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Research Article

Role of Preoperative Carbohydrate Loading for Length of Hospital Stay in Elective Surgery Patient: Meta-Analysis Study

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Abstract

Background: Preoperative administration of oral carbohydrates reduces insulin resistance and prevents catabolic metabolism. Preoperative oral carbohydrates have also been recommended by the Enhanced Recovery after Surgery (ERAS) protocol as part of a multimodal approach in an effort to reduce length of stay in surgical patients and rates of complications.

Methods: The study design was carried out using meta-analysis randomized controlled trials (RCTs) by conducting a literature review of RCTs published in the last 5 years. Article databases were searched systematically for RCTs comparing preoperative carbohydrate administration with water, a placebo drink, or fasting.A comprehensive literature search was carried out using PubMed and Google Scholar. Then the risk ratio (RR) is calculated with a 95% confidence interval using the fixed-effects model.

Results: Some 20 trials involving 1921 participants were included. Comparison of CHO and preoperative fasting showed that preoperative low-dose and high-dose carbohydrate administration decreased postoperatively length of stay by 0.4 day. There was no significant decrease in length of stay compared with water or placebo.

Conclusion: Administration of carbohydrates before elective surgery provided a slight reduction in postoperative hospital stay compared to fasting.

Keywords

Preoperative Carbohydrate, COMT enzyme

1. Introduction

Fasting before surgery is recommended for patients with elective surgery which aims to prevent the risk of aspiration by ensuring that the patient's gastric volume is minimal before anesthesia or during surgery. The length of time fasting depends on the various types of food the patient eats before induction of anesthesia [1]. Pulmonary aspiration of gasater has significant morbidity and mortality but is a rare case. In fact, the patient can fast longer than the recommended fasting time as part of the elective surgery preparation, so that the patient can experience a longer hypoglycemic state which is precisely the case. Independent risk factor for poor perioperative clinical outcome [2]. In addition, there is an increase in enzymes that can exacerbate metabolic stress conditions, such as Catechol-O-Methyltransferase (COMT) Enzyme [3].

Preoperative anxiety increases intraoperative and postoperative morbidity and mortality. Anxiolytic premedication drugs that exist so far have adverse side effects. Hypoglycemic conditions during fasting result in changes in anabolic metabolism to catabolic, as a consequence of the endocrine response and the body's metabolic response. The endocrine response that occurs is in the form of increased blood glucose and insulin resistance, while the metabolic response can be in the form of the breakdown of glycogen, protein, and lipolysis [4]. As a result of this hypoglycemia condition, it will occur a stress response which aims to provide homeostatic adjustments to the body resulting in physiological phenomena that try to protect the body against various kinds of aggression. However, if the stress response that occurs is too intense and lasts a long time, then in this condition the body will find it difficult to carry out defense mechanisms, so that it can easily experience an imbalance that can threaten the body's homeostasis. The metabolic response is characterized by tissue hypoperfusion and decreased overall metabolic activity and lasts 12-24 hours. In addition, there is hypermetabolism of protein and glucose, as well as changes in fluids and electrolytes [5].

During the surgical process there is an increase in sympatho-adrenal activity which has an effect on catecholamine release as an initial response, resulting in hepatic glycogenolysis and direct sympathetic stimulation of glycogen breakdown, which ultimately results in hyperglycemia. The surgery results in a longer catabolic phaseleads to increased insulin resistance and hyperglycemia. This high stress response lasts for 2 to 3 weeks, with hyperglycemia being most significant on postoperative days 1, 3, and 4. Condition Hyperglycemia as a poor clinical outcome after surgery is a very important problem to be addressed immediately because it can put patients at high risk for various complications, longer recovery period, increased length of stay, and can cause death [5].

Preoperative administration of oral carbohydrates reduces insulin resistance and prevents catabolic metabolism which has a positive impact on perioperative blood glucose control and prevents muscle glucose breakdown, thereby preventing hyperglycemia. Preoperative oral carbohydrates have also been recommended by the Enhanced Recovery After Surgery (ERAS) protocol as part of a multimodal approach in an effort to reduce length of stay in surgical patients and rates of complications [6].

