Perioperative carbohydrate loading in patients undergoing one-day surgery. A systematic review of randomized controlled trials

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Abstract

Introduction: It is suggested that preoperative carbohydrate loading may have beneficial effects, which is emphasised in Enhanced Recovery After Surgery protocols (ERAS). Recent data confirmed that carbohydrate loading shortens length of hospital stay.

Aim: In this systematic review we aimed to determine whether carbohydrate loading have positive effects in patients undergoing 1-day surgery.

Material and methods: We searched 5 databases and identified some randomized controlled trials which were reviewed independently by two reviewers. In the end 6 RCTs were included, involving 411 patients. Studies compared effects of carbohydrate loading vs. fasting and/or placebo on the following outcomes: thirst, hunger, postoperative nausea and vomiting (PONV), fatigue, pain and postoperative insulin resistance. In most cases data are inconclusive as studies reported opposite results.

Conclusions: It seems that carbohydrate loading did not have a significant impact when compared to fasting or placebo. Preoperative carbohydrate loading seems not to have significant benefits over fasting or placebo in patients qualified for 1-day surgery.

Key words: enhanced recovery after surgery, carbohydrate loading, pre-op, fasting, 1-day surgery, laparoscopic cholecystectomy.

Introduction

One of many aspects of Enhanced Recovery After Surgery protocols (ERAS) is perioperative nutrition and fluid management. Preoperative fasting and surgical injury increases insulin resistance leading to postoperative hyperglycaemia and further complications, such as impaired wound healing. This lengthens hospital stay [1]. However those detrimental metabolic effects can be alleviated to some degree with preoperative administration of a carbohydrate-rich drink [2], which is recommended by both ERAS and ESPEN guidelines [3, 4]. Postoperative nausea and vomiting is another factor known for delaying discharge after surgery, fortunately it can be lessened with a carbohydrate rich drink as well [5, 6]. The carbohydrate drink also improves general well-being after surgery [6, 7].

There are four meta-analyses assessing benefits of the preoperative carbohydrate drink [8–11], each proving that carbohydrate loading reduces length of hospital stay. However two of them, including the most recent one, show no difference compared to placebo [10, 11]. We have chosen to focus on day-care surgery to take a closer look on secondary outcomes as those previously mentioned reviews were inconclusive in that regard.

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Aim

The aim of this review was to determine how preoperative carbohydrate treatment impacts on recovery after elective ambulatory surgery compared to placebo.

Material and methods

Search strategy

The Medline, EBSCO, Scopus, Web of Science (WoS) and Cochrane databases were systematically and comprehensively searched in October 2021 according to Prisma guidelines. The search protocol was prospectively registered in the International prospective register of systematic reviews (PROSPERO) – CRD42021284397. Two reviewers (JK, KPS) independently evaluated each paper. If any disagreement occurred, the third reviewer (RO) was involved. The following data were extracted: title, first author, publication year, number of patients, patient age, sex, body mass index (BMI) and ASA status, inclusion criteria, exclusion criteria, intervention type, allocation, measured outcomes, amount of carbohydrates administered, type of surgery, duration of anaesthesia and surgery.

Search query

The following search query was used to extract articles from databases: ((preoperative or perioperative) and (carbohydrate or CHO or nutricia/nutrition or carbohydrates or maltodextrin or carbohydrate rich) and (drink or treatment or loading or oral or per os or load or administration)) and ((ambulatory or 1-day or elective or outpatient or ambu* or electiv* or fast-track) and (surgery or surgical procedures or procedure or sedation or anesthesia or surg* or general anaesthesia)).

Type of studies

We included randomised clinical trials comparing carbohydrate loading with controls in patients over 18 years old undergoing elective ambulatory surgery. Patients undergoing ambulatory surgery receiving clear liquid or nothing were treated as controls.

Inclusion criteria

- randomised controlled trial,
- results published in English,
- participants not younger than 18 years old,
- general anaesthesia or general anaesthesia combined with regional anaesthesia,
- any ambulatory or 1-day surgery,
- elective surgery,
- subjects received at least 45 g of the carbohydrate drink per os before surgery; controls received other clear liquid or nothing,
- hospitalisation under 24 h,
- results published in a reviewed journal.

Exclusion criteria

- not fulfilling inclusion criteria,
- basic science research,
- single-arm studies.

Main outcome

Comparison of the effectiveness of preoperative oral carbohydrate and fasting.

Additional outcomes

1. Metabolic effect
2. Impact on fatigue and general well-being
3. Impact on nausea and vomiting
4. Other outcomes: as defined and measured by trials’ authors.

