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Original Article

Anaesthesia Section

Clinical and Biochemical Effects of Preoperative Oral Carbohydrate Loading versus Fasting in Major Abdominal Surgeries: A Randomised Clinical Study

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ABSTRACT

Introduction: Surgery and preoperative fasting result in Perioperative Insulin Resistance (PIR) and can lead to increased postoperative morbidity, mortality and prolonged hospital stay. Enhanced Recovery After Surgery (ERAS) protocols advocate oral carbohydrate loading preoperatively, contrary to conventional fasting practices.

Aim: To compare preoperative oral carbohydrate loading with fasting in terms of mean changes in perioperative blood sugar, albumin levels and patient well-being in major abdominal surgeries.

Materials and Methods: This prospective randomised clinical study was conducted in the surgical gastroenterology operating theatre of Government Medical College Hospital, Kozhikode, Kerala, India, during 2021-2022 among 54 patients. Patients undergoing elective major abdominal surgeries under general anaesthesia were randomly divided into two groups. One group received preoperative oral carbohydrate loading (CHO) (n=27), while the other group followed conventional fasting (FAST) (n=27). Changes in perioperative blood sugar were the primary objective. Changes in perioperative albumin levels, subjective patient well-being, time for resumption of oral intake and duration of postoperative hospital stay were secondary objectives. Continuous variables were assessed using mean and standard deviation. The Student's t-test was used to statistically analyse quantitative data and the Chi-square test was employed for qualitative data.

Results: There was a significant difference in the perioperative blood sugar values (p-value <0.05) and the albumin levels (p-value <0.001) among patients who received preoperative carbohydrate loading and those who followed conventional fasting. The group that received preoperative oral carbohydrate loading had a significantly lower mean blood sugar value compared to the conventionally fasted group during the perioperative period. Postoperative serum albumin values were significantly higher in the carbohydrate-loaded group compared to the fasted group. The carbohydrate-loaded group reported better subjective well-being, shorter time for resumption of oral intake and a reduced duration of hospital stay (p-value <0.05).

Conclusion: Preoperative loading with oral carbohydrates stabilises perioperative blood sugar levels and albumin levels and improves patient well-being in major abdominal surgeries.

Keywords: Carbohydrate loading, Colorectal surgery, Enhanced recovery after surgery, Insulin resistance

INTRODUCTION

Fasting before anaesthesia is an accepted practice to reduce the risks of pulmonary aspiration. International guidelines recommend that patients refrain from fatty foods for eight hours, non human milk or a light meal for six hours and clear fluids for two hours before the induction of anaesthesia [1]. However, starvation causes a fall in blood glucose levels, which leads to a decrease in insulin secretion and an increase in counter-regulatory hormones, resulting in catabolism and gluconeogenesis. Hence, preoperative fasting is an important cause of PIR development. Surgery induces an endocrine stress response and activates inflammatory pathways that contribute to PIR. All this can lead to glycogenolysis, gluconeogenesis, hyperglycaemia, lipolysis and muscle protein loss [2]. Thus, PIR causes increased postoperative morbidity, mortality and prolongs hospital stays [3].

Preoperative fasting and surgical stress activate inflammatory pathways mediated by cytokines. An increase in the level of Interleukin-6 (IL-6) reduces insulin sensitivity and increases PIR. IL-6 stimulates the synthesis of acute-phase proteins, such as C-Reactive Protein (CRP) and inhibits the synthesis of albumin [4]. Prolonged fasting causes depletion of carbohydrates, proteins, lipids, electrolytes and vitamins. Prolonged fasting predisposes individuals to infection and delays wound healing, as well as optimal muscle function [5-7].

Modern surgical practice has started to adopt ERAS protocols that include early enteral feeding, even in patients undergoing gastrointestinal surgeries. Hausel J et al., conducted a randomised study in 2001 that showed a preoperative carbohydrate drink reduced discomfort in patients undergoing elective surgeries [8]. There are conflicting studies in the literature regarding the benefits of preoperative carbohydrate loading. Mathur S et al., in a randomised controlled study, postulated that preoperative carbohydrate loading did not improve postoperative fatigue or the length of hospital stay in major abdominal surgeries [9]. A Cochrane systematic review in 2014 concluded that preoperative carbohydrate loading resulted in only a short reduction in hospital stay and did not increase or decrease postoperative complications [10]. Bilku DK et al., in a systematic review, pointed out that the administration of an oral carbohydrate drink before surgery is safe and leads to positive perioperative outcomes [11].

