

Effect Of Preoperative Oral Carbohydrate Loading On Early Surgical Outcomes – A Randomised Controlled Study

ABSTRACT: Background Enhanced recovery after surgery (ERAS) protocols are designed to minimise the physiological stress associated with surgical procedures. A key component of these protocols is preoperative carbohydrate loading, which aims to optimise patients' metabolic status before surgery. This study investigated the impact of preoperative carbohydrate intake on early surgical outcomes and encouraged their integration into surgical practice. **Methods** In this randomised controlled trial, 40 patients who were scheduled for elective surgery under general anaesthesia were enrolled and divided into two groups via the sealed envelope method. The GLUC group received preoperative oral carbohydrate loading and the FAST group followed the conventional fasting guidelines. The primary outcome measured was blood glucose levels at two and 24 hours postoperatively. The secondary outcomes included serum cortisol and insulin levels at the same time points, postoperative complications classified according to the Clavien-Dindo system, and length of hospital stay. **Results** There were 20 participants in each group after randomisation. Statistical analysis revealed significant differences in blood glucose levels between the two groups at induction and 24 hours postoperatively ($p < 0.05$). Serum cortisol levels at 24 hours post surgery also significantly varied. Although the FAST group presented a incidence of surgical site infections (SSI) according to the Clavien-Dindo classification, this difference was not statistically significant. **Conclusion** The administration of carbohydrate-rich clear liquids up to two hours before surgery appears to be safe and may mitigate the surgical stress response. Despite the small sample size, this study lays the groundwork for larger-scale research, particularly in the Indian subcontinent, where the adoption of ERAS protocols is limited.

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Introduction

Enhanced recovery after surgery (ERAS) protocols are multimodal, evidence-based strategies in perioperative care designed to expedite recovery after surgical procedures. The primary philosophy of ERAS is to recognise and mitigate the profound physiological stress caused by surgery [1]. Preoperative carbohydrate loading is a cornerstone of the ERAS protocol. Administering a carbohydrate-rich drink before surgery helps maintain euglycemia, reduce the insulin surge, decrease the stress response, promote earlier recovery of bowel function, and shorten hospital stays [2-4].

The surgical stress response triggers the release of counter-regulatory hormones (such as catecholamines, glucagon, cortisol and growth hormone) and proinflammatory cytokines (including

tumor necrosis factor-alpha [TNF- α] and interleukins IL-1 and IL-6), leading to a state of insulin resistance. Insulin resistance is a significant factor influencing perioperative outcomes [5]. Insulin-dependent cells are protected by insulin resistance, causing most circulating glucose to enter cells that do not require insulin for uptake resulting in a cellular glucose overload. Inside the cell, glucose may either non-enzymatically glycosylate proteins (such as immunoglobulins) rendering them dysfunctional or enter glycolysis, generating excess superoxide radicals. These radicals can bind to nitric oxide (NO) and promote the formation of peroxynitrite, leading to mitochondrial dysfunction and apoptosis. Consequently, a growing body of evidence indicates that even moderate increases in blood glucose are associated with adverse surgical outcomes [6].

Despite substantial evidence supporting preoperative carbohydrate loading, data regarding its efficacy within the Indian population remain limited. Moreover, most studies have examined glucose loading as part of the broader ERAS protocol rather than as an isolated strategy. This study aims to elucidate the impact of preoperative oral carbohydrate loading on early surgical outcomes in terms of early recovery, shorter hospital stays and fewer postoperative complications among Indian patients undergoing elective surgery.

Methodology

A prospective randomised controlled study was conducted in a surgical unit of a large tertiary teaching hospital in New Delhi over a period of 12-months following approval from the institutional ethics committee. All patients aged 18-65 years who were scheduled for elective surgery under general anaesthesia were screened for the study with informed consent. Any participant with deranged carbohydrate metabolism, pregnancy or an abnormal BMI was excluded from the study. Eligible participants were randomly allocated into two groups: the GLUC group, which received preoperative oral carbohydrate loading, and the FAST group, which adhered to conventional fasting guidelines. Randomisation was achieved through computer-generated randomisation tables and a sealed envelope technique to ensure allocation concealment. A comprehensive preoperative assessment encompassing demographic details, medical history, and baseline investigations was conducted for all participants. Additionally, anthropometric measurements, including body mass index (BMI) were meticulously recorded.