The meta-analysis of Bilku, have previously examined the comparison of muscle mass in groups given preoperative oral carbohydrates and muscle mass given placebo, found a significant difference ($p < 0.05$) in manual muscle testing, and proved that preoperative oral carbohydrates were able to maintain mass. muscles and their functions [7]. Therefore, we conducted a systematic review to evaluate the efficacy and side effects associated with preoperative oral carbohydrate administration in elective surgery patients.

2. Methods

2.1. Research design

The study design was carried out using meta-analysis randomized controlled trials (RCTs) by conducting a literature review of RCTs published in the last 5 years. The search was conducted from 2013-2018. The literature reported at least one outcome such as Length of Stay (LOS) or length of ICU stay, postoperative vomiting, and preoperative well-being (anxiety, thirst, hunger, vomiting, dry mouth). A comprehensive literature search was carried out using PubMed and Google Scholar. Then the risk ratio (RR) is calculated with a 95% confidence interval using the fixed-effects model. The research design was adopted from the previous meta-analysis [8,9].

2.2. Eligibility criteria

Randomized controlled trials included in the inclusion criteria were studies evaluating preoperative oral administration of carbohydrates in surgical patients. Comparisons evaluated were patients with preoperative oral carbohydrates versus patients on preoperative fasting, and preoperative oral carbohydrates versus placebo (mineral water).

2.3. Search strategy

The literature taken has an accepted status for publication in English. Search using keywords in the form of "preoperative", "carbohydrates loading", "CHO", "glucose", "fasting", and "surgery". Keyword searches are also carried out using medical terms when this is needed. A search was also carried out on the ClinicalTrials.gov website to identify completed but unpublished RCTs. All searches were carried out independently and completed by discussion.

2.4. Data extraction

The research data was extracted and entered into Excel data. The data entered consists of: (1) Country; (2) Patient characteristics (age, gender); (3) Treatment protocols (intervention and comparison, sample size); (4) Measured results and effects. If the data is lacking in the article, we contact the first author or the author according to the information needed, but if the author of the article does not respond within 4 weeks, an in-depth search will be carried out from the available information data.

2.5. Variable

Primary outcomes assessment is Length of stay (LOS) or Length of postoperative (LOP). These primary outcomes are presented using sensitivity analysis and funnel plot.

2.6. Quantitative Level Assessment and Evidence

The methodological quality and level of evidence were evaluated, as well as according to the standards recommended in the Cochrane 5.0 guidebook, randomization, blinding, concealed allocation, baseline comparability, missing subjects at follow-up, intention-to-treat analysis, selection of reporting, incomplete outcome data, and another bias. To evaluate the quality of the methodology on the evaluated outcomes, the Grading of Recommentation Assessment, Development and Evaluation (GRADE) approach is used which consists of high, medium, low and very low quality evidence.

2.7. Data analysis

Data were analyzed using ProMeta 3 software program. Results are presented in the form of a risk ratio (RR) with a confidence interval (CI) of 95%, average difference (MD), or standard average difference (SMD) if the scale used is different in outcomes assessment. Data were collected using a fixed-effects model, but a random-effect model was also considered to ensure the robustness of the model. The percentage of trial variability can be found due to heterogeneity which can be described with a statistical estimate of I2 with a significant result of $p < 0.05$ or $I2 > 50\%$. Subgroup analysis was also performed by assessing different controls, namely the group given oral carbohydrates preoperatively versus the fasting

group, preoperative oral carbohydrates versus placebo, preoperative oral carbohydrates versus glucose infusion.

