The Effect of Preoperative Oral Carbohydrate Administration on Insulin Resistance and Comfort Level in Patients Undergoing Surgery

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Purpose: *The aim of this study was to evaluate the effect of preoperative oral carbohydrate solution (OCS) administration on postoperative insulin resistance and patient comfort in elective laparoscopic cholecystectomy.*
Design: *Randomized controlled clinical study.*
Methods: *The experimental group received OCS. The control group did not eat or drink before surgery. Glucose and insulin level were measured at baseline, 2 hours before surgery, and at the first and third hour after surgery. Insulin resistance was assessed by the homeostasis model assessment of insulin resistance (HOMA-IR). The visual analogue scale (VAS) and general comfort scale (GCS) were used to assess postoperative comfort level.*
Findings: *A significant increase in the glucose level was observed in both groups (P < 0.05). A change in glucose level was significantly higher in the control group (P = .014). HOMA-IR values did not change significantly in the OCS group (P = .160). In the OCS group VAS scores were significantly lower (P < .0001). The OCS group had significantly higher relief (P = .014), ease (P = .001), and transcendence (P < .0001) scores.*
Conclusions: *OCS decreases insulin resistance and increases comfort.*

Keywords: *insulin resistance, nursing, oral carbohydrate solution, comfort, surgery.*

SURGICAL INTERVENTION CAUSES A STRESS response in the body. It leads to the release of catecholamines, cortisol, glucagon, and growth hormone–induced insulin resistance by starting the release of stress hormones and cytokines.[1,2] Insulin resistance increases the risk of postoperative complications.[3] One of the factors that induces insulin resistance is perioperative fasting. The aim of the modern perioperative approach is to shorten the duration of patient fasting before and after the surgery. According to "The Enhanced Recovery After Surgery protocol," oral carbohydrate solution (OCS) is recommended for shortening the fasting duration of patients and the reduction of insulin resistance in the preoperative period.[4,5] The International Anesthesia

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Conflict of interest: None to report.

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Association indicates that the administration of OCS is safe and does not increase the general anesthesia–related risk of complications.[6,7] It has been reported that even a single dose of carbohydrate reduces insulin resistance postoperatively; decreases glyconeogenesis, glycogenolysis, and lipolysis; minimizes muscle protein catabolism; and allows glucose accumulation in the liver to be stored as glycogen.[8] On the other hand, some researchers point out that it has a positive role on intestinal peristaltism.[9-11] According to the guide published by the American Society of Anesthesiologists (ASA), patients can be given solid foods up to 6 hours before surgery, and clear liquids up to 2 hours before surgery.[12,13] However, carbohydrate-containing liquids are recommended instead of clear liquids as they do not provide adequate metabolic support.[2]

The aim of preoperative administration of carbohydrate solution before surgical intervention is to increase glycogen storage in the body and reduce possible tissue damage and insulin resistance.[14,15] Administration of these liquids during the perioperative period has been reported to increase patient comfort, reduce the patient's anxiety level, and shorten the hospital stay.[1,2,16] These solutions containing maltodextrin polymers increase the gastric emptying rate and reduce gastric secretion because of their low osmolality compared with standard glucose solutions.[17] It has been reported that the OCS given to the elective laparoscopic cholecystectomy (LC) patients before a surgical intervention passes through the stomach within 90 minutes.[5,12] It is recommended that these solutions should be given 100 g (800 mL) in the evening before the surgery and 50 g (400 mL) 2 hours before the surgery.[12,18] Also, recent advances in perioperative medicine have led to the recommendation of liberal fasting and preoperative oral carbohydrate ingestion as part of Enhanced Recovery After Surgery protocols.[19]

It is one of the basic responsibilities of surgical nurses to ensure that patients are kept fasting in the preoperative period in parallel with the guidelines.[20,21] The use of evidence-based information related to the preoperative food and liquids restraint by surgical nurses in cooperation with their team will reduce the complication rate, insulin resistance, and mortality in the postoperative period, have a positive influence on patient comfort because of the increased patient well-being, and shorten the hospital stay.[21] This study was a prospective randomized controlled study evaluating the effect of preoperative OCS administration on postoperative insulin resistance and patient comfort in patients undergoing elective LC.

Methods

Research Design

This study was a prospective, randomized controlled trial.

