Original Article

Effect of Preoperative Oral Carbohydrate Loading on Perioperative Hemodynamic in Patients Undergoing Laparoscopic Cholecystectomy: A Randomized Controlled Study

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Abstract

Background: Conventional preoperative fasting is associated with intravascular volume contraction, increased stress, hyperglycaemia in the perioperative period. Recently, the concept of preoperative carbohydrate loading is introduced. This study was conducted to reveal the relation between use of carbohydrate-rich fluid and perioperative hemodynamic, perfusion index, and glucose control of the patients, who were undergoing elective laparoscopic cholecystectomy under general anesthesia.

Methods: This study is a double-blinded prospective randomized control study. The patients, who met the inclusion criteria were randomly divided into 2 groups of 43 each with the help of computer-generated randomization method. Patients who received preoperative carbohydrate loading and patients who follow conventional preoperative fasting for surgery were labelled as Group E and Group S respectively. Incidence of hypotension was the primary outcome; variation in blood pressure, heart rate, perfusion index, and blood glucose level were the secondary outcomes.

Results: Intraoperative hypotensive episodes were significantly lower in the carbohydrate loading group in comparison to the conventional fasting group, p=0.023. The systolic, diastolic blood pressure and perfusion index were significantly lower in the conventional fasting group. Also, the heart rate was significantly higher in the conventional fasting group. Numeric rating scale, the score for pain taken at 1 hour postoperatively was significantly lower in the carbohydrate loading group. Blood glucose level postoperatively after 24 hours was significantly more in the conventional fasting group.

Conclusion: The carbohydrate loading group has better hemodynamic stability and optimal intravascular volume after induction and intraoperatively. Also, the carbohydrate loading group had better glycaemic control and better pain relief postoperatively.

Keywords

Carbohydrate loading, Hemodynamic, Blood Glucose, Perfusion index, Postoperative pain.

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Introduction

Pre-operative nil per oral (NPO) is a common practice to minimize the chance of aspiration throughout the perioperative period. However, pre-operative fasting results in shrinkage of intravascular volume and affects the internal milieu of the patient, which clinically manifests as tachycardia, hypotension, decreased stroke volume, and cardiac output of the patient.[1] Administration of anaesthetic agents additionally affects the hemodynamic of the

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patient. Once these two factors are combined, it causes vital alteration and results in hemodynamic instability. Prolonged fasting preoperatively leads to enhanced catabolic metabolism, muscle breakdown, insulin resistance, and hyperglycaemia.[2]

The idea of pre-operative carbohydrate loading is recently introduced to avoid unfavourable effects of prolonged fasting. The most recent literature is in favour and showed lesser side-effects, better pain control, and improved insulin sensitivity; however, there is a lack of studies on the effect of carbohydrate loading on perioperative hemodynamic.[3] Thus, this study was conducted to know the effect of oral carbohydrate-rich fluid pre-operatively on perioperative hemodynamic, perfusion index, and glucose control of the patients, who were undergoing laparoscopic cholecystectomy under general anesthesia.

Materials and Methods

The present study is a prospective, double-blinded, randomized control. The study protocol was approved by the institutional ethical committee (TS/MSSH/ DDN/ MHIL/ ANAES/ IEC/19-04) and registered in Clinical Trials Registry- India (CTRI/2020/04/024564). Written informed consent has been taken from all the patients before enrolment. Patients scheduled for elective laparoscopic cholecystectomy under general anesthesia, American Society of Anaesthesiology (ASA)- I and II, and with ages between 18 to 60 years during the pre-anaesthetic check-up were included. Patients with uncontrolled hypertension, ASA physical status grade III or higher, uncontrolled diabetes mellitus, any known significant renal/ cardiac disease, gastroesophageal reflux disease, BMI ≥30 Kg m^{-2}, moderate to severe respiratory disease, pregnancy and documented delayed gastric emptying or slow gastrointestinal motility were excluded. Included patients were randomly assigned into two equal groups of 43 each with the help of a computer-generated table of random numbers and concealed in opaque sealed envelopes. A total of 98 patients were assessed for eligibility from December 2019 to August 2020 in one of the tertiary centre in India.