Results

Search results

Databases yielded 3467 results, from those 2385 were screened for eligibility criteria based on the titles which gave 240 papers. Those were screened for eligibility criteria based on abstracts which have left 74 papers which were read in full text. After careful consideration against inclusion criteria, 6 papers were included in the review. Prisma flow diagram presents study search in detail (Figure 1).

Characteristics of included studies

Six studies published in 2012–2020 were included in the study [12–17]. The studies were conducted in Finland, Turkey, India and Brazil. Majority of patients were females under 50 years old who underwent elective laparoscopic cholecystectomy. Patients had ASA status I–II. In all studies patients received the amount of carbohydrates recommended by ERAS guidelines. The comparator was either fasting place-
bo or carbohydrates + glycine (GLN group). Detailed characteristics of the studies are presented in Table I.

**Quality assessment**

We followed Cochrane Collaboration guidelines regarding bias assessment. Each paper was assessed independently by two reviewers. Five databases were searched to ensure that all matching papers were included. In risk of bias assessment, several parameters were included: (I) random sequence generation, (II) allocation concealment, (III) blinding of participants and personnel, (IV) blinding of outcome assessment, (V) incomplete outcome data, (VI) selective reporting, (VII) other potential threats to validity. All studies have met baseline criteria for quality assessment. Typically, there were no issues regarding random sequence generation, however in most cases allocation concealment was not described. Unfortunately majority of the studies were single blinded, or blinding was not reported, also only one study by Helminen et al. published the protocol. We have not found other potential risks within the studies. A summary of biased assessment for each study is presented in Table II.

**Thirst and hunger**

Three studies examined whether carbohydrate loading can alleviate thirst and hunger [14–16]. Helminen et al. used VAS scale (0–100) while Gök et al. and Yildiz et al. measured nausea incidence. In studies by Gök et al. and Yildiz et al., the carbohydrate-rich drink decreased thirst preoperatively or preoperatively and postoperatively. However, Helminen et al. did not support that result (Table III).

In studies by Gök et al. and Yildiz et al., administration of a carbohydrate-rich drink decreased hunger preoperatively or preoperatively and postoperatively. However, Helminen et al. did not support that result (Table IV).
Nausea and vomiting

For studies including nausea as examined outcomes [14–17], Helminen et al. and Singh et al. used VAS scale while Gök et al. and Yildiz et al. measured nausea incidence. Data are inconsistent as Helminen et al. and Yildiz et al. did not observe any significant changes in nausea intensity. Meanwhile Singh et al. reported that in the early postoperative period nausea was less intensive in the group which received carbohydrates preoperatively, oppositely Gök et al. determined that nausea was more frequent in the pre-op group. Detailed results are presented in Table V.

Singh et al. and Gök et al. examined impact of carbohydrate administration on emesis occurrence [15, 17]. Singh et al. determined that vomiting occurred less frequently only in the first 4 h postoperatively, however this observation was not supported by the study of Gök et al. It seems that pre-op carbohydrate loading does not have a significant impact on vomiting occurrence more than 4 h after surgery. Moreover, Helminen et al. reported that there were no differences regarding need for antiemetics administration between carbohydrates and fasting group ($p = 0.84$). Results are presented in Table VI.

Pain

Two studies included in the analysis determined the effect of carbohydrates administration on the pain level post-operatively [16, 17]. Helminen et al.
measured pain with a visual analog scale (VAS; 0–100). Singh et al. also used VAS, however with a span of 0–10. In the study of Helminen et al., no changes between groups had been found. They also did not observe differences in demand for pain medication and opioids between groups ($p = 0.94$ and $p = 0.95$, respectively). Contrarily Singh et al. reported that pain intensity was lower in the CHO group in the first 12 h postoperatively. Based on those two studies it cannot be concluded whether the carbohydrate-rich drink administration has beneficial effects on pain alleviation. Detailed results of included studies are presented in Table VII.

**Tiredness**

Two studies included tiredness in their outcomes [14, 16]. Helminen et al. used the VAS scale (0–100), whereas Yildiz et al. measured tiredness incidence. It seems that the carbohydrate-rich drink did not impact tiredness after surgery. Data regarding the preoperative period are inconclusive as studies reported opposite results (Table VIII).

**Impact on metabolism**

Three studies measured impact of pre-op carbohydrate loading on glucose and/or insulin levels [12, 13, 16]. In all studies no differences between groups were found (Table IX).

