Brazilian Journal of Anesthesiology 2021;71(3):247–253

Sociedade Brasileira de Anestesiologia

Brazilian Journal of ANESTHESIOLOGY

CLINICAL RESEARCH

Effect of preoperative oral liquid carbohydrate intake on blood glucose, fasting-thirst, and fatigue levels: a randomized controlled study

Gökçen Aydın Akbuğa [a,*], Mürüvvet Başer [b]

[a] *Bozok University, Faculty of Health Sciences/Surgery Nursing, Yozgat, Turkey*
[b] *Erciyes University, Faculty of Health Sciences/Women's Health and Childbirth Nursing, Kayseri, Turkey*

Received 19 August 2019; accepted 25 February 2021
Available online 15 April 2021

KEYWORDS
Fasting;
Thirst;
Fatigue;
Blood glucose

Abstract

Background: This study aimed to analyze the effects of preoperative oral intake of liquid carbohydrate on postoperative blood glucose, fasting-thirst, and fatigue levels in patients undergoing arthroscopic surgery.

Methods: This randomized controlled clinical trial enrolled 82 patients, who were scheduled to undergo arthroscopic surgery, and divided them into two groups: (1) those who consumed a carbohydrate-rich drink, and (2) those not consuming anything after midnight. Pre- and postoperative fasting-thirst (visual analog scale) and blood glucose levels were measured. Likewise, the Brief Fatigue Inventory was applied to patients 24 hours after surgery.

Results: The mean blood glucose levels in the first postoperative hour were 90.90 ± 13.56 $mg.dL^{-1}$ and 107.00 ± 15.84 $mg.dL^{-1}$ in the intervention group and control group, respectively ($p < 0.001$). The postoperative mean thirst scores were 4.70 ± 1.59 and 6.36 ± 2.07 in the intervention group and control group, respectively ($p < 0.001$). Their corresponding postoperative mean fasting scores were 5.54 ± 1.76 and 5.86 ± 1.79 ($p > 0.05$) and the mean fatigue levels in the 24^{th} postoperative hour were 4.80 ± 2.13 and 5.48 ± 1.46, respectively ($p > 0.05$).

Conclusions: Oral intake of liquid carbohydrate before spinal anesthesia was found to have positive effects on patients' postoperative blood glucose and thirst levels.

* Corresponding author.
E-mails: gokcen86@windowslive.com (G.A. Akbuğa), mbaser@erciyes.edu.tr (M. Başer).

https://doi.org/10.1016/j.bjane.2021.02.053

Introduction

Surgical procedures performed for therapeutic reasons can cause physiological and psychological stress in the organism and can result in catabolism.[1,2] This is closely associated with factors that influence the management of symptoms, such as the duration of preoperative fasting, type and length of anesthesia, surgical techniques, hemorrhage, postoperative pain, nausea-vomiting, ileus, and fatigue.[2,3] Catabolism also causes patients to experience fatigue, lowers their resistance, prolongs their recovery and length of hospital stay, and increases their risk for postoperative complications; thus, it can result in an increased risk for mortality and morbidity.[3,4]

New evidence-based protocols have been developed. The use of traditional approaches for perioperative treatment and care of individuals has been avoided to lower their stress response and to accelerate their recovery. Enhanced recovery after surgery (ERAS) is a cycle-based protocol for perioperative strategies that requires multidisciplinary approaches.[5–7] The protocol aims to enable individuals to return to their basic performance and functions within the shortest time possible. ERAS also suppresses catabolism and enhances their quality of life because it prevents development of postoperative complications.[6,7]

Two of the protocol's predictors include shortened preoperative fasting duration and carbohydrate loading. Accordingly, individuals are told that they can consume solid foods up to 6 hours prior to surgery, clear liquid-based food up to 2 hours prior to surgery, 800 mL carbohydrate-rich drink at any time until midnight before surgery, and 400 mL carbohydrate-rich drink 2–3 hours before surgery.[5–7]