The two groups were - Group E: Patients who received preoperative carbohydrate loading, 800 ml of clear fluid containing 100 grams of carbohydrate in the evening before surgery and 400 ml of clear fluid containing 50 grams of carbohydrate 2 hours before surgery, and Group S: Patients who received conventional preoperative fasting for surgery, 8 hours fasting for solids and two hours for clear fluid. The sealed envelopes were opened by the nurse on the night before surgery for group allocation and thereafter follow-up by an anesthesiologist, who was blinded to the group allocation.

In the absence of any previous article on the incidence of hypotension, the sample size calculations have been done based on mean blood glucose level on the first postoperative day as reported by Weledji et al. According to their study, the mean and SD of blood glucose levels in the fasting and CHO group (carbohydrate loading) respectively are 146.20 ± 38.36 mg dL^{-1} and 123.06 ± 26.64 mg dL^{-1}. To be able to detect a mean difference of at least 20 mg dL^{-1} in these two groups with a power of 80% and a significance level of 5%, the sample size comes to at least 43 in each group.

The patient was shifted to the operating room and standard ASA monitors were attached. Baseline heart rate, systolic and diastolic blood pressure, oxygen saturation, and perfusion index were noted. Before induction of anesthesia, gastric volume was measured by using ultrasound (Sonosite M-Turbo®). A curvilinear, low-frequency transducer (2-5MHZ) was used. The ultrasonography was done first in the supine position and then in the right lateral position. Gastric volume was calculated by using the formula Perlaset et al. [Gastric volume (GV) (ml)=27.0+14.6 X right lateral CSA (cm^2)-1.28 X age (year)], antral cross-sectional area was measured by using two perpendicular diameters and formula of the area ellipse; CSA(cross-sectional area)= (AP XCC X 22/7)/4 AP=Antero-posterior diameter and CC=cranio-caudal diameter. The volume threshold of gastric fluid in patients was taken as 1.5 ml kg^{-1}. Patients who had a gastric fluid volume of >1.5 ml kg^{-1} were taken as the next case on the same day.

The patient was pre-oxygenated with 100% oxygen and induced with injection Fentanyl (2 µg kg^{-1}), Propofol (2 mg kg^{-1}), and Atracurium (0.5 mg kg^{-1}). After induction, the patient was intubated with a 7.5 internal diameter (ID) cuffed endotracheal tube in females and 8.5 ID in males. The position of the tube was confirmed by five-point auscultation and capnography and then fixed. Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), Heart Rate (HR), and perfusion index were monitored every 1 minute for 5 minutes, and at 15-minute, 30-minute, 45-minute, and 1 hour following induction of anesthesia. Decrease of systolic blood pressure to <100 mm Hg was considered a hypotensive episode and managed by fluid bolus and intravenous(iv) injection of Mephentermine 6 mg. Anesthesia was maintained by sevoflurane (Minimum alveolar concentration-1.2) and an intermittent bolus of atracurium 0.10 mg kg^{-1} iv and fentanyl 50µg iv. For postoperative nausea and vomiting prevention, an injection of Ondansetron 0.8 mg kg^{-1} iv was given. At the end of the surgery, the patient's residual neuromuscular paralysis was antagonized with an intravenous injection of neostigmine 0.05 mg kg^{-1} and glycopyrrolate 0.01 mg kg^{1}. Following satisfactory recovery, the patients were extubated and shifted to the post-anesthesia care unit.

The patient's vitals were monitored in the Post Anaesthesia Care Unit (PACU) for an hour. Postoperative pain was checked by NRS (numerical pain rating scale) rating between 0-10 (0-no pain and 10 highest pain) at the end of an hour following surgery. The blood sugar of the patient was checked preoperatively and at 24 hours post-surgery.

