group D	19(63%)	11(37%)	0(0%)
Group C	23(74%)	8(26%)	0(0%)
χ^2	0.838		
P	0.416		

3.3 Other Indicators

There were no significant differences in perioperative hunger, nausea, vomiting and exhaust time between the two groups (P < 0.05), see Table 4 for details.

Table 4: Comparison of Other Postoperative Observation Indexes between the Two Groups

Index	Group D	Group C	T/χ^2	*P*
Hunger	8/30(27%)	6/31(19%)	0.461	0.554
Nausea and vomiting	4/30(13%)	3/31(10%)		0.707[a]
Exhaust time(hours)	23.63±5.0	23.43±4.4	0.166	0.869

a: Tested by the exact probability method

4. Discussion

Shortening the duration of fasting and drinking before surgery is one of the core contents of enhanced recovery after surgery (ERAS) [1]. A number of studies have confirmed that eating

carbohydrate-containing drinks, such as maltodextrin fructose drinks, at 2h before surgery can not only reduce patients' perioperative discomfort, but also reduce postoperative insulin resistance and reduce perioperative complications [6]. Previous guidelines or studies are mostly for non-diabetic patients. In diabetic patients, due to impaired blood glucose control and slow gastric emptance, it is generally believed that oral administration of carbohydrates before surgery may lead to severe hyperglycemia and reflux aspiration, which makes its clinical safety questionable and limits its wide application. In diabetic patients, fasting and drinking for a long time is likely to lead to severe hypoglycemia [2], but their own insulin secretion deficiency, insulin resistance and surgical stress caused by fasting and drinking are also prone to severe conditions such as hyperglycemia, hypoglycemia, ketosis and even acid-base imbalance [3], which requires reasonable fasting and drinking and blood glucose management during the perioperative period. In clinical practice, there are great differences between different countries, regions and clinicians on whether patients with diabetes use carbohydrate drinks and the ingredients of drinks before surgery[7][8]. This very controversial hot topic requires more large sample studies and more powerful evidence.

Lee[9] et al. reported that patients with diabetes who took carbohydrate drinks orally before surgery would have large fluctuations in blood sugar, and suggested “careful giving”. In the study of Li et al. [10], after taking carbohydrate drinks orally and then administering insulin intravenously to regulate blood sugar according to elevated blood sugar, patients' perioperative thirst, hunger and other discomfort were significantly improved. The ideal perioperative blood glucose range for patients with diabetes is still controversial. Cheisson et al. [11] concluded that the perioperative blood glucose range of 4.4 ~ 10.0 mmol/L in patients with diabetes was too strict, which could not improve the prognosis except for frequent hypoglycemia. Ceriello et al. [12] found that, regardless of whether patients were diabetic or not, severe blood glucose fluctuations caused greater damage to endothelial function than sustained high blood glucose level (blood glucose maintained at 15mmol/L), which may increase the risk of postoperative cognitive dysfunction and cardiovascular adverse events. Therefore, large fluctuations in perioperative blood sugar should be avoided. In recent years, expert consensus[2][4] proposed that when fasting or random blood glucose ≥13.89mmol/L, surgery should be decided after comprehensive evaluation by multidisciplinary physicians. In this study, although the perioperative blood glucose in the diabetes group increased more significantly than that in the control group, 11 patients had at least one blood glucose value of more than 10.0 mmol/L during T0-T5, but none of them exceeded 13.9 mmol/L, and no other complications occurred.

With the increasing number of diabetic patients in clinical practice and the popularization of diabetes knowledge and medication, more and more diabetic patients have good compliance with daily medication and blood glucose monitoring, and their blood glucose control is ideal. In addition, with the promotion of minimally invasive and daytime operations in recent years, both surgeons and patients hope to recover to the “daily state” more quickly after surgery. For such patients, more “autonomous” blood glucose control may be used. In this study, type 2 diabetes patients with stable blood glucose control and medication were selected as the experimental group. After oral administration of carbohydrates 2 hours before surgery, patients were given the individualized medication plan to control blood glucose after eating once a day. Perioperative blood glucose control was satisfactory in the diabetic group, and no additional medication was needed for blood glucose control by clinicians, considering that such medication might be closer to the steady-state of daily blood glucose control in patients.

In addition, there were 3 patients in the control group whose perioperative blood glucose value exceeded 10.0 mmol/L at least once, and no insulin was added after postoperative infusion containing glucose, and their blood glucose did not increase significantly. The elevated blood glucose in these patients may be related to stress caused by perioperative inflammation or pain or

the patient's own impaired glucose tolerance.

In recent years, researchers began to pay attention to the risk of reflux aspiration after oral carbohydrate intake in diabetic patients. In several current research results, Cassady[13] et al. assessed the gastric emptying rate by detecting the blood paracetamol content after drinking liquid mixed with carbohydrates and paracetamol before operation, and concluded that there was no significant difference in the gastric emptying rate between the diabetic group and the non-diabetic group. In the study of Lin Xinqiang et al. [14], after taking different amounts of carbohydrates orally before surgery, the gastric volume obtained from the gastric antrum area was measured by ultrasound to assess the risk of reflux aspiration. It was concluded that the consumption of 300ml carbohydrate 2h before surgery had no significant effect on the stomach volume before anesthesia induction in diabetic patients. Lee Seohee et al. [15] performed Perlas A classification of gastroantrum for diabetic patients who took carbohydrates orally 2h before anesthesia, and the results showed that grade 0:67.3%; Level 1:32.7%; Grade 2 0%, similar to the results of antrum grading in this study. But the commodity category of carbohydrate drinks was not consistent between these studies; The course of diabetes, medication and related complications were not described in detail. Whether these factors have an effect on the gastric emptying of carbohydrate drinks remains to be further studied with large samples.

The studies of Lee[8], Li et al. [9] and Lin Xinqiang [14] all showed that oral administration of carbohydrates before surgery can significantly reduce the symptoms of hunger, nausea and vomiting, and significantly improve the comfort level of patients during perioperative period. Talutis et al. [16] reviewed preoperative oral carbohydrate cases (80 patients with diabetes and 275 patients without diabetes) in recent years, and concluded that there was no difference in postoperative complications. These are consistent with the results of this study. Patients with diabetes who take carbohydrates orally before surgery can get the same benefits as non-diabetic patients in terms of improving comfort level and accelerating rehabilitation during perioperative period.

The enrolled patients in this study underwent laparoscopic non-digestive tract surgery with little trauma and quick recovery, and most of them could return to normal diet soon after surgery. The experimental group were type 2 diabetes patients with good blood glucose control, and perioperative blood glucose fluctuations were significantly improved after combined with personalized medication (oral hypoglycemic agents or/and insulin). Whether this medication mode is also suitable for other more traumatic operations such as gastrointestinal surgery and open surgery; Whether it is also applicable to other diabetic patients, such as patients with poor blood sugar control, patients with liver and kidney function injury and patients with type 1 diabetes, should be guided by the clinical judgment of the surgical team, and further large sample study should be conducted according to the needs and characteristics of patients.

In conclusion, in type 2 diabetes patients, oral carbohydrate combined with individualized medication before surgery, the perioperative blood glucose fluctuation is relatively stable, no additional blood glucose regulation medication is required, and the risk of perioperative reflux aspiration is not increased. In addition, the patients can get the same benefits as non-diabetic patients in terms of improving comfort level and accelerating recovery during the perioperative period. It can bring more clinical benefits to diabetic patients and provide clinical basis for the wider application of oral carbohydrate in diabetic population before surgery.

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