Many studies have reported that a diet of clear liquid given 2 hours before surgery does not increase patients' gastric fluid volumes or gastric acidity and it poses no risk of aspiration.[8,9] Some other studies have revealed that oral intake of liquid carbohydrate suppresses catabolism by lowering the stress response induced both by surgical trauma and fasting, decreases insulin resistance, minimizes alterations in postoperative glucose levels, and reduces fasting-thirst feelings, nausea and vomiting, defecation time, length of hospital stay, and fatigue.[4,8–12]

This study aimed to investigate whether preoperative carbohydrate improves fasting-thirst, fatigue, and glucose levels compared with standard therapy.

Methods

Trial design

This randomized controlled trial was conducted at the orthopedic clinic of a research and application hospital in Turkey. The ethics committee approval was obtained from the Clinical Trials Ethics Committee (07/10/2016-2016/523). Institutional permission was obtained from the related research and application hospital. Participants were informed about the purpose of the study, and they had all signed the informed consent form. Blinding or masking was not performed in the study.

If scheduled for surgeries performed under spinal anesthesia at the orthopedic clinic, patients should not eat anything after midnight; moreover, they start to eat based on regimen I (pulpless, grain-free clear liquid diet) at the second postoperative hour. Arthroscopy lasts for 45–90 minutes. Then, patients are sent home after undergoing the recommended blood tests and physical examinations and return to the clinic on the morning of surgery. In this study, patients were told to come to the clinic 2 hours before surgery. The first patients who underwent arthroscopic surgery between 08:00 and 10:00 a.m. by the same orthopedic surgeon were included in the sample. The patients were not administered any intravenous fluid after surgery. As a standard, a 10–15 $mL.kg^{-1}$ of balanced solution (Isolen-S) was given to the patients in the intraoperative period. They received 1000–1500 mL of intravenous fluid on average. Spinal anesthesia took place using 15 mg of 0.5% bupivacaine HCl (Marcaine) through the intervertebral space (L3–4). As far as is known, bupivacaine, used for spinal anesthesia, has no effect on glucose metabolism. Those included in the study were $\geq$ 18 years old, indicated for arthroscopic surgery, and could communicate enough to be able to answer the research questions. Individuals diagnosed with any psychiatric disorder, endocrine disorder, renal and hepatic failure, gastroesophageal reflux, sour cherry allergy, and body mass index of > 25 $kg.m^{-2}$ were excluded from the study.

Sample size calculation and patient randomization

A power analysis was carried out to determine the sample size of the study. For this purpose, the arithmetic mean difference (3.3) between the blood glucose levels of the intervention and control groups mentioned by Yagci et al.[8] was used. After the arithmetic mean and standard deviation were used to calculate the sample size (95% confidence interval, 95% power), 30 patients should be included in each group. When the desired number of the calculated data was reached, the power analysis was repeated over the study data. The margin of error in the post-hoc power analysis was 5%. According to the blood glucose level in the first postoperative hour, the effect size of 1.095 and power of the study was calculated as 99%.

Therefore, 70 patients were randomly divided into two groups using a computerized table of random numbers. After the random numbers were placed in opaque envelopes, the envelopes were numbered sequentially, and they were opened just before the start of the procedure. Patients were assigned to the intervention and control groups.

The study was conducted on a total of 61 patients including 31 in the intervention group and 30 in the control group.

Data collection tool

A patient information form, physiological measurement chart, visual analog scale (VAS) for fasting-thirst levels, and Brief Fatigue Inventory (BFI) were all used to collect the data.