3. Result

3.1. Eligible studies

A total of 6313 studies were published between 2013-2018 with keyword searches, 1 journal in Japanese, 47 articles relevant to keyword searches, but only 20 articles were randomized controlled trials that matched the inclusion and exclusion criteria. The total number of patients obtained from this article was 1921 patients (range 20-324 patients per study), with 945 patients in the oral glucose and glucose infusion treatment group, and 922 patients in the control group. In the research of Asakura, there were 16 lost follow-up patients [10], besides that there are several studies found 38 patients [11–18], drop-out during the research process. The characteristics of the included research studies are shown in Table 1. The randomization method was carried out using a computer random number generator (20 studies) [10–29,], sealed envelope (7 studies) [10,11,17,18,20,24,28], simple randomization (17 studies) [10,12-14,16-23,25–29], and block randomization (3 studies) [11,15,24]. In addition, allocation concealment was reported in 7 studies using sealed envelopes [10,11,18,20,24,28] and password-protected (web-data) [17]. Five randomized controlled trials using triple blind trials [13,18,25,28,29] double blind in 8 studies [11,16,17,20,21,24,26,27], single blind in 1 study [12], and 6 studies did not explain the blinding method used [10,14,15,19,22,23]. Inclusion and exclusion criteria were defined in all research studies included in this meta-analysis.

3.2. Patient characteristics

The literature included in this study consisted of patients undergoing abdominal surgery [21], maxillofacial surgery [23], coronary artery bypass or spinal surgery [16,24], laparoscopic roux-en-y gastric bypass [14], Laparoscopic Cholecystectomy [18,27,29]. ASA grade I was reported as 141 patients, ASA grade II was 345 patients and ASA grade III 58 patients. A total of 647 patients were only reported to be in the ASA grade I-III range, whereas 730 patients had no explanation of ASA. A recapitulation of the articles in the study is shown in Table 1.

3.3. Length of Hospital Stay

Length of postoperative stay was the main and most frequently reported outcome in patients undergoing elective surgery. Figure 1 represents the Forest plot of the effect of preoperative oral carbohydrate treatment on length of hospital stay in patients undergoing elective surgery. The mean length of postoperative stay in patients undergoing elective surgery in the CHO group was 5.1 days, while in the fasting group it was 5.7 days. This shows that the mean length of stay of patients given carbohydrate loading is shorter.

Figure 2 shows that the results of the meta-analysis presented in the forest plot, show that the combined studies are homegene with I2 of 39%, but there is only 1 study that states that the fasting group has a better length of postoperative stay than the CHO group. Overall, this meta-analysis shows that carbohydrate loading can reduce the length of postoperative stay of patients undergoing elective surgery under general anesthesia.

4. Discussion

Research by Hausel, showed that administering carbohydrate drink (CHO) improved preoperative well-being compared to placebo (water) intake or overnight fasting. This treatment relieves thirst, hunger, anxiety before surgery. Furthermore, it is more effective than placebo in reducing hunger, thirst, and anxiety.

In a meta-analysis conducted by Bilku et al, giving carbohydrates improved thirst, hunger, anxiety, and malaise in two randomized controlled trials. In contrast, the Cochrane review found no difference in the well-being of patients during postoperative care between the group given carbohydrates and the group that was fasting before surgery [6,7,30].

Several meta-analyzes have also shown previously that the oral carbohydrate group decreased postoperative length of stay (0.4 days) compared to fasting patients, this was also followed by an increase in insulin sensitivity [9,31].

Table 1: Characteristics of studies of preoperative carbohydrate treatment in patients undergoing elective surgery.

Research	Patient	Randomization method	Envelopes	Blinding	Inclusion and exclusion	Describe dropouts and withdrawals
Tran et. al (2013)	Coronary Artery Bypass or Spinal Surgery	Block randomization	sequen- tially numbered opaque envelopes	Double blind	Yes	Not stated
Sada et. al (2014)	abdominal surgery	Simple randomization	Not stated	Double blind	Yes	Not stated
Azagury et. al (2015)	Laparoscopic Roux-en-Y gastric bypass	Simple randomization	Not stated	Not blinded	Yes	Not stated
Singh et. al (2015a)	maxillofacial surgery	Simple randomization	Not stated	Not stated	Yes	Not stated
Pedziwiatr et. al (2015)	laparoscopic cholecystectomy	Simple randomization	sealed opaque envelopes	Triple blind	Yes	Not stated
Lee et. al (2018)	Laparoscopic Cholecystectomy	Simple randomization	Not stated	Double blind	Yes	Not stated