Thus, there is conflicting data in the literature regarding preoperative carbohydrate loading. Therefore, the present study was conducted to compare the advantages and likely complications of carbohydrate loading against conventional fasting, specifically in major abdominal surgeries. The primary objective was to compare the mean changes in perioperative blood sugar levels. The secondary objectives were to compare perioperative albumin levels, subjective well-being in relation to fatigue, thirst, hunger, nausea and vomiting using the Visual

Analogue Scale (VAS), the time for resumption of postoperative oral intake and the length of the postoperative hospital stay.

MATERIAL AND METHODS

The present prospective randomised single-blinded clinical study was conducted in the surgical gastroenterology operating theatre of Government Medical College Hospital, Kozhikode, Kerala, India, from August 2021 to September 2022. Clearance from the Institutional Ethics Committee was obtained (GMCKKD/RP2021/IEC/201). Informed written consent was obtained from all participants.

Inclusion criteria: Patients of both sexes scheduled for elective major abdominal surgery (lateral pancreatojejunostomy and colorectal surgery), aged between 20 and 65 years, with American Society of Anaesthesiologists (ASA) physical status I or II and having a BMI of 20-30 kg/m² were included.

Exclusion criteria: Patients with a history of previous abdominal surgery, diabetes mellitus, hypothyroidism, disseminated malignancy and an increased risk of aspiration of gastric contents {such as Gastroesophageal Reflux Disease (GERD), obesity, pregnancy, sliding hernia of the stomach, or a previous history of intestinal obstruction} were excluded.

Sample size calculation: The sample size was calculated assuming a power of 80 percent using the following formula:

$$n=\frac{2(Z\alpha+Z\beta)^2.SD^2}{d^2}$$

Substituting the Standard Deviations (SD) of blood sugar levels from the study by Rizvanovic N et al., (FAST group SD=1.1, CHO group SD=0.6), the mean SD was 0.85. Taking d as 0.65, the sample size in each group is 27 [6]. A total of 54 patients were included.

Study Procedure

The procedure was explained to each eligible patient and informed written consent was obtained from those willing to participate. They were allocated into either the FAST group or the CHO group using a computer-generated random number table. Those included in the CHO group were instructed to take the carbohydrate drink. Participants in the FAST group followed ASA fasting guidelines. Only one patient was selected per day and was scheduled as first on the operation list. During the preoperative visit, patients were instructed on how to use the VAS scale for fatigue, thirst, hunger, nausea, or vomiting. Intake of solid food was stopped eight hours before surgery, while clear fluids were allowed up to two hours prior to surgery. Patients in the CHO group received 400 mL of clear carbohydrate drink (12.5 g/100 mL maltodextrin, pH 5.0) at 10 PM the night before surgery and another 200 mL of the drink two hours before anaesthetic induction [6]. The resident conducting the preoperative visit was entrusted with administering the drink but was not informed of the details by the principal investigator. Intravenous Fluids (IVF) were not administered preoperatively. The night before surgery, patients received 0.25 mg of alprazolam and 150 mg of ranitidine orally.

Patients were shifted to the operating theatre and standard monitors were connected, including an Electrocardiogram (ECG), peripheral Oxygen Saturation (SpO_2), Non Invasive Blood Pressure (NIBP), End-tidal Carbon Dioxide ($ETCO_2$) and temperature. Before the induction of anaesthesia, patients received premedication with Midazolam at 0.02 mg/kg, Morphine at 0.1 mg/kg, Glycopyrrolate at 0.2 mg and Ondansetron at 0.1 mg/kg intravenously. An epidural catheter was placed at levels T9-T12. After preoxygenation with 100% oxygen for three minutes, anaesthesia was induced with Propofol at 2 mg/kg. Neuromuscular blockade was achieved with Atracurium at 0.5 mg/kg and preservative-free Lignocaine at 1.0 mg/kg was administered intravenously 90 seconds before intubation. Anaesthesia was maintained with a mixture of O_2 and air, isoflurane at 0.2-1.0%, along with intermittent bolus doses of Atracurium and an epidural block using 0.25% Bupivacaine at a rate of 3-5 mL/hr.

