MediDrink OpLoad

MEDIFOOD

PRODUCT MONOGRAPH

FOOD FOR SPECIAL MEDICAL PURPOSES FOR THE PREOPERATIVE DIETARY MANAGEMENT OF SURGERY PATIENTS

1. Metabolic changes caused by surgery

Malnutrition has an unfavourable effect on recovery, wound healing, frequency of complications (e.g. infections, decubitus), prognosis, mortality, tolerability of therapies, quality of life, and healthcare use (e.g. visits, consultations, number and length of hospital stays) (Martyn et al. 1998, Löser 2010). Studley has demonstrated a direct relationship between preoperative weight loss and surgical mortality already in 1936 (Studley 1936).

Surgery is a great metabolic stress for the patient that can induce numerous metabolic and physiologic changes. In response to such stress, the body increases its basal metabolic rate (BMR), uses its nitrogen stores up and creates a negative nitrogen balance (Bozzetti et al. 2011). The body scavenges for the required nutrients during such times of stress, which if continue unchecked for prolonged periods of time could lead to adverse consequences (Abunnaja et al. 2013). The increase in intestinal permeability during periods of surgical stress, which can be even fourfold greater in some patients, is paralleled a decrease in villous height, leading to malabsorption and an impaired ability of the gut to act as a barrier against endogenous bacteria and toxins (Ward et al. 2003, Beattie et al. 2000, Fujita et al. 2012, van der Hulst et al. 1998). Malnutrition and surgery can also both present a stress on the heart. Patients undergoing cardiac surgery are frequently found to be malnourished, resulting in alteration in the structure of myocytes and depleting the substrates utilized by the heart for mechanical work. It is therefore hypothesized that by addressing the undernourished state of the patient prior to surgical intervention, cardiovascular performance can be improved and cardiac complications after surgery as well as perioperative mortality can be lowered (Thorell et al. 1999).

Perioperative nutritional supplementation, therefore, should blunt the catabolic effects of such a high energy state (Martyn et al. 1998).

Preoperative fasting has been an established practice aimed to mitigate the risk of pulmonary aspiration and ensuing pulmonary injury in surgical patients. ‘Nil by mouth from midnight’ of the day preceding elective surgery was the empirically enforced traditional method used to assure a fasted state (Pillinger et al. 2018). However, perioperative fasting generates an unfavourable metabolic state additive to that caused by surgical stress (Carli 2015).

Short-term fasting (<12 hours) reduces insulin-mediated glucose uptake into skeletal muscle, slows metabolism and reduces total energy expenditure by 5%–10%. After an overnight fast, most of the body’s energy is derived from free fatty acids, but the body continues to consume glucose – the source of which is glyconeogenesis performed by the liver. Six hours of preoperative fasting induces peripheral insulin resistance (Pillinger et al. 2018). Prolonged fasting (>12 hours) leads to a proportional increase in peripheral insulin resistance and hepatic glycogen consumption. The glycogen stores get depleted after 18–24 hours, meaning that there is no readily available energy substrate for critical tissues (e.g. nervous system) (Pillinger et al. 2018).

Skeletal muscle is used to generate a pool of amino acids, adding to the protein loss due to surgical stress. Increase of the inflammatory citokines (interleukin-6 / IL-6, tumor necrosis factor / TNF) is likely to facilitate the development of postoperative insulin resistance, that in turn leads to an impaired glucose transporter type 4 (GLUT4) translocation in skeletal muscle cells. Due to these changes, a catabolic cascade may be initiated that may lead to an even clinically significant muscle loss (Pillinger et al. 2018). In normal adults, the loss of protein may be as much as 300 g of protein per day during starvation (Pillinger et al. 2018).

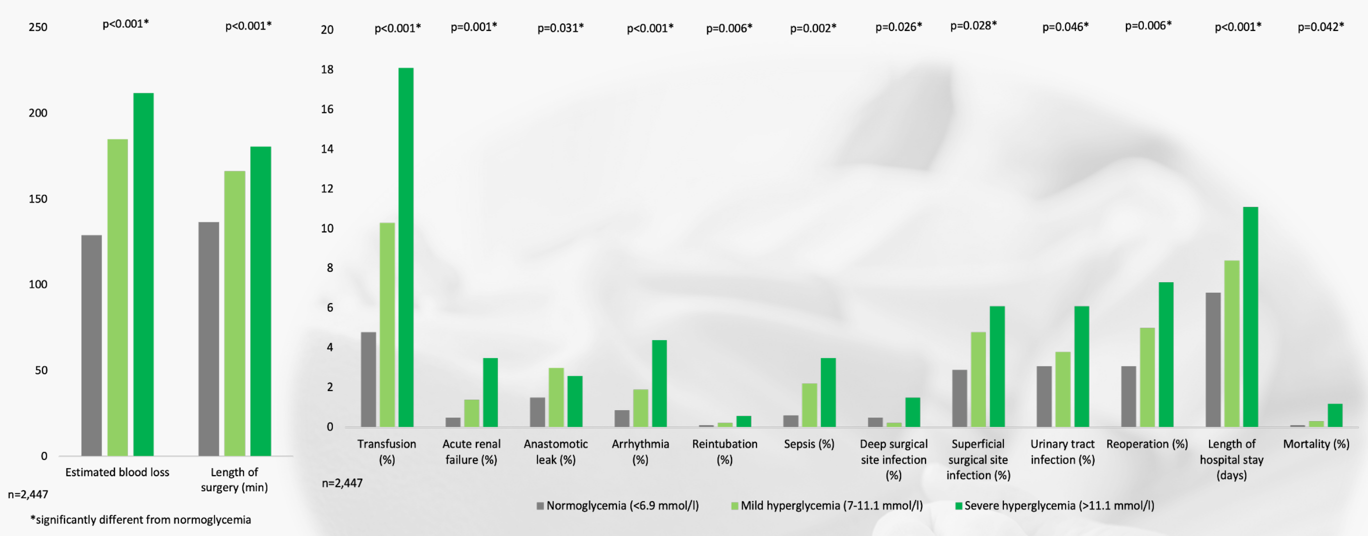
Thus, surgical trauma and perioperative fasting both contribute to the development of perioperative insulin resistance that positively correlates to surgical invasiveness and occurs even after minor surgery, such as laparoscopic cholecystectomia and open inguilnal hernia repair (Pillinger et al. 2018). Mitochondrial defects are also thought to be related to the development of insulin resistance (Pillinger et al. 2018). Persistence of the insulin resistant state depends on the length of surgery – in upper gastrointestinal tract surgery, insulin resistance has been found to persist for at least 5 days and could exist for even weeks (Thorell et al. 1994).