Patient information form

This form was prepared by the researcher upon literature review.[4,8,12] It includes 10 questions about the characteristics of the patients such as age, sex, marital status,

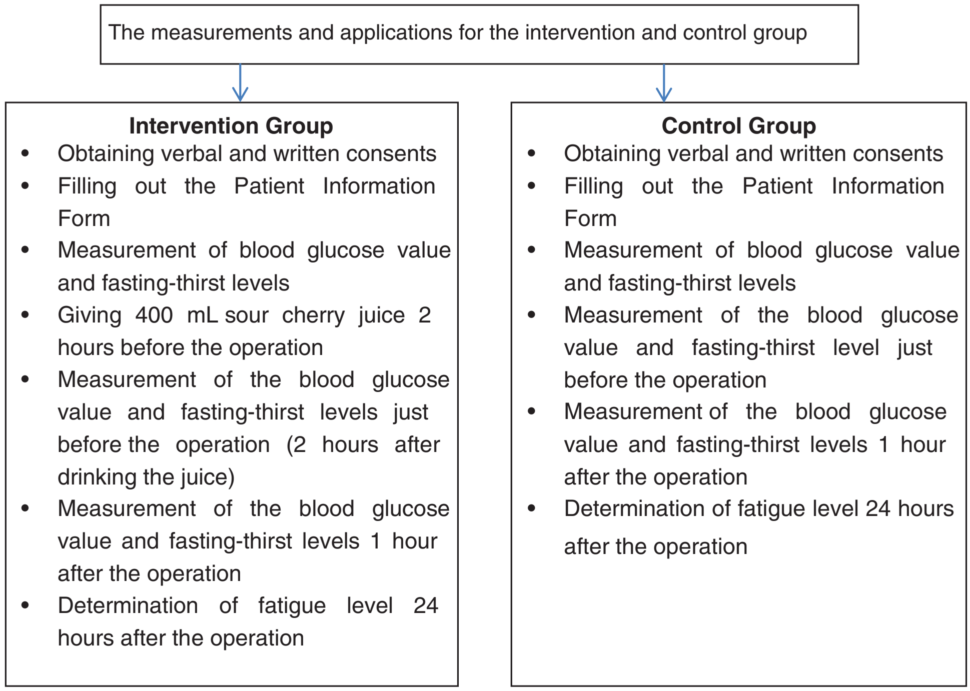

Figure 1 The measurements and applications for the intervention and control group.

educational level, occupation, income level, presence of any chronic disease, and surgery duration.

BFI

This inventory was developed by Mendoza et al.[13] and adapted by Cinar et al.[14] for the Turkish population. Cronbach's alpha internal consistency coefficient of the inventory is 0.98. BFI has nine items and evaluates the fatigue severity (now, always, worst) (1, 2, 3) and the effect of fatigue on the activities of daily living (4a, 4b, 4c, 4d, 4e, 4f). Each item is rated between 0 and 10 points. The higher the score, the more severe the fatigue is, and the more does it affect daily living activities.[15] In this study, Cronbach's alpha internal consistency coefficient of BFI was 0.74.

Intervention

Figure 1 shows the measurements and applications for the intervention and control groups.

Applications in the intervention group

Based on the literature review and opinions of three experts − a dietitian, an anesthesiologist, and a biochemist −400 mL of grain-free sour cherry juice from a fixed brand (with value of 200 kcal and deemed suitable for a clear diet) was given to the patients in the intervention group 2 hours before surgery (Fig. 1).[4]

Applications in the control group

Those in the control group did not drink the liquid carbohydrate (i.e., sour cherry juice). Rather, they only received routine treatment and hospital care services (Fig. 1).

Statistical analysis

Patients' descriptive characteristics are presented in number and percentage distributions in tables. The Shapiro−Wilk W test was used to determine whether the numerical data were normally distributed. Parametric tests were applied for analysis of normally distributed data. The independent samples *t*-test was used to identify whether the blood glucose, fasting-thirst, and fatigue levels of both groups are different from one another.

Repeated measures analysis of variance was employed to determine the difference between the mean scores of the repeated measures in both groups. The Bonferroni multiple comparison test was applied to identify which group caused the difference between intervention and control groups. The significance level in all comparisons was 0.05.