In the GLUC group, participants were administered a standardised oral carbohydrate solution comprising 75 grams of glucose dissolved in 1 liter of water, to be consumed 2 to 4 hours prior to the scheduled surgical intervention. Conversely, participants in the FAST group were instructed to adhere to standard of care (conventional fasting guidelines) routinely followed in our hospital, refraining from oral intake for a minimum of 6 hours before surgery. All of the above investigations and interventions were ensured and recorded by surgical resident who participated in this study and were posted in the same surgical unit where the study was conducted. Preoperatively, blood

glucose, serum cortisol, and serum insulin levels were measured in all patients on the morning of surgery and again intraoperatively at the time of induction. The participants were monitored for changes in postoperative blood glucose levels and the secondary end points were changes in serum cortisol and insulin levels, operative time, and duration of hospital stay. Postoperative complications, including surgical site infections (SSI), were diligently monitored and graded according to the Clavien-Dindo Classification,[7] for a period of 14 days.

Postoperative hyperglycaemia and surgical stress were assessed by measuring the aforementioned blood parameters at 2 hours and 24 hours postoperatively. All the outcomes were assessed by the resident who recorded the initial demographic details. The minimum sample calculated from a previous study by Weledji EP et al,[8] using blood glucose levels at 24 hours as primary endpoint. Assuming a confidence interval of 90% and power of 80%, the total sample size was calculated using formula given below:

$$k=n2/n1=1$$

$$n1= (\sigma1^2+\sigma2^2/K) (z1-\alpha/2+z1-\beta)^2 / \Delta^2$$

$$\Delta = |\mu2-\mu1| = \text{absolute difference between two means}$$

$$\sigma1, \sigma2 = \text{variance of mean \#1 and \#2}$$

$$\text{Mean, group 1} = 123.06 \pm 26.64$$

$$\text{Mean, group 2} = 146.20 \pm 38.36$$

$$n1 = \text{sample size for group \#1}$$

$$n2 = \text{sample size for group \#2}$$

$$\alpha = \text{probability of type I error} = 0.1$$

$$\beta = \text{probability of type II error} = 0.2$$

$$z = \text{critical Z value for a given } \alpha \text{ or } \beta$$

$$k = \text{ratio of sample size for group \#2 to group \#1}$$

Hence by using the above study parameters, the sample size was 17 in each group but we followed 20 patients in each group, with a total sample size of 40.

The post-hoc power analysis was done with following parameters:

$$\text{Mean, group 1} = 130.80 \pm 23.50$$

$$\text{Mean, group 2} = 155.85 \pm 28.99$$

$$\alpha = \text{significance} = 0.1$$

$$\text{Post-hoc power was calculated to be } 91.3\%$$

This is very small sample size study to impress upon importance of ERAS protocol in perioperative outcomes and not for obtaining results by measuring outcomes. The intervention is done in one group only therefore; the study could not be blinded. To reduce measurement bias, researchers standardized participant care—like additional treatments, follow-up frequency, and complication management—and ensured that the outcomes measured were as objective as possible [9].

Statistical analysis:

The data were recorded and analyzed via MS-Excel via SPSS 25.0 version. Statistical analysis was performed using Chi-square test and Mann-Whitney tests, with p-values <0.05 deemed statistically significant. Subgroup analyses were conducted to explore potential variations in outcomes on the basis of the nature of surgery and the presence of surgical site infections. AOC analysis was used to estimate the period of hyperglycemia. Since, it is a small sample size study with low statistical power, not much statistical comparisons have done [10]. Therefore, no correction method was used.