**Other outcomes**

Some outcomes have been described only in one study, here we discuss the selected few. Helminen et al. did not observe any significant changes between groups regarding mouth dryness, time to be able to drink, eat, ambulate or discharge [16]. Dock-Nascimento et al. investigated selected biochemical parameters and they found significant differences between the groups in HOMA-IR, albumin, C-reactive protein and interleukin 6 levels [12]. Another study by Dock-Nascimento et al. found that there are no differences in gastric residual volume between groups [13]. Yildiz et al. have found that weakness, malaise and concentration difficulty are less prominent in patients receiving a carbohydrate-rich drink [14].

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Table II. Risk of biases in selected studies

| Authors                  | Random sequence generation | Allocation concealment | Blinding of participants and personnel | Blinding of outcome assessment | Incomplete outcome data | Selective reporting | Other risks | Reference |
|--------------------------|---------------------------|------------------------|----------------------------------------|-------------------------------|------------------------|---------------------|-------------|-----------|
| Helminen et al.          | Low risk                  | Low risk               | High risk – single blinded              | Unclear – not described       | Low risk – balanced dropouts | Low risk            | Low risk    | [16]      |
| Singh et al.             | Low risk                  | Unclear – not described | Unclear – not described                | Unclear – no information regarding dropouts | Unclear – protocol not published | Low risk            |            | [17]      |
| Gök et al.               | Low risk                  | Unclear – not described | Unclear – not described                | Unclear – no information regarding dropouts | Unclear – protocol not published | Low risk            |            | [15]      |
| Dock-Nascimento et al.   | Low risk                  | Unclear – not described | High risk – surgeons were not blinded   | Unclear – not described       | Low risk – balanced dropouts | Unclear – protocol not published | Low risk    | [12]      |
| Dock-Nascimento et al.   | Unclear – not described   | Unclear – not described | High risk – single blinded              | Unclear – not described       | Low risk – balanced dropouts | Unclear – protocol not published | Low risk    | [13]      |
| Yildiz et al.            | Low risk                  | Unclear – not described | High risk – single blinded              | Unclear – no dropouts         | Low risk – protocol not published | Low risk            |            | [14]      |
Table III. Summary of the results regarding thirst occurrence and intensity

| Study Group | Participants | Thirst pre-op. n (%) | Thirst 0–4 h post-op. n (%) | Thirst 4–12 h post-op. n (%) | Thirst 12–24 h post-op. n (%) | P-values | Reference |
|-------------|--------------|----------------------|-----------------------------|-----------------------------|-------------------------------|----------|-----------|
| Helminen et al. | CHO n = 57 | 22 (6–50) | 41 [20–60] | 28 [9–61] | 12 [0–50] | 0.682 | [16] |
| | Fasting n = 56 | 40 [8–63] | 46 [24–70] | 20 [0–50] | 10 [0–50] | | |
| Gök et al. | CHO n = 21 | 12 (57.1%) | n/a | n/a | n/a | 0.032 | [15] |
| | Placebo n = 21 | 19 (90.5%) | n/a | n/a | n/a | | |
| Yildiz et al. | CHO n = 30 | 3 (10%) | 13 (43.3%) | n/a | 4 (13.3%) | < 0.05 | [14] |
| | Fasting n = 30 | 26 (86.7%) | 30 (100%) | n/a | 10 (33.3%) | | |

CHO – patients receiving carbohydrates, IQR – interquartile range, pre-op. – preoperatively, post-op. – postoperatively.

Table IV. Summary of the results regarding hunger occurrence and intensity

| Study Group | Participants | Hunger pre-operatively n (%) | Hunger 0–4 h post-op. n (%) | Hunger 4–12 h post-op. n (%) | Hunger 12–24 h post-op. n (%) | P-values | Reference |
|-------------|--------------|-----------------------------|-----------------------------|-----------------------------|-------------------------------|----------|-----------|
| Helminen et al. | CHO n = 57 | 26 (2–48) | 10 [0–34] | 10 [0–34] | 0 [0–8] | 0.529 | [16] |
| | Fasting n = 56 | 30 [19–55] | 5 [0–30] | 5 [0–30] | 0 [0–11] | | |
| Gök et al. | CHO n = 21 | 9 (42.9) | n/a | n/a | n/a | 0.003 | [15] |
| | Placebo n = 21 | 19 (90.5%) | n/a | n/a | n/a | | |
| Yildiz et al. | CHO n = 30 | 1 (3.3%) | 5 (16.7%) | n/a | 4 (13.3) | < 0.05 | [14] |
| | Fasting n = 30 | 19 (63.3%) | 26 (86.7%) | n/a | 9 (30%) | | |

CHO – patients receiving carbohydrates, GLN – patients receiving carbohydrates and glycine, IQR – interquartile range, pre-op. – preoperatively, post-op. – postoperatively.

