**Effects of Preoperative Glucose (Dextrose/Carbohydrate) Administration via Intravenous versus Oral Route on Recovery Outcome in the Post-anesthesia Care Unit**

Mitra Jablameli, Behzad Nazemroaya*, Ladan Salehfard

**Background:** Human body exposure to any trauma, such as surgical procedures stimulates neurohumoral and catabolic responses. This process includes; increased metabolism of proteins, carbohydrates, and lipids along with water and sodium retention, resistance to insulin, and furthermore, increased levels of blood sugar. One of the factors that has been assumed to influence postoperative complications is preoperative fasting duration.

**Methods:** In this double-blind, randomized clinical trial, 90 patients aged 18 to 70 years, referred for elective surgery were randomly allocated to three groups of 30. Group A (IV-CHO): Within 6 hours of fasting, this group was treated with one gram per kilogram of carbohydrate dissolved in 50 ml of normal saline and then injected. Group B (Oral-CHO): Within 6 hours of fasting, this group was treated with one gram per kilogram of carbohydrate dissolved in 50 ml of normal saline and then administered orally. Group C (Ni-CHO): Within 6 hours of fasting, 50 ml of normal saline was administrated orally in this group. Patients were requested to score their pain following the surgical procedure using a scale of 0-10 scoring (VAS). Besides, the [need for] analgesics before [transfer] to the general ward, at the end of recovery stay were recorded as well.

**Results:** According to the results of our study, evaluation (and) comparison of VAS scores was significantly different among groups prior to the surgical procedure (p=0.004). Postoperative pain assessments showed significant difference among groups (p=0.002). Scheffe test showed significantly less pain score in the IV-CHO group than the oral-CHO (p=0.029) and control group (p=0.010).

**Conclusion:** Preoperative use of carbohydrate whether intravenously or orally could efficiently affect postoperative adverse effects in a positive manner while some aspects were not statistically changed to a more desirable status.

**Keywords:** Intravenous carbohydrate; Oral carbohydrate; Post-anesthesia care unit

Human body exposure to any trauma such as surgical procedures stimulates neurohumoral and catabolic responses [1]. This process includes increased metabolism of proteins, carbohydrates and lipids along with water and sodium retention, resistance to insulin, and furthermore increased levels of blood sugar [2-3].

Varieties of factors have been assumed to influence postoperative complications such as type of the surgery, type, and technique of anesthesia, preoperative fasting duration and perioperative bleeding [4-5]. The technique of the surgery is among the estimated factors influencing postoperative related adverse effects such as resistance to insulin, nausea, vomiting, pain and duration of hospitalization. Therefore, several studies have been conducted and are in progress by the anesthesiologists to minimize mentioned complications [6].

Preoperative 6-8 hours of fasting is an old theory since 1994 to prevent gastric contents aspiration during anesthesia [7]. This is while further evaluations revealed that postoperative insulin resistance and complications related to hunger and water retention are directly associated with this long time of fasting [8].

Preoperative infusion of carbohydrates could successfully reduce dehydration related adverse effects and insulin resistance, a main underlying etiology for catabolic state of surgical procedure [8]. Further evaluations presented that preoperative oral carbohydrate within 2 hours prior to the surgical procedure not only can reduce operation related complications including thirst, hunger, headache, nausea and vomiting but has no adverse effects due to gastric content aspiration as the transit time of this solution is less than two hours [9-10].

Most of the studies have assessed efficacy of carbohydrate administration prior to the surgical procedure regardless of the administration way. The current study has aimed to assess effects of oral and intravenous carbohydrate and fasting on postoperative adverse effects and then compare these three approaches.
Methods

This is a prospective double-blinded randomized clinical trial (RCT) conducted on 90 patients referred for elective surgeries to Alzahra Hospital, affiliated to Isfahan University of Medical Sciences, from April 2016 to August 2017.

Inclusion criteria: 18 to 70 years old, ASA class I or II who presented their willingness for participation in the current study were included.

