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Original Article

The Effect of Preoperative Oral Carbohydrate Loading on Postoperative Insulin Resistance and Recovery Following Orthognathic Surgery: A Randomized Placebo-controlled Trial in Healthy Volunteers

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Abstract

Objectives: This study aimed to investigate the effect of preoperative oral carbohydrate loading on postoperative insulin resistance, inflammation, and recovery following orthognathic surgery.

Methods: Twenty healthy patients were evenly randomized to receive 12.5% oral carbohydrate drink (CHO group) which is 50 g of glucose (400 ml) or placebo drink three hours before surgery. Insulin resistance, determined by homeostatic model assessment (HOMA-IR), and interleukin-6 (IL-6) levels were measured before and after orthognathic surgery. Length of stay, time to readiness for discharge (TRD) from postanesthetic care unit (PACU), postoperative complications, and quality of postoperative recovery were also documented. Regression analysis was used to explore independent effect of preoperative carbohydrate loading.

Results: Postoperative HOMA-IR and IL-6 levels showed no statistically significant difference between groups. TRD from PACU was significantly shorter in CHO group (p=0.01). No significant differences of length of stay, postoperative complications, and quality of recovery were observed.

Conclusions: Preoperative carbohydrate loading did not improve postoperative insulin resistance and inflammation following orthognathic surgery. However, this intervention significantly enhanced recovery in postanesthetic care unit.

Keywords: carbohydrate loading, inflammation, insulin resistance, orthognathic surgery, post-surgery recovery time

Introduction

Traditionally, a 6-8-hour period of preoperative fasting has been recommended to decrease gastric volume and acidity in prevention of pulmonary aspiration. However, previous studies demonstrated that overnight fasting brings on preoperative discomfort and associates with adverse physiologic events, such as dehydration, muscle wasting, and a weakened immune system.[1] Several studies also documented that oral intake of clear fluid at two hours prior to induction of anesthesia reduces preoperative discomfort[2] and does not increase the risk of pulmonary aspiration.[3] Thus, this strict routine practice has been questioned on the necessary and true benefit for patients. Surgical stress response results in an increased metabolic rate and a state of hypermetabolism.[4] This accelerated situation leads to metabolic alterations and systemic inflammatory response (SIRs) mediated by various cytokines.[5] IL-6 levels can be predicted the severity of SIRs and markedly increased after orthognathic surgery.[6]

Recently, the fasted state before surgery has been emphasized on metabolic implications and represented an additional stress.[7] After surgical stress occur, the body will shortly develop a state of insulin resistance (IR) which associated with higher postoperative morbidity and mortality. Currently, several anesthesia societies change their guidelines and recommend intake of clear fluids up until two hours prior to elective surgery and anesthesia.

Preoperative carbohydrate loading (PCL) with 12% carbohydrate-rich clear drink was developed to suit the preoperative setting with safety.[2] Preoperative carbohydrate drink improves patient's wellbeing, reduces in IR, minimize inflammation, and shorten length of stay.[8-12] PCL also became one component of the Enhanced Recovery After Surgery protocol which is multimodal perioperative care developed to execute early recovery after surgical procedures. The roles of preoperative carbohydrate drink have been investigated in various types of surgery, but no current evidence is related to orthognathic surgery.[13] The present study aimed to evaluate the efficacy of preoperative oral carbohydrate drink (CHO), comparing the differences between preoperative carbohydrate drink and placebo on postoperative IR, plasma interleukin-6 (IL-6) level, time to readiness for discharge (TRD) from PACU, length of stay in hospital (LOS), quality of recovery (QoR), and complications in orthognathic surgery.

Materials and Methods

Trial design

This was a single-centered, stratified (one jaw and double jaw of orthognathic surgery, with equal randomization), triple-blind, placebo-controlled, parallel-group study. This study was registered on the Thai Clinical Trials Registry (TCTR20200424001) and approved by the Human Experimentation Committee, Faculty of Dentistry, Chiang Mai University (NO. 33/2019).

Participants

Eligible participants were healthy patients (ASA class I or II), aged from 18 to 40 years, those who require orthognathic surgery, both one jaw and double jaw, and those who were willing to participate the study. The exclusion criteria were smoking or pregnant patients, patients who have body mass index (BMI)≥25, patients who have a history of gastroesophageal reflux disease (GERD), upper gastrointestinal tract surgery and metabolic disease, including diabetes mellitus, dyslipidemia, hypertension, hypothyroidism and malnutrition. The patients who present fasting blood glucose greater than or equal to 100 mg/dL, at shortly before drink intake, was withdrawn from study. All participants provided written informed consent.