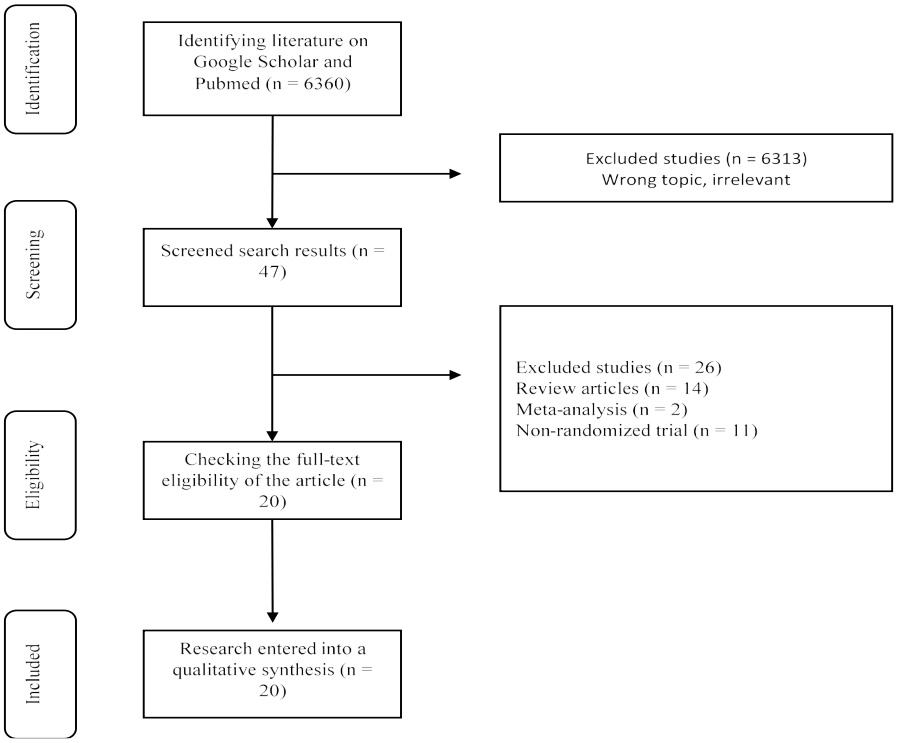

Figure 1: PRISMA diagram.

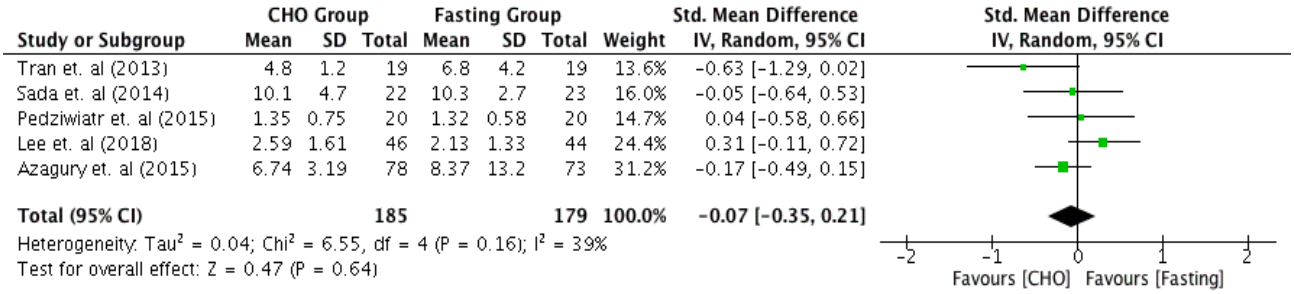

Figure 2: Forest plot of the effect of preoperative oral carbohydrate treatment on length of hospital stay in patients undergoing elective surgery. Abbreviations: CI- confidence interval; IV- inverse variance.

The limitations of this study are the validity of the degree of research quality, the large number of which do not present complete data and the non-uniform number of samples from each study. In addition, poorly designed placebo-controlled trials were excluded from this study, particularly leading to the combination of placebo and water as one group.

Current anaesthetic guidelines recommend for patients clear fluids for up to 2h before surgery, based on the established safety of this practice in patients who are not at high risk of aspiration. Recently published ERAS guidelines strongly recommend the routine use of oral carbohydrate loading before a variety of elective procedures [32].

5. Conclusion

Administration of carbohydrates before elective surgery provided a slight reduction in postoperative hospital stay compared to fasting.

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