The consequence of insulin resistance, postoperative hyperglycemia, originates not solely from postoperative insulin resistance – other metabolic processes taking place during fasting (glycogenolysis, glyconeogenesis, increased serum glucagone level), and increased serum cortisol and catecholamine levels (as part of the stress response to surgery) also contribute to the development of postoperative hyperglycemia (Pillinger et al. 2018).

In a study of 10 patients undergoing elective cholecystectomy, all patients showed markedly decreased insulin sensitivity on the first day after operation, and there was no correlation between the preoperative sensitivity to insulin and the relative reduction found on the first day after surgery, nor did the duration of surgery correlate with the extent of the decrease after surgery. The decreased insulin sensitivity was present during at least the first 5 days after surgery (Thorell et al. 1994). The type and duration of surgery performed, perioperative blood loss, and also the degree of postoperative insulin resistance significantly influence the length of hospital stay in elective surgery patients (Thorell et al. 1999).

2. The consequences of postoperative hyperglycemia

In the analysis of 16,404 postoperative glucose measurements for 2,447 nondiabetic surgery patients, 66.7% of patients experienced postoperative hyperglycemia. Degree of hyperglycemia correlated with increasing American Society of Anesthesiologists class and surgical severity measured by blood loss. Hyperglycemia was associated with infectious and noninfectious complications and mortality, the rates of these complications increasing with the degree of hyperglycemia. Hyperglycemia was independently associated with septic complications (p=0.024) (Kiran et al. 2013).



Postoperative hyperglycemia increases complications in nondiabetic surgery patients (Kiran et al. 2013)

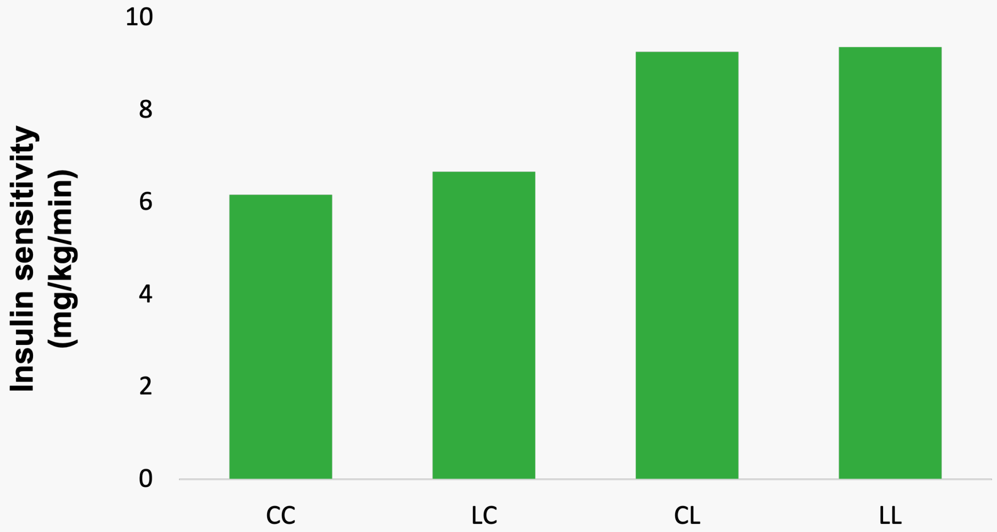
In 143 nondiabetic and 130 diabetic patients scheduled for elective cardiac surgery, diabetic patients with poor glycemic control had a greater incidence of major complications (p=0.010) and minor infections (p=0.006), received more blood products and spent more time in the intensive care unit (p=0.030) and in the hospital (p=0.001) than nondiabetic patients. For each 1 mg/kg/min decrease in insulin sensitivity, the incidence of major complications increased significantly (p=0.004) (Sato et al. 2010).

One strategy to overcome postoperative hyperglycemia would be to administer parenteral insulin. However, to achieve the same glucose uptake during total parenteral nutrition, even 8 times more insulin might be needed after surgery (Brandi et al. 1990, Thorell et al. 1994).

3. Preoperative carbohydrate loading in surgery patients

The scientific basis for the ”nil by mouth from midnight” practice has lately been questioned and attitude towards preoperative fasting changed (Ljungqvist & Soreide. 2003). Recent guidelines support a more liberal approach and patients are now encouraged to consume clear fluids (water, carbonated drinks, clear tea, black coffee, pulpfree juices) up to two hours before elective surgery (Smith et al. 2011, American Society of Anesthesiologists Committee 2017). The aim of this strategy is to ensure that patients are in a fed status during surgery, and thus to prevent the unwanted metabolic changes induced by fasting and surgical trauma and therefore improve clinical outcomes. A more recent approach is to provide carbohydrate supplementation for surgery patients with specifically designed clear carbohydrate-rich foods for special medical purposes.