Randomization and allocation

A web-based random sequence generator was utilized to assign eligible patients (1:1 allocation ratio) to receive CHO or placebo. Random permuted blocks of four, stratified with types of orthognathic surgery (one jaw and double jaw), was used to ensure close balance of the numbers and characteristics in each group. Allocation concealment was done with sealed opaque envelopes which was opened by nursing staffs at ward, 3 hours prior to the surgery. The allocation was blinded to anesthesiologists, surgeons, participants, and co-investigators assessing outcomes until completion of the study.

Intervention and procedure

All participants were screened with physical examination and laboratory investigation, including complete blood count (CBC), urine analysis and coagulogram, at two weeks prior to surgery. Then the participant was admitted on the day before surgery and underwent overnight fasting. Preoperatively, no intravenous fluid

was administered until completion of CHO or placebo intake. CHO group received 12.5% in-house carbohydrate drink (50 g of glucose monohydrate, 400 ml). Placebo group received plain water in the same amount. Both carbohydrate drink and placebo were formulated with the same color and flavor, and participants were not informed about characteristics, also taste, of carbohydrate drink and placebo. At 3 hours prior to induction of anesthesia, participant received either CHO or placebo, regarding allocation. All surgeries were performed by only single surgical team. One jaw orthognathic surgery included only bilateral sagittal split ramus osteotomy (BSSRO). Double jaw orthognathic surgery included both BSSRO and Le Fort I osteotomy simultaneously. General anesthesia was induced with propofol 1.0-2.5 mg/kg and atracurium 0.5-0.6 mg/kg or cistracurium 0.1-0.15 mg/kg. Sevoflurane or isoflurane was used for maintenance of anesthesia, with intermittent bolus doses of fentanyl and neuromuscular blockage. Perioperative fluid administration was restricted to a glucose-free intravenous solution and the participants would obtain blood transfusion with packed red cell, if indicated. At the end of operation, the neuromuscular block was reversed with neostigmine 0.05 mg/kg and atropine 0.02 mg/kg. Subsequently, participant was monitored at post anesthetic care unit (PACU) and assessed Modified Aldrete Score every 15 minutes until discharge to hospital ward. Cefazolin was used as perioperative antibiotic prophylaxis and clindamycin was an alternative. Perioperative dexamethasone was routinely administrated to decrease swelling of oropharynx and risk of airway compromise. After operation, participants received only oral carbohydrate fluid (13 g of glucose monohydrate, 150 ml) as needed and glucose-free intravenous fluid administration until postoperative blood sample drawing was done. Fentanyl was used to relieve acute pain in PACU. At hospital ward, participant received parecoxib once daily as primary analgesic. Intravenous morphine sulfate was available for breakthrough pain. Ondansetron was used for postoperative nausea and vomiting, as needed.

Study endpoints

The primary endpoints were postoperative IR and IL-6 level. Peripheral venous blood samples were collected for biochemical assay of plasma glucose, insulin, and IL-6 level at shortly before carbohydrate drink or placebo intake (T0) and 24 hours after surgery (T1). Plasma glucose was measured by blood glucose meters (Accu-Chek®, Roche, Thailand). While Plasma insulin level was measured by Human Insulin ELISA Kit (ab100578) (Abcam, Cambridge, U.K) sensitivity 4 μU/ml and range 4.69-300 μu/ml and plasma IL-6 level was measured by Human Interleukin-6 ELISA Kit (ab178013) (Abcam, Cambridge, U.K) sensitivity 1.6 pg/ml and range 7.8-500 pg/ml. These investigations were duplicated. The homeostatic model assessment is a method used to quantify insulin resistance using the formula by Matthews *et al*[14]: HOMA-IR = (Blood glucose [mg/dL] x Blood insulin [μU/ml]) / 405.