Non-inclusion criteria: Severe respiratory disease, severe cardiovascular disease, Body mass index above 30 kg/m2, diabetes mellitus, gastroesophageal reflux and any history of post operation nausea and vomiting or any history of motion sickness.

Exclusion criteria: Vomiting after oral carbohydrate administration, any change in the anesthesia technique and over 10 hours of fasting.

The study protocol was approved by Isfahan University of Medical Sciences Ethic Committee (No.IR.MULMED.REC.1398.010). Thereafter, the study protocol was thoroughly presented to the participants and they were requested to sign their written consent form of participation in this study.

Study population were selected through convenient sampling until achieving the goal number of participants. Then participants were randomly divided into three groups using Random Allocation software. Therefore each patient was provided with a specific number allocating him/her to each of the groups.

Participants were blinded to the type of approach used for him/her. In addition, the anesthesiologists who assessed postoperative complications were different from the person presented at the surgery and was blinded to the type of the remedy used for each of the patients. Study population was randomly allocated to three groups; all of the participants were treated with injection of 10 cc per kilograms of a serum containing normal saline in one third proportions and dextrose water 5% in two third remained proportions during fasting. Group A (IV-CHO): Within 6 hours of fasting, this group was treated with one gram per kilogram of carbohydrate dissolved in 50 ml of normal saline and then injected. Group B (Oral-CHO): Within 6 hours of fasting, this group was treated with one gram per kilogram of carbohydrate dissolved in 50 ml of normal saline and then injected. Group C (Ni-CHO): Within 6 hours of fasting, 50 ml of normal saline was administered orally. Group C (Ni-CHO): Within 6 hours of fasting, 50 ml of normal saline was administered orally in this group. Prior to the anesthesia induction, preoxygenation was performed for 5 minutes using mask containing 100% oxygen. Then anesthesia was induced for patients using 5 mg/kg of sodium thiopental and 0.15 mg/kg of atracurium. The anesthesia induction went on using 50% oxygen and 50% dinitrogen oxide (N2O). Gathered data in the checklist included age, gender, weight, duration of the surgery, duration of recovery stay, nausea and vomiting incidence during the recovery stay.

Furthermore, presence or absence of thirst, hunger, anxiety and fatigue prior to and following the surgical procedure were entered as well. In addition, patients were requested to score their pain following the surgical procedure using 0-10 scoring visual analogue scale (VAS) [9]. Besides, requirement of analgesics before transmission to the general ward, at the end of recovery stay were recorded as well.

Obtained data were analyzed using SPSS-20 (IBM; Chicago; The United States). Descriptive information was presented in mean and percentages. For analytics, Chi-square tests, ANOVA, McNemar test and ANOVA were used. P-value of less than 0.05 was considered as significant level.

Results

In this study 90 patients divided in three equal groups of 30-member including IV-CHO, oral-CHO and control group were evaluated. Mean age of study population was 49.92±16.91 years with gender distribution of 62.2% of females and 37.8% of males.

Based on (Table 1), three groups were not statistically different regarding demographics including age (p=0.52), gender distribution (p=0.13), weight (p=0.90) and height (p=0.18). Comparison of three groups regarding recovery stay revealed significant difference as group oral-CHO presented significant less duration of recovery time in comparison to group IV-CHO (p=0.023). Two by two comparison of other groups presented no statistical difference (p>0.05) (Table 1).

| Table 1- Comparison of demographic information and recovery time in three groups' participants (intravenous carbohydrate (IV-CHO), oral-carbohydrate (Oral-CHO) and control group (Ni-CHO)) |
| Variable | Group IV-CHO | Group Oral-CHO | Group Ni-CHO | P-Value | Test |
| Gender *(female/male)* | 16/14 | 23(7) | 17(13) | 0.13 | Chi Squared |
| Age ** | 52.80 (18.13) | 48.53 (17.85) | 48.43 (14.75) | 0.52 | ANOVA |
| Weight ** | 79.70 (20.32) | 72.03 (7.50) | 77.77 (19.10) | 0.18 | ANOVA |
| Height ** | 167.87 (7.33) | 167.03 (7.51) | 167.77 (8.24) | 0.90 | ANOVA |
| Recovery stay ** | 74.83 (23.39) | 58.57 (15.44) | 72.20 (25.08) | 0.013 | ANOVA |

* N, ** mean (std)

Evaluation Comparison of VAS scores was significantly different among groups prior to the surgical procedure (p=0.004). Postoperative pain assessments showed significant different among groups (p=0.002). Scheffe test showed significant less pain score in IV-CHO group than oral-CHO (p=0.029) and controls (p=0.010). Comparison of pain scores prior to the surgery with VAS scores following the surgery presented no statistical difference (p=0.054) (Table 2).