In a randomised, crossover, unblinded study of 6 healthy volunteers, the participants underwent four protocols in a crossover-randomised order. In protocol CC (Control-Control) no drink was given. In protocol LC (Loading-Control) the volunteers ingested 800 ml of 12.6% carbohydrate drink (50 kcal/100 ml) between 7 PM and midnight during the evening before the day of the clamp. In protocol CL, 400 ml of the drink was ingested at 8 AM in the morning before the clamp, and in protocol LL the volunteers received the drink both in the previous evening (800 ml) and in the morning before the measurement (400 ml). In the evening before all investigations, the volunteers were allowed food intake until 7 PM after which only intake of water was allowed ad libitum. After basal blood sampling, the drink was given to CL and LL immediately before the time point 0 minute. Blood sampling for glucose and insulin was collected at 30, 60, 90, 120, 180, 210 and 240 minutes. Additional samples for measurement of blood glucose were taken every 5–10 minutes after commencement of insulin infusion (after 120 min). Insulin sensitivity was higher in CL and LL (9.2±1.5 and 9.3±1.9 mg/kg/min, respectively) compared to CC and LC (6.1±1.6 and 6.6±1.9 mg/kg/min, p<0.01 vs. CL and LL). The authors concluded that a carbohydrate-rich drink enhances insulin action 3 h later by approximately 50% (Svanfeldt et al. 2005).



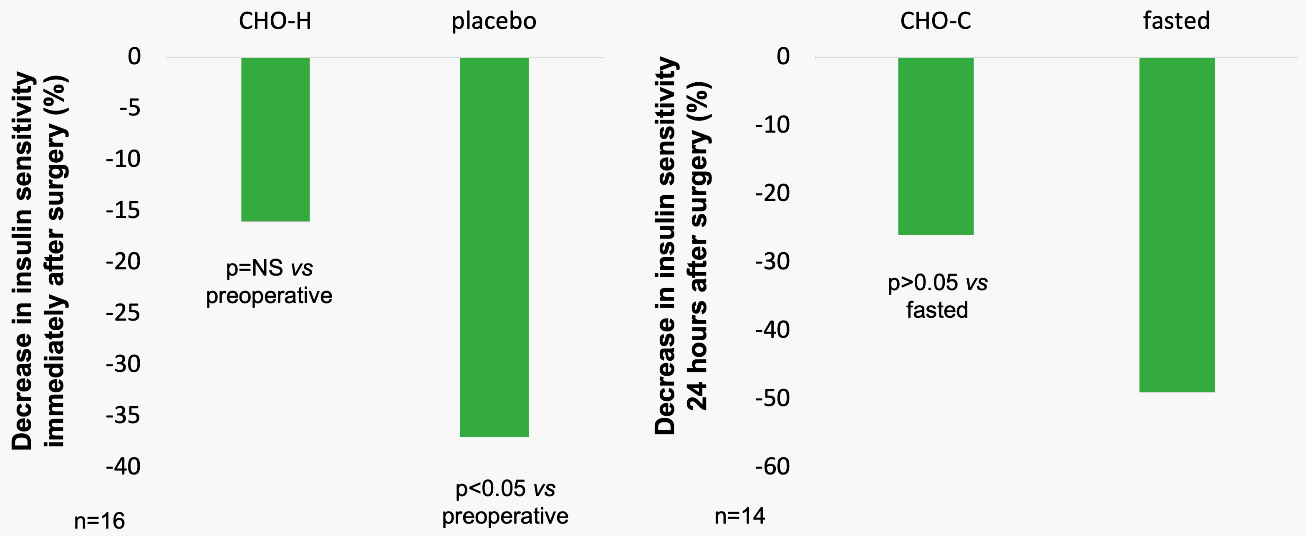
n=6

*p<0.01

CC: overnight fasting, LC: sigle evening dose (800 ml) of carbohydrate drink, CL: single morning dose (400 ml) of carbohydrate drink, LL: evening and morning doses of carbohydrate drink

Carbohydrate drink given in the evening and in the morning prior to surgery increases insulin sensitivity (Svanfeldt et al. 2005)

Insulin sensitivity and glucose turnover were measured using hyper-insulinemic, normoglycemic clamps before and after elective surgery in 16 patients undergoing total hip replacement, and 14 patients undergoing elective colorectal surgery. Total hip replacement patients were randomly assigned to preoperative oral carbohydrate administration (CHO-H, n=8) or the same amount of a placebo drink (n=8) before surgery. Insulin sensitivity was measured before and immediately after surgery. Patients undergoing elective colorectal surgery were studied before surgery and 24 h postoperatively (CHO-C (n=7), and fasted (n=7), groups). The fasted group underwent surgery after an overnight fast. In both studies, the CHO groups received 800 ml of an isoosmolar carbohydrate rich beverage the evening before the operation (100 g carbohydrates), as well as another 400 ml (50 g carbohydrates) 2 h before the initiation of anesthesia. Patients given a carbohydrate drink shortly before elective surgery displayed less reduced insulin sensitivity after surgery as compared to patients undergoing surgery after an overnight fast (Nygren et al. 1999).