The secondary outcomes were TRD from PACU, LOS, QoR, and surgery or anesthesia related complications. TRD was defined as the number of minutes to achieve Modified Aldrete Score over 8. Postoperative quality of recovery was measured by Thai QoR-35 questionnaire at 12-24 hours after surgery. Thai QoR-35, modified from QoR-40, is a 35-item questionnaire that covers five domains of recovery outcomes, including physical comfort, emotional state, physical independence, psychological support, and pain.[15] Thai QoR-35 has a total score of 175 points. The higher scores reflect better quality of recovery. Surgery-related complication was defined as a composite of oropharyngeal swelling with potential airway compromise and surgical site infection within the first 3 weeks of surgery.[16] Anesthesia-related complication was defined as pulmonary aspiration. Demographic data, including age, sex, and BMI, were recorded on the day of admission. Total operative time, intraoperative blood loss, the amount of blood transfusion received were obtained. The amount of postoperative carbohydrate intake and medication was measured by nursing staff on ward. Postoperative opioid used was recorded as total morphine equivalent dose.

Statistical analysis

This study calculated sample size based on previous study by Nermina *et al.*[17] Considered with the power of 90%, the enrollment of 20 participants would detect a mean reduction of 28.6±17.2 pg/ml in IL-6 level in CHO group at an alpha level of 0.05, allowing for a loss to drop out of 10%.

All data were analyzed using Stata Statistical Software: Release 17 (College Station, TX: StataCorp LLC). The Shapiro–Wilk test was used to explore normal distri-

bution. Numeric data is presented as mean and standard deviation or median and interquartile range. Categorical data is presented as number and percentage. The mean difference of CHO and placebo group were analyzed by independent sample t-test in normally distributed data, while abnormally distributed data were analyzed with Man-Whitney U test. Fisher's exact test was used to analyzed categorical data. In addition, the independent effect of preoperative oral carbohydrates loading on HOMA-IR and IL-6 level was analyzed with regression analysis. A *p*-value of less than 0.05 was considered to be statistically significant.

Results

Study population and clinical characteristics

Regarding screened 21 patients who underwent orthognathic surgery, only one patient was excluded due to a history of GERD. A total of 20 participants underwent randomization and completed the study. The average age was 24.85±5.14 (19 to 40 years). Each group consisted of seven single-jaw surgeries and three double-jaw surgeries. Baseline demographic and clinical characteristics were shown in Table 1.

Primary endpoints

Plasma glucose, insulin and HOMA-IR levels increased after surgery in both groups and were higher in CHO group, compared to placebo group at T0 and T1. No significant difference in plasma glucose, insulin and HOMA-IR levels was observed during all study periods. After surgery (T1), the total increase in HOMA-IR was lower in placebo group, compared to the CHO group. IL-6 level also increased after surgery in both groups, and CHO group tended to increase lesser than placebo group. There was no significant difference in IL-6 between CHO and placebo group during all study periods. The primary endpoints were presented in Table 2.

The regression analysis, adjusted for age, BMI, type of orthognathic surgery, intraoperative blood loss, the amount of blood received, and postoperative carbohydrate intake, was considered to explore the independent effect of PCL (Table 3). The model showed that PCL resulted in increase of plasma glucose level (95%CI; -25.61-42.87, p=0.59) and decrease of insulin (95%CI; -9.32-3.20, p=0.31), HOMA-IR (95%CI; -4.73-2.06, p=0.40) and IL-6 (95%CI; -2.48-0.78, p=0.28) level.

Secondary endpoints

TRD from PACU was significantly shorter in CHO group, compared to placebo group (p=0.01). LOS was found to be similar between groups (p=0.29). Thai QoR-35 scores in all domains were not significantly different between CHO and placebo groups. Ondansetron was greater frequently used in placebo group, but the result showed no significant difference between groups (p=0.05). Moreover, no significant difference was also observed in the total morphine equivalent dose among groups (p=0.80). There was no incidence of surgery-related and anesthesia-related complications in this study. The details of secondary endpoints were presented in Table 4.

Discussion

Surgical stress response after traditional preoperative fasting results in unfavored metabolic alteration. In fasted state, glucose will be increased through mechanism of liver glycogenolysis and gluconeogenesis. Although the insulin-mediated glucose reuptake into peripheral tissue is reduced while occurring of gluconeogenesis, insulin action still needs for the glucose supplied-energy pathways. Due to prolonged fasting, the endoplasmic Reticulum (ER) regulation of liver gluconeogenesis is continuously activated which sequentially led to IR.[18] The development of IR was widely reported to correlate with poor recovery and clinical outcomes. Besides, the rising in level of IL-6 could lead to sepsis and increase the mortality after surgery.[19] PCL was introduced to reverse the undesirable effects of fasted state, but the precise physiologic mechanism of this intervention remains unclear.