Results

The study was completed on a total of 61 patients, including 31 in the intervention group and 30 in the control group (Fig. 2). Table 1 shows the demographic characteristics of the patients. Both groups had comparable characteristics ($p > 0.05$, Table 2), and the mean blood glucose levels in the first postoperative hour were 90.90 ± 13.56 $mg.dL^{-1}$ in the intervention group and 107.00 ± 15.84 $mg.dL^{-1}$ in the control group, and their difference was statistically significant ($p < 0.001$).

The fasting mean scores of both groups 2 hours before surgery, immediately before surgery, and 1 hour after surgery were similar to one another ($p > 0.05$, Table 3).

The mean thirst score just before surgery was 4.90 ± 2.11 in the intervention group and 6.20 ± 1.98 in the control

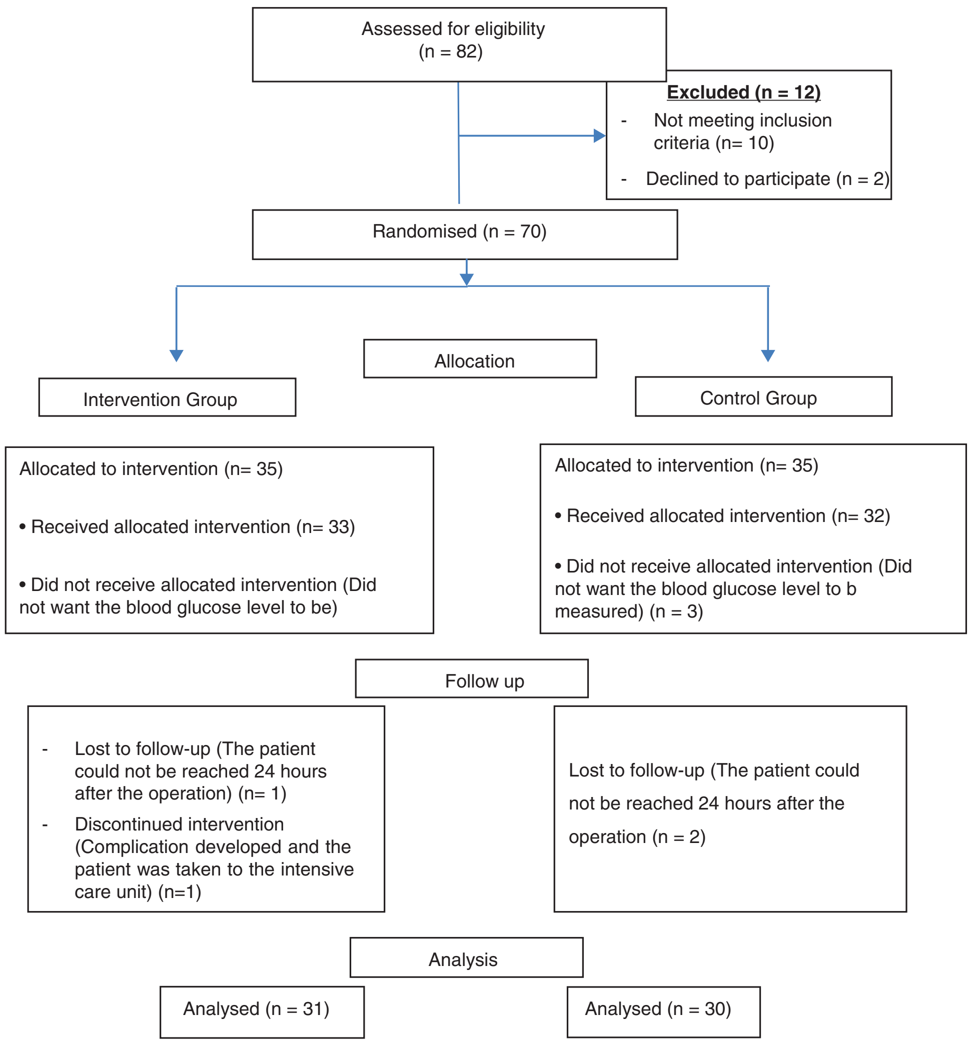

Figure 2 Consort Flowchart of the study.