Study Population

The universe of this research consisted of patients who were scheduled for elective LC and operated on by the same surgeon between February 22, 2016 and July 20, 2016 at the General Surgery Clinic of Karabuk University Training and Research Hospital in Turkey. A total of 90 patients were scheduled for elective LC by the same surgeon. Two patients did not agree to participate in the study. Thirty-five of the 88 individuals involved in the sampling were excluded from the study because of exclusion criteria. The remaining 53 patients were randomized into two groups, OCS ($n = 26$) and control ($n = 27$). The sealed envelope randomization method was performed for the process. The envelopes were prepared by another researcher who was not involved in the study. All the envelopes were similar to each other and each was numbered consecutively. After the conformity of the patient was assessed and the consent form was filled in, an envelope was opened for each patient. The operation was delayed for a control group patient who was found to have a history of aspirin use. The operation shifted from LC to open surgery for one of the control group patients. In addition, the operation was delayed for an OCS group patient because of high blood pressure. As a result, the data from a total of 50 patients, 25 in each group, were analyzed (Figure 1).

PARTICIPANTS/ELIGIBILITY.

Inclusion Criteria.

- Scheduled for LC.
- Age more than 18 years and less than 65 years.

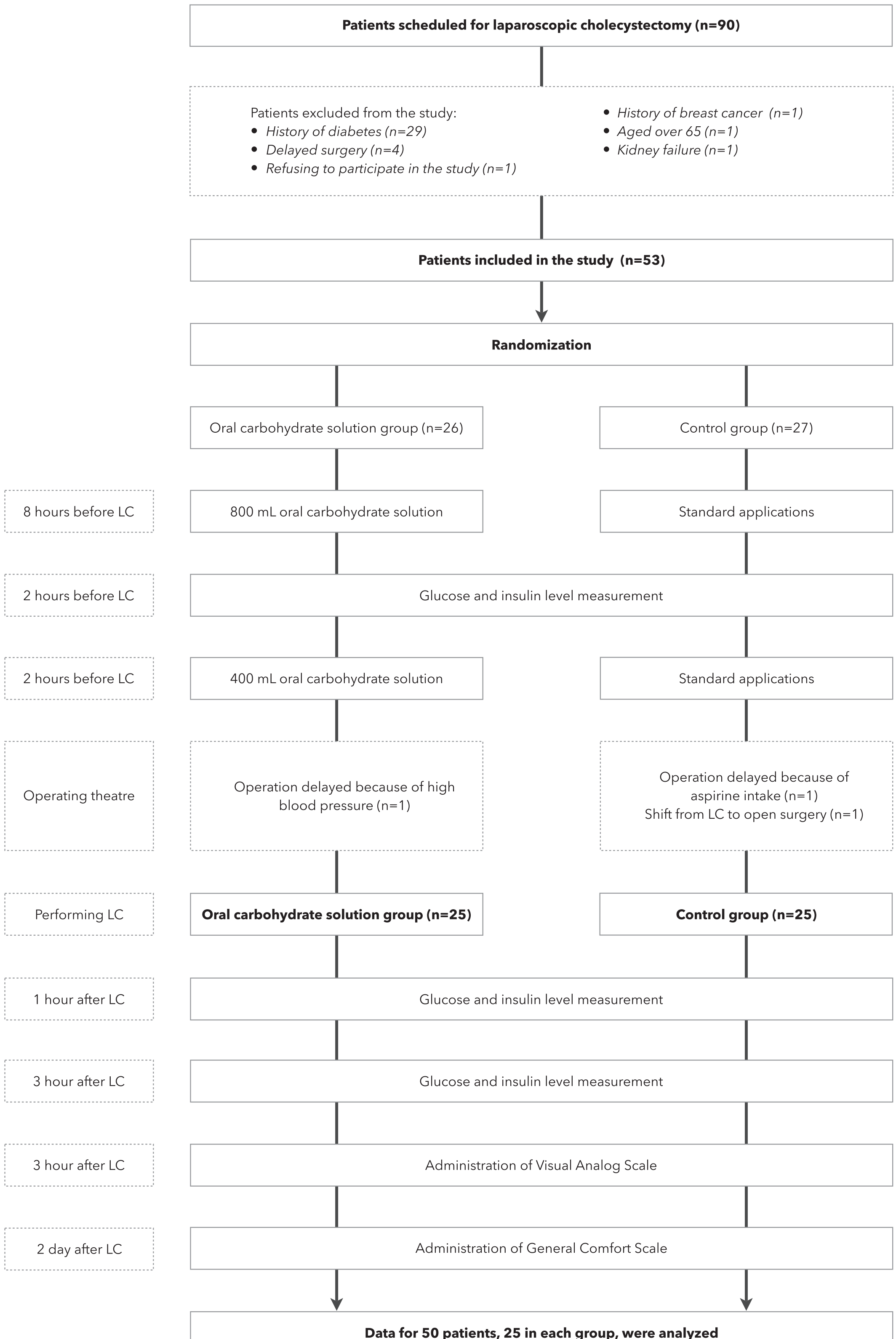

Figure 1. CONSORT diagram. LC, laparoscopic cholecystectomy.

