Original Article

Role of preoperative carbohydrate loading for prevention of perioperative ketoacidosis in elective cesarean delivery

Ankita Sharma, Udeyana Singh, Gurpreeti Kaur, Anju Grewal[1], Sahil Maingi, Swati Tidyal

Dayanand Medical College, Ludhiana, Punjab, [1]All India Institute of Medical Sciences Bathinda, Punjab, India

Abstract

Background and Aims: Starvation of long duration during third trimester of pregnancy is undesirable as it is associated with accelerated fasting leading to hypoglycemia, raised plasma free fatty acid (FFA) levels, and increased plasma/urinary ketones. Carbohydrate (CHO)-rich drinks given preoperatively may ameliorate these deleterious effects. The enhanced recovery after surgery (ERAS) guidelines for perioperative care recommend that oral CHO fluid supplementation 2 h before cesarean delivery may be offered to nondiabetic pregnant women. The aim of the study was to evaluate the role of preoperative oral CHO loading for the prevention of perioperative ketoacidosis in elective cesarean deliveries.

Material and Methods: One hundred and twenty American Society of Anesthesiologists (ASA) II/III parturients undergoing elective cesarean section under subarachnoid block (SAB) were divided into two groups of 60 each after they gave written informed consent. Group A parturients received 400 ml of filtered water 2 h before surgery. Group B parturients received 400 ml of nonparticulate CHO drink 2 h before surgery. The primary outcome was the incidence of ketonuria studied by the dipstick method. Secondary outcomes included hunger and thirst scores, anxiety score, dominant hand grip strength, and the quality of recovery score.

Results: The urine ketone levels were positive (+1) in 8.3% parturients in group A and 1.7% parturients in the CHO group (*P* value- 0.094). The hunger and thirst scores as well as the modified Beck's anxiety scores were significantly lower in the CHO group (*P* value- 0.002). Dominant hand grip strength was preserved in both the groups (*P* value- 0.827). The quality of recovery score was significantly improved in the CHO group (*P* value- 0.002). No serious adverse effects were noted in either group.

Conclusion: Oral CHO drink is safe when administered 2 h before uncomplicated elective cesarean deliveries. It may have a positive influence on a wide range of perioperative markers of clinical outcome.

Keywords: Cesarean section, ERAS guidelines, oral carbohydrate drink, urinary ketones

Introduction

The strict "nil per orally" (NPO) from midnight rule before elective surgery was initiated to ensure an empty stomach at the time of induction of anesthesia in order to reduce the risk of gastric regurgitation and pulmonary aspiration. During prolonged fasting, especially in expecting mothers, carbohydrate (CHO) stores are rapidly depleted, leading to muscle catabolism, raised plasma free fatty acids (FFAs), and elevated urinary ketone body concentration.[1] Surgical stress also results in insulin resistance, leading to an exacerbation of existing postoperative catabolic state with marked loss of body fat and protein stores.[2,3]

In a nondiabetic parturient, third trimester fasting glucose levels are lower relative to the pregravid state due to the

Address for correspondence: Dr. Udeyana Singh, Department of Anaesthesiology, Dayanand Medical College and Hospital, Ludhiana, Punjab - 141 001, India.
E-mail: udeyana@yahoo.co.in

Access this article online

Quick Response Code:

Website: https://journals.lww.com/joacp

DOI: 10.4103/joacp.joacp_172_23

How to cite this article: Sharma A, Singh U, Kaur G, Grewal A, Maingi S, Tidyal S. Role of preoperative carbohydrate loading for prevention of perioperative ketoacidosis in elective cesarean delivery. J Anaesthesiol Clin Pharmacol 2024;40:439-44.

Submitted: 21-Apr-2023 **Revised:** 22-Jul-2023
Accepted: 31-Jul-2023 **Published:** 08-Feb-2024

dilutional effects of the increased maternal circulating blood volume and increased glucose use by the growing feto-placental unit. Despite the relative reduction in fasting glucose levels, maternal insulin sensitivity decreases, hepatic gluconeogenesis increases, and fatty acid levels increase. Postprandial glucose levels are raised relative to pregravid levels because of impaired insulin action due to human placental lactogen and placentally derived human growth hormone (GH-V) and inflammatory mediators, altered pancreatic insulin secretion, and increased hepatic gluconeogenesis.[4] Starvation of long duration is associated with the development of hypoglycemia, increased urinary nitrogen excretion, raised plasma levels of FFAs, and increased plasma and urinary ketones. This set of events is referred to as "accelerated starvation."[5]