Results

A total of 50 patients aged 18-65 years, who were scheduled for elective surgery under general anesthesia between August 2021 and April 2022, were screened for the study. The consort diagram of the study is shown in figure 1.

Analysis of baseline characteristics revealed comparable demographic profiles and surgical characteristics between the GLUC and FAST groups is shown in table 1. Figure 2 illustrates the glucose tolerance levels among all 40 patients, as represented by their preoperative HbA1c values. Table 2 presents the distribution of surgeries performed in the GLUC and FAST groups. The duration of hospital stay was also similar in both study groups (Table 3). Tables 3 and Figures 4, 5, and 6 illustrate the variation in parameters such as blood glucose, serum insulin, and serum cortisol at four different intervals during the perioperative period between the FAST and GLUC groups.

Table 1: Comparison of baseline parameters between the two study groups

DEMOGRAPHICS	GLUC Group (n=20)	FAST Group (n=20)	p value
AGE in years Mean (Range, SD)	38.80 (19-65, 12.23)	41.55 (21-65, 13.52)	0.127
BMI Mean (Range, SD)	21.61(18.18-28.67, 3.05)	21.59 (18.43-28.16, 3.09)	0.567
SEX (M: F)	M: F = 1:9	M: F = 1:9	1
Smoking	Yes=15% No=85%	Yes=20% No=80%	0.677
Alcohol	Yes=10% No=90%	Yes=10% No=90%	1
Duration of surgery in hours Mean (Range, SD)	2.81 (1-6, 1.44)	2.85 (1.30-7, 1.32)	0.494
HbA1c (Range)	5.37 (4.7-6.1)	5.28 (4.8-6.2)	