In this study, PCL did not significantly attenuate postoperative IR following orthognathic surgery, which postoperative IR was higher in CHO group compared with placebo. In contrast, Tran and colleagues found that PCL insignificantly reduces IR more than it does in the placebo group.[20] Previous meta-analysis also demonstrated a statistically significant decrease of IR in patients receiving preoperative carbohydrate (mostly 45-55 g) loading.[21] The degree of postoperative IR has been found to be proportional to the magnitude of the surgical trauma and the effect of PCL on IR seemed to be different among various types of surgeries.[22] This intervention might suit to decrease IR in patients undergoing colorectal surgery, and

Table 1: Demographic data and clinical characteristics of patients included.

Parameter	CHO Group (*n*=10)	Placebo group (*n*=10)	*p* value
Female[a]	8 (80)	2 (20)	0.33
Age (years)[b]	24.5 (23-27)	22 (22-24)	0.12
BMI (kg/m^2)[c]	22.60±4.04	23.00±3.95	0.82
Total operative time (minutes)[b]	252.5 (200-320)	192.5 (170 -370)	0.32
Intraoperative blood loss (ml)[b]	375 (200-500)	500 (300-1000)	0.21
Blood transfusion (ml)[b]	0 (0-0)	0 (0-250)	0.21
Number of patients receiving blood transfusion[a]	0 (0)	1 (10)	-
Total amount of postoperative carbohydrate intake (g)[c]	11.70±9.59	15.60±10.25	0.37
Number of patients intaking postoperative carbohydrate[a]	7 (70)	6 (60)	-

CHO, preoperative carbohydrate drink; BMI, body mass index
[a]Data are reported as count (percentage), [b]Data are reported as median (Q1-Q3), [c]Data are reported as mean ± standard deviation
*Statistically significant

Table 2: Insulin resistance and inflammatory response parameters according to the CHO group and placebo group at different time points.

Parameters		CHO Group (*n*=10)		Placebo Group (*n*=10)		*p* value
		Median (Q1-Q3)	95% CI	Median (Q1-Q3)	95% CI	
Plasma glucose (mg/dl)	T0	94 (88-96)	86.46-98.93	96 (91-104)	91.75-102.04	0.40
	T1	151 (130-168)	132.43-172.16	140.5 (132-147)	125.66-169.53	0.62
	T1-T0	53 (44-72)	40.28-78.91	39.5 (32-60)	27.22-74.17	0.20
Insulin (μIU/ml)	T0	9.56 (8.94-11.91)	9.03-11.96	10.11 (9.88-10.5)	8.74-10.75	0.90
	T1	13.31 (11.44-20.19)	11.49-18.00	12.06 (10.81-17.84)	10.27-19.95	0.73
	T1-T0	4.14 (0.93-5.47)	1.65-6.84	3.22 (0.78-7.65)	0.73-9.98	0.85
HOMA-IR	T0	2.28 (2.07-2.79)	2.02-2.79	2.34 (2.25-2.44)	2.11-2.51	0.85
	T1	5.5 (3.87-6.62)	4.20-6.84	4 (3.29-6.43)	3.022-8.76	0.40
	T1-T0	3.17 (1.48-3.94)	1.91-4.31	1.77 (0.93-3.74)	0.74-6.41	0.60
IL-6 (pg/ml)	T0	1.32 (0.42-3.5)	0.53-3.21	1.48 (1.06-3.61)	1.05-2.82	0.60
	T1	6.57 (6.22-7.28)	5.81-8.59	7.63 (7.19 -8.5)	7.05-8.74	0.05
	T1-T0	5.35 (4.64-6.22)	4.04-6.61	6.01 (4.83-6.78)	4.82-7.09	0.33

CHO, preoperative carbohydrate drinks; CI, confident interval; HOMA-IR, Insulin resistance determined by homeostatic model assessment; IL-6, interleukin-6
*Statistically significant

Table 3: Independent effect of preoperative carbohydrate loading on parameters at regression analyses[a].