Over the last decade, as part of enhanced recovery after surgery (ERAS) guidelines, a plethora of studies in other surgical fields have proven that there is no requirement for such a prolonged preoperative fasting period and have shown that not only can more liberal rules be applied while ensuring patient safety, it may also be of considerable benefit to the patient by ensuring early recovery and preserved muscle strength.Until now, most of the studies have excluded pregnant women due to the perceived risk of aspiration related to maternal hormones causing delayed gastric emptying, increased intra-abdominal pressure, and reduced lower esophageal sphincter tone. However, the American College of Obstetrics and Gynecology Committee on Obstetric Practice[6] specifically states that "the patient without complications undergoing elective cesarean delivery may have modest amounts of clear liquids up to 2 h before induction of anesthesia," which is congruent with the American Society of Anesthesiologists' guidelines. Various ultrasound-guided studies[7,8] on gastric emptying of pregnant women have suggested that up to 400 ml of a clear liquids could be safely consumed up to 2 h before elective surgery.

The use of intravenous glucose (10%–20% to avoid fluid overload) to maintain glucose levels and to prevent accelerated starvation requires concomitant insulin infusion, access to large veins, and frequent monitoring of blood glucose levels by trained staff. These disadvantages can be overcome by using the enteral route, which is a more physiological pathway to provide CHO preload as suggested by the ERAS guidelines. Thus, a CHO-rich beverage may safely be given shortly before surgery.[9] Intake of 400 ml (50 g) CHO stimulates a release of insulin similar to that seen after a mixed meal (plasma concentrations: 60 mU/ml).[9,10] Osmolality is low (285 mOsm/kg), allowing a gastric transit time of 90 min for 400 ml.[9]

We hypothesized that oral CHO drink given 2 h before elective cesarean delivery would ameliorate the state of accelerated starvation, thus decreasing perioperative ketoacidosis. This would be reflected in urine ketone analysis by reagent strip method. This study was designed to evaluate the efficacy of preoperative oral CHO loading for the prevention of perioperative ketoacidosis as a marker of insulin resistance as well as the quality of recovery in the postoperative period in elective cesarean deliveries.

Material and Methods

This randomized study was conducted after approval from the Institutional Ethics Committee was obtained. The trial has been registered in the Clinical Trials Registry of India (CTRI Reg. No. –CTRI/2021/10/037435). A total of 132 patients were recruited for the study after they gave written informed consent. Three of them showed high random blood sugar RBS readings on multiple occasions, thus raising doubt of undiagnosed gestational diabetes. Two parturients went into labor and in five parturients, there was delay of more than 4 h after oral drink administration due to lack of operating room (OR) availability. Two parturients withdrew consent. The remaining 120 parturients were randomly assigned equally to either of the two groups A and B by computer-generated randomized codes contained in sealed, sequentially numbered envelopes [Figure 1].

The study included parturients aged above 18 years and weighing 50–100 kg with American Society of Anesthesiologists (ASA) physical status II and III who were undergoing elective lower segment cesarean section under subarachnoid block (SAB) with healthy singleton pregnancy. We excluded diabetic parturients, parturients with severe gastroesophageal reflux disease, parturients with failed SAB or planned general anesthesia (GA), severe cardiovascular or cerebrovascular disease in mother, known fetal abnormality, anticipated excessive intraoperative blood loss, and patients with previous gastrointestinal surgery. Group A parturients received 400 ml of filtered water 2 h before surgery, while Group B parturients were given nonparticulate CHO drink (0.5 g/kg of Glucon-D powder containing 99.4% glucose) formulated in 400 ml of filtered water 2 h before surgery.

A thorough preanesthesia check-up was done before each surgery. Parturients were explained about the study being conducted, and written informed consent was taken from them. All parturients were advised to be nil orally for 8 h for solid before the scheduled time of surgery. Blood sugar was measured immediately before giving the drink, immediately before taking the patient to OR, and immediately postoperative. They were asked to consume the drink within

