International Journal of Innovative Research in Medical Science (IJIRMS)
Volume 07, Issue 10, October 2022,
https://doi.org/10.23958/ijirms/vol07-i10/1501

Original article

Effect of Carbohydrate Loading on the Well-Being of Patients Undergoing Elective Surgery

Attila Enyedi MD PhD [1], István Takács MD PhD [1], Ferenc Győry MD PhD [1], Csongor Váradi MD [1], Gergely Kóder MD [1], Gábor Mudriczki MD [1], Tamás Végh MD PhD [2], Katalin Szamos MD [2], Edit Nádasi MD PhD [3], Bálint Szőllőssy-Csoma MD [3], Gellért György Cseh MD [3]

[1]Department of Thoracic Surgery, University of Debrecen, H-4032 Debrecen, Móricz Zsigmond Krt. 22, Hungary
[2]University of Debrecen, Department of Anesthesiology and Intensive Care, H-4032 Debrecen, Móricz Zsigmond Krt. 22, Hungary
[3]Medifood Hungary Innovation Kft, H-2045 Törökbálint, Tópark u. 3, Hungary

*Corresponding author: Bálint Szőllőssy-Csoma; *balint.szollossycsoma@medifoodinternational.com*

Received 02 September 2022; Accepted 28 September 2022; Published 01 October 2022

Abstract

Elective surgery is one of the main treatment modalities in modern medicine. Approximately 5% of the population undergo elective surgery each year. Traditional preoperative management calls for patients being fasted from midnight of the evening prior to surgery in order to decrease the risk of aspiration. For many years, this practice has been enforced, but over the past decades the scientific basis for fasting has been challenged. Perioperative fasting and surgical trauma contribute to increased postoperative morbidity and length of hospital stay.

Preoperative oral carbohydrate loading recommended by the European Society of Anaesthesiology (ESA), Enhanced Recovery After Surgery (ERAS) and European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines has been shown to reduce the development of insulin resistance by approximately 50% on the day after surgery. Moreover, it significantly reduces perioperative discomfort such as hunger, thirst, tiredness, weakness, and inability to concentrate.

This clinical trial aimed to determine the efficacy and safety of a food for special medical purposes (FSMP) versus standard dietary management (fasting) in patients scheduled for elective surgery.

The study was designed as a randomized, controlled, open-label, single centre clinical trial with an intervention (n=25) and a control group (n=25). Patients ages 18 years and older who were scheduled for elective surgery and required to fast the night and morning prior to surgery were enrolled into the study.

The primary endpoint was thirst assessed during the morning of surgery. Secondary endpoints were assessed hunger, assessed feeling of agitation, feeling of fatigue, assessed feeling of weakness, and overall well-being.

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.

In our view, the use of the formula improves the well-being of patients. Our hypothesis is that the consumption of food for special medical purposes in the form of a transparent liquid containing only carbohydrates, instead of fasting before surgery, improves the well-being of patients. Our results suggest that MediDrink OpLoad can be an effective alternative to the standard dietary care of patients undergoing major surgery, and it can positively affect patient well-being.

Keywords: ***preoperative, carbohydrate loading, preoperative fasting, surgery, well-being, OpLoad***

Introduction

Elective surgery is one of the main treatments in modern medicine. Approximately 5% of the population undergo elective surgery each year (Ljungqvist 2000). Traditional preoperative management calls for patients being fasted from midnight of the evening prior to surgery. The rationale for preoperative fasting is to mitigate the risk of pulmonary aspiration and aspiration pneumonia (Pillinger 2018). For many years, this practice has empirically been enforced, but over the past decades the scientific basis for fasting has been challenged (Pillinger 2018).

During prolonged fasting, glycogen stores get virtually depleted (approximately in 18-24 hours), which means that there will be no readily available energy substrate for the obligate glucose tissues (e.g. central nervous system, bone marrow, red blood cells, peripheral nerves). Therefore, the body increasingly relies on gluconeogenesis, during which skeletal muscle is broken down to generate a pool of amino acids, thus adding to the protein loss due to surgical stress (Pillinger 2018).