- Agreeing to participate in the study and signing the informed consent form.

Exclusion Criteria.

- Those with a history of diabetes (type 1 and 2).
- Those who have a history of gestational diabetes.
- Body mass index (BMI) of 40 kg/m^2 or more (BMI = body weight/height^2).
- ASA group III or IV.
- Those who were administered intravenous fluid before surgery.
- Those with liver and kidney failure.
- Drug users whose blood glucose levels will be impacted.
- Those who have previously undergone abdominal surgery.
- Those with a history of acute cholecystitis or acute pancreatitis.
- Patients for whom CO_2 insufflation is inconvenient in terms of anesthesia (heart failure, chronic obstructive pulmonary disease, and so forth).
- Those who have bleeding diathesis.
- Those receiving immunosuppressive treatment.
- Patients with any infectious disease.

Materials and Methods

SETTINGS. In OCS group (n = 25), the patients were given an oral glucose solution (Nutricia preop) containing 12.5% glucose, first 800 mL at 12 a.m., and then 400 mL at 6 a.m., 2 hours before the surgery. The solution was ingested in 10 minutes. Nutricia preop, one of the OCSs containing maltodextrin and electrolytes, contains 12.5% glucose. It passes through the stomach in 90 minutes. Its osmolality is 285 mosm/kg/H_2O and it has 50 kcal/100 mL. In addition, it contains 0.46 mg/mL sodium and 1.93 mg/mL potassium. Food and water were cut off in the control group (n = 25) as of 12 a.m. the night before surgery. Both groups were not given intravenous fluid before surgery. The surgical intervention began between 8 and 9 a.m. in the morning in all patients. During intubation, 2 mg/kg propofol, 2 mcg/kg fentanyl (Fentanyl), and 0.5 mg/kg rocuronium (Esmeron) were used for induction. As maintenance, 1.5 L/min of oxygen, 1.5 L/min of air, sevoflurane, and 2 mcg/kg/min of remifentanil infusion were administered. No complications were observed during induction, monitoring, or waking up-recovery.

To provide the standardization of treatment after surgery, both groups were treated with 2,000 mL 5% dextrose plus 1,500 mL saline solution, cefazolin sodium (according to our country's infection control committee suggestion) 1 g 2 x 1, tenoxicam 20 mg 2 x 1, ranitidine 50 mg 3 x 1, and metocloramide HCL.

THE PARAMETERS. After the patients were scheduled for LC, the venous blood samples taken from the patients were analyzed for the insulin level and HbA1c, as well as the routine biochemistry values before any surgery. Glucose and insulin levels were reanalyzed and recorded 2 hours before LC, and at first and third hour after LC. All serum samples were studied in the biochemical laboratory of the hospital where the study was conducted. The Advia 2400 automated analyzer (Siemens Healthcare Diagnostics) and the Advia Centaur XP immunoassay system (Siemens Healthcare Diagnostics) were used.

MEASUREMENT OF INSULIN RESISTANCE. The euglycemic-hyperinsulinemic glucose clamp method is accepted as the gold standard for measuring insulin sensitivity. But the euglycemic-hyperinsulinemic glucose clamp method is practically impractical because of the need for insulin infusion and repeated blood withdrawal. To measure insulin sensitivity, insulin resistance (IR) was calculated according to the homeostatic model assessment (HOMA) method, which is most commonly used in clinical practice. In normal individuals, the HOMA value is reported to be lower than 2.7, and values greater than 2.7 reflect insulin resistance at different degrees.[22] HOMA-IR values were calculated using glucose and insulin levels (fasting insulin $\times$ fasting glucose/405).

ASSESSMENT OF COMFORT LEVEL. At the third hour of LC, the visual analog scale (VAS) and on the second day, the general comfort scale (GCS) were administered.

GENERAL COMFORT SCALE. This scale was used to determined the requirements of comfort and evaluate nursing interventions providing comfort and the state where an increase in the anticipated comfort was reached.[23] With the GCS the situations of relief, ease, and transcendence were assessed. Relief, relieving the suffering of the individual who is satisfied with the needs; ease, peaceful and calm state is coming from previously mentioned problems; the individual can transcendent with problems by increasing his or her power. The Cronbach's α score of our scale was 0.94. The GCS was performed 2 days after the operation because the anxiety level in the patients started with hospital admission and was high for 2 days after surgery.[24]

VISUAL ANALOG SCALE. Patient well-being, hunger, thirst, pain, and anxiety were assessed using VAS scores of 1 to 10 cm. It was used to quantify certain values that are subjective and not numerically measured. On a 10-cm linear scale, the patient is asked to mark how he feels at that moment, either by putting a mark or by drawing a line between the two statements about his or her current state. The average of the values obtained is calculated for the assessment.[25,26]

Data Analysis

Data were analyzed using IBM SPSS Statistics for Windows Version 21.0. (IBM Corp, Armonk, NY). The anthropometric data are presented as means and standard deviation. The numerically determined data were expressed in numbers and percentages. To compare the difference between the two groups, the independent samples *t* test, Mann-Whitney *U* test, χ^2 test, and Fisher's exact test were used. Changes in glucose, insulin, and HOMA-IR values in the study groups were compared with variance analysis. Multiple comparisons of measurements at different times were performed by applying the "Bonferroni" correction. A significance level of .05 was used in the study.