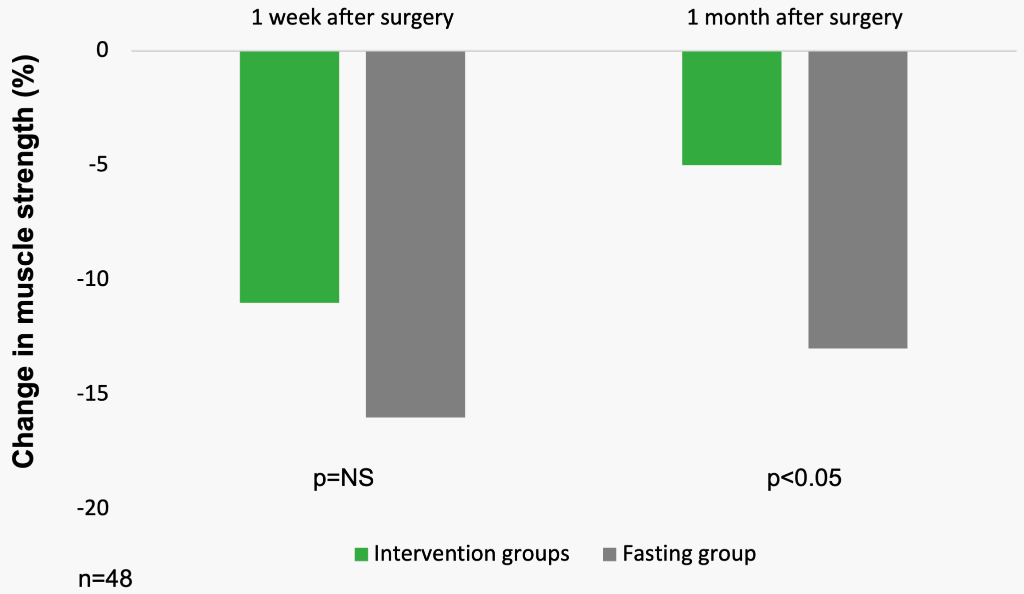


CHO-H: carbohydrate drink before surgery in total hip replacement patients
CHO-C: carbohydrate drink before surgery in elective colorectal surgery patients

Carbohydrate drink given shortly before surgery attenuates insulin sensitivity reduction after surgery (Nygren et al. 1999)

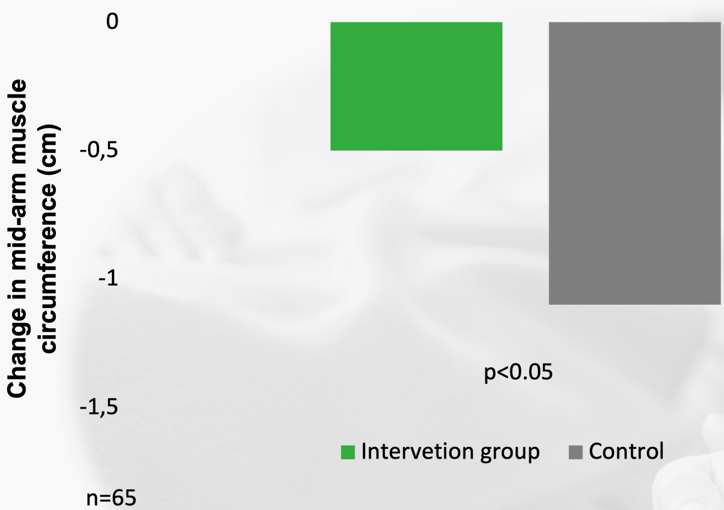
In a double-blind clinical trial, 52 patients undergoing elective open colorectal surgery have been randomised to preoperative carbohydrate loading (n=18), to placebo (n=17) or to fasting (n=17). Median blood glucose and insulin levels were significantly lower for carbohydrate loading than for fasting (p=0.002) and placebo (p=0.001) by the end of surgery. Although median levels of HOMA-IR in all three groups had increased significantly by the end of surgery, they were significantly lower in the carbohydrate loading group than in the other two groups (p<0.001). Subjective well-being measured on a 100-mm visual-analogue scale (VAS) was significantly better in the carbohydrate and placebo groups compared the fasting group, mainly due to the reduction in thirst (p=0.005) and hunger (p=0.041) (Wang et al. 2010).

In a study of patients admitted for elective bowel resections (n=48), patients were randomized into 3 groups to 12.5% carbohydrate-rich drink preoperatively, to 12.5% carbohydrate + 3.5% hydrolyzed sy protein drink, or to fast overnight with water allowed only. The basic postoperative regimen for all groups were immediate oral nutrition and early enforced mobilization. A significant decrease in the glycogen synthase (rate-limiting enzyme of glucose storage) activity (p<0.05) was found in the vastus lateralis muscle in the fasting group, while remained unchanged in the intervention groups. A 10—11% decrease in voluntary strength occurred after the first postoperative week in the two intervention groups as compared to a 16% decrease in the control group. After 1 month, both intervention groups were 5% below the initial level, whereas the control group was still 13% below (p<0.05). After 2 months, the two intervention groups were above the preoperative level, and the control group was still slightly below (Henriksen et al. 2003).



Preoperative carbohydrate drink helps retain quadriceps strength in elective surgery patients (Henriksen et al. 2003)

In a study of patients with elective abdominal surgery, patients were randomised to receive either a 12.6% carbohydrate drink (n=31) or placebo (n=34) preoperatively (800 ml on the evening before surgery and 400 ml on the day of surgery 2–3 hours before the induction of anaesthesia). Postoperatively, no significant difference in the change in BMI between the two groups occurred, but loss of muscle mass (measured by change in mid-arm muscle circumference) from baseline to discharge, was significantly greater in the control group (1.1±0.15 cm *vs* 0.5±0.16 cm, $p<0.05$) (Yuill et al. 2005).



Preoperative carbohydrate drink may attenuate muscle mass depletion after surgery (Yuill et al. 2005)

Glucose and protein kinetics and substrate oxidation (indirect calorimetry) were studied at baseline and during hyperinsulinaemic normoglycaemic clamping before and on the first day after colorectal resection in a randomised clinical trial of 15 patients who received a preoperative carbohydrate beverage with high (125 mg/ml) or low (25 mg/ml) carbohydrate content. After surgery, whole-body protein balance did not change in the high oral carbohydrate group, whiles it was more negative in the low oral carbohydrate group after surgery at baseline (p=0.003) and during insulin stimulation (p=0.005). Insulin-stimulated endogenous glucose release was similar before and after surgery in the high oral carbohydrate group, but was higher after surgery in the low oral carbohydrate group (p=0.013) and higher compared to the high oral carbohydrate group (p=0.044). The authors cocluded that whole-body protein balance and the suppressive effect of insulin on endogenous glucose release are better maintained when patients receive a carbohydrate-rich beverage before surgery (Svanfeldt et al. 2007).

4. Micronutrients in wound healing

4.1. Vitamin C

Vitamin C has important functions in the synthesis of collagen connective tissue protein at the level of hydroxylation of procollagen, in fibroblast proliferation, in capillary formation, and in neutrophil activity. Vitamin C deficiency results in clinical scurvy, which is characterized, among other complications, by poor wound healing (Stechmiller JK. 2010).