Perioperative fasting and surgical trauma both contribute to perioperative insulin resistance. Insulin resistance correlates to the magnitude of surgical trauma (Thorell 1993), and occurs even following minor surgery (Thorell 1993, Faria 2009). Besides surgical magnitude, pain and bed rest also contribute to perioperative insulin resistance (Carli 2015). Hyperglycemia due to insulin resistance increases morbidity after surgery (van den Berghe 2003,

Krinsley 2004), while insulin resistance is an independent factor affecting length of postoperative hospital stay (Thorell 1999).

Preoperative oral carbohydrate loading recommended by the European Society of Anaesthesiology (ESA), Enhanced Recovery After Surgery (ERAS) and European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines (Smith 2011, Gustaffson 2012, Feldheiser 2016, Dort 2017, Weimann 2017) has been shown to reduce the development of insulin resistance by approximately 50% on the day after surgery (Nygren 1998). Moreover, it significantly reduces perioperative discomfort such as hunger, thirst, tiredness, weakness, and inability to concentrate (Hausel 2001). Clear, carbohydrate-rich drinks administered up to 2 hours prior to elective surgery are also safe (Smith 2011), since gastric emptying of a 50 g oral carbohydrate load has been complete within 90 minutes after the intake (Nygren 2001).

Since the volume to be consumed likely affects patient compliance, we have developed a low-volume-high-carbohydrate clear drink for preoperative carbohydrate load in surgery patients. The clinical trial aimed to determine the efficacy and safety of this food for special medical purposes (FSMP) versus standard dietary management (fasting) in patients scheduled for elective surgery.

Methods

The study has been designed as a randomized, controlled, open-label, single centre clinical trial with an intervention (n=25) and a control group (n=25). Patients at or above the age of 18 years scheduled for elective surgery and required to fast the night and morning prior to surgery were enrolled into the study. Further inclusion criteria were the ability of enteral nutrition, life expectancy at least 6 months according to the treating physician, and a written informed consent. Exclusion criteria included pregnancy or breastfeeding, diabetes or decreased glucose tolerance, medication influencing glucose tolerance, >10% weight loss in the past 6 months, distant metastasis proved by computer tomography, liver failure (Child-Pugh state ≥B), proven gastro-esophageal reflux, conditions slowing gastric emptying (e.g. ileus), co-morbidity with special dietary requirements (e.g. renal failure, diabetes mellitus), oral or parenteral steroid (expect local and inhalation steroids) within 1 month prior to surgery, known intolerance or allergy to any component of the interventional FSMP, uncontrolled nausea and/or vomiting, chronic diarrhea, participation in any clinical trial. The study has been approved by the National Public Health and Medical Officer Service. Written informed consent has been obtained from all participants.

Patients were recruited at the Department of Surgery, University of Debrecen. Patients were randomized to the interventional FSMP, or to standard dietary management (fasting prior to surgery) according to their order of appearance at the treating physician. Patients had to consume 2 packs (200 kcal, 50 g carbohydrates in 400 ml) of the interventional FSMP at the night prior to surgery, and 1 pack (100 kcal, 25 g carbohydrates in 200 ml) of the interventional FSMP 2 hours prior to surgery. 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 FSMP has also been measured at each timepoint (**Figure 1**).