Dependent variable	Overall population (*n*=20)		
	coefficient (standard error)	95% Confidence interval	*p* value
Δ glucose, mg/dl	8.63 (15.56)	-25.61-42.87	0.59
Δ insulin, IU/ml	-3.06 (2.85)	-9.32-3.20	0.31
Δ HOMA-IR	-1.34 (1.54)	-4.73-2.06	0.40
Δ IL-6, pg/ml	-0.85 (0.76)	-2.48-0.78	0.28

Δ, difference [postoperative value (T1) – preoperative value (T0)]; HOMA-IR, insulin resistance determined by homeostatic model assessment; IL-6, interleukin-6
[a]Models were adjusted for age, BMI, type of orthognathic surgery, intraoperative blood loss, the amount of blood received, and postoperative carbohydrate intake
*Statistically significant

Table 4: Secondary endpoints in the CHO group and the placebo group.

Secondary endpoints	CHO Group (*n*=10)	Placebo group (*n*=10)	*p* value
Thai QoR-35 (total)[a]	136.2±23.64	143.7±21.31	0.46
Domain 1: Physical comfort	47.8±11.66	49.6±7.69	0.68
Being able to enjoy food	4.5±0.70	4.5±1.27	1.00
Nausea	4.3±1.25	4.2±0.92	0.48
Vomiting	4.5±1.27	4.8±0.63	0.54
Domain 2: Emotional state	27.9±4.77	28±4.69	0.96
Having a general feeling of well-being	4.5±0.71	4.5±0.53	0.82
Feeling anxious	3.6±1.17	3.7±0.67	0.94
Domain 3: Psychological support	11.5±4.92	13.5±4.60	0.36
Domain 4: Physical independence	26.6±2.50	28.1±3.17	0.25
Domain 5: Pain	22.4±4.74	24.5±3.86	0.29
Moderate pain	3.6±0.93	4.1±0.99	0.24
Severe pain	4.1±0.99	4.4±0.96	0.50
Total amount of ondansetron (mg)[a]	8.4±1.26	10±2.1	0.05
Total amount of morphine equivalent (mg)[a]	1.9±2.2	1.65±1.93	0.80
TRD from PACU (minutes)[a]	48±15.49	63±9.48	0.01*
LOS in hospital (days)[a]	3.1±0.32	3.3±0.48	0.29
Surgery-related complication[b]	0 (0)	0 (0)	-
Anesthesia-related complication[b]	0 (0)	0 (0)	-

TRD, time to readiness to discharge; PACU, post-anesthetic care unit; LOS, length of stay

[a]data presented as mean ± standard deviation

[b]data presented as count (percentage)

*Statistically significant

no significant effects were observed for any of the other surgeries evaluated.[23] Although the resemble amount of blood transfusion was noted among groups, the level of containing plasma glucose and insulin were not evaluated. This could result in an uncertain increase of plasma glucose and insulin after blood transfusion.

Following surgery, the main cytokine released are interleukin-1 (IL-1), tumour necrosis factor-α (TNF-α) and IL-6. These cytokines stimulate the development of acute phase response, directly relating with the level of initial tissue injury and predicting poor outcomes in injured and surgical patients. IL-6 is the crucial cytokine responsible for inducing the acute phase response, representing the systemic inflammatory response associated with unfavorable postoperative outcomes.[24] In the presence of IR, blood glucose levels are not regulated well. High amount of glucose can promote oxidative stress, reactive oxygen species (ROS) production, the formation of advanced glycation end products (AGEs), and the secretion of the pro-inflammatory cytokines as IL-6.[25] Consecutively, inflammation exaggerates IR, becoming a vicious cycle26. PCL was also significantly effective in reducing IL-6 level.[16] In present study, IL-6 level was lesser increased in CHO group, similar to Tran *et al*[27], but there was not statistically significance. The increase of IL-6 level is directly related to the stress of surgery. Compared with other surgeries, the IL-6 level in this study was distinctly lower because the magnitude of orthognathic surgery was less severe. Kasahara *et al.* reported that IL-6 detected in orthognathic surgery (2.5-9 hours) was less than 20 pg/ml within 24 hours after surgery.[28] All patients in this study were given dexamethasone, opioids, and parecoxib, which can significantly reduce IL-6 level as well.[29] Although, the surgical response, in terms of stress, glucose response, insulin state, and inflammation, among different sex remains unclear, the higher number of females in the CHO group should be concern.