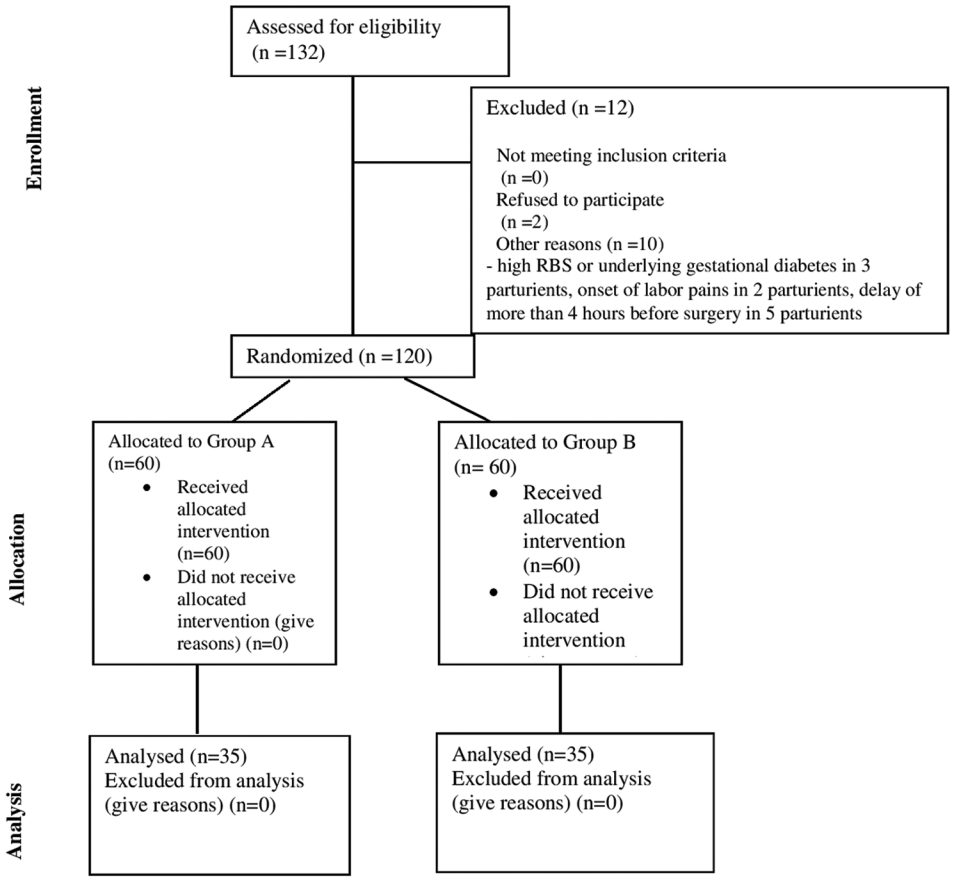

Figure 1: CONSORT flow diagram. CONSORT = consolidated standards of reporting trials

half an hour, 2 h before entering the operation theater (OT). This administration of either filtered water or CHO drink was supervised or monitored by the attending anesthesiologist. After administration of the oral drink, an 18 G intravenous cannula was secured and balanced salt solutions were initiated. Anxiety score was measured in all the parturients on a modified Beck anxiety scale[11] immediately before they entered OT. Hunger and thirst scores were also assessed before entry into OT on a numeric rating scale (NRS) by asking the parturient to rate hunger/thirst on a scale of 0–10, with 0 being no hunger or thirst and 10 being hungriest or thirstiest they had ever felt. Dominant hand grip strength was measured by taking the mean of three readings using an electronic dynamometer (Camry 200 lb or 90 kg digital hand dynamometer) immediately before the participants entered OR.

On arrival in OR, the parturient was positioned on the operating table in a supine position with a 30° left lateral tilt with a wedge under the right thigh. Standard ASA monitors were applied. After full aseptic precautions were taken and skin infiltration was performed with lignocaine hydrochloride 2% (w/v), a 26G Quincke's needle was inserted in L3–L4 or L4–L5 vertebral interspace. After confirmation of free flow of the cerebrospinal fluid, a total of 2.5 ml of drug comprising 2 ml (10 mg) of hyperbaric bupivacaine and 0.5 ml (25 μg) of fentanyl was injected intrathecally. The parturient was then catheterized with Foley catheter and 5 ml of urine was collected to assess the urinary ketone levels using reagent strips (Mission urinalysis reagent strips) or dipstick method, which was documented. At the end of the surgery, the surgical incision was infiltrated with 40 ml of 0.2% ropivacaine (isobaric). Postoperative analgesia regimen consisted of injection tramadol 1–1.5 mg/kg intravenously every 8 h, injection paracetamol 10 mg/kg intravenously six hourly infused over 15 min, and diclofenac patch 200 mg (Nupatch200) applied over the abdomen. Any breakthrough pain was treated by injection fentanyl 2 μg/kg intravenously. Postoperatively, the quality of recovery score was measured after 24 h of surgery using the ObsQoR-11 score.[12] Muscle strength was measured using hand dynamometer 24 h postoperatively.

