Nutrición Hospitalaria

Nutr Hosp. 2014;29(3):681-686
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original / *Otros*

# Safe intake of an oral supplement containing carbohydrates and whey protein shortly before sedation to gastroscopy; a double-blind, randomized trial

José Eduardo de Aguilar-Nascimento[1,2], Cervantes Caporossi[1], José Sebastião Metelo[1], Guilherme Henrique Tanajura[1], Mariana Canevari-de-Oliveira[1] and Rodrigo da Cunha Costa[1]

*[1]All authors are from the Department of Surgery, Federal University of Mato Grosso. Cuiaba. Brazil. [2]Medical School, University of Varzea Grande. UNIVAG. Brazil.*

**Abstract**

***Objective:*** **To investigate the gastric emptying of an oral supplement containing carbohydrate plus whey protein drunk before sedation for gastroscopy.**

***Methods:*** **This is a randomized double-blind trial including adult patients (ages 18-65) with a chief complaint of epigastric burning and who were candidates to elective gastroscopy. After overnight fast subjects were randomized to drink 200 mL of an oral nutritional supplement containing maltodextrine in addition to whey protein 150 to 210 min before the gastroscopy (intervention group, n = 12) or to undergo the endoscopic procedure with no supplement (control group, n = 12). The residual gastric volume (RGV) suctioned and measured during the exam was the main endpoint of the study.**

***Results:*** **There were no complications during all exams. The median (range) fasting time was greater (P < 0.001) in control group (770 min, ranging from 660-917 min) than in the study group (175min ranging from 150 to 210 min). The median (range) RGV was similar in between the two groups (control group: 25 (10-70) mL *versus* intervention group: 10 (0-100) mL; p = 0.32).**

***Conclusion:*** **Gastric emptying 150-210 min after the ingestion of an oral supplement containing carbohydrate plus whey protein is similar to an overnight fasting condition. Although limited by the number of cases, the sedation for endoscopic procedures is safe with this fasting protocol.**

(*Nutr Hosp.* 2014;29:681-686)

**DOI:10.3305/nh.2014.29.3.7161**

Keywords: *Residual gastric volume. Preoperative fasting. Whey protein. Randomized trial.*

**Correspondence:** José Eduardo de Aguilar-Nascimento.
Rodovia Helder Candia, 2755.
Condominio Country, casa 15.
78048-150 Cuiabá. Mato-Grosso. Brazil.
E-mail: aguilar@terra.com.br

Recibido: 3-IX-2013.
1.ª Revisión: 22-XI-2013.
Aceptado: 1-XII-2013.

**INGESTA SEGURA DE UN SUPLEMENTO ORAL QUE CONTIENE HIDRATOS DE CARBONO Y PROTEÍNAS DE SUERO DE LECHE POCO ANTES DE SEDACIÓN PARA ENDOSCOPIA; UN ENSAYO DOBLE CIEGO Y ALEATORIZADO**

**Resumen**

***Objetivo:*** **Investigar el vaciado gástrico de un suplemento oral que contiene hidratos de carbono, más proteínas de suero de leche tomado antes de la sedación para endoscopia.**

***Método:*** **Se trata de un estudio doble ciego aleatorizado, que incluyó pacientes adultos (18-65 años de edad) por presentar epigastralgia y que eran candidatos a gastroscopia electiva. Después de una noche de ayuno los pacientes fueron asignados aleatoriamente para tomar 200 ml de un suplemento nutricional oral que contiene maltodextrina y proteína de suero de leche, de 150 a 210 minutos antes de la sedación, para gastroscopia (grupo de intervención, n = 12) o continuar en ayuno para el procedimiento endoscópico (grupo control, n = 12). El volumen gástrico residual (RGV) aspirado y medido durante el examen fue la variable de evaluación principal del estudio.**

***Resultados:*** **No hubo complicaciones durante los exámenes. El tiempo medio de ayuno (rango) fue mayor (P <0,001) en el grupo control (770 min, 660 - 917 min) que en el grupo de estudio (175 min, 150-210 min). El RGV (mediana y rango) fue similar entre los dos grupos (grupo control: 25 (10-70) ml y grupo de intervención: 10 (0-100) ml, p = 0,32).**

***Conclusión:*** **El vaciado gástrico 150-210 minutos después de la ingestión de un suplemento oral que contiene hidratos de carbono y proteína de suero de leche es similar al ayuno tradicional durante toda la noche. Aunque limitado por el numero de casos, la sedación para procedimiento endoscopico es segura con este protocolo de ayuno.**

(*Nutr Hosp.* 2014;29:681-686)