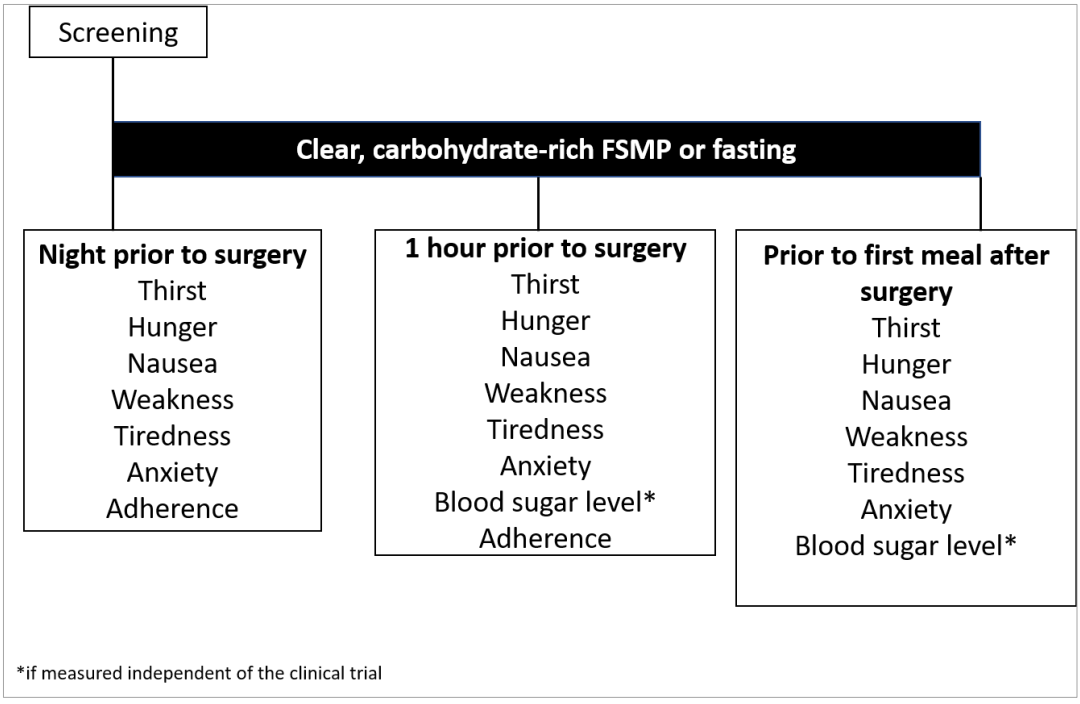

Figure 1. Flowchart of study procedures.

Sample size calculation was based on the magnitude of type I and II errors, the expected change in the primary outcome, and the experiences in previous clinical studies. The conventional 5% type I error and the 20% type II error have been used in our clinical study ensuring a statistical power of 80%. A similar clinical trial [Wang 2010] found that the expected change in thirst when patients are fasted is 34 points, while the expected change in thirst in patients consuming the interventional FSMP is 20 points. Considering the probability of dropouts, the number of patients in both study groups were determined as 25.

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 are 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.

Our hypothesis is that instead of preoperative starvation, the consumption of carbohydrate-only food in a transparent liquid form for special medical purposes improves patients' well-being.

Results

Baseline patient characteristics and demographic analysis

Gender: In the case of the two patient groups, it can be said that the number of genders is almost the same, in the MediDrink OpLoad faculty the majority of the men and in the standard dietary care faculty the majority of the women.

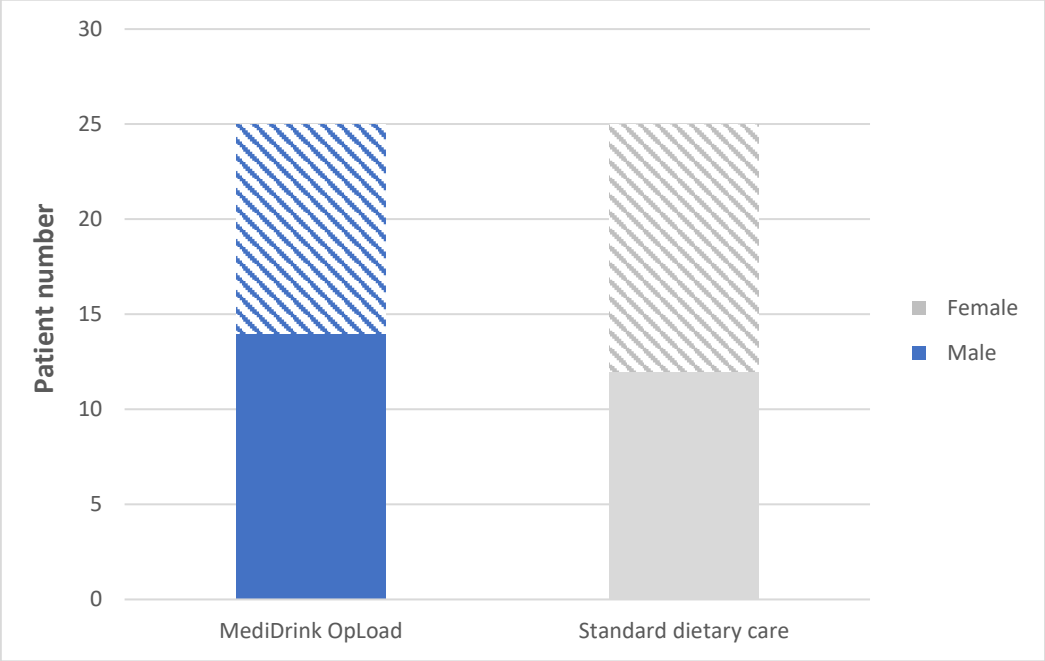

Fig 2. Number of patients by gender and dietary regimen

Age: Regarding the age of the subjects included in the study, it can be said that the subjects in the standard dietary care group were selected from a wider range (23-86 years vs. 29-76 years), however, the average age and the median value were almost the same in each group (63 vs. 64 years).