Based on findings prior to and after surgical procedure, the highest rate of all variables during recovery stay was found in the control group. Prior to the surgery, the least positive responses to nausea (10%), vomiting (6.7%), thirst (20%), hunger (13.3%) and anxiety (30%) were found in oral-CHO.
group while antiemetic agent requirement (0%) and analgesics requirements (6.7%) and fatigue (3.3%) were presented by IV-CHO. Further evaluations on postoperative recovery stay factors showed the least nausea (10%),

antiemetic agent use (0%), analgesics use (23.3%) and fatigue (10%) in IV-CHO. Other variables were presented in the least distribution in oral-CHO group (Table 3).

Table 2 - Comparison of pain score among participants of three groups (intravenous carbohydrate (IV-CHO), oral-carbohydrate (Oral-CHO) and control group (Ni-CHO))

| Variable     | Group IV-CHO | Group Oral-CHO | Group Ni-CHO | P-Value | P-Value* |
|--------------|--------------|----------------|--------------|---------|---------|
|              | Before       | after          |              | t-paired | difference mean |
| Vas mean(std) | 2.27±.98     | 2.83±1.74      | 0.11         |         |         |
|              | 3.13±1.33    | 4.73±1.72      | <0.001       | 0.054   |         |
|              | 3.27±1.36    | 3.97±1.49      | 0.029        |         |         |
| P-Value      | 0.004*       | 0.002**        |              |         |         |

Table 3- Comparisons of three groups regarding recovery stay variables (intravenous carbohydrate (IV-CHO), oral-carbohydrate (Oral-CHO) and control group (Ni-CHO))

| Variable     | Group IV-CHO | Group Oral-CHO | Group Ni-CHO | P-Value (McNemar test) |
|--------------|--------------|----------------|--------------|------------------------|
| Nausea       |              |                |              |                        |
| (Yes/No)     |              |                |              |                        |
| P-Value      |              |                |              |                        |
| Vomit        |              |                |              |                        |
| (Yes/No)     |              |                |              |                        |
| P-Value      |              |                |              |                        |
| Antiemetic agents |        |                |              |                        |
| (Yes/No)     |              |                |              |                        |
| P-Value      |              |                |              |                        |
| Analgesics   |              |                |              |                        |
| (Yes/No)     |              |                |              |                        |
| P-Value      |              |                |              |                        |
| Thirst       |              |                |              |                        |
| (Yes/No)     |              |                |              |                        |
| P-Value      |              |                |              |                        |
| Hunger       |              |                |              |                        |
| (Yes/No)     |              |                |              |                        |
| P-Value      |              |                |              |                        |
| Anxiety      |              |                |              |                        |
| (Yes/No)     |              |                |              |                        |
| P-Value      |              |                |              |                        |
| Fatigue      |              |                |              |                        |
| (Yes/No)     |              |                |              |                        |
| P-Value      |              |                |              |                        |
Discussion

Surgical procedures pose catabolic state, insulin resistance and dehydration that may be accompanied with postoperative complications such as nausea, vomiting, increased blood sugar, hunger, thirst and anxiety. Various anesthetic agents and techniques have been recommended in order to decrease mentioned postoperative complications. There are studies presenting that long term fasting may deteriorate these conditions [11-12].

In the current study, we tried to compare three approaches of intravenous, oral carbohydrate and carbohydrate free regimens on postoperative associated complications. Participants of the groups in our study were similar regarding age, gender distribution, weight and height eliminating probable role of demographics on the eventual outcomes of our study.