Outcomes

The primary outcome of interest was the incidence of hypotension following the induction of anesthesia. The secondary outcomes were perioperative systolic/diastolic blood pressure and heart rate variation, Perfusion Index (PI) at baseline and following induction, blood glucose level on the first postoperative day in both the groups and severity of postoperative pain at 1 hour after surgery.

Statistical Analysis

The collected data was coded and saved within the MS Excel spreadsheet program. SPSS v23 (IBM Corp.) was utilized for information analysis. The continuous variables were analyzed by descriptive statistics and were elaborated in the form of medians/IQRs and means/standard deviations. The categorical variables were elaborated in the percentages and frequencies. To compare proportions, inferential statistics were used by using the Fisher's exact or Chi-square test. The student's t-test and Mann-Whitney U test were used for the comparison of means in the two groups as applicable. The paired t-test was used for the comparison of continuous variables at two points in time. Multiple logistic regression analysis was used to document independent predictors of desired outcomes.

Results

There was no statistically significant difference between the groups in regards to age, sex, weight, height, BMI, ASA grade, gastric volume distribution, duration of anesthesia, and duration of surgery (Table 1).

Intraoperative hypotension episodes were significantly lower in the carbohydrate loading group (Group E) 9/43 (20.9%) in comparison to the conventional fasting group (Group S) 20/43 (46.5%), $\chi 2 = 5.20$, $p=0.023$.

The mean arterial pressure (MAP) at the time of induction and for the first 5 minutes of post-induction was significantly lower in Group S in comparison to Group E (Table 2).

The systolic blood pressure (SBP) at the time of induction and for the first 5 minutes of post-induction

Table 1: Association between Group and Parameters

Parameters	Group S (n = 43)	E (n = 43)	p value
Age (Years)	47.42 ± 9.65	44.47 ± 10.72	0.210[1]
Age			0.160[2]
21-30 Years	2 (4.7%)	8 (18.6%)	
31-40 Years	10 (23.3%)	6 (14.0%)	
41-50 Years	12 (27.9%)	14 (32.6%)	
51-60 Years	19 (44.2%)	15 (34.9%)	
Gender			0.353[2]
Male	16 (37.2%)	11 (25.6%)	
Female	27 (62.8%)	32 (74.4%)	
Height (cm)	160.07 ± 8.83	159.28 ± 7.71	0.893[1]
Weight (Kg)	65.51 ± 10.42	64.07 ± 8.08	0.476[3]
BMI (Kg/m2)	25.52 ± 3.11	25.30 ± 3.29	0.754[3]
ASA Grade			0.824[2]
I	26 (60.5%)	28 (65.1%)	
II	17 (39.5%)	15 (34.9%)	
Gastric Volume (mL)	47.57 ± 14.51	41.25 ± 7.74	0.082[1]
Duration of Surgery (Minutes)* **	47.42 ± 7.27	47.93 ± 3.03	0.214[1]
Duration of Anesthesia (Minutes)* **	62.05 ± 7.39	62.70 ± 3.56	0.245[1]