Ethical Issues

The approval of Clinical Research Ethics Committee, Bülent Ecevit University, was obtained with decision number 2015/11 of November 18, 2015. All patients were informed about the study, and their written consent was obtained.

Budget of the Study

This study was carried out as the Scientific Research Project of Karabük University with project number KBÜ-BAP-15/2-YL-051. Our study did not have any financial burden on the patients or the institution.

Results

There was no statistically significant difference between the groups in terms of patient age (median, 43; interquartile range, 26 vs median 54; interquartile range, 14; P = .148, respectively), gender (80% vs 68% female; P = .333, respectively), and BMI (28.3 ± 3.7 vs 29.0 ± 3.3; P = .452, respectively). The study groups were similar to each other in terms of operative time (P >.05) (Table 1). Complications (fever, aspiration, and surgical site infection) did not develop in the patients in either group. No statistically significant difference was found between the OCS and control groups in terms of initial glucose level, insulin level, HOMA-IR values, and other parameters (P < .05).

Changes in Glucose Levels

Both groups were observed to have an increase in glucose levels over time. In the OCS group, mean glucose levels were 97 (±9), 98 (±10), 102 (±11), and 105 (±13) at baseline, 2 hours before, and at the first and third hour of LC, respectively. These values were 99 (±8), 101 (±12), 108 (±20), and 119 (±19), respectively, in the control group. The increase in the glucose levels of the control group occurring over time was found to be statistically significant ($F(3, 72)$ = 4.97, P = .003) (Figure 2).

In the control group, glucose levels at the third hour of surgery were significantly higher than baseline (difference = +9.64, P = .017) and those 2 hours before the operation (difference = +7.48, P = .039) (Table 2).

Changes in Insulin Levels of the Patients

The descriptive data on insulin levels measured at different times in the control groups are shown in Figure 3. The mean insulin values measured at different times were not different from each other

Table 1. Characteristics of Patient Groups

	Control Group (n = 25)	OCS Group (n = 25)	*P* Value
Age (y)			
Median	54	53	.425
Interquartile range	14	16	
Body mass index (kg/m^2)			
Median	29.0	28.3	.452
Standard deviation	3.3	3.7	
Sex			
Female	17 (%68)	20 (%80)	.333
Male	8 (%32)	5 (%20)	
Operation time (min)			
Mean	78.25 ± 25.97	77.37 ± 21.50	.968

OCS, oral carbohydrate solution.

($F(3, 144) = 1.12$, $P = .342$). It was found that the "group × time" interaction was not significant in terms of the change in insulin levels ($F(3, 144) = 0.640$, $P = .590$). In addition, no difference was found between patient groups regarding insulin levels ($F(1, 48) = 0.954$, $P = .334$) (Table 3).

Changes in HOMA-IR Values of the Patients

In the OCS group, mean HOMA-IR levels were 2.34 (±0.24), 2.21 (±0.34), 2.35 (±0.40), and 2.45 (±0.61) at baseline, 2 hours before, and at the first and third hour of LC, respectively, whereas they were 2.25 (±0.28), 2.16 (±0.67), 2.26 (±0.94), and 2.81 (±0.82) in the control group, respectively (Figure 4). It was determined that there was no significant change in the HOMA-IR values in the OCS group over time ($F(2.54, 60.86) = 1.83$, $P = .160$), whereas a statistically significant increase was observed in the control group ($F(3, 72) = 5.63$, $P < .002$). The HOMA-IR values at the third hour of the surgical intervention in the control group were found to be significantly higher than those of baseline (difference = +0.567, $P < .009$) and those 2 hours before the surgery (difference = +0.649, $P = .005$). The increase in HOMA-IR values of both groups was statistically significant ($F(3, 144) = 7.005$, $P < .001$) (Table 4).