Primary outcome was the measurement of urinary ketone levels using reagent strips as a marker of postoperative catabolic state. Secondary outcomes included the hunger and thirst scores recorded immediately before entering the operating

room, anxiety score on modified Beck's scale, dominant hand grip strength recorded using electronic dynamometer, and the quality of recovery score postoperatively recorded using the ObsQoR-11 score.

Sample size was estimated from the results of a previous study[13] using the urinary ketone levels as the parameter, which was the primary outcome of our study. This utility calculates the sample size required to estimate the proportion (18%) with a specified level of confidence and precision. The sample size was calculated as $n = (Z^2 \times P (1 - P))/E^2$ $n = 116$ (approximately), where Z = value from standard normal distribution corresponding to desired confidence level ($Z = 1.96$ for 95% confidence interval [CI]), P (0.18) is the expected true proportion, and E (0.07) is the desired precision. Thus, the total sample size taken was taken as 120 with 10% dropout rate.Therefore, a total of 132 parturients were recruited. The statistical analysis was carried out using IBM Statistical Package for Social Sciences (SPSS) statistical version 20. The analysis included frequency table, bar, pie chart, association of variables based on Chi-square and Fisher's exact test, and risk ratio estimates with 95% CI. All quantitative variables were estimated using measures of central location (mean and median) and measures of dispersion (standard deviation). Normality of data was checked by Kolmogorov–Smirnov test. For normally distributed data, the mean values were compared using the *t*-test and one-way analysis of variance (ANOVA). For non-normally distributed data, the medians were compared using the Mann–Whitney U test and the Kruskal–Wallis test. All statistical tests were seen at two-tailed level of significance ($P \leq 0.01$ and $P \leq 0.05$).

Results

A total of 120 parturients were randomly assigned equally to either of the two groups A and B [Figure 1] by computer-generated randomized codes contained in sealed, sequentially numbered envelopes. The demographic characteristics including age, height, weight, as well as the ASA physical status were well matched between the two groups [Table 1]. The urine ketone levels were positive (+1) in 8.3% parturients in group A and 1.7% parturients in group B, with a *P* value of 0.094 [Table 2]. The duration of fasting for solids as well as liquids was also comparable in both the groups. There was no statistically significant difference in the mean RBS in both the groups at all times during the study. The hunger and thirst scores were significantly higher in group A (5.63 ± 2.69) than in group B (4.20 ± 2.35), with a *P* value of 0.002 [Table 3]. The modified Beck's anxiety score was also significantly higher in group A (24.45 ± 8.33) in comparison to group B (19.40 ± 3.49), with a *P* value of 0.001 [Table 3]. The muscle strength was preserved in both the groups (*P* value- 0.827 preoperatively and 0.889 postoperatively). The vital parameters, that is, heart rate, systolic blood pressure, diastolic blood pressure, and oxygen saturation, were comparable in both the groups. The APGAR scores were also comparable for both the groups at 1 and 5 min. The quality of recovery score was significantly higher in group B (79.97 ± 13.12) than in group A (72.2 ± 13.60), with a *P* value of 0.002 [Table 4].

Table 1: Demographic characteristics of patients: Distribution of subjects according to age, height, and weight

	Water group		CHO group		*t*	*P*
	Mean	SD	Mean	SD		
Age	29.72	4.29	30.07	4.69	−0.427	0.670
Height (cm)	159.35	4.15	159.17	4.22	0.240	0.811
Weight (kg)	72.48	6.50	72.84	7.56	−0.278	0.781

CHO=carbohydrate, SD=standard deviation

Discussion

This study was designed to evaluate the role of preoperative oral CHO loading for the prevention of perioperative ketoacidosis as a marker of insulin resistance as well as the quality of recovery in the postoperative period in elective cesarean deliveries. We measured the urine ketone levels as the primary outcome with the help of reagent strips/dipstick method (Mission urinalysis reagent strips) at the time of catheterization of the bladder immediately before surgery.