Vitamin C supplementation at 100 to 200 mg/d isrecommended for patients who have vitamin C deficiency or wounds, including stage I or II pressure ulcers. For more complex wounds, including stage III or stage IV pressure ulcers or severe trauma, supplementation of 1,000 to 2,000 mg/d orally has been suggested until healing occurs. Vitamin C supplementation has also been shown to enhance healing of wounds and burns (Stechmiller JK. 2010).

4.2. Zinc

Zinc is an essential mineral required for the catalytic activity of approximately 100 enzymes, and playing a role in immune function, DNA synthesis, protein and collagen synthesis, cellular proliferation, and wound healing (Stechmiller JK. 2010).

The recommendation for zinc supplementation to enhance wound healing is up to 40 mg (176 mg zinc sulfate) for 10 days. Zinc sulfate 220 mg twice daily (25-50 mg elemental zinc) has been used as a standard adult oral replacement dose, but no specified duration of therapy is available in the literature (Stechmiller JK. 2010). In a retrospective, controlled study of 16 inpatients with a stage 2, 3, or 4 pressure ulcer, only patients receiving additional arginine (9 g/day), vitamin C (500 mg/day), and zinc (50 ng/day) demonstrated a clinically significant improvement in pressure ulcer healing (9.4±1.2 vs. 2.6±0.6; baseline and week 3, respectively; $p<0.01$) (Desneves et al. 2005).

5. MediDrink OpLoad

5.1. Product description

MediDrink OpLoad is a 1.0 kcal/ml, ready-to-consume food for special medical purposes for the preoperative dietary management of surgery patients.

MediDrink OpLoad must be used under medical supervision.

5.2. Product composition

COMPONENT	per 100 ml	per 100 kcal
Energy (kcal)	100	
Protein (g)	0.0	0.0
energy %	0%	0%
Fat (g)	0.0	0.0
of which saturates (g)	0.0	0.0
monounsaturates (g)	0.0	0.0
polyunsaturates (g)	0.0	0.0
energy %	0%	0%
Carbohydrates (g)	25.0	25.0
energy %	100%	100%
Fibre (g)	0.0	0.0
energy %	0%	0%
Vitamin C (mg)	20.0	20.0
Zinc (mg)	5.0	5.0

5.3. Target groups

MediDrink OpLoad is indicated for the preoperative carbohydrate loading of adult surgery patients and pediatric surgery patients above 3 years of age.

MediDrink OpLoad is lactose-free, and is gluten-free, therefore, can be administered to patients with lactose- or gluten-intolerance.

Medidrink OpLoad should be used with caution in patients with insulin resistance or diabetes and in children aged 3-6 years.

5.4. Recommended dosage

Recommended dosage for adults is 2 packs (400 ml) 12 hours prior to surgery, and an additional 1 pack (200 ml) 2 hours before surgery. MediDrink OpLoad must not be consumed within 2 hours prior to surgery.

5.5. Precautions

MediDrink OpLoad is not suitable for patients with insulin resistance, diabetes mellitus, delayed gastric emptying, hereditary fructose intolerance (fructosemia), and for children below 3 years of age.

5.6. Packaging

MediDrink OpLoad is currently available in lemonade flavour. MediDrink RC comes in liquid format in 200 ml Tetra Pak packaging in a ready-to-drink form, with a foil-wrapped straw on each individual pack.

6. Efficacy, safety, and adherence

6.1. Efficacy

The efficacy of MediDrink OpLoad has been investigated in a randomized, controlled, open-label trial of adult patients scheduled for elective surgery. Of the 50 patients enrolled, 25 patients received 400 ml MediDrink OpLoad in the evening prior to surgery and 200 ml MediDrink OpLoad 2 hours prior to surgery, and 25 patients were required to fast the night and morning prior to surgery (Enyedi et al. 2022).

Patients were recruited at the Department of Surgery, University of Debrecen. Patients were randomized to the interventional carbohydrate drink, or to standard dietary management (fasting prior to surgery) according to their order of appearance at the treating physician. Study visits were performed at the night before surgery, the morning of surgery, and prior to the first meal after surgery. Data of well-being and blood sugar level (only if measured independently of the study) were collected at each visit. The primary endpoint was thirst in the morning of surgery. Secondary endpoints consisted of hunger, thirst, weakness, tiredness, anxiety, and nausea at the night prior to surgery; hunger, weakness, tiredness, anxiety, nausea, and blood sugar level (if measured independently of the study) in the morning prior to surgery; and hunger, thirst, weakness, tiredness, anxiety, nausea, and blood sugar level (if measured independently of the study) prior to the first meal after surgery. Adherence to the clear, carbohydrate-rich drink has also been measured at each timepoint (Enyedi et al. 2022).

Descriptive statistics were used for the presentation of results: mean and standard error in case of continuous variables, and distribution in case of discrete variables. To perform the descriptive statistics-related hypothesis testing, parametric statistical probes, such as independent paired-sample t-test, one-way ANOVA in case of continuous variables, while $\chi 2$ test and Fisher’s exact test in case of discrete variables have been used. Regression analyses were applied when multiple variables were concerned. The type of regression analysis was defined on the basis of the outcome tested (e.g., in case of survival-like data, Cox regression model was used). The applicability criteria were examined during the statistical hypothesis analyses (Enyedi et al. 2022).

There was no significant difference ($p=0.052$) detected between the two groups when assessing thirst during the morning of surgery. There were significant differences between the two populations regarding hunger ($p<0.001$), feelings of agitation ($p=0.012$), feelings of fatigue ($p<0.001$) and overall well-being both before ($p=0.001$) and after surgery ($p<0.001$). No significant difference ($p=0.398$) was detected between the two populations regarding feelings of weakness (Enyedi et al. 2022).