**DOI:10.3305/nh.2014.29.3.7161**

Palabras clave: *Ayuno preoperatorio. Proteína de suero de leche. Volumen gástrico residual. Estudio controlado aleatorizado.*

## Introduction

The main reason for the traditional prescription of 6-8 hours (h) of preoperative fasting for either gastroscopy or elective operations is to reduce the volume and acidity of stomach contents, thus decreasing the risk of regurgitation and aspiration recognized as Mendelson's syndrome[1]. In the 1980s, it was already known that gastric emptying of water and other noncaloric fluids followed an extremely fast exponential curve in volunteers[2,3]. Various randomized controlled studies[4-6] and a meta-analyse[7] have consistently documented that oral intake of water and other clear fluids up to 2 h before induction of anesthesia does not increase gastric volume or acidity. The use of carbohydrate (CHO)-rich beverage in the immediate preoperative period is not only safe, but may also reduce the catabolic stress response, nausea, vomiting, and thus enhance postoperative recovery[8,9].

Several studies have also shown the nutritional qualities of soluble whey proteins. Whey protein contains a high level of essential amino acids especially branched-chain amino acids[10]. The branched-chain amino acids (leucine, isoleucine, and valine) are rapidly used by skeletal muscle during stress and highly stimulate protein synthesis. In addition, they are precursors of endogenous synthesis of glutamine, the main energy source for enterocytes[11,12]. Whey protein has also been described as an excellent source of cysteine, a precursor of glutathione synthesis, which acts as an endogenous antioxidant. Moreover, whey protein has a high degree of digestibility and rapid absorption in the small bowel[10-12].

However, only a few studies have investigated the gastric emptying of formulas containing carbohydrate combined with a nitrogen source such as protein or amino acids[13,14]. This is most important because these formulas could be prescribed 2-3 h before either gastroscopy or surgical procedures needing light sedation or general anesthesia[15,16]. We thought that gastroscopy would be an excellent tool to verify the contents of the gastric camera and assess the safety in the use of such drinks before general anesthesia for elective operations. Moreover the visualization of the entire gastric camera and the duodenum is essential for providing excellence in diagnostic and therapeutic endoscopy and data are most necessary on this matter. Thus, the aim of the study was to investigate the residual gastric volume (RGV) found during a gastroscopy 150-210 minutes after the ingestion of a carbohydrate plus whey protein enriched-drink.

## Materials and methods

This was a randomized, double-blind, clinical study carried out at Gastroclinica, Cuiaba, Brazil. The study was approved by the Julio Muller Hospital Research Ethics Committee registered under number 194294/CEP-HUJM/13 and is in accordance with the ethics principals set out in the Helsinki Declaration (2000), and meets Brazilian national legal specifications. The study was registered in ClinicalTrails.gov under the number NCT01828645.

Adult patients scheduled to upper digestive endoscopy due to chief complaint of epigastric burning were eligible for inclusion in this trial. Exclusion criteria were: decline to participate, American Society of Anesthesiologists (ASA) score above II, diabetes mellitus, pregnancy, history of renal or hepatic failure, gastro-esophageal reflux, acute cholecystitis, use of corticosteroids up to 6 months previously, use of any prokinetic drug up to 6 weeks previously, and any noncompliance or violation on the assigned protocol of preoperative fasting. Patients who ingested the drink either less than 150 minutes (min) or more than 210 min before of the exam were also excluded.

### Randomization

A staff not involved with the study was in charge of the randomization process. A computer program generated random numbers to assign patients to the two groups. Patients were randomized to receive either an overnight fast (minimum of 8 hours; control group) or fast for solids for the same period and drink 200 milliliters (mL) of an oral nutritional supplement (Composition per 200 mL: 0g lipids; 8 g whey protein; 67g carbohydrate being 88% maltodextrin and 12% sacharose; osmolality: 680 mOsm/L; and total energy: 300 kcal; Fresubin Jucy, Fresenius Kabi, Brazil) 150-210 minutes before the exam (intervention group).

### Preoperative protocol

All patients received both oral and written information about the protocol at the outpatient clinic. Gastroscopies were scheduled to begin at 8:30 AM. The evening before operation patients were allowed to ingest solid food until 11:00 PM. The patients belonging to the intervention group received written instructions to ingest the above beverage at 6:00 AM (200 mL), and be at the endoscopy unit at 7:00 AM.

