Clinical Nutrition 32 (2013) 34–44

Contents lists available at SciVerse ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Meta-analyses

A meta-analysis of randomised controlled trials on preoperative oral carbohydrate treatment in elective surgery☆

Sherif Awad [a,d], Krishna K. Varadhan [a,d], Olle Ljungqvist [b,c,e], Dileep N. Lobo [a,*,e]

[a] Division of Gastrointestinal Surgery, Nottingham Digestive Diseases Centre National Institute for Health Research Biomedical Research Unit, Nottingham University Hospitals, Queen's Medical Centre, Nottingham NG7 2UH, UK
[b] Department of Surgery, Örebro University Hospital, SE-701 85 Örebro, Sweden
[c] Institution for Surgery and Molecular Medicine, Karolinska Institutet, Stockholm, Sweden

ARTICLE INFO

Article history:
Received 19 June 2012
Accepted 12 October 2012

Keywords:
Oral carbohydrate
Surgery
Hospital stay
Insulin resistance
Complications
Meta-analysis

SUMMARY

Background & aims: Whilst preoperative carbohydrate treatment (PCT) results in beneficial physiological effects, the effects on postoperative clinical outcomes remain unclear and were studied in this meta-analysis.

Methods: Prospective studies that randomised adult non-diabetic patients to either PCT (≥50 g oral carbohydrates 2–4 h pre-anaesthesia) or control (fasted/placebo) were included. The primary outcome was length of hospital stay. Secondary outcomes included development of postoperative insulin resistance, complications, nausea and vomiting. Methodological quality was assessed using GRADEpro® software.

Results: Twenty-one randomised studies of 1685 patients (733 PCT: 952 control) were included. No overall difference in length of stay was noted for analysis of all studies or subgroups of patients undergoing surgery with an expected hospital stay ≤2 days or orthopaedic procedures. However, patients undergoing major abdominal surgery following PCT had reduced length of stay [mean difference, 95% confidence interval: −1.08 (−1.87 to −0.29); $I^2 = 60\%$, $p = 0.007$]. PCT reduced postoperative insulin resistance with no effects on in-hospital complications over control (risk ratio, 95% confidence interval, 0.88 (0.50–1.53), $I^2 = 41\%$; $p = 0.640$). There was significant heterogeneity amongst studies and, therefore, quality of evidence was low to moderate.

Conclusions: PCT may be associated with reduced length of stay in patients undergoing major abdominal surgery, however, the included studies were of low to moderate quality.

1. Introduction

Preoperative fasting and surgery cause metabolic-stress and insulin resistance,[1] which is characterised by hyperglycaemia and decreased responsiveness of tissues (mainly skeletal muscle and liver) to the biological actions of insulin.[1] Development of insulin resistance is associated with increased morbidity,[2] mortality[2] and length of hospital stay.[3] Measures to attenuate development of insulin resistance, such as preoperative oral treatment with complex carbohydrates may, therefore, be clinically beneficial. A number of studies have examined the effects of preoperative carbohydrate treatment on postoperative insulin resistance and glucose kinetics,[4,5] protein balance and body composition,[5,6] postprandial hormonal and metabolic responses,[7–9] immune function,[10] gene and protein expression,[8,11] residual gastric volume,[7,12] drink-related complications,[6,13,14] patient well-being[15,16] and length of hospital stay.[6,14,17] Whilst the safety[6,14] and physiological benefits of preoperative carbohydrate treatment have been demonstrated,[1] data regarding the effects on important clinical endpoints such as length of hospital stay are conflicting; with some studies demonstrating a reduction[17] and others no reduction[6,14] in length of stay. Reasons for these inconsistencies include small numbers of participants and study of heterogeneous groups of patients undergoing surgical procedures of differing magnitudes.[18]

Meta-analysis of studies on the effects of preoperative carbohydrate treatment on clinical endpoints has hitherto not been

☆ Preliminary findings from this paper were presented at the Annual Conference of the Society for Academic and Research Surgery, Nottingham, January 2012 and were published in abstract form [Br J Surg 2012; 99(S4):43]. The final dataset was presented at the Annual Congress of the European Society for Clinical Nutrition and Metabolism, Barcelona, September 2012 and was in abstract form in Clin Nutr Suppl 2012; 7:29.

* Corresponding author. Division of Gastrointestinal Surgery, Nottingham University Hospitals, Queen's Medical Centre, Nottingham NG7 2UH, UK. Tel.: +44 115 8231149; fax: +44 115 8231160.
E-mail address: Dileep.Lobo@nottingham.ac.uk (D.N. Lobo).
[d] SA and KKV have contributed equally to this paper.
[e] OL and DNL are joint senior authors.

0261-5614/$ – see front matter © 2012 Elsevier Ltd and European Society for Clinical Nutrition and Metabolism. All rights reserved.
http://dx.doi.org/10.1016/j.clnu.2012.10.011

performed. The aims of the present meta-analysis were to determine the effects of preoperative carbohydrate treatment in patients undergoing elective surgery on: 1) length of hospital stay; 2) development of postoperative insulin resistance; 3) occurrence of drink-related (vomiting, aspiration and pneumonia) and postoperative complications; and 4) occurrence of postoperative nausea and vomiting.