The presence of urinary ketones was selected as the primary outcome because it was a simple, noninvasive test of metabolic state of the parturient. Other similar studies assessing the effectiveness of preoperative CHO drinks have used a hyperinsulinaemic clamp and the Homeostatic Model Assessment of insulin resistance HOMA-IR technique to detect perioperative insulin resistance.[14,15] However, these tests add to the expense of the patient as well as cause discomfort because of repeated needle pricks. Our study

Table 2: Urine ketone levels

Urine ketone levels	Water group		Carbohydrate group		Total	Chi-square value	*P*
	No. cases	%	No. cases	%			
1+	5	8.3%	1	1.7%	6	2.807	0.094
Negative	55	91.7%	59	98.3%	114		

Table 3: Hunger and thirst score and Beck's anxiety score

	Water group		CHO group		*Z*	*P*
	Mean	SD	Mean	SD		
Hunger and thirst score	5.63	2.69	4.20	2.35	3.107	0.002
Modified Beck's anxiety score	24.45	8.33	19.40	7.50	3.491	0.001

CHO=carbohydrate, SD=standard deviation

Table 4: Quality of recovery score

	Water group		Carbohydrate group		*Z*	*P*
	Mean	SD	Mean	SD		
Quality of recovery score	72.20	13.60	79.77	13.12	−3.103	0.002

SD=standard deviation

showed positive urine ketones in 8.3% parturients in the group that was given water (group A) and in 1.7% parturients in the group that received CHO drink (group B), with a *P* value of 0.094. RBS measured at all time points (before the drink, immediately preoperative, immediately postoperative) was similar in both the groups without any significant difference. Even after ingestion of CHO drink, RBS remained within normal range, which may be explained by the accelerated starvation state in the third trimester of pregnancy, giving evidence for the need of continued CHO supplementation and avoiding prolonged starvation which may be detrimental for the parturient and the fetus.

Thirst has been suggested to be the main determinant of preoperative discomfort, followed by anxiety, preoperative insomnia, and hunger.[16] In our study, hunger and thirst scores were significantly lower in the CHO group compared to the placebo group, reflecting an improvement in maternal comfort ahead of surgery. Modified Beck's anxiety scores[9] were also significantly lower in the CHO group, suggesting CHO drinks could play a beneficial role in ameliorating anxiety levels in parturients. Hand grip strength has been used as a marker of physical performance, indirectly measuring the muscle loss in the perioperative period due to prolonged NPO regimens. It has been measured in the clinical trials assessing the impact of CHO drinks in the perioperative period. Our study showed no effect of oral CHO loading on the muscle strength of the patient when compared to the placebo group, presumably due to shorter postoperative NPO status. As part of ERAS protocols, oral feeding was allowed early in the parturients after cesarean section.

Few studies have also shown that CHO supplementation improves cardiac function in the setting of surgical stress.[17,18] In our study, the hemodynamics of the two groups was well maintained with lesser requirement of vasopressors. This could be due to maintenance of intravascular volume with isobalanced salt solutions after NPO schedule was implemented. We found no significant difference in terms of adverse anesthetic outcomes, that is, perioperative episodes of hypotension, hypertension, bradycardia, nausea, and vomiting, between the groups. The quality of recovery score ObsQOR-11,[12] which includes various aspects of maternal well-being post-cesarean delivery, was significantly improved in the CHO group compared to the placebo or water group.

One of the limitations of our study is the limited number of parturients included. Large multicentric trials could help to establish the safety and efficacy of CHO loading before cesarean deliveries. Secondly, better and more sensitive biochemical indices, such as HOMA-IR and Homeostatic Model Assessment 2 HOMA 2 index, could be used to know insulin resistance among fasting parturients. These can, however, add to the expense as well as discomfort to the patient due to their invasive techniques. Thirdly, we did not address the length of hospital stay, which is an important outcome of the ERAS guidelines. So, in a follow-up study, the length of hospital stay may be included as part of the outcomes. There may also have been confounders that were not identified in this study, such as the nursing staff was not always the same due to change in their shift duty timings. Nonetheless, our results suggest that the preoperative administration of CHO-rich fluids is safe and improves the overall quality of recovery in pregnant patients for elective cesarean deliveries, and hence, they can be added safely to the routine protocols for elective uncomplicated cesarean deliveries of ASA II–III parturients.