Figure 1: Consort diagram

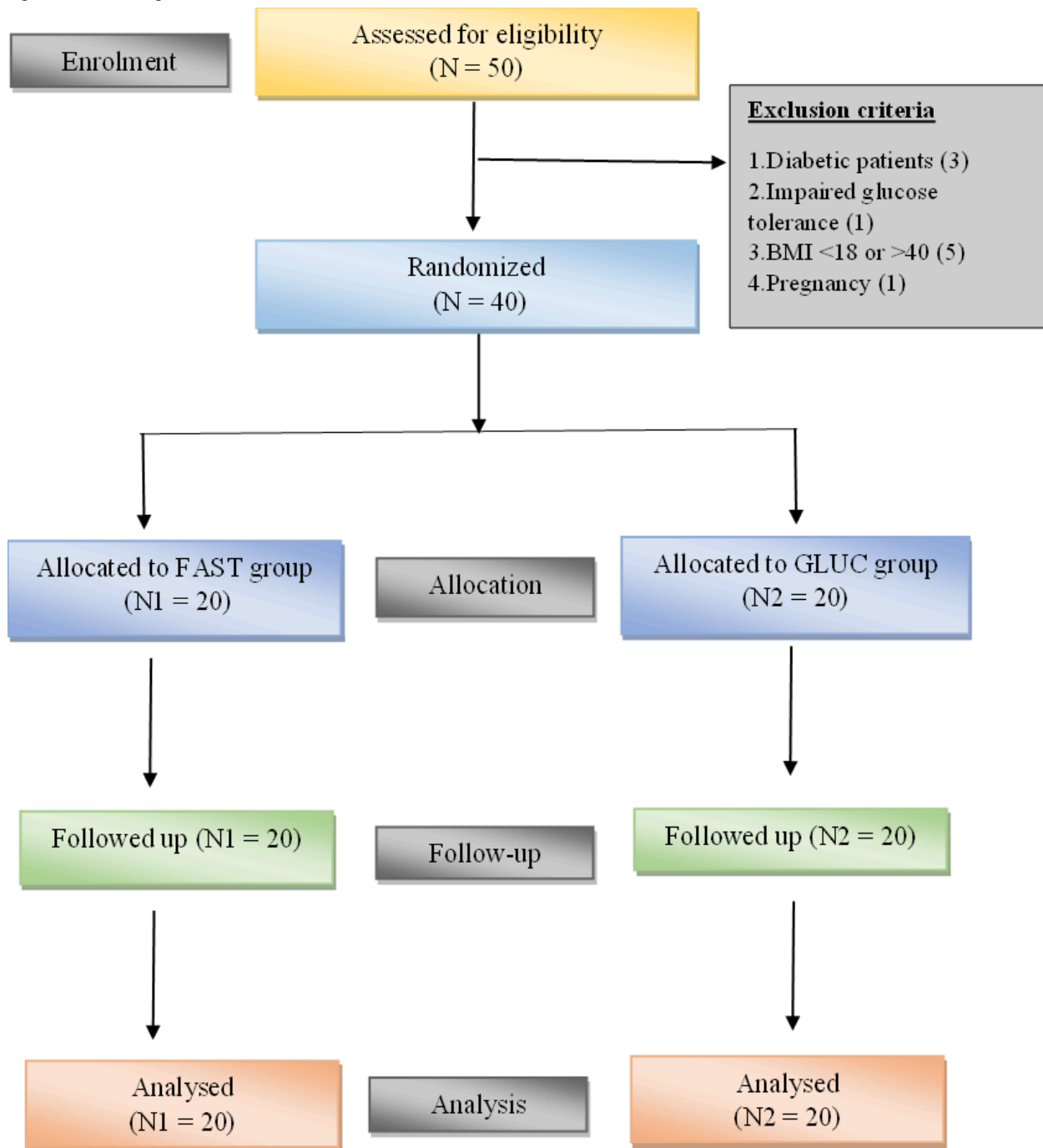
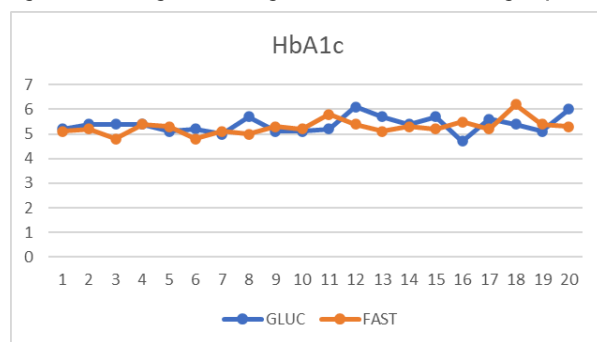
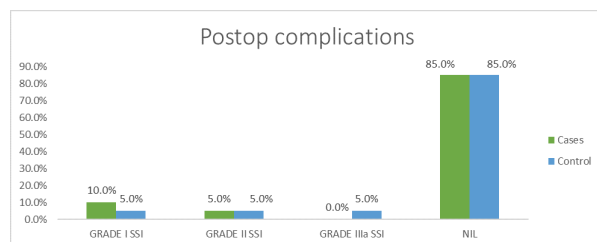
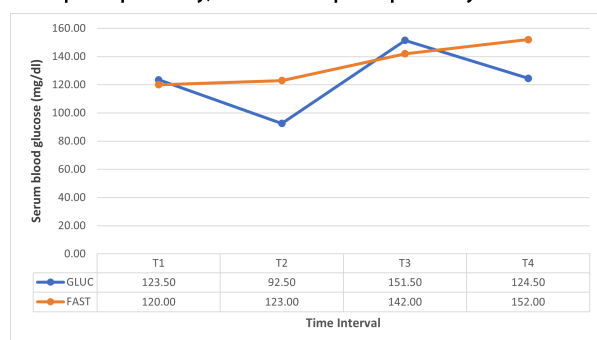
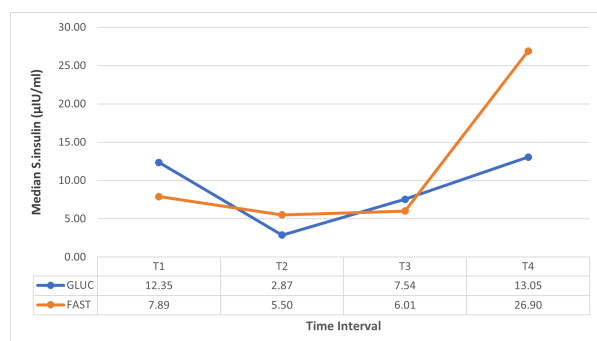
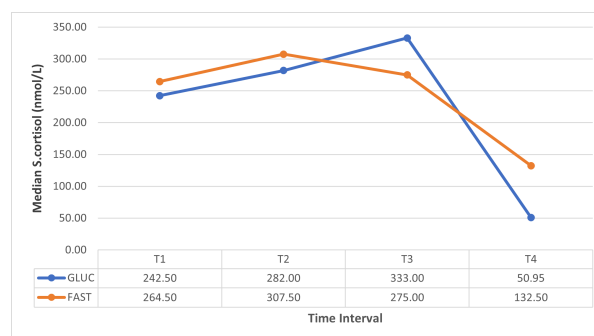