Comparison of the Patients' Comfort

It was observed that hunger (0.12 ± 0.44 vs 6.44 ± 2.97, $P < .0001$), thirst (0.64 ± 0.91 vs 7.8 ± 2.50, $P < .0001$), anxiety (0.12 ± 0.44 vs 5.12 ± 2.77, $P < .0001$), and pain (0.92 ± 0.81 vs 6.12 ± 2.54, $P < .0001$) were significantly lower in the OCS group (Table 5). In the experimental group, the scores for "relief" (3.50 ± 0.37 vs 3.24 ± 0.35, $P = .014$), "relaxation" (3.81 ± 0.34 vs 3.51 ± 0.27, $P = .001$), and "transcendence" (3.64 ± 0.49 vs 3.08 ± 0.40, $P < .0001$) were significantly higher than those of the control group (Table 6).

Discussion

In our study, the patients in OCS group, who received OCS at two different times and underwent elective LC after the randomization of the patients, were compared with the patients of the control group, who had standard fasting in terms of insulin resistance and patient comfort.

Our study groups were well matched for age, BMI, and duration of surgery. This study showed that intake of liquid formula with 12.5% of the maltodextrin content helped attenuate the organic response of LC. The relevance of this study consists of ingestion of maltodextrin, already established in the literature for abbreviation of preoperative fasting for 2 hours. Since the early studies with fasting abbreviation, no morbidity or adverse events have been reported. This is confirmed by the observation of more than 2,000 patients in clinical studies and more than 2 million patients who have had shortened fasting duration in clinical practice.[13,26]

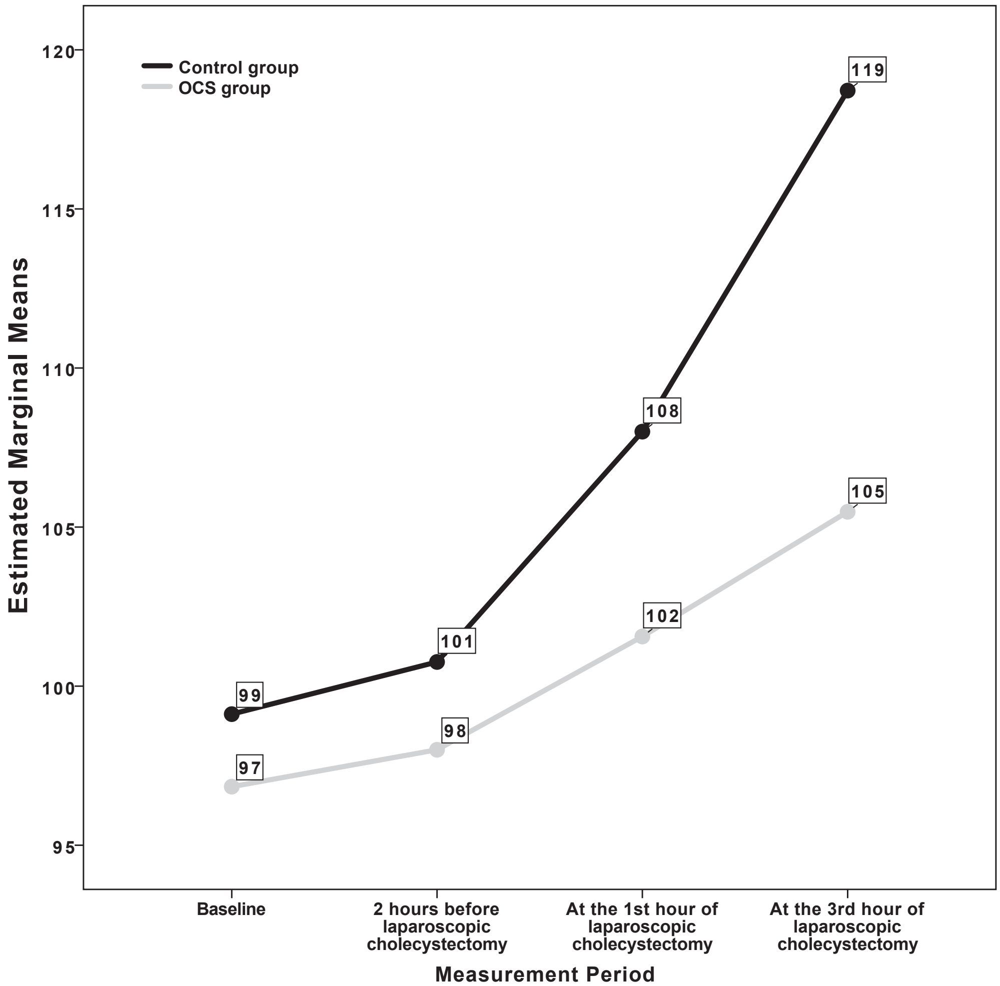

Figure 2. Changes in patients' glucose levels. OCS, oral carbohydrate solution.