Table 1 Distribution of socio-demographic characteristics of individuals in Intervention and Control groups.

Characteristics	Intervention Group (n = 31)		Control Group (n = 30)		Test
Gender	n	%	n	%	
Female	14	45.2	15	50.0	p = 0.705
Male	17	54.8	15	50.0	
Age (year, mean*.±SD) (min–max)	47.58 ± 11.24 (25–60)		45.30 ± 9.43 (25–59)		p = 0.395
Educational status					
Literate	4	12.9	4	13.3	
Primary education	18	58.1	20	66.7	p = 0.709
High school and higher	9	29.0	6	20.0	
Presence of chronic disease					
Yes	3	9.7	7	23.3	p = 0.150
No	28	90.3	23	76.7	
Operation time (minute, mean*.±SD)	74.19 ± 13.60		80.16 ± 20.10		p = 0.178

group, and their difference was statistically significant (p = 0.017). The mean thirst score in the first postoperative hour was 4.70 ± 1.59 in the intervention group and 6.36 ± 2.07 in the control group, and the difference between them was statistically significant (p = 0.001, Table 3).

The mean score of fatigue severity was 4.80 ± 2.13 in the intervention group and 5.48 ± 1.46 in the control group ($p > 0.05$). The mean fatigue score affecting daily life activities was 4.33 ± 1.53 in the intervention group and 4.26 ± 1.86 in the control group ($p > 0.05$, Table 4).

Table 2 Distribution of blood glucose level mean scores according to the follow-up hours of Intervention and Control groups.

Blood glucose level (mg.dL^{-1})	Intervention Group (n = 31) X ± SD	Control Group (n = 30) X ± SD	p^d
2 hours before the operation	98.93 ± 14.45	94.76 ± 15.83[a]	0.287
Just before the operation	97.38 ± 16.62	99.23 ± 14.78[a]	0.649
1 hour after the operation	90.90 ± 13.56	107.00 ± 15.84[b]	< 0.001
p^c	0.101	0.001	

[a,b]Superscripts show within-group differences. There is no difference in the measurements with the same letters.
[c] Repeated measures Anova.
[d] Independent samples *t*-test.

Table 3 Distribution of fasting-thirst level mean scores in terms of the follow-up hours of the individuals in intervention and control groups.

Fasting level	Intervention group (n = 31) X ± SD	Control group (n = 30) X ± SD	p^d
2 hours before the operation	6.22 ± 1.68	7.30 ± 11.94	0.622
Just before the operation	5.54 ± 2.15	5.76 ± 1.63	0.658
1 hour after the operation	5.54 ± 1.76	5.86 ± 1.79	0.488
p^c	0.095	0.7267	
Thirst level			
2 hours before the operation	5.19 ± 1.88	5.53 ± 1.96[b]	0.493
Just before the operation	4.90 ± 2.11	6.20 ± 1.98[a]	0.017
1 hour after the operation	4.70 ± 1.59	6.36 ± 2.07[a]	0.001
p^c	0.273	0.002	

[a,b]Superscripts show the within-group differences. There is no difference in the measurements with the same letters.
[c] Repeated measures Anova.
[d] Independent samples *t*-test.

Table 4 Distribution of brief fatigue inventory mean scores of the individuals in Intervention and Control groups.

BFI	Intervention Group (n = 31) X ± SD	Control Group (n = 30) X ± SD	p^a
Fatigue Severity	4.80 ± 2.13	5.48 ± 1.46	0.152
The effect of fatigue on activities of daily living	4.33 ± 1.53	4.26 ± 1.86	0.879

[a] Independent samples t-test.