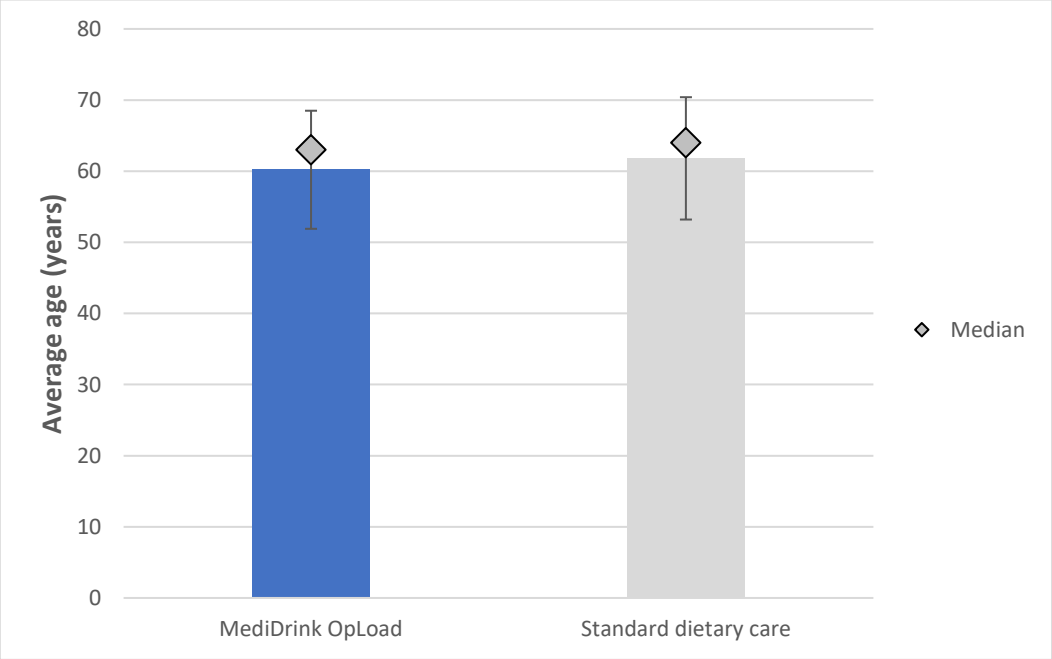

Fig 3. Average age of patients on the two arms

Comorbidities

In accordance with the study protocol, investigators were required to record the comorbidities of the patients involved that result in the patient receiving regular therapy. All the indicated comorbidities persisted during the study period. The number of comorbidities is shown in Table 1 and the number of diseases by their main groups in Table 2.

Table 1: Number of comorbidities by dietary regimen

Comorbidities	MediDrink OpLoad n = 25 (100%)	Standard dietary care n = 25 (100%)	Statistical method	p value
No	1 (4,0%)	3 (12,0%)	Fisher test	0,609
Yes*	24 (96,0%)	22 (88,0%)		
Number of comorbidities			Fisher test	0,839
1	9 (37,5%)	10 (45,5%)		
1-2	16 (66,7%)	15 (68,2%)		
1-3	22 (91,7%)	19 (86,4%)		
>3	2 (8,3%)	3 (13,6%)		

Table 2: List of comorbidities by dietary regimen

Comorbidities	MediDrink OpLoad n = 24 (100%)	Standard dietary care n = 22 (100%)	Statistical method
Musculoskeletal system	2 (8,3%)	1 (4,5%)	Fisher-test
Malignancy	0 (0,0%)	2 (9,1%)	
Gastrointestinal	0 (0,0%)	1 (4,5%)	
Endocrine, metabolic disorders	10 (41,7%)	4 (18,2%)	
Infectious and parasite	1 (4,2%)	0 (0,0%)	
Cardiovascular system	18 (75,0%)	16 (72,7%)	
Respiratory System	3 (12,5%)	9 (40,9%)	
Mental and cognitive disorders	1 (4,2%)	3 (13,6%)	
Eye disorders	1 (4,2%)	1 (4,2%)	
Haematology	1 (4,2%)	0 (0,0%)	

The baseline patient characteristics of the patients treated in the two arms did not differ significantly.