Insulin resistance is a transitory phenomenon of the metabolic response to trauma. In uncomplicated operations, it lasts for 2 to 4 weeks postoperatively and is directly related to the magnitude of the injury.[6,27] The fasting status caused by conventional fasting protocols aggravates this resistance and induces greater hyperglycemia.[28]

The results of our study indicate that the abbreviation of preoperative fasting with maltodextrin is safe and is associated with reduced organic response to surgical trauma by improving insulin sensitivity evaluated by the HOMA-IR test. HOMA-IR is commonly used and is well validated in the literature.[6,18,29] Administration of carbohydrate-rich fluids can have a positive

Table 2. Comparison of the Change in Glucose Levels of the Groups

	Degree of Freedom/Error	*F* Value	*P* Value	Partial η^2
Time effect	2.8/132.6*	14.292	< .0001	0.229
Time × group interaction	2.8/132.6*	2.231	.093	0.044
Group effect	1/48	6.563	.014	0.12

*(χ^2(5) = 14.733, P = .012) the degree of freedom was corrected using the Huynh-Feldt spherical estimate (ε = 0.850).

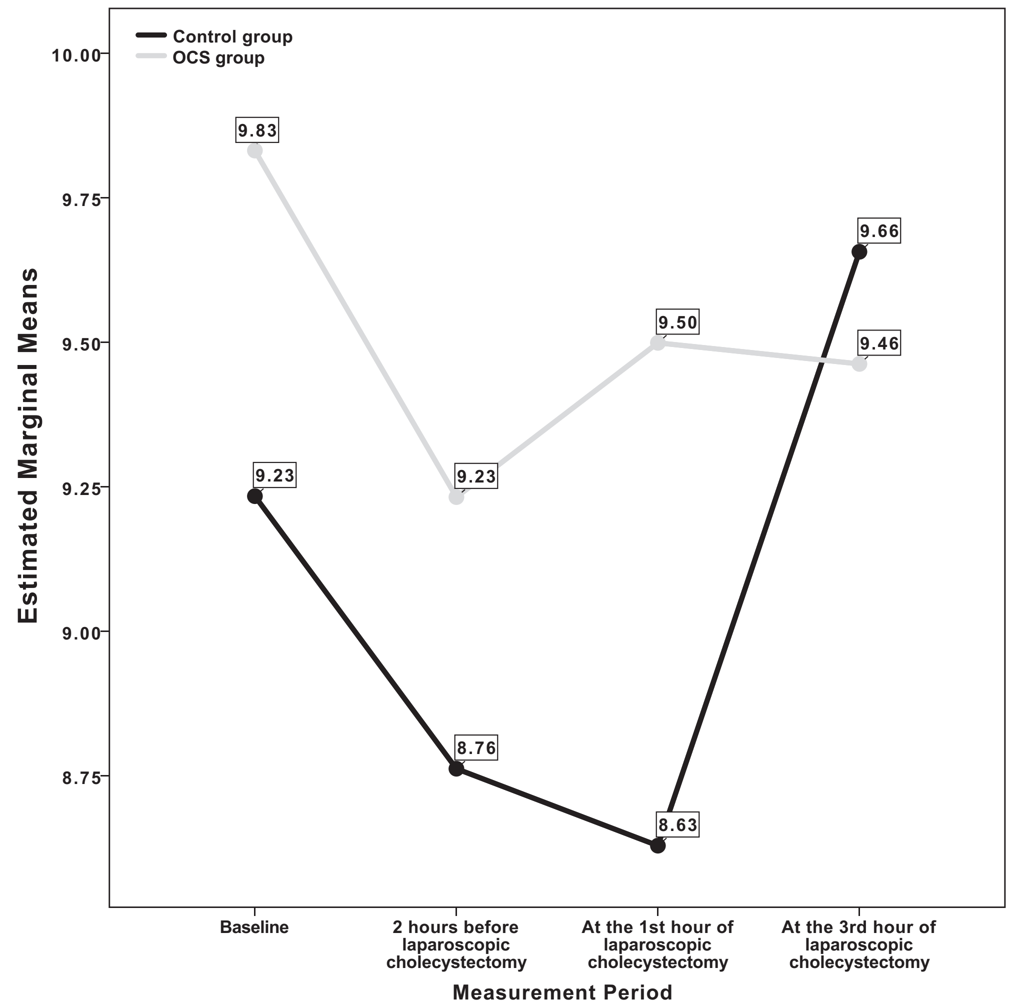

Figure 3. Changes in insulin levels of the patients. OCS, oral carbohydrate solution.

influence by decreasing insulin resistance to surgical stress.