6.2. Safety

Assessment of the patient's gastric contents is the key to avoiding aspiration incidents. Studies have shown that preoperative oral carbohydrate loading can improve the discomfort induced by fasting, but there are different perspectives on their safety (Jin et al. 2023).

In a study of 12 patients scheduled to undergo elective laparoscopic cholecystectomy (n=11) or parathyroid surgery (n=1), consumption of 400 ml 12.0% carbohydrate drink compared to 400 ml water 4 hours prior to surgery led to no difference in gastric emptying despite the increased anxiety experienced by patients before surgery. Initially, water emptied more rapidly than the carbohydrate drink, but after 90 minutes, the stomach was emptied regardless of the solution administered (3.2±1.1% remaining in the stomach in the carbohydrate group versus 2.3±1.2% remaining in the stomach in the water group) (Nygren et al. 1995).

Effect of ingesting 400 ml of a carbohydrate drink at midnight and freely up to 2 hours before anesthesia (n=32) compared to nil per os after midnight before surgery (n=32) has been investigated in a study of 64 patients scheduled for elective laparoscopic benign gynecologic surgery. When measured by ultrasound, gastric antral cross-sectional area in right lateral decubitus position was not different between the nil per os group (6.25±3.79 cm^2) and the carbohydrate group (6.21±2.48 cm^2; $p=0.959$), thus, preoperative carbohydrates ingested up to 2 hours before anesthesia did not delay gastric emptying compared to midnight fasting, as evaluated with gastric ultrasound (Cho et al. 2021).

In a non-randomized, non-inferiority comparative study of 60 patients aged over 65 years scheduled for total knee arthroplasty. patients either fasted from midnight (fasting group) drank 400 ml of a carbohydrate-containing fluid (carbohydrate ingestion group) two hours prior to surgery. The mean (standard deviation) gastric volume measured by ultrasound was not significantly different between the groups (mean difference in gastric volume -1.9 ml, 95% confidence interval [CI]: -17.9 - 14.2) (Shin et al. 2022).

A prospective, randomized, controlled study of 180 cirrhotic patients with gastroesophageal varices scheduled for elective therapeutic endoscopy under intravenous anesthesia found that patients randomised to no carbohydrate supplementation and to carbohydrate supplementation 4 hours prior to endoscopy had no residual gastric volume >1.5 ml/kg, while 6 patients (11%) in the group randomised to carbohydrate supplementation 24 hours before endoscopy had a residual gastric volume of >1.5 ml/kg, hence, were at a risk of regurgitation and aspiration. VAS scores for 6 parameters (thirst, hunger, mouth dryness, nausea, vomiting, and fatigue) in the 2 hours group and 3 parameters (thirst, hunger, and mouth dryness) in the 4 hours group were significantly lower than those in the control group, suggesting a beneficial effect on cirrhotic patients' well-being. The study concluded that avoiding preoperative fasting by consuming carbohydrates 4 hours prior to anesthesia had considerable advantages in improving the well-being of patients with cirrhosis undergoing therapeutic endoscopy, without increasing their risk of regurgitation (Wang et al. 2021).

Paediatric patients younger than 18 yr old undergoing elective surgery were enrolled in a study investigating the gastric volume measured by ultrasound before and after drinking carbohydrate fluids before surgery. Initial ultrasound assessment of gastric volume was performed after fasting for 8 hours. Two hours before surgery, patients were given carbohydrate drinks: 15 ml/kg for patients younger than 3 years old and 10 ml/kg for those more than 3 yr old. Carbohydrate fluids ingested 2 hours before surgery reduced the gastric volume (mean±SD 1.85±0.94 *vs* 2.09±0.97 cm^2, p=0.01) and did not cause serious complications in paediatric patients. Parents were satisfied with the preoperative carbohydrate drink (Song et al. 2016).

In a randomized, controlled trial, 120 children (mean age 11 years, range 2-18 years) scheduled for gastroscopy under general anaesthesia were randomised to either a control group of standard preoperative fasting or to receive a carbohydrate beverage. Compared with fasting, carbohydrate loading was associated with significantly less gastric content (p=0.01), and fewer patients experiencing postoperative nausea (p=0.028), with no significant difference in postoperative vomiting. High preoperative VAS scores (>5) were recorded for 1 child in the carbohydrate group vs 5 children in the fasting group (Tudor-Drobjewski et al. 2018).

The effects of preoperative carbohydrate loading with a 12.5% carbohydrate fluid was investigated in 25 patients (45–73 years) with type 2 diabetes and 10 healthy control subjects (45–72 years. Type 2 diabetic patients showed no signs of delayed gastric emptying, suggesting that a carbohydrate rich drink may be safely administrated 180 minutes before anaesthesia without risk of hyperglycaemia or aspiration pre-operatively (Gustafsson et al. 2008).

No treatment-related death, serious, or other significant adverse events were reported in the MediDrink OpLoad randomized, controlled, open-label, single-centre clinical trial. On the MediDrink OpLoad arm, 1 patient reported nausea, fullness, abdominal pain and feeling unwell (Enyedi et al. 2022).

6.3. Adherence

In the clinical trial, 1 patient refused to consume MediDrink OpLoad in the morning prior to surgery due to nausea, abdominal pain, and feeling full and unwell. The patient later consumed the required dose of MediDrink OpLoad (Enyedi et al. 2022).

7. Guidelines recommendations on preoperative carbohydrate loading

Numerous clinical guidelines recommend preoperative carbohydrate loading.

The guidelines of the European Society of Anaesthesiology endorse a 2-hour fasting interval for clear fluids and a 6-hour interval for solids. They recommend that adults and children should be encouraged to drink clear fluids (including water, pulp-free juice and tea or coffee without milk) up to 2 hours before elective surgery including caesarean section, since drinking carbohydrate-rich fluids before elective surgery improves subjective wellbeing, reduces thirst and hunger and reduces postoperative insulin resistance. Moreover, drinking carbohydrate-rich drinks up to 2 hours before elective surgery is deemed safe for patients including diabetics (Smith et al. 2011).