Table 2: Distribution of surgeries in both groups

	GLUC	FAST
B/L TEP	0	1
Bowel anastomosis	2	0
Distal gastrectomy and bilroth II	0	1
Extended Cholecystectomy	1	0
Ilioinguinal Lymph dissection Left side	1	0
Lap -> Open Left Nephrectomy	1	0
Lap Appendectomy	1	0
Lap CBD exploration and stent placement and subhepatic drain placement	0	1
Lap cholecystectomy and open rectus repair	1	0
Laparoscopic appendectomy	2	0
Laparoscopic cholecystectomy	4	6
Laparoscopic cholecystectomy and total thyroidectomy	1	0
Laparoscopic IPOM and open paraumbilical hernia repair	1	0
Left Hemithyroidectomy	0	1
Left MRM + axillary dissection	1	0
Left Nephrectomy	0	1
Open CBD exploration and stent in situ and subhepatic drain	0	1
Open Cholecystectomy	0	2
Open hernia repair and mesh placement	1	0
Open left Pyeloplasty	0	1
Open Mesh hernioplasty	1	2
Radical cystectomy and Ileal conduit	0	1
Right Lap ureterolithotomy	0	1
Right simple mastectomy	1	0
Wide local excision	1	1

Table 3: Mean and median values of blood parameters according to the groups and study time points.

	GLUC group (n=20), Mean ± SD				FAST group (n=20), Mean ± SD			
Parameter	T1	T2	T3	T4	T1	T2	T3	T4
Glucose (mg/dl)	133.05 ± 45.21	97.55 ± 22.37	164.65 ± 52.56	130.80 ± 23.50	119.10 ± 11.54	124.60 ± 22.00	171.45 ± 58.97	155.85 ± 28.99
Insulin (µU/ml)	38.66 ± 67.49	9.40 ± 16.99	14.81 ± 19.05	32.00 ± 74.75	8.63 ± 6.43	5.83 ± 4.08	8.87 ± 8.65	39.47 ± 56.47
Cortisol (nmol/L)	259.34 ± 76.33	312.17 ± 154.90	534.95 ± 481.00	127.33 ± 142.69	267.12 ± 87.71	376.16 ± 362.87	461.70 ± 428.50	299.19 ± 414.69
Duration of hospital stay in days Mean (Range, SD)	5 (2-13, 3.09)				6.10 (2-23, 5.49)			
*T1= 6 hours before surgery, T2= At the time of induction of anaesthesia, T3= Two hours post-operatively, T4= 24 hours post-operatively								

Figure 2: Line diagram showing HbA1c values in both the groups**Figure 3: Clustered column graph depicting post-operative complications.****Figure 4: line diagram showing trend of median blood glucose values at different intervals of time in two groups. *T1= 6 hours before surgery, T2= At the time of induction of anesthesia, T3= Two hours post-operatively, T4= 24 hours post-operatively.****Figure 5: line diagram showing trend of median serum insulin values at different intervals of time in two groups. *T1= 6 hours before surgery, T2= At the time of induction of anesthesia, T3= Two hours post-operatively, T4= 24 hours post-operatively.****Figure 6: line diagram showing trend of median serum cortisol values at different intervals of time in two groups. *T1= 6 hours before surgery, T2= At the time of induction of anesthesia, T3= Two hours post-operatively, T4= 24 hours post-operatively.**