Pedziwiatr et al found no differences between their study groups with regard to OCS loading in LC. But the difference between this study and theirs is that they had two measurements, one right after the surgery and the other 24 hours after the surgery. In addition, their intervention group received OCS loading (400 mL Nutricia preoperatively) just 2 hours before the surgery and the control group received a placebo.[11] In our study, the OCS group received 800 and 400 mL of OCS solution at midnight, the night before the surgery, and

Table 3. Comparison of the Change in Insulin Levels of the Groups

	Degree of Freedom/Error	*F* Value	*P* Value	Partial η^2
Time effect	3/144	1.122	.342	0.023
Time × group interaction	3/144	0.640	.590	0.013
Group effect	1/48	0.954	.334	0.019

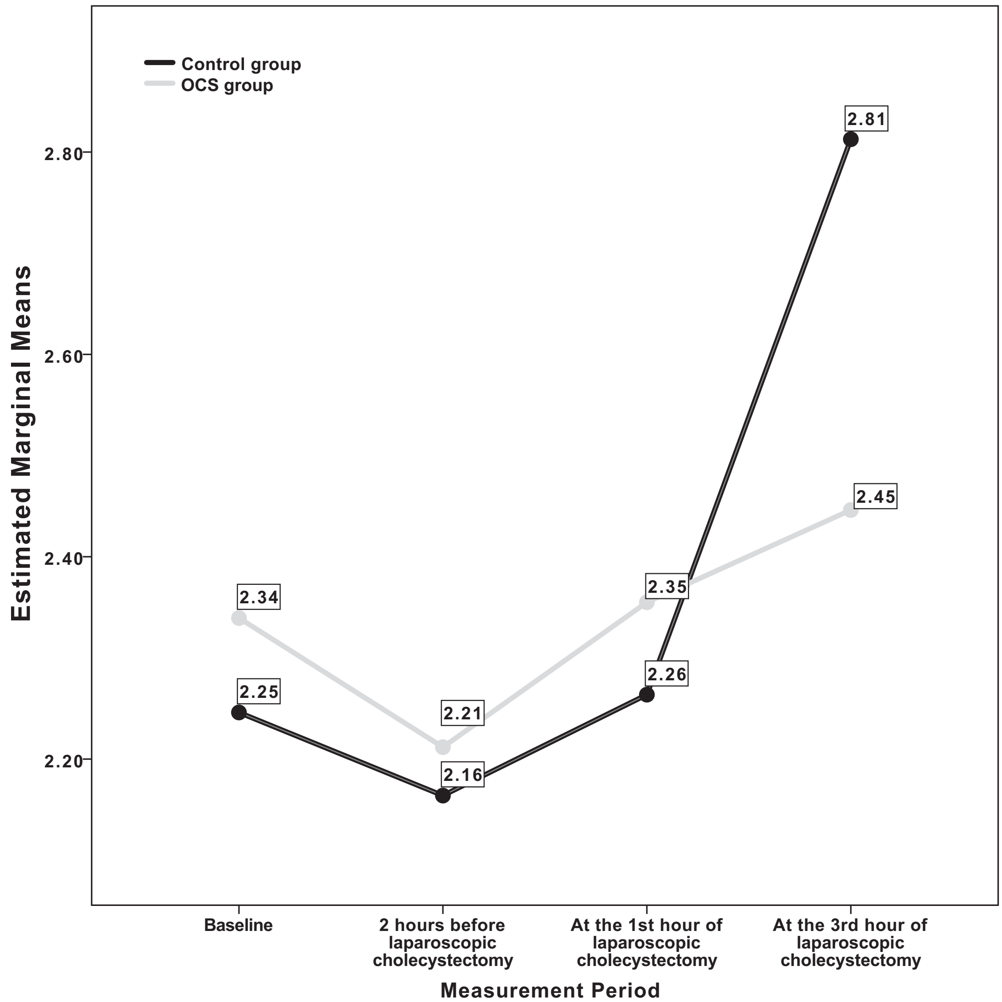

Figure 4. Changes in HOMA-IR values of the patients. HOMA-IR, homeostasis model assessment of insulin resistance; OCS, oral carbohydrate solution.

2 hours before the surgery, whereas the control group did not eat and drink at all after midnight the night before the surgery.

In our study, all the patients in conventional fasting group had high blood glucose after 3 hours of LC, whereas the patients with shortened fasting with a drink enriched in OCS showed no associated high insulin. In the study, the oral carbohydrate administration caused a significant reduction in the insulin release and, therefore, a reduction in insulin resistance. Administration of OCS may cause more physiological metabolism of glucose and insulin to plasma because of increased insulin

Table 4. Comparison of the Change in HOMA-IR Values

	Degree of Freedom/Error	*F* Value	*P* Value	Partial η^2
Time effect	3/144	7.005	< .001	0.127
Time × group interaction	3/144	2.392	.071	0.047
Group effect	1/48	0.092	.763	0.002

HOMA-IR, homeostatic model assessment of insulin resistance.