Intraoperative fluid management was limited to glucose-free solutions, with no exogenous insulin administration. At the end of the surgery, neuromuscular blockade was reversed with Neostigmine at 0.05 mg/kg and Glycopyrrolate at 0.01 mg/kg. Patients were extubated when fully awake. The average duration of the surgeries was between 2 to 3 hours. Postoperative care was standardised as clinically indicated. Epidural analgesia was continued for 48 hours at a rate of 5.0 mL/hour of 0.125% Bupivacaine. Early postoperative mobilisation was encouraged. Biochemical parameters were assessed from peripheral venous blood samples. Blood glucose levels were assessed on the preoperative day (T1), two hours before surgery (T2), six hours after surgery (T3), at 06:00 on Postoperative Day (POD) 2 (T4) and at 06:00 on postoperative day 3 (T5). Postoperative day 2 was considered the day after surgery. Serum albumin was measured on the preoperative day (Ta1) and at 06:00 on postoperative day 3 (Ta2).

Subjective patient well-being in terms of fatigue, thirst, hunger, nausea and vomiting was assessed using the VAS, where no discomfort was rated as 0 and the most severe discomfort as 10 cm. This assessment was conducted by the principal investigator, who was unaware of the group to which the patient belonged. The assessment was performed prior to anaesthesia induction and repeated after surgery at four-hour intervals until 12 hours post-surgery and then again at the 24th hour.

The return of gut function was assessed by noting the time of postoperative oral intake. The duration of hospital stay after surgery was recorded.

STATISTICAL ANALYSIS

Microsoft Excel was used to create the graphs and data were analysed using the statistical software Statistical Package for the Social Sciences (SPSS) version 21.0. To summarise continuous variables, means with standard deviations were calculated. The Chi-square test was used to compare different independent variables between the groups. Statistical significance was determined by a p-value of less than 0.05. The Student's t-test was used to statistically analyse the quantitative data, while the Chi-square test was employed for qualitative data.

RESULTS

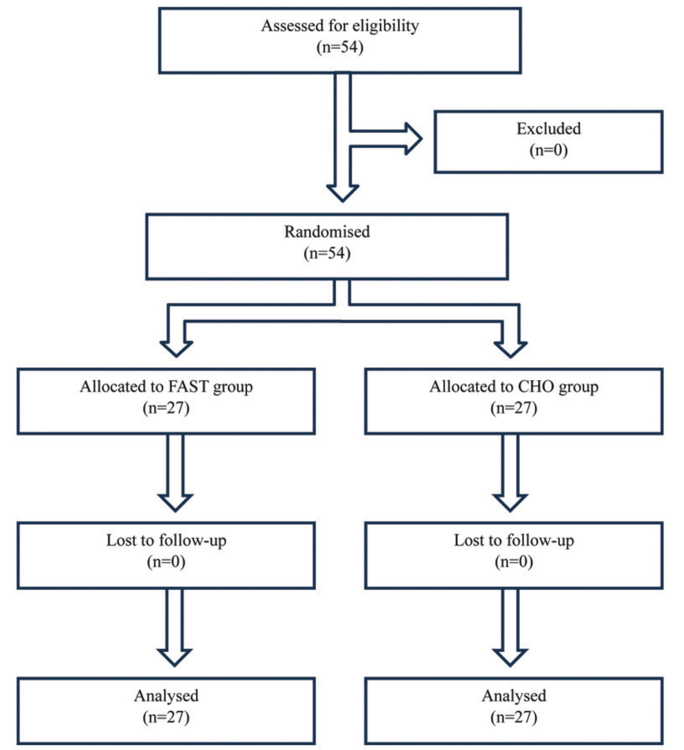
A total of 54 patients who met the inclusion criteria (27 in each group) participated in the study. There were no dropouts, resulting in a response rate of 100% [Table/Fig-1]. Demographic data, including age, height, weight, Body Mass Index (BMI), distribution of gender and ASA physical status, were comparable between the two groups [Table/Fig-2]. Analysis of blood glucose [Table/Fig-3] and albumin [Table/Fig-4] across the study groups showed statistically significant differences at the various follow-up time points.