Discussion

The enhanced recovery after surgery (ERAS) model of care was introduced in 1997 by a group of general surgeons from Northern Europe, led by Henrik Kehlet, with expertise in colorectal fast-track surgery [11]. The key elements of the ERAS protocol are categorised into preadmission, preoperative, intraoperative, and postoperative phases, forming a multimodal perioperative care pathway designed to promote early recovery for patients undergoing major surgical procedures [11].

Carbohydrate loading is one of the recommended strategies for managing the metabolic response, allowing patients to enter surgery in a fed rather than a fasted state [12]. Insulin, the body's major anabolic hormone, is adversely affected by surgical stress, leading to a state of insulin resistance. This insulin resistance reduces peripheral glucose uptake, resulting in hyperglycemia, while also increasing gluconeogenesis in the liver—a phenomenon referred to as “Diabetes of injury” [1]. Administering carbohydrate-rich drinks two hours before surgery has been shown to reduce insulin resistance by 50%, thereby shortening hospital stays, reducing postoperative complications,[13,14] and minimising muscle catabolism [15-17].

In our study, the blood glucose variability patterns differed between the two groups because after consuming a carbohydrate drink, the body entered a carbohydrate-storing metabolic state, as anticipated. However, when surgical injury occurs, the body releases mediators that counteract this state. These mediators reduce glucose uptake in muscles and

stimulate glucose production, collectively contributing to insulin resistance. If a patient is pretreated with carbohydrates, the metabolic baseline is more anabolic, which allows the body to respond to surgical stress with a less pronounced catabolic state. In contrast, patients who fast overnight start from a catabolic baseline, leading to a more severe catabolic response to surgical stress. This variability is also confirmed in our study as patients in GLUC group had lower values of blood glucose just before the patient was anaesthetised as compared to patients who were in fasted state which was statistically significant.

The ERAS protocol is not only applicable in complex surgeries; it is just a multimodal pathway to improve perioperative outcomes. So, we enrolled different types of surgeries in our study and not only the complex studies.

The difference in blood glucose levels at the time of induction between the two groups was statistically significant, with a p-value of 0.001 (CI 95%). At 24 hours postoperatively, the mean blood glucose values were also statistically significant ($p = 0.006$, CI 95%). No significant difference was observed between the GLUC and FAST groups at baseline on the morning of surgery ($p = 0.208$, CI 95%) or at 2 hours postoperatively ($p = 0.766$, CI 95%). We noted that in the FAST group, persistent elevated blood glucose levels were observed preoperatively and postoperatively. The blood glucose in GLUC group showed a plateau in postoperative period owing to less surgical stress and insulin resistance in individuals loaded with a carbohydrate drink preoperatively.

Additionally, a significant difference in mean serum cortisol levels was observed at 24 hours postoperatively between the two groups ($p = 0.05$), compared to serum cortisol values at other time intervals: morning of surgery ($p = 0.766$), time of induction of anaesthesia ($p = 0.735$), and 2 hours postoperatively ($p = 0.665$). Furthermore, patients in the FAST group remained under greater surgical stress, as evidenced by increased serum cortisol levels compared to GLUC group during the studied perioperative period.

The difference in mean serum insulin levels preoperatively between the groups was statistically

significant ($p = 0.036$, CI 95%). However, no significant differences were found in mean serum insulin levels at the time of induction of anaesthesia ($p = 0.401$, CI 95%), 2 hours postoperatively ($p = 0.304$, CI 95%), or 24 hours postoperatively ($p = 0.152$, CI 95%). In our study, we observed reduced postoperative surgical stress in patients who received carbohydrate loading on the morning of surgery. Insulin resistance was also more pronounced in fasted individuals, which was correlated with elevated glucose levels.