Discussion

Our study indicated that oral intake of liquid carbohydrate before spinal anesthesia had a positive effect on the patients' blood glucose and thirst levels after surgery, but it did not affect their fasting and fatigue levels.

In this study, the normal range (80–110 mg.dL^{-1}) of fasting glucose was considered as the baseline value. Accordingly, the findings were within the normal range for blood glucose. However, fluctuations in blood glucose levels were interpreted through the control and intervention groups.

In this study, the preoperative blood glucose levels of the intervention and control groups were comparable. However, a difference was found between their blood glucose levels in the first postoperative hour. The blood glucose level (107.00 ± 15.84 mg.dL^{-1}) was higher in the control group than in the intervention group, which did ingest the liquid carbohydrate (90.90 ± 13.56 mg.dL^{-1}) ($p < 0.001$). The blood glucose level of both groups remained within normal limits (80–110 mg.dL^{-1}). However, the blood glucose level of the control group increased significantly after surgery ($p = 0.001$).

Such situation may be advantageous for patients. We can think that oral intake of liquid carbohydrate can lower postoperative blood glucose fluctuations and suppress catabolism because it lowers the stress response induced by fasting and surgical trauma.

Prolonged fasting before surgery causes the depletion of glycogen stores because it suppresses the liver's response to insulin and produces glucose from lipids and proteins, thus resulting in a faster neuroendocrine stress response due to surgical trauma. With the onset of catabolism, the patients are observed to experience fluctuations (i.e., a spike) in their blood glucose levels, as well as symptoms such as feeling hungry, thirsty, and tired.[16,17]

In the context of this study, the oral intake of liquid carbohydrate 2 hours before surgery was thought to suppress catabolism by preventing hyperglycemia, thus allowing the patient to recover.

A meta-analysis revealed that oral intake of liquid carbohydrate lowered patients' insulin resistance, thus preventing their blood glucose levels from fluctuating. The literature points to a number of studies that have reported similar findings.[4,8,9,18,19] In their study, Svanfeldt et al.[20] found that giving patients 400 mL of liquid carbohydrate 2 hours before surgery prevented stress-induced hyperglycemia.

Ozdemir et al.[8] reported that the blood glucose levels of the control and placebo groups returned to normal 24 hours after surgery and then gradually increased.

However, some other studies have indicated that oral intake of liquid carbohydrate has no significant effect on blood glucose levels.[3,13] The type and length of surgery, type of anesthesia used, and type of liquid carbohydrate might have influenced these findings.

Gunawardhana[21] investigated preoperative fasting practices and revealed that 51.5% of patients who had not eaten for 13 hours did not feel hungry. Similarly, in their study, Crenshaw and Winslow[22] asked patients who fasted before surgery to score their fasting level on a scale between 0 and 10 and found that their mean fasting level was 5. In this study, the oral intake of liquid carbohydrate was thought not to have created any difference in fasting levels between the intervention and control groups because it is liquid and therefore stays in the stomach only for a short time period and does not lead patients to feel discomfort.

Another problem caused by preoperative fasting is the feeling of thirst. A long-term interruption in nourishment can decrease gastrointestinal and salivary secretions, increase thirst and mouth dryness and even lead to dehydration. Hausel et al.[23] found that patients who underwent colorectal surgery consumed either a carbohydrate-rich liquid or water to reduce the feeling of thirst. George[15] examined preoperative fasting practices and found that patients consuming oral drinking liquid carbohydrate 2 hours before surgery felt significantly less thirsty based on the ERAS protocol. Gebremenhn and Nagaratnam[24] also examined patients who fasted before surgery and found that 49% of the patients experienced severe thirst as the most common symptom.