The European Society of Clinical Nutrition and Metabolism (ESPEN) guidelines for clinical nutrition in surgery (Weimann et al. 2017, Weimann et al. 2021) state that preoperative fasting from midnight is unnecessary in most patients. Patients undergoing surgery, who are considered to have no specific risk of aspiration, shall drink clear fluids until 2 hours before anaesthesia. Solids shall be allowed until 6 hours before anaesthesia (recommendation 1). To reduce perioperative discomfort including anxiety oral preoperative carbohydrate treatment (instead of overnight fasting) the night before and 2 hours before surgery should be administered. To impact postoperative insulin resistance and hospital length of stay, preoperative carbohydrates can be considered in patients undergoing major surgery (recommendation 2).

According to the 2023 American Society of Anesthesiologists Practice Guidelines for Preoperative Fasting (Joshi et al. 2023), fasting duration is often substantially longer than recommended and prolonged fasting has well described adverse consequences. Therefore, to avoid prolonged fasting in children, efforts should be made to allow clear liquids in healthy children as close to 2 hours before procedures as possible. The task force reaffirms the previous recommendations for clear liquids until 2 hours preoperatively. Simple or complex carbohydrate-containing clear liquids appear to reduce hunger compared with noncaloric clear liquids.

The Enhanced Recovery After Surgery (ERAS) guidelines also recommend the preoperative carbohydrate loading 12 hours and 2 hours prior to surgery. Such perioperative carbohydrate loading is recommended in the ERAS guidelines for gastrointestical surgery (Feldheiser et al. 2016), for colorectal surgery (Gustafsson et al. 2019), for liver surgery (Melloul et al. 2016), for pancreatoduodenectomy (Melloul et al. 2020), for gastrectomy (Mortensen et al. 2014), for gynecologic oncology surgery (Nelson et al. 2019), for vulvar and vaginal surgery (Altman et al. 2020), for cytoreductive surgery with or without hyperthermic intraperitoneal chemotherapy (Hübner et al. 2020), and by the American Society for Enhanced Recovery and Perioperative Quality Initiative Joint Consensus Statement on Nutrition Screening and Therapy (Wischmeyer et al. 2018).

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8. Summary

Total preoperative starvation has not been shown to reduce the risk of perioperative aspiration and related diseases.

Surgical stress enhances postoperative insulin resistance, immunosuppression, and patient discomfort. Recommendations from the European Society of Anaesthesiology and Intensive Care (ESAIC), the European Society for Clinical Nutrition and Metabolism (ESPEN), the American Society of Anaesthesiologists, the American Society for Enhanced Recovery and Perioperative Quality, and the Enhanced Recovery After Surgery (ERAS) guidelines all recommend the preoperative use of clear, carbohydrate-rich fluid as it reduces perioperative discomfort, postoperative insulin resistance, the risk of postoperative complications, length of hospital stay, postoperative muscle loss, and consequential hospital costs.

Developed in accordance with ESAIC, ESPEN and ERAS guidelines, MediDrink OpLoad is a food for special medical purposes for the preoperative dietary management of patients undergoing major surgery.

9. References

Abunnaja S. Enteral and parenteral nutrition in the perioperative period: state of the art. *Nutrients* 2013;5:608-23.

Altman AD. et al. Guidelines for vulvar and vaginal surgery: Enhanced Recovery After Surgery Society recommendations. *Am J Obstet Gynecol* 2020;223:475-85.

Beattie AH. et al. A randomised controlled trial evaluating the use of enteral nutritional supplements postoperatively in malnourished surgical patients. *Gut* 2000;46:813-8.

Bozzetti F. Nutritional support in oncology patients: Where we are and where we are going. *Clin Nutr* 2011;30:714-7.

Brandi LS. et al. Insulin resistance after surgery: normalization by insulin treatment. *Clin Sci* 1990;79:443-50.

Carli F. Physiologic considerations of Enhanced Recovery After Surgery (ERAS) programs: implications of the stress response. *Can J Anesth* 2015;62:110-9.

Cho E-A. et al. Gastric ultrasound assessing gastric emptying of preoperative carbohydrate drinks: A randomized controlled noninferiority study. *Anesth Analg* 2021;133:690-7.

Desneves KJ. et al. Treatment with supplementary arginine, vitamin C and zinc in patients with pressure ulcers: a randomised controlled trial. *Clin Nutr* 2005;24:979-87.

Enyedi A. et al. Effect of carbohydrate loading on the well-being of patients undergoing elective surgery. *Int J Innov Res Med Sci (IJIRMS)* 2022;7:504-9.

Feldheiser A. et al. Enhanced Recovery After Surgery (ERAS) for gastrointestinal surgery, part 2: consensus statement for anaesthesia practice. *Acta Anaesthesiol Scand* 2016;60:289-334.

Fujita T. et al. Early enteral nutrition reduces the rate of life-threatening complications after thoracic esophagectomy in patients with esophageal cancer. *Eur Surg Res* 2012;48:79-84.

Gustafsson UO. et al. Guidelines for Perioperative Care in Elective Colorectal Surgery: Enhanced Recovery After Surgery (ERAS) Society Recommendations: 2018. *World J Surg* 2019;43:659-95.

Gustafsson UO. et al. Pre-operative carbohydrate loading may be used in type 2 diabetes patients. *Acta Anaesthesiol Scand* 2008;52:946-51.

Henriksen MG. et al. Effects of preoperative oral carbohydrates and peptides on postoperative endocrine response, mobilization, nutrition and muscle function in abdominal surgery. *Acta Anaesthesiol Scand* 2003;47:191-9.

Hübner M. et al. Guidelines for perioperative care in cytoreductive surgery (CRS) with or without hyperthermic IntraPEritoneal chemotherapy (HIPEC): Enhanced Recovery After Surgery (ERAS®) Society Recommendations - Part I: Preoperative and intraoperative management. *Eur J Surg Oncol* 2020;46:2292-310.