Discussion

In this review we included 6 studies with a total of 411 patients undergoing elective 1-day surgery. We aimed to determine whether perioperative carbohydrate-rich drink administration may be beneficial in this group. The results are inconclusive as some of the studies had opposite results.

Preoperative carbohydrate treatment is over 20-year-old idea, with first findings reported in the late 1990s [18, 19]. Over the years reduction in length of hospital stay caused by carbohydrate loading was confirmed in several meta-analyses [8–11]. However the exact mechanism of action remains uncertain as studies provide conflicting data regarding proposed rationale of increasing postoperative insulin sensitivity [8–11]. We chose to restrict the scope of this review to day-care surgery in order to improve homogeneity, allowing us to focus on outcomes considered as secondary in previous studies. Also, there is a significant gap in knowledge whether carbohydrate loading can be beneficial in relatively healthy individuals who are typically qualified to be 1-day cases. This proved futile as inconsistent findings across all the studies suggest that carbohydrate loading has little to no impact on measured parameters.
Table V. Summary of the results regarding nausea occurrence and intensity

| Study Group | Participants | Nausea 0–4 h post-op. n (%) | Nausea 4–12 h post-op. n (%) | Nausea 12–24 h post-op. n (%) | P-values | Reference |
|-------------|--------------|-----------------------------|-----------------------------|-----------------------------|----------|-----------|
| CHO         | n = 57      | 0 [0–14]                    | 0 [0–4]                    | 0 [0–3]                     | 0.476    | [16]      |
| Fasting     | n = 56      | 0 [0–6]                     | 0 [0–10]                   | 0 [0–3]                     |          |           |
| Singh et al. | CHO       | n = 40                     | 0.65 (0.7)                 | 0.7 (0.823)                | 0.25 (0.439) | 0.001 (0–4 h) | 0.066 (4–12 h) | 0.357 (12–24 h) |
| Placebo     | n = 40      | 1.3 (0.853)                 | 0.83 (0.636)               | 0.43 (0.501)               |          |           |
| Fasting     | n = 40      | 1.23 (1.097)                | 1.05 (0.815)               | 0.35 (0.483)               |          |           |
| Gök et al.  | CHO         | n = 21                     | 21 (100%)                  | 15 (71.4%)                 | 6 (28.6%) | 0.048 (0–4 h) | 0.014 (4–12 h) | 0.093 (12–24 h) |
| Placebo     | n = 21      | 16 (76.25%)                 | 6 (28.6%)                  | 1 (4.8%)                   |          |           |
| Yildiz et al. | CHO      | n = 30                     | 17 (56.7%)                 | n/a                        | 1 (3.3%) | > 0.05 (0–4 h) | > 0.05 (4–12 h) | > 0.05 (12–24 h) |
| Fasting     | n = 30      | 17 (56.7%)                 | n/a                        | (6.7%)                      |          |           |

CHO – patients receiving carbohydrates, IQR – interquartile range, SD – standard deviation, pre-op. – preoperatively, post-op. – postoperatively.

The studies included in this review seem to demonstrate that the carbohydrate-rich drink did not have a significant impact on thirst and hunger. Similarly, Li et al. showed inconsistent results regarding hunger. As for thirst, they observed a significant difference when compared to fasting but not when compared to placebo [9]. With postoperative nausea and vomiting being one of the most common side effects of general anaesthesia [20] early findings about carbohydrate treatment seemed promising [21]. However, our results did not support this as no significant differences were found. This is consistent
with previous analyses [8–11] and guidelines [22]. Considering that safe, effective painkillers are readily available and routinely administered during and after general anaesthesia, it is difficult to assess whether carbohydrate loading has any impact on pain response. Consequently, no significant difference in pain response was found. To the best of our knowledge, it is the first comprehensive assessment of such kind. Moreover, carbohydrate loading has no impact on either glucose or insulin levels. This is unexpected as alleviating postoperative insulin resistance was one of reasons to consider preoperative carbohydrate treatment in the first place [2, 18, 23]. Those results fall in line with previous works [8–11]. Lastly carbohydrate treatment did not affect postoperative tiredness, which is coherent with previous findings [10, 11].

Our work, being a review, is only as good as the included studies and while they met baseline quality criteria, several limitations should be mentioned. The amount of carbohydrates used differs between studies (67–150 g), though all studies fulfilled ERAS guidelines in this matter. Authors used visual analog scales and incidence reporting, as one could expect when working with parameters of such subjective nature. Those methods rely heavily on patients’ compliance, which in itself is a source of discrepancies, even more so considering side effects of general anaesthesia. As for postoperative insulin resistance, none of the studies used hyperinsulinemic-euglycemic-euglycemic-euglycemic clamp, which is a gold standard for such assessment.