Likewise, this study revealed that that intervention group was less thirsty 2 hours after surgery (4.90 $\pm$ 2.11) than the control group (6.20 $\pm$ 1.98) (p = 0.001). Similar findings were obtained 1 hour after surgery as well: the control group was thirstier 1 hour after surgery (6.36 $\pm$ .2.07) than the intervention group (4.70 $\pm$ 1.59) (p = 0.017).

One of the postoperative symptoms is fatigue. Unnecessary preoperative fasting intensifies fatigue because it increases cell destruction products; leads to catabolism, hydrogen, and lactic acid accumulation; and stimulates glucose production from lactates and amino acids, thus resulting in protein degradation. Additionally, postoperative fatigue can occur because of tissue damage caused by surgical intervention, immobility, and stress. Fatigue adversely affects patients' physical and mental well-being, prolongs their recovery and length of hospital stay, and increases their stress response to surgical trauma.[25,26]

In this study the intervention group had less fatigue 24 hours after surgery (4.80 $\pm$ 2.13) than the control group (5.48 $\pm$ 1.46); this difference, however, was not statistically significant ($p > 0.05$).

Ozdemir et al.[8] discovered that patients who drank liquid carbohydrate had less fatigue 12 hours after surgery than those who did not.

Kaya and Sentura[26] found that fatigue began before surgery and increased mostly immediately after surgery. Rubin et al.[27] revealed that patients who underwent a major surgery (abdominal, gynecology, or cardiovascular surgery) had higher fatigue levels than those who underwent an orthopedic surgery.

In this study, patients' fatigue levels were assessed 24 hours after surgery and were found not affected by fasting alone. Other subjective factors such as anxiety, insomnia, and pain were found to play a role, albeit such factors were not identified in any of the participants. Given that arthroscopic surgery can be categorized as a minor operation, patients are likely to feel more energetic and vigorous. The fatigue levels did not differ between the groups because of these reasons. Further studies involving cases with long-term follow-up are needed to determine the effects of drinking liquid carbohydrate on fatigue. In light of these findings, further studies are needed on cases with long surgery duration as well as in cases undergoing anesthesia techniques other than spinal anesthesia to determine the effect of drinking liquid carbohydrate on fatigue and fasting.

As limitations of the study, findings were obtained from patients without history of genetic or chronic diseases, who underwent arthroscopic surgery, and were directed to spinal anesthesia. Moreover, their body mass indexes were not measured. This study's findings cannot be generalized to other patients undergoing surgery under spinal anesthesia.

Conclusion

Oral intake of liquid carbohydrate before spinal anesthesia was found to have a positive effect on patients who underwent arthroscopic surgery, in terms of their postoperative blood glucose and thirst levels. However, it appeared to have no effect on their fasting feel and fatigue levels.

Conflicts of interest

The authors declare no conflicts of interest.

References

1. Aksoy G, Kanan N, Akyolcu N. Surgery Nursing 1. Nobel Bookstore; 2012. p. 11–26.
2. Erdil F, Özhan NÖ. Surgery Nursing. Ankara, IV. Printing, Aydoğdu Ofset; 2001. p. 101–13.
3. Çeliksular C, Saraçoğlu A, Yentür E. The Influence of oral carbohydrate solution intake on stress response before total hip replacement surgery during epidural and general anaesthesia. Turk J Anaesthesiol Reanim. 2016;44:117–23.
4. Awad S, Varadhan KK, Ljungqvist O, et al. A meta-analysis of randomised controlled trials on preoperative oral carbohydrate treatment in elective surgery. Clin Nutr. 2013;32:34–44.
5. Hübner M, Addor V, Slieker J, et al. The impact of an enhanced recovery pathway on nursing workload: A retrospective cohort study. Int J Surg. 2015;24:45–50.
6. Demirhan İ, Pınar G. Enhanced recovery after surgery and nursing practicesenhanced recovery and nursing. Yıldırım Beyazıt Univ Faculty Health Sci Nurs E-J. 2014;2.
7. Bozkırlı OB, Gündoğdu HR, Ersoy EP, et al. ERAS protokolü kolorektal cerrahi sonuçlarımızı etkiledi mi? Turkish J Surg. 2012;28:149–52.