LOS cannot be shortened by PCL in this study consistent with previous meta-analysis.[30] Several studies reported that PCL can significantly reduce LOS for major

open abdominal surgeries. Both plasma glucose level higher than 200 mg/dl and the incidence of postoperative complications can prolong patients staying in the hospital.[31] This study found that mean plasma glucose of CHO and placebo group at T0 represented normal fasting plasma glucose, while mean plasma glucose of both group at T1 seemed to be high even CHO group was collected the blood after PCL more than 24 hours and placebo group did not receive any carbohydrate drink. However, plasma glucose at T1 was possibly high by the stress of an operation. The physical trauma associated with surgery can affect the increasing of stress hormone as cortisol and catecholamines which result in increased IR consequently elevating of plasma glucose. Nevertheless, all mean plasma glucose was less than 200 mg/dl, and no complications were observed. In our center, all patients also require blood drainage tube placement at least 24 hours after surgery and stable occlusion must be warranted before discharge from hospital. TRD from PACU was significantly reduced in this study. This result should be interpreted with caution because the early phase of postoperative recovery was also influenced by anesthetic medication and management.

This study did not show the benefit of PCL on quality of postoperative recovery, which similar to previous study using QoR-40 questionnaire.[32] Several studies have also investigated perioperative thirst, hunger, malaise, fatigue, and anxiety, measured by VAS score, on patients receiving PCL. The meta-analysis by Smith *et al.* found no difference in these variables during hospital stay among PCL versus fasting groups.[33] The non-significant difference of this study may relate to a small reduction of postoperative insulin resistance and inflammation. Postoperative pain and nausea remain concern and adversely affect the experience of patients. There was no significant difference of nausea and vomiting score regarding Thai QoR-35, but the insignificantly greater amount of ondansetron was observed in placebo group. Thus, the PCL tended to decrease the incidence of postoperative nausea and vomiting following orthognathic surgery. Recent meta-analysis found that a reduction in nausea score was observed in CHO group and there was no statistically significant difference in the incidence of vomiting.[34] This study showed that the mean postoperative pain and the morphine equivalent dose receiving were not different like previous studies.[11] It showed that carbohydrate administration before surgery did not relieve postoperative pain. Furthermore, all patients will be routinely given parecoxib as a primary analgesic which remains effective in controlling of postoperative pain following orthognathic surgery in our center. In fact, orthognathic surgery is not the high-magnitude surgery, like colorectal surgery, with short period of hospital stay and fast recovery in nature. Thus, the PCL may not have crucial effect in term of overall postoperative recovery.

Both intravenous and oral carbohydrate administration were reported to improve insulin sensitivity, preoperative tiredness, and weakness. CHO is non-invasive and more feasible and demonstrated a decrease of preoperative thirsty and hungry. The significant improvement in insulin action was also observed after the morning dose of oral carbohydrate administration on the day of surgery.[35] The essential component of CHO is maltodextrin, which is reliably emptied from the stomach after 2 hours. The common formulation is a 50 g maltodextrin, diluted to 400 ml to make 12.5% carbohydrate drink. Because maltodextrin is rare and available commercial products remains expensive, this study prepared in-house carbohydrate drink using 50 g glucose, diluted in 400 ml to make 12.5% carbohydrate drink. Overall, the administration of this in-house carbohydrate drinks appeared safe, and no pulmonary aspiration was observed during anesthesia in this study.

Some limitations should be discussed in this study. First, the patients were routinely allowed to intake clear sweeten liquid after surgery, as needed. The time interval between last clear sweeten liquid intake and blood sample drawing can confound the plasma level of insulin and glucose, although the total amount of glucose intake postoperatively between groups were similar. Second, this study did not allocate the participants to the traditional over-fasting group. Subsequently, it is not possible to determine the different effects, compared to the traditional over-fasting group. Lastly, this study recruited only healthy patients who present normal fasting blood glucose, insulin and HOMA-IR status. Therefore, the effect of PCL may be insignificant. Further investigation including metabolic alterations such as pre-diabetic or diabetic patients may be beneficial.

The PCL, with 12% in-house carbohydrate drink and 3 hours prior to induction, is safe for healthy patients undergoing orthognathic surgery. The PCL appeared to

improve recovery time in PACU. However, there is no significant benefits on postoperative insulin resistance, inflammation, and other clinical outcomes under current standard perioperative care in our center. The routine practice of PCL could be promised in orthognathic surgery, although more sample sizes are necessary to justify the true clinical benefit. Furthermore, this study is demonstrated in healthy participants who have normal, insulin and HOMA-IR status, PCL in other groups with metabolic alterations may be affected.

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Conflicts of interest

The authors declare no conflicts of interest.

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