The mean preoperative blood sugar value for the CHO group was 99.11±14.3 mg/dL, while that of the FAST group was 104.9±27.8 mg/dL. This was comparable between both groups (p=0.34). Mean blood sugar values at all other time points showed a statistically significant lower value in the CHO group compared to the FAST group ($p<0.05$) [Table/Fig-3].

The preoperative serum albumin value for the CHO group was 4.1±0.3 g/dL, while that of the FAST group was 4.0±0.7 g/dL (p=0.497). Albumin levels on postoperative day three were 3.8±0.29 g/dL in the CHO group and 3.1±0.3 g/dL in the FAST group, showing a statistically significant difference ($p<0.001$) [Table/Fig-4].

The incidence of fatigue, thirst, hunger, nausea and vomiting was higher in the fasting group (FAST) at all follow-up time points ($p<0.001$) [Table/Fig-5].

The mean number of days for resumption of oral intake was 2.8 days for the CHO group compared to 3.4 days for the FAST group



[Table/Fig-1]: Consolidated Standards of Reporting Trials (CONSORT) flow diagram.

Characteristics	CHO group	FAST group	p-value
Age (years) *	48.5±13.7	50.7±14.7	0.58
Sex (Male:Female)†	18 (58.1): 9 (39.1)	13 (41.9): 14 (60.9)	0.16
ASA physical status (I or II)†	17(53.1): 10 (45.4)	15 (46.9): 12 (54.6)	0.58
Height (cm)*	161.8±6.7	164.3±5.5	0.58
Weight (kg)*	61.4±8.3	63.5±7.7	0.33
BMI (kg/m²)*	23.3±2.3	23.4±2.1	0.90

[Table/Fig-2]: Demographic data and ASA status of CHO and FAST groups.
*Mean±SD, †Frequency (%)

Time period	CHO group Mean±SD	FAST group Mean±SD	p-value
Preoperative (T1)	99.1±14.3	104.9±27.8	0.34
2 hours before surgery (T2)	102.2±10.4	129.1±8.7	0.004
6 hours after surgery (T3)	103.4±10.1	136.9±48.3	<0.001
6 am on POD 2 (T4)	104.8±10.2	135.7±46.2	0.001
6 am on POD 3 (T5)	101.7±12.5	127.6±33.9	<0.001

[Table/Fig-3]: Perioperative blood sugar values in mg/dL of CHO and FAST groups.

Time period	CHO group Mean±SD	FAST group Mean±SD	p-value
Preoperative (Ta1)	4.1±0.3	4±0.7	0.497
6 am on POD 3 (Ta2)	3.8±0.5	3.1±0.3	<0.001

[Table/Fig-4]: Perioperative albumin values of CHO and FAST groups in g/dL at two time points.

(p<0.001). The mean length of hospital stay was also shorter in the CHO group compared to the FAST group (p<0.001) [Table/Fig-6].

DISCUSSION

In the present study, the demographic parameters and ASA physical status were comparable between both groups. Analysis of blood glucose across the study groups showed statistically significant differences at the various follow-up time points, with the CHO group demonstrating lower blood sugar levels. A decline in perioperative blood sugar values was noted with statistical significance, which was consistent with the findings of Rizvanovic N et al., (who used a clear carbohydrate drink containing 50 g of maltodextrin in 400 mL) and Rajan S et al., (who administered 250 mL of apple juice in a tetra pack containing 39 grams of carbohydrate for thyroidectomy patients) [6,12].