An initial study by Ljungqvist et al.,[18] in 1994 demonstrated a 50% reduction in postoperative insulin resistance through carbohydrate loading [19]. Preoperative oral carbohydrate (POC) loading has been recommended at a dosage of 800 ml (400 kcal) the evening before surgery, followed by a repeat dose of 400 ml (200 kcal) two hours prior to the initiation of anaesthesia [20].

In a study by Akbuga et al.,[21] the mean blood glucose levels during the first postoperative hour were statistically significant ($p < 0.001$). Another study by Weledji et al.,[8] reported statistically significant mean blood glucose levels on the first postoperative day (POD1) ($p = 0.005$). Additionally, there was a significant difference in postoperative infections between the fasted group (15.75%) and the carbohydrate-loaded group (4.28%) ($p = 0.034$, CI 1.23-19.47). Although not statistically significant, the mean length of hospital stay was 3 days longer in the fast group than in the carbohydrate group ($p = 0.315$).

A systematic review by Smith et al.,[22] demonstrated a modest reduction in the overall length of hospital stay (0.3 days, 95% CI 0.56–0.04 days) with a more significant reduction of 1.6 days for patients undergoing abdominal surgery, alongside a shorter time for the passage of flatus (0.39 days, 95% CI 0.70–0.07 days).

This study addresses a gap in the existing literature, particularly for the Indian population, where this area is underexplored. Being a randomised controlled trial, the results are more dependable. The findings could have implications for broader adoption in the future, potentially influencing policy, clinical practise, or further research in India, and lay the groundwork for more extensive studies within the Indian context.

A limitation of our study is the small sample size, which was affected by the COVID-19 pandemic and related shutdowns. Our study is single centre study as it is an academic research project carried out in one of the surgical units in the department of surgery of a tertiary teaching hospital. A larger sample size and multicentric study would increase the study's robustness and allow for a more comprehensive evaluation of the ERAS protocol across various surgical types. While the procedural heterogeneity in our study was noted, it still served to demonstrate initial feasibility and importance of oral carbohydrate loading, one of the components of ERAS by this study. The duration of surgery comparison is also not very reliable and cannot be generalised because all the procedures included in the study were not complex surgeries only.

Even if methodological precautions described in methodology were incorporated in our study the results could not be validated maximally because of lack of blinding, another limitation of our study. Despite considering all limitations stated above, the above results are largely generalisable even beyond this centre.

Carbohydrate-rich clear liquids have been shown to be safe when administered up to two hours before surgery, enhancing patient comfort without increasing the risk of aspiration. Carbohydrate drinks attenuate the inflammatory response, reduce insulin resistance, and consequently shorten hospital stays while decreasing postoperative complications. However, proving these theoretical benefits and favorable outcomes solely attributable to preoperative carbohydrate loading remains challenging in a small sample study.

Conclusion

In conclusion, preoperative oral carbohydrate loading is a crucial advancement in perioperative care, particularly within enhanced recovery after surgery (ERAS) protocols. By mitigating insulin resistance, stabilizing blood glucose levels, and reducing stress-induced catabolic responses, this intervention enhances postoperative recovery and reduces complications such as surgical site infections. Perioperative care practitioners (anesthesiologists, surgeons, and nurses) are central to the successful

implementation of preoperative carbohydrate loading by educating patients about the benefits and safety of carbohydrate loading. They play a major role in administering or ensuring the appropriate intake of carbohydrate drinks according to guidelines and monitoring patients' glucose levels and overall well-being during the perioperative period.

For anesthesiologists, surgeons, and perioperative nurses, integrating carbohydrate loading into standard preoperative care can optimize patient outcomes, shorten hospital stays, and improve surgical recovery. Understanding its benefits equips perioperative professionals with evidence-based strategies to increase metabolic homeostasis, minimize fasting-related stress, and improve overall surgical care, particularly in elective procedures requiring general anesthesia.

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