Efficacy Analysis - Endpoint Results

Primary endpoints

Thirst assessed during the morning of surgery

On the morning of surgery, 9 individuals reported feeling some degree of thirst, two in the MediDrink OpLoad faculty and 7 in the standard diet care faculty. No significant difference (p = 0.052) was detected using the Mann-Whitney U-test. It should be noted, however, that the standard deviation value on the MediDrink OpLoad arm is much higher on the NPO arm. One patient experienced nausea, abdominal pain, and a feeling of fullness, which increased the values of the examined endpoints. Without taking this patient data into account, there was a significant difference (p = 0.017) between the two populations.

Secondary endpoints

Assessed hunger

In terms of feeling hungry, no one felt hungry in the MediDrink OpLoad faculty the night before surgery, whereas only two of those on standard dietary care indicated this. Using the Mann-Whitney U test, a significant difference (p <0.001) was detected. On the morning of surgery, one person felt some degree of hunger in the MediDrink OpLoad arm, in contrast to the standard diet care arm, where there are 24 individuals. Using the Mann-Whitney U test, a significant difference can be detected. 10 patients reported some degree of hunger in the MediDrink OpLoad faculty, all of whom received standard dietary care. There was a significant difference (p <0.001) between the two populations.

Assessed feeling of agitation

Fifteen individuals did not feel excited in the evening before surgery, 12 of them in the MediDrink OpLoad faculty. The Mann-Whitney U test shows a significant difference (p = 0.005). Feeling agitated during the morning of surgery had the highest median and mean value in both faculties. Only 6 individuals (MediDrink OpLoad faculty: 5 people, Standard dietary care: 1 person) indicated that they had no sense of excitement. There was a significant difference (p = 0.012) between the two populations using the Mann-Whitney U test. In both arms, 2-2 people reported some degree of agitation after surgery. There was no significant difference (p = 0.492) between the two populations.

Feeling of fatigue

In the evening before surgery, 13 patients rated it as not feeling tired in the MediDrink OpLoad arm, 14 in the other arm. No significant difference (p = 0.352) was found using the Mann-Whitney U test. Thirteen individuals did not feel tired on the morning of surgery, 10 individuals in the MediDrink OpLoad arm, and 3 in the standard diet care arm. Based on the obtained values, a significant difference (p = 0.005) can be detected between the two populations. 9 people did not feel tired in the MediDrink Opload faculty, and 1 person in the standard diet care faculty after surgery. There was a significant difference (p <0.001) using the Mann-Whitney U test.

Assessed feeling of weakness

On the preoperative evening, 14 patients indicated that they did not feel weak in the MediDrink OpLoad arm, and 16 patients indicated that they received standard dietary care. No significant difference (p = 0.398) was detected between the two populations. Prior to surgery, there were no weaknesses in 13 patients in the MediDrink arm and 15 patients in the standard diet. No significant difference was detected. 16 people in the MediDrink OpLoad faculty reported some degree of weakness, 23 of those in the standard dietary faculty after the surgery. There is a significant difference between the populations of the two arms.

3-3 patients indicated on the visual analog scale that they felt some degree of thirst in the evening before surgery, no significant difference (p = 0.486) was found. After surgery, only one person was not thirsty in the standard dietary care arm, 9 people in the MediDrink OpLoad arm indicated that they did not feel thirsty. There was a significant difference (p <0.001) between the two populations.

Assessing overall well-being

On the morning of surgery, the mean and median scores are lower in the MediDrink faculty than in those receiving standard dietary care. There is a significant difference between the populations of the two arms. Prior to surgery, the mean and median scores are lower in the MediDrink faculty than in those receiving standard dietary care. There was a significant difference (p = 0.001) between the two populations. Following surgery, the mean and median scores are lower in the MediDrink faculty than in those receiving standard

dietary care. There was a significant difference (p <0.001) between the two populations.

Adherence

One patient was recorded on the MediDrink Opload arm on the morning of the day of surgery, and the patient later consumed his drink. The reason for this was that she felt nauseous, full, abdominal, and was unwell.

Safety analysis

On the visit records, the doctor was required to record any side effects that occurred during the study.