The Randomised Controlled Trial (RCT) conducted by Rizvanovic N et al., showed that PIR was 30% lower (p<0.03) and insulin sensitivity was 15% higher (p<0.05) in the carboloaded group compared to the conventionally fasted group among patients undergoing colorectal surgery [6]. Results comparable to the present study were obtained by Kumar SM et al., who conducted an RCT involving patients undergoing colorectal surgery, in which one group received preoperative oral carbohydrate loading while the other followed conventional fasting [13]. There was a significant decrease in insulin resistance on the day of surgery, on Postoperative Day 1 (POD 1) and on Postoperative Day 3 (POD 3).

Another RCT conducted by Lai Y et al., on type 2 diabetics undergoing knee arthroplasty demonstrated significantly lower insulin resistance and lower blood sugar levels in a group that received oral carbohydrates two hours prior to surgery compared to a group that received oral carbohydrates four hours prior to surgery; both groups performed better than a placebo group [14].

The Glasgow Prognostic Score (GPS), a valuable measure for predicting infectious complications, morbidity and mortality after colorectal surgery, is the ratio of inflammatory to nutritional variables: CRP/albumin [15]. Albumin levels on postoperative day three were 3.1 g/dL and 3.8 g/dL in the FAST and CHO groups of the present study, respectively, showing a statistically significant difference. The RCT conducted by Kumar SM et al., demonstrated similar results [13]. Their study indicated a significant decrease in inflammatory response parameters such as CRP and IL-6 throughout the postoperative period in the group that received preoperative oral carbohydrates compared to the conventionally fasted group. Additionally, the fasted group exhibited significantly lower albumin levels and consistently higher GPS at all follow-up time points (p<0.001). An RCT conducted by Chaudhary NK et al., concluded that preoperative carbohydrate loading helped to stabilise blood albumin levels in the perioperative period compared to conventional fasting in patients undergoing surgery for fractured femur [16]. However, another meta-analysis conducted by Lu J et al., found the opposite, concluding that preoperative carbohydrate loading does not have a significant effect on postoperative glycaemic control in patients undergoing colorectal

Parameters	Groups	VAS scores at time intervals Mean±SD					
		Pre induction	4 hr after surgery	8 hr after surgery	12 hr after surgery	24 hr after surgery	p-value
Fatigue	CHO	0.96±0.6	0.96±0.6	0.77±0.6	0.7±0.6	0.6±0.7	<0.001
	FAST	5.7±0.9	5.7±1.1	5.2±1.1	5.2±1.2	4.8±1	
Thirst	CHO	0.8±0.5	0.44±0.5	0.6±0.6	0.8±0.6	0.4±0.5	<0.001
	FAST	5.4±0.9	5.4±1.2	5.0±1.2	4.8±1.2	4.7±0.9	
hunger	CHO	0.48±0.7	0.74±0.7	0.6±0.7	0.4±0.5	0.5±0.6	<0.001
	FAST	5.7±1.2	4.5±1.3	4.2±1.2	4.2±1.1	4.4±1.1	
Nausea and vomiting	CHO	0.7±0.6	0.7±0.6	0.5±0.5	0.7±0.8	0.4±0.7	<0.001
	FAST	5.2±1.3	5.0±1.3	4.8±1.2	4.7±1.2	4.7±1.1	

[Table/Fig-5]: Perioperative incidence of fatigue, thirst, hunger, nausea or vomiting at various intervals in CHO and FAST groups.

Parameters	CHO group Mean±SD	FAST group Mean±SD	p-value
Time for oral intake (days)	2.8±0.3	3.4±0.5	<0.001
Length of hospital stay(days)	5.1±0.5	5.8±0.8	<0.001

[Table/Fig-6]: Time of resumption of oral intake and length of postoperative hospital stay in CHO group and FAST group.

surgery, although it was associated with a faster return of bowel function and shorter length of stay [17].