Comparison of recovery stay among three groups revealed that patients under oral carbohydrate therapy prior to surgery had shorter recovery stay in comparison to other groups. A systematic review by Bilku et al. tried to assess advantages of oral preoperative carbohydrate use on surgical procedure postoperative complications. They presented improved recovery duration in all of the surgical procedures whether minor or major surgeries [13]. Their findings were confirmed by other authors conducting on varieties of surgical procedures [6] while Lauwick et al. presented contrary findings in their study comparing advantages of preoperative oral carbohydrate versus placebo following thyroidectomy [9]. This benefit was presented by Kiellhorn et al. assessing efficacy of intravenous carbohydrate as well [14].

Postoperative pain assessment showed significant less pain complaint among patients under intravenous carbohydrate treatment in comparison to other groups. Furthermore, patients allocated to intravenous carbohydrate therapy presented no statistical change in their pain while comparing their score prior to the surgical procedure with post operation. It is while two other groups presented significant increase in their pain sensation postoperatively. Neslihan Yılmaz et al. conducted a case-control study and declared superiority of oral-CHO to fasting regarding pain assessment [8] confirmed by other studies as well [15]. This is while there are numerous studies presenting considerable change in pain scores following oral preoperative CHO use [16-17]. Kaska et al. in 2010 [15] and also Haasel et al. in 2001 [18] conducted their studies assessing effectiveness of preoperative intravenous CHO on pain relief following colorectal surgery and laparoscopic cholecystectomy and presented no considerable change in pain scores as compared either with placebo treated group or with oral-CHO treated group.

Nausea, vomiting, hunger, anxiety and fatigue as the postoperative complications were significantly better controlled by CHO administration whether intravenous or orally as compared to fasting. These findings were confirmed by numerous studies [6, 19-21] while some opposed our findings [22-23].

Conclusion

Based on findings of our study, preoperative use of carbohydrate whether intravenous or orally could efficiently affect postoperative adverse effects in positive manner while some aspects were not statistically changed to better statuses. Findings of the current study were consistent with some of the previous papers while in contrast to others. In general, consideration of preoperative use of carbohydrate is recommended as its benefits. Further evaluations are strongly recommended.