No treatment-related death, serious, or other significant adverse events were reported during the study. In one patient, it was recorded in the MediDrink Opload faculty that the patient felt nausea, fullness, and abdominal pain and was unwell.

Discussion

The aim of the research was to investigate the efficacy and safety of MediDrink OpLoad food for special medical purposes in the dietary care of patients undergoing major surgery in comparison with the standard dietary care (nil per os, NPO) used in surgical care.

Our research is justified by the increasing number of data showing that it is not possible to demonstrate a reduction in the risk of perioperative aspiration and related diseases in connection with established practice, i.e. complete starvation ordered from midnight the day before surgery. Preoperative starvation of a patient is downright detrimental because surgical stress enhances postoperative insulin resistance, immunosuppression, and the patient's sense of discomfort. Another common surgical preparation procedure is to allow the patient to consume only clear fluids (e.g., water, tea) before surgery and in the early postoperative period. As a result, starvation depletes glycogen stores within a few hours and begins gluconeogenesis, during which the body uses the raw materials and energy obtained from the breakdown of muscles and visceral proteins for carbohydrate synthesis. For this reason, the patient is given a carbohydrate-rich fluid the evening before the planned operation and for 2 hours before the operation, which demonstrably reduces the harmful effects of preoperative starvation. The clear carbohydrate-only clear fluid given preoperatively increases insulin sensitivity, improves insulin resistance, and patient well-being. The carbohydrate-containing clear fluid given before surgery also preserves the predominance of protein build-up in the body for the postoperative period.

MediDrink OpLoad is recommended in the following cases:

- Patients scheduled for elective major surgery, regardless of diagnosis or type of surgery, in case food intake prior to surgery is prohibited;
- The patient can no longer eat or drink after midnight before surgery, he can take the morning medicine with a sip of water if necessary;
- Adult patient (≥18 years);
- Able to consume enteral nutrition;
- Life expectancy of at least 6 months (at the discretion of the doctor).

In our view, the use of the formula improves the well-being of patients. Our hypothesis is that the consumption of food for special medical purposes in the form of a transparent liquid containing only carbohydrates, instead of fasting before surgery, improves the well-being of patients.

As a result of the final analysis, we came to the conclusion that the well-being of patients can be significantly improved by consuming the formula.

There was no significant difference in the baseline characteristics of the patients in the two arms. For the thirst sensation defined as the primary endpoint, 9 individuals on the morning of surgery indicated that they were experiencing some degree of thirst: two in the MediDrink OpLoad faculty and seven in the standard diet care faculty.

For each of the secondary endpoints, the median scores on the visual analog scale were either the same in the two arms or higher in the standard dietary care arm. A higher value indicates a worse value.

In the evening before surgery, there was a significant difference in hunger and agitation at the 5% significance level (p <0.001). Taking all the variables into account and treating them together, it can be said that there is a significant difference in well-being (p = 0.001).

On the morning of the operation, there was a significant difference (p <0.001) in the case of three indicators: the feeling of hunger, the feeling of excitement and the feeling of tiredness at the 5% significance level. We can also see a significant difference (p <0.001) in the assessment of well-being during these visit data.

No one reported nausea after surgery. There was a significant difference (p <0.001) in weakness, fatigue, hunger, and thirst at a 5% significance level.

Safety Results: No death, serious, or other significant adverse events occurred during therapy.

Our results suggest that MediDrink OpLoad can be an effective alternative to the standard dietary care of patients undergoing major surgery, and it can positively affect patient well-being.

Ethics approval and consent to participate

The ethics approval of the study was issued by the Hungarian Medical Research Council's Scientific and Research Ethics Committee (ETT-TUKEB); case file number: IV/478-2/2020/EKU.

List of abbreviations

ESA: European Society of Anaesthesiology
ERAS: Enhanced Recovery After Surgery
ESPEN: European Society for Clinical Nutrition and Metabolism
FSMP: Food for special medical purposes
NPO: nil per os/nothing by mouth

Data Availability

The data underlying the findings of this study are available upon request. The following e-mail address can be used for requests: balint.szollossycsoma@medifoodinternational.com.

Conflicts of Interest

Edit Nádasi, Bálint Szőllőssy-Csoma, and Gellért György Cseh are affiliated with Medifood Hungary Innovation Kft., the manufacturer of MediDrink OpLoad, the product used for preoperative carbohydrate loading.