***Significant at p<0.05, 1: Wilcoxon-Mann-Whitney U Test, 2: Chi-Squared Test, 3: t-test

Table 2: Comparison of the Two Groups in Terms of change in MAP (mmHg) over time

MAP (mmHg)	Group S		E		P value for comparison of the two groups at each of the timepoints (Wilcoxon-Mann-Whitney U Test)
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
Pre-Induction	94.45 (10.45)	96.67 (16.67)	92.81 (7.94)	93.33 (14.33)	0.506
Induction	85.28 (10.22)	85.33 (13.00)	92.32 (6.27)	93.33 (9.67)	<0.001
1 Minute Intra-Operative	79.73 (7.53)	79.33 (8.67)	88.36 (5.14)	89.33 (7.00)	<0.001
2 Minutes Intra-Operative	77.95 (7.26)	79.00 (9.00)	88.35 (5.49)	88.67 (6.33)	<0.001
3 Minutes Intra-Operative	80.19 (6.91)	80.67 (8.17)	88.56 (5.24)	88.00 (7.00)	<0.001
4 Minutes Intra-Operative	84.34 (7.34)	83.33 (6.67)	88.50 (4.80)	88.67 (6.00)	<0.001
5 Minutes Intra-Operative	84.91 (8.51)	83.33 (12.00)	89.31 (4.57)	90.67 (6.00)	0.007
15 Minutes Intra-Operative	89.14 (8.58)	90.00 (11.33)	91.38 (5.15)	91.33 (6.00)	0.270
30 Minutes Intra-Operative	92.86 (8.65)	92.00 (7.17)	92.09 (4.30)	92.67 (4.50)	0.812
45 Minutes Intra-Operative	94.24 (8.32)	92.67 (12.33)	92.69 (4.60)	92.67 (5.67)	0.397
1 Hour Intra-Operative	95.07 (6.32)	94.67 (8.67)	94.93 (4.02)	96.00 (6.00)	0.849
15 Minutes Post-Operative	93.05 (6.52)	93.33 (12.67)	93.68 (3.89)	94.00 (4.67)	0.846
30 Minutes Post-Operative	91.64 (4.60)	91.33 (6.67)	92.70 (4.16)	92.67 (4.33)	0.165
45 Minutes Post-Operative	94.31 (4.56)	94.00 (4.83)	94.43 (4.22)	94.67 (4.83)	0.839
1 Hour Post-Operative	93.36 (5.41)	93.33 (6.67)	94.12 (4.40)	94.00 (5.83)	0.628

The diastolic blood pressure (DBP) at the time of induction and for the first 5 minutes of post-induction, and at 1 hour postoperatively was significantly lower in Group S in comparison to Group E. Overall comparison of the change in diastolic BP (mmHg) over time between the two groups was significantly different, $p<0.001$.

The heart rate (HR) at the time of induction, 1 and 2 minutes post-induction, and 1 hour postoperatively were significantly higher in Group S in comparison to Group E. Overall comparison of the change in heart rate (BPM) over time between the two groups was significantly different (Table 3).

The perfusion index at the time of induction, for the first 5 minutes, at 15, 30, 45, and 60 minutes of post-induction was significantly lower in Group S in comparison to Group E, $p<0.001$ (Figure 2).

Blood sugar in Group S increased significantly in comparison to Group E after 24 hours postoperatively, $p<0.001$ (Table 4).

There was a significant difference between the two groups in terms of the distribution of NRS (1 Hour) ($\chi2 = 6.943$, $p = 0.031$). There was no significant difference between the total volumes of intraoperative fluid among the two groups ($p=0.748$).

Discussion

This study compared the effects of preoperative oral carbohydrate drinks on perioperative haemodynamics, perfusion index, and blood glucose in patients, who underwent laparoscopic cholecystectomy. Patients who received preoperative carbohydrate drink was found to have significantly fewer intraoperative hypotensive episodes after induction in comparison to patients with conventional fasting, $p=0.023$. In our study, we found significantly less tachycardia at certain time points in the carbohydrate loading group in comparison to the conventional fasting group, which

Table 3: Comparison of the Two Groups in Terms of change in Heart Rate (BPM) over time