2. Materials and methods

2.1. Eligibility

2.1.1. Inclusion criteria

We included prospective studies that randomised adult patients undergoing elective surgery to either preoperative oral treatment with complex carbohydrates using $\geq$50 g oral carbohydrate in the preoperative morning serving of the drink or a control arm. The latter may have been either ingestion of an equivalent volume of placebo drink containing no nutrients or preoperative fasting.

2.1.2. Exclusion criteria

Randomised controlled trials that administered intravenous carbohydrate, utilized $<$50 g oral carbohydrate in the preoperative morning serving of the drink, that did not compare preoperative carbohydrate treatment against a placebo/preoperative fasting control arm, in which study outcomes were not measured, and those that included patients with diabetes mellitus were excluded. Additionally, non-randomised, case–control, retrospective, healthy volunteer studies, and other studies that did not fulfill the inclusion criteria were also excluded.

2.1.3. Type of intervention

Preoperative carbohydrate treatment using $\geq$50 g oral carbohydrate (with or without additional additives) compared with control.

2.1.4. Outcomes

The primary outcome measure was the effect of preoperative carbohydrate treatment on length of primary hospital stay, (defined as number of postoperative days in hospital, until discharge). Secondary outcomes included the effects of preoperative carbohydrate treatment on development of postoperative insulin resistance, occurrence of drink-related (vomiting, aspiration or pneumonia) and postoperative complications, and occurrence of postoperative nausea and vomiting.

2.1.5. Types of groups and subgroups of patients analysed

We defined *a priori* subgroup analyses to examine the effects of preoperative carbohydrate treatment on length of stay in: 1) all patients who received preoperative carbohydrate treatment; 2) patients undergoing major abdominal surgery; 3) operative procedures with an expected length of stay $\leq$2 days (e.g. laparoscopic cholecystectomy, hernia repair and thyroidectomy); and 4) orthopaedic surgery.

2.2. Search strategy

Studies published in all languages between January 1980 and April 2012 in Medline, Embase, Science Citation Index and Cochrane Library databases were searched using the MeSH search terms preoperative, postoperative, protein, insulin resistance, insulin sensitivity, oral, loading, glucose, hospital stay, nausea, vomiting, pulmonary, complication, well-being, thirst, hunger, pain and anxiety. These results were combined with carbohydrate and surgery in combination with the Boolean operators AND, OR and NOT. Additionally, bibliographies of published randomised controlled trials were scanned for studies that were missed in the initial electronic search. Commercial companies that produced preoperative carbohydrate drinks were contacted for any unpublished data. Corresponding authors of the relevant publications were approached for additional or missing data when necessary.

2.3. Data collection

The randomised controlled trials identified were examined independently by two authors (SA and KKV) and were considered as eligible for inclusion for meta-analysis if they met predefined inclusion criteria. Data collected included age of participants, type of surgery, presence of diabetes, American Society of Anesthesiologists (ASA) grade, total quantity and timing of carbohydrate ingestion preoperatively, study reported outcomes, length of hospital stay, changes in insulin resistance, occurrence of pulmonary and surgical complications and postoperative nausea and vomiting. Outcomes measures were recorded either as intention to treat analysis or per protocol, as mentioned in the included RCTs.

2.4. Assessment of quality and risk of bias of included studies

The quality of studies was assessed for patient selection, comparability of the two study groups, and outcome measures used. Each randomised controlled trial was assessed for method of randomisation, allocation concealment, blinding, protocol violation, description of withdrawals/dropouts. Any disagreement was resolved by consensus discussions with the other members of the review team (OL and DNL). Graphic exploration with funnel plots was also used to evaluate publication bias.

The overall quality of the evidence obtained from the included studies, for the outcome measures used in this meta-analysis was assessed comprehensively using GRADEpro® (http://http://ims.cochrane.org/revman/other-resources/gradepro/download). Judgements of the quality of specific outcomes were based on presence or absence of the following variables in individual randomised controlled trials: limitations of study design and execution, inconsistency, indirectness and imprecision of results and risk of bias. Overall quality of the evidence for each outcome was a pooled result of the assessments in the above domains and was graded as very low, low, moderate or high. Strength of recommendations for either preoperative carbohydrate treatment or control was based on the combined results of the aforementioned systematic assessments.

2.5. Statistical analysis

Two authors (KKV and SA) performed the statistical analysis using RevMan 5.1 software (The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark, http://http://ims.cochrane.org/revman/download) using standard methods recommended by the Cochrane Collaboration. Effect sizes for dichotomous outcomes were reported as risk ratio with 95% confidence intervals and continuous outcomes as mean differences. A random-effects model with the inverse variance method was used for pooled analyses. Differences were considered significant at $p < 0.05$. Quantitative assessment of heterogeneity was calculated first using both 'fixed' and 'random' effect models for all outcomes. Test for homogeneity was then assessed using χ^2 and the I^2 statistic with values of I^2 less than or equal to 25%, 50%, and 75%, representing low, moderate, and high heterogeneity, respectively. If the I^2 test rejected the assumption of homogeneity of studies, then the random-effect analysis was reported.