The incidence of fatigue, thirst, hunger, nausea and vomiting, as assessed subjectively using the VAS scale, was higher in the FAST group at all follow-up time points, including pre-induction as well as postoperative hours 4, 8, 12 and 24 (p<0.001). This finding is comparable with the observations of Rizvanovic N et al., who demonstrated a reduction in the perception and incidence of fatigue, thirst, hunger, nausea and vomiting [6]. The incidence and severity of postoperative nausea and vomiting were reduced in the fed group in a South Indian study conducted by Rajan S et al., involving thyroidectomy patients [12]. The findings were also consistent with the RCT conducted by Kumar SM et al., in which thirst, hunger, nausea, anxiety and dry mouth, as assessed by VAS score, were significantly higher in the conventionally fasted group compared to the oral carboloaded group (p<0.00) in patients undergoing colorectal surgery [13]. No significant differences in thirst and hunger were observed by Ackerman RS et al.,; this discrepancy could likely be attributed to variations in study population, co-morbidity and other study characteristics across the different study settings (p=0.27) [18].

In the present study, the mean time for resumption of oral feeds was 2.8 days in the CHO group, which was significantly lower compared to 3.4 days in the fasting group (p<0.01). This finding is comparable with the RCT by Rizvanovic N et al., where the carboloaded group demonstrated a significantly earlier return of gastrointestinal function, including earlier bowel sounds, time to first flatus, defaecation and oral intake following colorectal surgery [6]. In the RCT conducted by Kumar SM et al., among patients undergoing colorectal surgery, the group that received preoperative oral carbohydrates also experienced an earlier return of bowel function; however, this was not statistically different from the fasted group [13].

The length of hospital stay was 5.8 days in the FAST group and 5.1 days in the CHO group, with a p-value of <0.001. An RCT conducted by Wang B et al., among patients undergoing gynaecological laparoscopic surgery indicated that those who received preoperative carbohydrate loading and early oral feeding had a shorter hospital stay compared to the control group [19]. The RCT conducted by Kumar SM et al., also demonstrated that patients who received a preoperative carbohydrate drink had a significantly reduced hospital stay compared to fasted patients (p<0.001) [13]. The meta-analysis by Amer MA et al., published in 2017, summarised that compared to fasting, preoperative low-dose and high-dose carbohydrate administration reduced the duration of hospital stay by only 0.4 and 0.2 days, respectively and there was no additional significant benefit compared to water or placebo [20].

It has now been demonstrated that due to significant surgical stress, open colorectal surgery alters metabolic homeostasis and causes significant PIR [6,21]. The Accelerated Recovery After Surgery (ERAS) programme, which includes preoperative carbohydrate loading, is primarily employed after colorectal surgery to decrease the stress response, insulin resistance and length of hospital stay. The role of a preoperative carbohydrate drink has long been debated, but several researchers now support its use.

A strong point of the present study is that only a limited amount of literature is available from South India regarding perioperative blood sugar and albumin levels, subjective patient well-being and surgical clinical outcomes when a preoperative carbohydrate drink is administered in major abdominal surgeries [13]. Although current guidelines recommend fasting for clear fluids two hours prior to elective surgery, many patients are still kept fasting after midnight due to an undue fear of aspiration [22]. A more liberal preoperative fasting protocol should be implemented, except for patients at risk of aspiration, such as those with gastro-oesophageal reflux disease, obesity, pregnancy, sliding hernia of the stomach, or a previous history of intestinal obstruction.

Limitation(s)

It was a single-centre study and a larger population of patients was necessary to arrive at a definitive conclusion. Additionally, an ultrasound-guided gastric volume assessment of the participants prior to the induction of anaesthesia was not performed, which might have helped to confirm the emptying of the administered drink.

CONCLUSION(S)

In contrast to traditional fasting, patients undergoing major abdominal surgeries who were administered preoperative oral carbohydrate loading exhibited stable perioperative blood sugar and albumin levels. The preoperative administration of an oral carbohydrate drink significantly reduced the incidence of fatigue, nausea and vomiting, thirst and hunger during the perioperative period. These patients also experienced better surgical outcomes, including a shorter time for the resumption of oral intake and a reduced length of hospital stay. The present research challenges the long-standing belief that preoperative fasting is an essential safety measure. Further studies investigating its impact on a larger scale and across varied populations are crucial to fully realise its clinical benefits.

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