Heart Rate (BPM)	Group S Mean (SD)	Group S Median (IQR)	Group E Mean (SD)	Group E Median (IQR)	P value for comparison of the two groups at each of the timepoints (Wilcoxon-Mann-Whitney U Test)
Pre-Induction	81.77 (10.03)	82.00 (13.50)	78.33 (7.10)	79.00 (6.00)	0.066
Induction	83.09 (12.31)	82.00 (16.00)	75.98 (7.19)	77.00 (10.00)	0.006
1 Minute Intra-Operative	82.09 (13.23)	82.00 (21.50)	75.51 (7.70)	76.00 (7.50)	0.044
2 Minutes Intra-Operative	80.26 (12.74)	80.00 (22.50)	74.58 (7.39)	75.00 (8.50)	0.044
3 Minutes Intra-Operative	76.49 (10.08)	77.00 (15.00)	74.74 (7.65)	76.00 (6.50)	0.492
4 Minutes Intra-Operative	74.79 (10.37)	74.00 (15.00)	73.58 (7.53)	74.00 (7.00)	0.595
5 Minutes Intra-Operative	72.98 (9.59)	73.00 (16.00)	73.51 (7.24)	75.00 (8.00)	0.707
15 Minutes Intra-Operative	71.88 (10.27)	72.00 (14.00)	70.67 (6.53)	71.00 (8.00)	0.464
30 Minutes Intra-Operative	71.93 (9.37)	72.00 (11.50)	69.70 (5.71)	70.00 (7.50)	0.150
45 Minutes Intra-Operative	72.30 (10.24)	70.00 (13.50)	70.40 (5.19)	70.00 (4.50)	0.768
1 Hour Intra-Operative	73.56 (9.45)	74.00 (12.00)	73.70 (6.54)	75.00 (6.00)	0.862
15 Minutes Post-Operative	80.67 (13.53)	79.00 (13.00)	76.53 (4.89)	78.00 (6.00)	0.051
30 Minutes Post-Operative	79.02 (6.07)	79.00 (7.00)	78.19 (4.45)	78.00 (6.50)	0.323
45 Minutes Post-Operative	79.91 (10.36)	80.00 (6.00)	78.35 (3.63)	79.00 (2.50)	0.280
1 Hour Post-Operative	79.86 (5.76)	80.00 (7.50)	77.74 (3.62)	78.00 (4.50)	0.020

Table 4: Comparison of Blood Glucose level of the two groups

Blood Glucose (mg/dL)	Group S Mean (SD)	Group S Median (IQR)	Group E Mean (SD)	Group E Median (IQR)	P value for comparison of the two groups at each of the timepoints (Wilcoxon-Mann-Whitney U Test)
Pre-induction	97.91 (4.88)	98.00 (7.00)	99.98 (5.02)	101.00 (4.50)	0.037
24 Hours	140.88 (10.36)	143.00 (12.50)	117.93 (6.50)	118.00 (8.00)	<0.001
Absolute Change	-42.98 (10.75)	-46.00 (11.50)	-17.95 (6.29)	-17.00 (7.50)	<0.001
Percent Change	-44.2% (11.6)	-47.1% (12.6)	-18.1% (6.8)	-17.6% (7.4)	<0.001