References

1. Wolf AR. Effects of regional analgesia on stress responses to pediatric surgery. Paediatr Anaesth. 2012; 22(1):19-24.
2. Haga Y, Wada Y, Takeuchi H, Ikejiri K, Ikenaga M, Kimura O. Evaluation of modified estimation of physiologic and surgical stress in gastric carcinoma surgery. Gastric cancer. 2012; 15(1):7-14.
3. Junı RP, Ducksck HJ, Vanhoutte PM, Virmani R, Moens AL. Oxidative stress and pathological changes after coronary artery intervention. Am Coll Cardiol. 2013; 61(14):1471-81.
4. Liu J, Ma C, Elkasabany N, Fleisher LA, Neuman MD. Neuraxial anesthesia decreases post-operative systemic infection risk compared to general anesthesia in knee arthroplasty. Anesth Analg. 2013; 117(4):1010-6.
5. Bayazıt EG, Karaşlan K, Ozturan K, Serin E, Kocgoğlu H. Effect of epidural levobupivacaine and levobupivacaine with fentanyl on stress response and postoperative analgesia after total knee replacement. Int J Clin Pharmacol Ther. 2013; 51(8):652-9.
6. Çeliksular MC, Saracoğlu A, Yentür I. 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(3):117-23.
7. Ljungqvist O, Thorell A, Gunia M, Häggborg T, Efendic S. Glucose infusion instead of preoperative fasting reduces postoperative insulin resistance. J Am Coll Surg. 1994; 178(4):329-36.
8. Yılmaz N, Çekmén N, Bilgin F, Ertan E, Özhan MÖ, Coşar A. Preoperative carbohydrate nutrition reduces postoperative nausea and vomiting compared to preoperative fasting. Journal of research in medical sciences. J Res Med Sci. 2013; 18(10):827-32.
9. Lauwick S, Kaba M, Maweja S, Hamoir E, Joris JL. Effects of oral preoperative carbohydrate on early postoperative outcome after thyroidectomy. Acta Anaesthesiol Belg. 2009; 60(2):67-73.
10. Doo AR, Hwang H, Ki MJ, Lee JR, Kim D-C. Effects of preoperative oral carbohydrate administration on patient well-being and satisfaction in thyroid surgery. Korean J Anesthesiol. 2018; 71(5):394-400.
11. Akbarzadeh M, Eftekhar MH, Shafa M, Alipour S, Hassanzadeh J. Effects of a New Metabolic Conditioning Supplement on Perioperative Metabolic Stress and Clinical Outcomes: A Randomized, Placebo-Controlled Trial. Iran Red Crescent Med J. 2016; 18(1):e26207.
12. Doo AR, Hwang H, Ki MJ, Lee JR, Kim DC. Effects of preoperative oral carbohydrate administration on patient well-being and satisfaction in thyroid surgery. Korean J Anesthesiol. 2018; 71(5):394-400.
13. Bilku D, Denisson A, Hall T, Metcalfe M, Garcea G. Role of preoperative carbohydrate loading: a systematic review. The Annals of The Royal College of Surgeons of England. 2014; 96(1):15-22.
14. Bangbde Kielhorn BA, Senagore AJ, Aasegirsson T. The benefits of a low dose complex carbohydrate/citrulline electrolyte solution for preoperative carbohydrate loading: focus on glycemic variability. The American Journal of Surgery. 2018; 215(3):373-6.
15. Kaška M, Grossmanová Tá, Havel E, Hyšpler R, Petrová Z, Brtko M, et al. The impact and safety of preoperative oral or intravenous carbohydrate administration versus fasting in colorectal surgery—a randomized controlled trial. Wiener klinische Wochenschrift. 2010; 122(1-2):23-30.
16. Bisaizard T, Kristiansen V, Hjortso N, Jacobsen L, Rosenberg J, Kehlet H. Randomized clinical trial comparing an oral carbohydrate beverage with placebo before laparoscopic cholecystectomy. British journal of surgery. 2004; 91(2):151-8.
17. Henriksen M, Hessov I, Dela F, Vin Hansen H, Haraldsted V, Rodt SA. Effects of preoperative oral carbohydrates and peptides on postoperative endocrine response, mobilization, nutrition and muscle function in abdominal surgery. Acta anaesthesiologica
18. Hausel J, Nygren J, Lagerkranser M, Hellström PM, Hammarqvist F, Almström C, et al. A carbohydrate-rich drink reduces preoperative discomfort in elective surgery patients. Anesthesia & Analgesia. 2001; 93(5):1344-50

19. Hausel J, Nygren J, Thorell A, Lagerkranser M, Ljungqvist O. Randomized clinical trial of the effects of oral preoperative carbohydrates on postoperative nausea and vomiting after laparoscopic cholecystectomy. British Journal of Surgery: Incorporating European Journal of Surgery and Swiss Surgery. 2005; 92(4):415-21.

20. Çakar E, Yilmaz E, Çakar E, Baydur H. The Effect of Preoperative Oral Carbohydrate Solution Intake on Patient Comfort: A Randomized Controlled Study. J Perianesth Nurs. 2017; 32(6):589-599.

21. Ömer Faruk ŞAVLUK1, Mehmet Ali KUŞCU1, FG, MEG, ERKILINÇ1 A, DÇ, et al. Do preoperative oral carbohydrates improve postoperative outcomes in patients undergoing coronary artery bypass grafts? Turkish Journal of Medical Sciences 2017; 47:1681-6.

22. Kehlet TBBKNCRLHJSJRJH. Randomized clinical trial comparing an oral carbohydrate beverage with placebo before laparoscopic cholecystectomy. British Journal of Surgery. 2004; 91(2):151-8.

23. Mathur SI, Plank LD, McCall JL, Shapkov P, McIlroy K, Gillanders LK, et al. Randomized controlled trial of preoperative oral carbohydrate treatment in major abdominal surgery. Br J Surg. 2010; 97(4):485-94.