Jin Y. et al. A convenient machine learning model to predict full stomach and evaluate the safety and comfort improvements of preoperative oral carbohydrate in patients undergoing elective painless gastrointestinal endoscopy. *Ann Med* 2023;55:2292778.

Joshi GP. et al. 2023 American Society of Anesthesiologists Practice Guidelines for Preoperative Fasting: Carbohydrate-containing clear liquids with or without protein, chewing gum, and pediatric fasting duration - a modular update of the 2017 American Society of Anesthesiologists Practice Guidelines for Preoperative Fasting. Anesthesiology 2023;138:132-51.

Kiran RP. et al. The clinical significance of an elevated postoperative glucose value in nondiabetic patients after colorectal surgery: evidence for the need for tight glucose control? *Ann Surg* 2013;258:599-604.

Ljungqvist O. & Soreide E. Preoperative fasting. *Br J Surg* 2003;90:440-6.

Löser C. Malnutrition in hospital: the clinical and economical implications. *Dtsch Arztebl Int* 2010;107:911-7.

Martyn CN. et al. Effect of nutritional status on use of health care resources by patients with chronic disease living in the community. *Clin Nutr* 1998;17:119-23.

Melloul E. et al. Guidelines for perioperative care for liver surgery: Enhanced Recovery After Surgery (ERAS) Society recommendation. *World J Surg* 2016;40:2425-40.

Melloul E. et al. Guidelines for perioperative care for pancreatoduodenectomy: Enhanced Recovery After Surgery (ERAS) recommendations. *World J Surg* 2020;44:2056-84.

Mortensen K. et al. Consensus guidelines for enhanced recovery after gastrectomy. Enhanced Recovery After Surgery (ERAS®) Society recommendations. *Br J Surg* 2014;101:1209-29.

Nelson G. et al. Guidelines for perioperative care in gynecologic/oncology: Enhanced Recovery After Surgery (ERAS) Society recommendations - 2019 update. *Int J Gynecol Cancer* 2019;29:651-68.

Nygren J. et al. Preoperative gastric emptying: effects of anxiety and oral carbohydrate administration. *Ann Surg* 1995;222:728-34.

Nygren J. et al. Preoperative oral carbohydrates and postoperative insulin resistance. *Clin Nutr* 1999;18:117-20.

Pillinger NL. et al. Nutritional prehabilitation: physiological basis and clinical evidence. *Anaesth Intensive Care* 2018;46:453-62.

Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: An updated report by the American Society of Anesthesiologists Task Force on preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration. *Anesthesiology* 2017;126:376-93.

Sato H. et al. The association of preoperative glycemic control, intraoperative insulin sensitivity, and outcomes after cardiac surgery. *J Clin Endocrinol Metab* 2010;95:4338-44.

Shin H-J. et al. Ultrasound assessment of gastric volume in older adults after drinking carbohydrate-containing fluids: a prospective, nonrandomized, and noninferiority comparative study. *Can J Anaesth* 2022;69:1160-6.

Smith I. et al. Perioperative fasting in adults and children: guidelines from the European Society of Anaesthesiology. *Eur J Anaesthesiol* 2011;28:556-69.

Song I-K. et al. Ultrasound assessment of gastric volume in children after drinking carbohydrate-containing fluids. *Br J Anaesth* 2016;116:513-7.

Stechmiller JK. Understanding the role of nutrition and wound healing. *Nutr Clin Pract* 2010;25:61-8.

Studley HO. Percentage of weight loss: A basic indicator of surgical risk in patients with chronic peptic ulcer. *JAMA* 1936;106:458-460.

Svanfeldt M. et al. Effect of ‘‘preoperative’’ oral carbohydrate treatment on insulin action - a randomised cross-over unblinded study in healthy subjects. *Clin Nutr* 2005;24:815-21.

Svanfeldt M. et al. Randomized clinical trial of the effect of preoperative oral carbohydrate treatment on postoperative whole-body protein and glucose kinetics. *Br J Surg* 2007;94:1342-50.

Thorell A et al. Insulin resistance: A marker of surgical stress. *Curr Opin Clin Nutr Metab Care* 1999;2:69-78.

Thorell A. et al. Insulin resistance after abdominal surgery. *Br J Surg* 1994;81:59-63.

Tudor-Drobjewski BA. et al. Randomised controlled trial comparing preoperative carbohydrate loading with standard fasting in paediatric anaesthesia. *Br J Anaesth* 2018;1231:656-61.

van der Hulst RR. et al. Gut permeability, intestinal morphology, and nutritional depletion. *Nutrition* 1998;14:1-6.

Wang Y. et al. Effects of preoperative oral carbohydrate on cirrhotic patients under endoscopic therapy with anesthesia: A randomized controlled trial. *Biomed Res Int* 2021;2021:1405271.

Wang ZG. et al. Randomized clinical trial to compare the effects of preoperative oral carbohydrate versus placebo on insulin resistance after colorectal surgery. *Br J Surg* 2010;97:317-27.

Ward N. Nutrition support to patients undergoing gastrointestinal surgery. *Nutr J* 2003;2:18.

Weimann A et al. Clinical nutrition in surgery. *Clin Nutr* 2017;36:623-50.

Weimann A et al. ESPEN practical guideline: Clinical nutrition in surgery. *Clin Nutr* 2021;40:4745-61.

Wischmeyer PE. et al. American Society for Enhanced Recovery and Perioperative Quality Initiative joint consensus statement on nutrition screening and therapy within a surgical enhanced recovery pathway. *Anesth Analg* 2018;126:1883-95.

Yuill KA. et al. The administration of an oral carbohydratecontaining fluid prior to major elective upper-gastrointestinal surgery preserves skeletal muscle mass postoperatively - randomised clinical trial. *Clin Nutr* 2005;24:32-7.