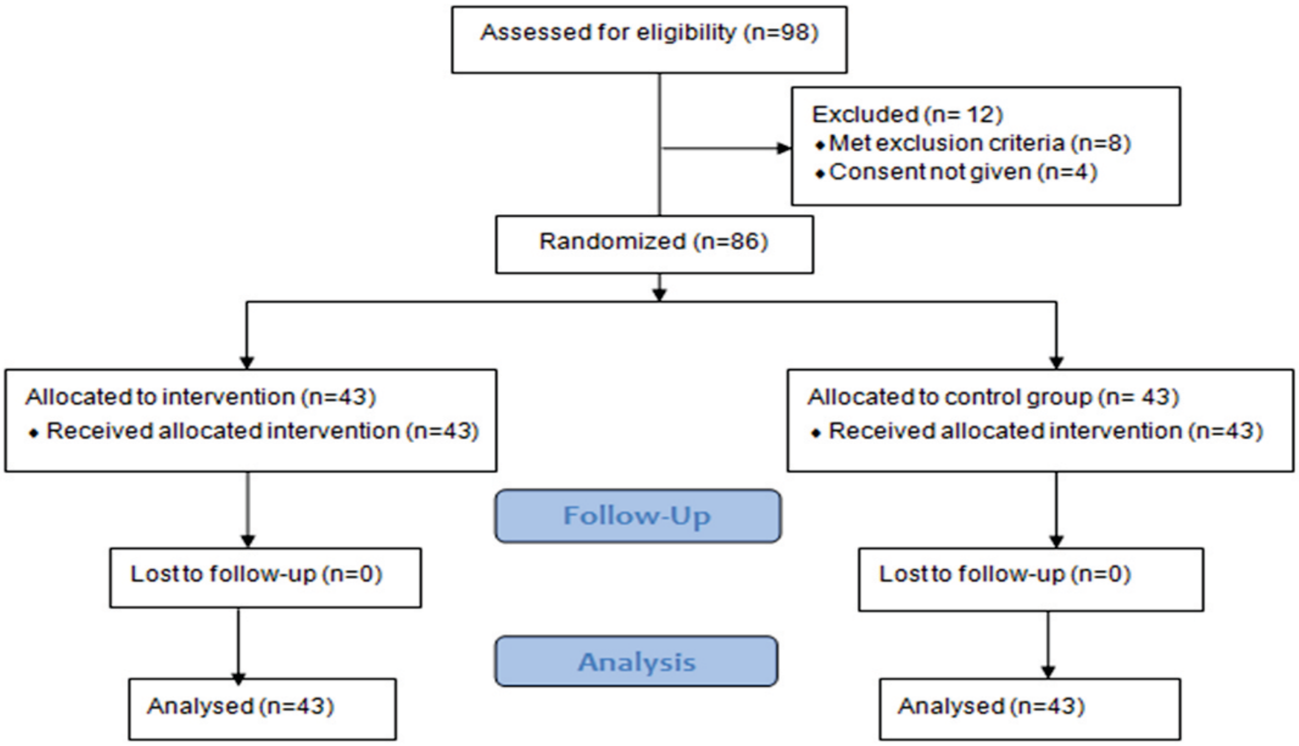

Figure 1: Consort flow diagram

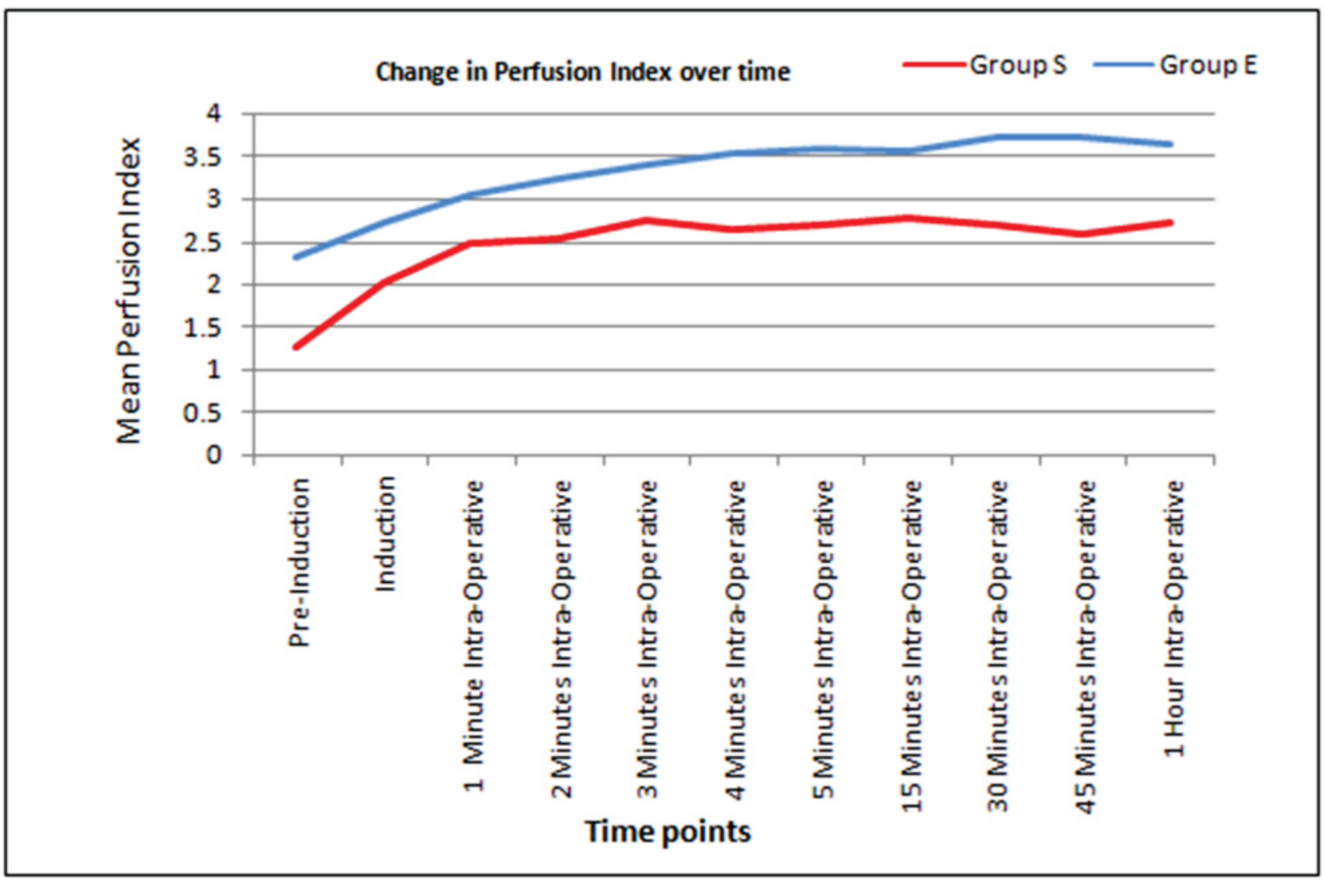

Figure 2: Line diagram showing the change in Perfusion Index over time

corresponded with a study conducted by Lee et al.[4] In patients with prolonged fasting, there is volume contraction and decline in the vascular capacity, this effect is more prominent in hypertensive and elderly patients; thus more hypotensive state following induction of general anaesthesia. In contrast, to a study by lee et al., who found no significant difference in mean arterial pressure, our study showed significantly lower systolic, diastolic, and mean arterial pressure in patients with conventional fasting for up to 5 minutes following induction.[5]

Our study showed that the perfusion index was significantly lower in the conventional fasting group in comparison to the carbohydrate loading group but there was no significant difference in the trend of the Perfusion Index over time in both groups. Perfusion Index is a ratio of pulsatile blood flow to static blood in the peripheral tissue and it's a non-invasive, rapid, and continuous predictor of tissue perfusion, which can be easily measured by pulse oximeter at various sites. Perfusion index can be used for the assessment of tissue hypoperfusion because of low intravascular volume. The tissue perfusion can also be assessed by various clinical (skin turgor, capillary refill time) and biochemical (mixed venous oxygen saturation and serum lactate) methods.[5-8]

The conventional fasting practice before surgery results in insulin resistance and depletion of hepatic glycogen-enhanced gluconeogenesis.[9,10] This is further escalated by insulin resistance because of surgical stress.[11] Ljungqvist et al first questioned the practice of conventional fasting in patients undergoing surgery under general anesthesia. The postoperative insulin resistance was found to be reduced by 50% and hepatic glycogen content was increased by 65% in the patients receiving overnight intravenous glucose infusion.[12-13] Nygren et al.[12] first advocated the use of high carbohydrate drinks preoperatively; it was constituted of polymers to decrease the osmotic effect of the drink on gastric emptying. They demonstrated with the help of a gamma camera, that the carbohydrate drink emptied from the stomach in 90 minutes after ingestion on the morning of surgery. None of the studies reported an increase in adverse events following preoperative oral carbohydrate loadings, like aspiration, nausea, and vomiting during or after surgery.[14]