Conclusions

From our results, we conclude that allowance of clear fluids or nonparticulate CHO drink up till 2 h before surgery is safe for the parturient. It may help to improve the preoperative indices of patient discomfort, including hunger, thirst, and anxiety. Quality of recovery with respect to postoperative maternal experience with pain, nausea, vomiting, and overall comfort improved with CHO loading. Thus, administration of oral CHO drinks before surgery is safe before elective cesarean deliveries and may have a positive influence on a wide range of perioperative markers of clinical outcome.

Key message

Oral carbohydrate drink is safe when administered 2 h before uncomplicated elective cesarean deliveries. It may have a positive influence on perioperative starvation ketosis.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Gillis C, Carli F. Promoting perioperative metabolic and nutritional care. Anesthesiology 2015;123:1455-72.
2. Toohill J, Soong B, Flenady V. Interventions for ketosis during labour. Cochrane Database Syst Rev 2008;2008:CD004230.
3. Thorell A, Nygren J, Ljungqvist O. Insulin resistance: A marker of surgical stress. Curr Opin Clin Nutr Metab Care 1999;2:69-78.
4. Angueira AR, Ludvik AE, Reddy TE, Wicksteed B, Lowe Jr WL, Layden BT. New insights into gestational glucose metabolism: Lessons learned from 21st century approaches. Diabetes 2015;64:327-34.
5. Freinkel N. Effects of the conceptus on maternal metabolism during pregnancy. In: Leibel BS, Wrenshall GA, editors. On the Nature and Treatment of Diabetes. Amsterdam: Excerpta Medica; 1965. p. 679-91.
6. Practice Guidelines for Obstetric Anesthesia: An updated report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia and the Society for Obstetric Anesthesia and Perinatology. Anesthesiology 2016;124:270-300.
7. Popivanov P, Irwin R, Walsh M, Leonard M, Tan T. Gastric emptying of carbohydrate drinks in term parturients before elective caesarean delivery: An observational study. Int J Obstetr Anesth 2020;41:29-34.
8. Van de Putte P, Vernieuwe L, Perlas A. Term pregnant patients have similar gastric volume to non-pregnant females: A single-centre cohort study. Br J Anaesth 2019;122:79-85.
9. Nygren J, Thorell A, Jacobsson H, Larsson S, Schnell PO, Hylén L, *et al*. Preoperative gastric emptying. Effects of anxiety and oral carbohydrate administration. Ann Surg 1995;222:728-34.
10. McMahon MO, Marsh H, Rizza R. Comparison of the pattern of postprandial carbohydrate metabolism after ingestion of a glucose drink or a mixed meal. J Clin Endocrinol Metab 1989;68:647-5.
11. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: Psychometric properties. J Consult Clin Psychol 1988;56:893-7.
12. Ciechanowicz S, Setty T, Robson E, Sathasivam C, Chazapis M, Dick J, *et al*. Development and evaluation of an obstetric quality-of-recovery score (ObsQoR-11) after elective Caesarean delivery. Br J Anaesth 2019;122:69-78.
13. Clark A, Litchfield K, Hannah S, Love C, Slade K, Lake K, *et al*. Pre-operative carbohydrate loading prior to elective caesarean delivery: A randomised controlled trial. Int J Obstet Anesth 2021;45:21-7.
14. Dock-Nascimento DB, de Aguilar-Nascimento JE, MagalhaesFaria MS, Caporossi C, Slhessarenko N, Waitzberg DL. Evaluation of the effects of a preoperative 2-hour fast with maltodextrine and glutamine on insulin resistance, acute-phase response, nitrogen balance, and serum glutathione after laparoscopic cholecystectomy: A controlled randomized trial. J Parenter Enteral Nutr 2012;36:43-52.
15. Soop M, Nygren J, Thorell A, Weidenhielm L, Lundberg M, *et al*. Preoperative oral carbohydrate treatment attenuates endogenous glucose release 3 days after surgery. Clin Nutr 2004;23:733-41.
16. Madsen M, Brosnan J, Nagy VT. Perioperative thirst: A patient perspective. J Peri Anesth Nurs 1998;13:225-8.
17. Quiros G, Ware J. Cardiovascular and metabolic alterations caused by hemorrhage in fed and starved rats. Acta Physiol Scand 1983;117:397-403.
18. Kotfis K, Jamioł-Milc D, Skonieczna-Żydecka K, Folwarski M, Stachowska E. The effect of preoperative carbohydrate loading on clinical and biochemical outcomes after cardiac surgery: A systematic review and meta-analysis of randomized trials. Nutrients 2020;12:3105.