Table 5. Comfort Analysis in Study Groups Using the Visual Analog Scale

	Control Group (n = 25)	OCS Group (n = 25)	*P* Value
Hunger	6.44 ± 2.97	0.12 ± 0.44	< .0001
Thirst	7.8 ± 2.50	0.64 ± 0.91	< .0001
Anxiety	5.12 ± 2.77	0.12 ± 0.44	< .0001
Pain	6.12 ± 2.54	0.92 ± 0.81	< .0001

OCS, oral carbohydrate solution.
Low values from the visual analog scale are indicative of recovery.

production and increased sensitivity. We concluded that preoperative carbohydrate therapy may reduce endogenous glucose release during the postoperative period.

Surgery inevitably induces a metabolic stress response and reduces insulin sensitivity. Our results showed that the conventional preoperative fasting reduced insulin sensitivity, even after a minimally invasive procedure, such as elective LC. Insulin sensitivity can be reduced by more than 50% even in healthy nondiabetic patients undergoing elective surgery.[30,31] Insulin resistance occurs within hours after the initiation of surgery and subsequently results in hyperglycemia, a catabolic state characterized by deterioration of stored glycogen, fat and protein, prolonged recovery, and even increased morbidity.[32,33] We believe in the underlying protective role of preoperative OCS supplementation in reducing the development of postoperative insulin resistance.

VAS was used to assess each patient's comfort using the following variables: hunger, thirst, anxiety, and pain. The carbohydrate preparation led to significant reductions in hunger, thirst, anxiety, and pain ($P < .0001$). Henriksen et al used VAS assessment and obtained no differences between their study groups with regard to thirst, hunger, anxiety, well-being, fatigue, pain, and nausea. However, in that study, the patients given carbohydrates reported significantly decreased hunger and mouth dryness.[34] Şavluk et al used VAS assessment for patient well-being, mouth dryness, hunger, anxiety, and nausea in their study, in which the patients underwent a coronary artery bypass graft and reported that the carbohydrate preparation led to significant reductions in mouth dryness and hunger, but the improvements in nausea and anxiety were similar for the fasting and carbohydrate groups.[35] Our results suggest that improved preoperative comfort extended in the early postoperative period in the OCS-treated group.

In terms of perioperative nutritional support, oral carbohydrate loading has been applied to patients undergoing elective surgery to improve clinical outcomes. Preoperative oral carbohydrate-rich drinks can improve patient well-being as well as reduce metabolic stress and insulin resistance. The results of the present study may be explained partly by the relatively short fasting time.

On the other hand, it was found in our study that comfort values of the LC patients were significantly higher in the OCS group compared with those of the control group, an outcome that was found as a result of GCS performed on the second day of LC ($P < .0001$).

OCS loading can decrease three levels of GCS (relief, ease, and transcendence), which can theoretically justify its use in cholecystectomy. All these beneficial effects of preoperative OCS may be related to a reduction in insulin resistance and subsequently better preservation of metabolic homeostasis.[10]

The administration OCS at midnight, at 12 a.m. the night before the surgery, and 2 hours before the surgery is safe and improves insulin sensitivity and comfort in patients undergoing elective LC. This evidence supports the clinical application of a shortened fasting time before LC.

Table 6. Comfort Analysis in Study Groups Using the General Comfort Scale

	Control Group (n = 25)	OCS Group (n = 25)	*P* Value
Relief	3.24 ± 0.35	3.50 ± 0.37	.014
Ease	3.51 ± 0.27	3.81 ± 0.34	.001
Transcendence	3.08 ± 0.40	3.64 ± 0.49	< .0001

OCS, oral carbohydrate solution.
High values from the general comfort scale are indicative of increased comfort.

The results of this study indicate that preoperative OCS administration had positive effects on surgical patient's insulin resistance and comfort in elective LC. The strength of our study is that it supports other related studies and provides important evidence. On the other hand, there is a limitation in our study. Our population did not include elderly patients, high-risk patients, or patients with an ASA Physical Status of III or higher; the safety and efficacy of preoperative OCS intake in these patients remain unclear. Further study is needed to evaluate the efficacy of OCS for these patients.

Conclusions

This study indicates that OCS given before LC lowers the postoperative stress response and insulin resistance and improves patient comfort, and poses no risk at all. We believe that this study will contribute to future research, in that it is the first study to evaluate patient comfort using GCS in LC patients. However, if this view is to be supported, new randomized controlled clinical trials should be performed with a greater number of patients.

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