All other authors (Attila Enyedi, István Takács, Ferenc Győry, Csongor Váradi, Gergely Kóder, Gábor Mudriczki, Tamás Végh, Katalin Szamos) declare that there is no conflict of interest regarding the publication of this paper.

Authors' contributions

Attila Enyedi performed the patient selection, coordinated the study, helped in data collection, and analyzed the data.
István Takács, Ferenc Győry, Csongor Váradi, Gergely Kóder and Gábor Mudriczki contributed to data collection.

Tamás Végh and Katalin Szamos performed anesthesia, performed the preoperative evaluation of patients and intraoperative monitoring of patients.
Edit Nádasi helped write the original protocol of the study, helped organize the study and wrote the original outlines of the article.
Bálint Szőllőssy-Csoma proofread the article and wrote the abstract.
Gellért György Cseh wrote the original protocol of the study, helped organize the study, helped write the article and proofread the article.

Acknowledgements

We express our gratitude to Bela E Toth (Medix Ltd) for his excellent medical writing support and services during the composition of the manuscript.

Funding

The clinical trial has been supported by the grant of the National Office for Research, Development, and Innovation 2018-1.1.1-MKI.

References

[1] Ljungqvist O, Nygren J, Thorell A. Insulin reisitance and elective surgery. Surgery 2000;128:757-60.
[2] Pillinger NL, Robson JL, Kam PCA. Nutritional prehabilitation: physiological basis and clinical evidence. Anaesth Intensive Care 2018;46:5.
[3] Thorell A, Efendic S, Gutniak M, et al. Development of postoperative insulin resistance is associated with the magnitude of operation. Eur J Surg 1993;159:593-9.
[4] Faria MSM, de Aguilar-Nascimento JE, Pimenta OS, et al. Preoperative fasting of 2 hours minimizes insulin resistance and organic response to trauma after video-cholecystectomy: a randomized, controlled clinical trial. World J Surg 2009;33:1158-64.
[5] van den Berghe G, Wouters PJ, Bouillon R, et al. Outcome benefit of intensice insulin therapy in the critically ill: insulin dose versus glycemic control. Crit Care Med 2003;31:359-66.
[6] Krinsley JS. Effect of an intensive glucose management protocol ont he mortality of critically ill adult patients. Mayo Clin Proc 2004;79:992-1000.
[7] Thorell A, Nygren J, Ljungqvist O. Insulin resistance: a marker of surgical stress. Curr Opin Clin Nutr Metab care 1999;2:69-78.
[8] Carli F. Physiologic considerations of Enhanced Surgery After Recovery (ERAS) programs: implications of the stress response. Can j Anaesth 2015;62:110-9.
[9] Nygren J, Soop M, Thorell A, et al. Preoperative oral carbohydrate administration reduces postoperative insulin resistance. Clin Nutr 1998;17:65-71.
[10] Hausel J, Nygren J, lagerkranser M, et al. A carbohydrate-rich drink reduces preoperative discomfort in elective surgery patients. Anesth Analg 2001;93:1344-50.
[11] Smith I, Kranke P, Murat I, et al. Perioperative fasting in adults and children: guidelines from the European Society of Anaethesiology. Eur J Anaesthesiol 2011;28:556-69.
[12] Gustaffson UO, Scott MJ, Schwenk W, et al. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS) Society recommendations. Clin Nutr 2012;31:783-800.
[13] Feldheiser A, Aziz O, Baldini G, et al. Enhanced Recovery After Surgery (ERAS) for gastrointestinal surgery, part 2: consensus statement for anaesthesia practice. Acta Anaesth Scand 2016;60:289-334.
[14] Dort JC, Farwell DG, Findlay M, et al. Optimal Perioperative Care in Major Head and Neck Cancer Surgery With Free Flap Reconstruction: A Consensus Review and Recommendations From the Enhanced Recovery After Surgery Society. JAMA Otolaryngol Head Neck Surg 2017;143:292-303.
[15] Weimann A, Braga M, Carli F, et al. Clinical nutrition in surgery. Clin Nutr 2017;36:623-50.
[16] Nygren J, Thorell A, Ljungqvist O. Preoperative oral carbohydrate nutrition: an update. Curr Opin Clin Nutr Metab care 2001;4:255-9.
[17] Wang ZG, Wang Q, Wang WJ 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.