In our study, we found that there is a significant rise in blood sugar after 24 hrs postoperatively in the conventional fasting group in comparison to the carbohydrate loading group. This may occur because of the more and progressive rise in insulin resistance in the conventional fasting group than in the carbohydrate loading group. This finding corresponds with many studies which demonstrated higher insulin resistance in patients with conventional preoperative fasting in contrast to preoperative carbohydrate loading.[15-16] The prior studies suggest improvement in insulin sensitivity by up to 50% when carbohydrate loading gave on the surgery day, two hours before surgery.[17] There were some important benefits of carbohydrate supplementation found in some studies. Both groups experienced a rise in circulating blood glucose concentrations postoperatively; this rise, however, was significantly higher in those who fasted longer before surgery. Perrone et al. suggested the addition of whey protein to carbohydrate drinks and demonstrated further improvement in insulin sensitivity and reduction in acute-phase markers in contrast to carbohydrate drinks alone.[18] The surgical stress releases cytokines and stress hormones, which are responsible for insulin resistance leading to postoperative hyperglycaemia. The preoperative anabolic state by reducing fasting duration, pain control, and carbohydrate loading improves insulin sensitivity and perioperative sugar control.[19]

In our study, we found a significant difference between the two groups in terms of the distribution of NRS score at 1 Hour postoperatively. The patients in the carbohydrate-loading group experienced lesser pain. This result corresponded to the study conducted by Lauwick et al. who found that oral carbohydrate loading before thyroidectomy improves postoperative analgesia, but does not affect the PONV.[20] The postoperative pain can result in increased analgesic requirements, decreased ambulation or mobility, which may result in patient discomfort, decreased gut motility, increased side effects such as nausea and vomiting, and ultimately increases hospital stay. Patients from the carbohydrate loading group required lesser postope-rative acetaminophen for 24 hours postoperatively than the control group. However, combined with a multi-modal analgesia regimen preoperative carbohydrate loading may further improve postoperative analgesia. Studies suggest that sucrose-induced pain relief is related to the activation of the endogenous opioid system.[21] Sucrose analgesia is mediated at the spinal level and activates the brainstem area involved in descending pain modulation.[22]

Our study demonstrated no significant difference in the total volumes of intravenous fluid intraoperatively administered between the two groups. This finding corresponds with the study conducted by Lauwick et al. who also found no difference in the volumes of intraoperative administration of intravenous fluid among the two groups.[21] Perioperative fluid management is an integral part of enhanced recovery after surgery pathways, the excessive intravenous fluid administration is associated with increased morbidity and mortality over a range of surgical specialties. The volume overload can lead to interstitial tissue edema, impaired bowel anastomotic healing, and reduced gastrointestinal function; whereas sub-optimal intravenous fluid administration can result in tissue hypoperfusion and hypoxia, which can also lead to postoperative gastrointestinal dysfunction and anastomotic complications.[23]

We have found the following limitation in our study; As we didn't find any literature on the effect of carbohydrate loading over hemodynamic parameters before the start of the study, therefore sample size was calculated based on a secondary outcome parameter. The effect of pneumoperitoneum parameters and outcome measures was not considered. The surgeon's skills and experience were not noted. The postoperative complications were not taken into consideration.

Conclusions:

We conclude that with carbohydrate loading preoperatively, there is better hemodynamic stability during surgery under general anesthesia. Perfusion index was more with carbohydrate drink preoperatively, indicating better intravascular volume. Also, there is better pain relief and glycaemic control postoperatively. And, we recommend in favour of carbohydrate drink during the preoperative period up to two hours before surgery.

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Conflict of interest

There are no conflicts of interest.

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