8. Yağci G, Can Fatih M, Özturk E, et al. Effects of preoperative carbohydrate loading on glucose metabolism and gastric contents in patients undergoing moderate surgery: A randomized, controlled trial. Nutrition. 2008;24:212−6.
9. American Society of Anesthesiologists. ''Committee 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 report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters''. Anesthesiology. 2011; 114:495.
10. Zareba K, Czygier M, Kamocki Z, et al. Parenteral Nutrition and preop preparation in prevention of post-operative insulin resistance in gastrointestinal carcinoma. Adv Med Sci. 2013;58:150−5.
11. Soop M, Nygren J, Myrenfors P. Preoperative oral carbohydrate treatment attenuates immediate postoperative insulin resistance. Am J Physiol Endocrinol Metab. 2001;280:576−83.
12. Özdemir F, Eti Z, Dinçer P, et al. The Effect of preoperative oral carbohydrate loading on stress response in patients undergoing major or minor surgery. Türkiye Clinics J Med Sci. 2011;31:1392−400.
13. Mendoza TR, Wang SX, Cleeand SC, et al. The rapid assessment of fatigue severity ın cancer patients: use of brief fatigue inventory. Cancer. 1999;85:1186−96.
14. Çınar S, Sezerli M, Sarsmaz N, et al. Hemodiyaliz akut yorgunluk sendromuna neden olabilir mi? J Nurs Forum. 2000;3:28−33.
15. Kobe JA. Assessing Preoperative Fasting Practice Among Adult Patients At Kenyatta National Hospital, Surgical Department, Thesis (MNutr (Human Nutrition). University of Stellenbosch; 2015, 101.
16. Yıldız H. New approaches during preoperative poverty process. AÜTD. 2006;38:1−5.
17. Azhar RA, Bochner B, Catto J, et al. Enhanced recovery after urological surgery: a contemporary systematic review of outcomes, key elements, and research needs. Eur Urol. 2016;70:176−87.
18. Crenshaw JT. Preoperative Fasting: Will the Evidence Ever Be Put into Practice? Am J Nurs. 2011;111:38−43.
19. Korkmaz Ö. Operasyon Öncesi Oral sıvı karbonhidrat Solüsyonu Alımının Stres Yanıta Etkisi, Specialization thesis. Department of Anesthesiology, Istanbul University Cerrahpaşa Medical Faculty; 2004, 58.
20. Svanfeldt M, Thorell A, Hausel J, et al. Effect of þreoperativeöral carbohydrate treatment on insulin action—a randomised cross-over unblinded study in healthy subjects. Clin Nutr. 2005;24:815−21.
21. Gunawardhana A. Knowledge, attitudes and practice of preoperative fasting guidelines in the National Hospital of Sri Lanka. Sri Lankan J Anaesthesiol. 2012;20:92−5.
22. Crenshaw JT, Winslow EH. Preoperative fasting: old habits die hard. Am J Nurs. 2002;102:36−44.
23. 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.
24. Gebremedhn EG, Nagaratnam VB. Audit on preoperative fasting of elective surgical patients in an african academic medical center. World J Surg. 2014;38:2200−4.
25. Yurtsever S. The fatigue in chronic illnesses and nursing care. Cumhuriyet Univ J Nurs School. 2000;4:16−20.
26. Kaya S, Şenturan L. The investigation of fatigue of the patients undergoing coronary artery by-pass graft surgery. JAREN. 2016;2:59−67.
27. Rubin GJ, Hardy R, Hotopf M. A systematic review and meta-analysis of the incidence and severity of postoperative fatigue. J Psychosom Res. 2004;57:317−26.