### Table VIII. Summary of the results regarding tiredness

| Study             | Group  | Participants | Pre-op. | Post-op. | P-values for glucose | Pre-op. | Post-op. | P-values for insulin |
|-------------------|--------|--------------|---------|----------|-----------------------|---------|----------|----------------------|
|                    |        |              | Tiredness |          | Tiredness | Tiredness | Tiredness |
|                   |        |              | n (% ) | Median [IQR] | n (% ) | Median [IQR] | n (% ) | Median [IQR] |
| Helminen et al.   | CHO    | n = 57      | 30 [10–56] | 49 [20–70] | 42 [8–70] | 20 [4–48] | 0.582 |
|                   | Fasting| n = 56      | 20 [5–46] | 53 [30–61] | 40 [10–50] | 25 [0–46] |          |
| Yildiz et al.     | CHO    | n = 30      | 4 (13.3%) | 19 (63.3%) | n/a | 9 (42.9%) | < 0.05 |
|                   | Fasting| n = 30      | 14 (46.7%) | 21 (70%) | n/a | 13 (43.3%) | > 0.05 |

**CHO** – patients receiving carbohydrates, **GLN** – patients receiving carbohydrates and glycine, **IQR** – interquartile range, **SD** – standard deviation, **pre-op.** – preoperatively, **post-op.** – postoperatively.

### Table IX. Summary of the results regarding pre- and post-operative levels of glucose and insulin

| Study             | Group  | Pre-op. glucose | Post-op. glucose | P-values for glucose | Pre-op. insulin | Post-op. insulin | P-values for insulin | Reference |
|-------------------|--------|-----------------|------------------|----------------------|-----------------|------------------|---------------------|-----------|
|                    |        | Mean (SD)       | Mean (SD)        |          | Mean (SD)       | Mean (SD)       |          |                     |
| Helminen et al.   | CHO    | 6.0 (1.6)       | 6.4 (1.1)        | 0.1 (preoperative) | n/a             | n/a             | n/a                  | [16]      |
|                   | Fasting| 5.4 (0.5)       | 6.4 (1.1)        | 0.37 (postoperative)| n/a             | n/a             | n/a                  |          |
| Dock-Nascimento et al. | Control | 4.4 (0.06) | 6.1 (0.3) | 0.16 (preoperative) | 10.6 (2.1) | 9.7 (2.4) | 0.17 (preoperative) | [12]      |
|                   | Placebo| 4.3 (0.11) | 5.8 (0.2) |                     | 8.1 (1.0) | 6.4 (0.9) |                     |          |
|                   | CHO    | 4.3 (0.2) | 5.9 (0.3) |                     | 13.3 (4.5) | 8.5 (1.2) |                     |          |
|                   | GLN    | 4.3 (0.2) | 5.7 (0.3) |                     | 9.6 (1.0) | 9.9 (1.9) |                     |          |
| Dock-Nascimento et al. | Fasting | 4.5 (0.1) | 6.6 (0.2) | > 0.05 for all comparisons between groups | 12.0 (3.2) | 13.0 (3.6) | > 0.05 for all comparisons between groups | [13]      |
|                   | CHO    | 4.3 (0.2) | 6.0 (0.4) |                     | 18.6 (5.3) | 8.6 (1.4) |                     |          |
|                   | GLN    | 4.3 (0.2) | 5.4 (0.4) |                     | 8.0 (0.8) | 6.5 (0.7) |                     |          |
mic clamp method. Considering the short hospital stay there were no follow-up; nonetheless no readmissions were reported.

Interestingly, there seems to be no advantages of using the carbohydrate-rich drink over placebo for several outcomes. Usually artificially flavoured water was used for this purpose. Given the fact that the carbohydrate-rich drink affects neither hydration [24] nor hemodynamic parameters [25], nor causes significant metabolic changes, any beneficial findings could be associated with a psychosomatic effect. However carbohydrates have been proven not to alter mood in any significant way in healthy adults [26]. While current guidelines recommend carbohydrate loading, any clear liquid, with or without carbohydrate content, is allowed for up to 2 h before surgery [3]. This gives an opportunity to pursue a more cost-effective alternative to meticulously manufactured carbohydrate-rich drinks. However, this idea should be further examined and confirmed.

Conclusions

The quality of evidence regarding preoperative carbohydrate loading in patients qualified for one-day case is relatively low. However, it seems that this procedure does not have beneficial effects.

Conflict of interest

The authors declare no conflict of interest.

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