### Endoscopic procedure

All endoscopic procedures were performed by one board-certified endoscopist (JSM) who was blind to the study design. Sedation was performed by a certified anesthesiologist who was also blind to the investigation with a bolus intravenous injection of 2 mL of lidocaine hydrochloride (Astra Zeneca, Sao Paulo, Brazil) in association of 100 to 150 mg of propofol before endoscopy. Digital oximetry was carried out throughout the procedure. Patients were positioned in left lateral recumbent throughout the endoscopy. A

flexible electronic videoendoscope (EG2770K; Pentax Corporation, Tokyo, Japan), 9 mm in outer diameter, was used for conventional and sedated endoscopy, according to a standard protocol recommended by the manufacturer. Special attention was done for the RGV. All gastric fluid was thoroughly suctioned through an endoscope side port, measured to the nearest mL and recorded.

### Outcome variables

The main endpoint of the study was the RGV. Secondary endpoint was the judgment of the endoscopist on how confident he was to visualize all the gastric and duodenal mucosa. The satisfaction of the patient with the exam was also registered. Satisfaction with the protocol fast was evaluated by patients 2-4 weeks after the gastroscopy using a four-point scale (1, very good; 2, good; 3, moderate; 4, not satisfactory) after the question: "please rate your level of satisfaction with the fasting protocol?".

### Statistical analysis

The sampling calculation was based on a previous study which reported that 80% of patients had less than 25 mL of RGV after either an overnight fast or 2-3 h after the ingestion of a carbohydrate alone or in addition to peptides enriched-drink[16]. A quantity of 12 cases in each study arm was judged to be sufficient to ensure 80% power (beta error) and 5% significance (alpha error) expecting a difference of a maximum of 25% in the RGV between the groups. Correlation between the fasting time and the RGV was done with the Pearson test. Comparison of RGV between the two groups was done by the Mann-Whitney test. A 5% level was adopted for significance. Data was presented as median (interquartile range) and range. All the calculations were made on a computer using the Statistical Package for the Social Sciences (SPSS) for Windows 11. 0.

## Results

There were no complications during the endoscopic procedures. The two groups had homogeneous demographics and clinical characteristics (table I). Overall patient satisfaction was excellent, with no difference between groups. The gastroscopist reported that in all cases, the aspiration of gastric contents was very easy and did not increase the time of the procedure. In all cases the gastroscopist was confident on his diagnosis, meaning that he had seen the entire gastric cavity, and the first portions of the duodenum. All patients had an endoscopic diagnosis of gastritis. Figure 1 shows the flowchart of the study. Forty six patients were eligible and 11 declined to participate. From the 35 randomized subjects 11 were subsequently excluded due to either current use of prokinetic agents (4 in control group) or noncompliance with the protocol (7 in intervention group). In all noncompliance cases the individuals ingested the drink out of the range of the protocol (less than 150 minutes or more than 210 minutes from the exam). No more patients were excluded and the analysis was done in 12 patients in each group. The median (range) fast period was greater ($p < 0.001$) in control group (770 min, ranging from 660-917 min) than in the study group (175 min ranging from 150 to 210 min).

**Table I**
*Demographics and clinical characteristics of the patients in the two groups. Data are the mean (range) or the number of cases (%)*

| *Variable* | *Control group* | *Intervention group* | *p* |
|---|---|---|---|
| Sex (n,%) | | | 1.00 |
| Female | 10 | 9 | |
| Male | 2 | 3 | |
| Age (years) | 40 (23-53) | 35 (21-49) | 0.88 |
| Weight (kg) | 72 (53-96) | 70 (52-97) | 0.83 |
| Body mass index (kg/m$^2$) | 27 (19-35) | 24 (21-38) | 0.89 |
| ASA* score | | | |
| I | 11 | 10 | |
| II | 1 | 2 | |

*, American Society of Anesthesiologists.

The findings of RGV in the two groups can be seen in figure 2. There was no correlation between the fasting time and the RGV ($R = 0.10$; $p = 0.66$). Only two cases in each group had a RGV of 60 mL or above (2 cases with 60 mL in each group, one case with 70mL in control group, and one case with 100 mL in the intervention group). A median (interquartile range) of 25 (27) ranging from 10 to 70 mL was found in the control group and 10 (55) ranging from 0 to 100 mL in the intervention group ($p = 0.32$).

## Discussion

Modern guidelines of various societies of anesthesiologists, and perioperative care now recommend 6-8h fast for solids and allow clear fluids or beverages containing carbohydrate up to 2h before surgery[17-19]. The findings of this randomized trail showed that the abbreviation of fasting up to 2 hours with 200 mL of an oral nutritional supplement containing whey protein along with carbohydrate was safe and was not associated with complications during the sedation for upper digestive endoscopy. Furthermore the RGV was similar in either fasted patients or in the group treated with abbreviation of the procedure fasting to 150-210 minutes. Moreover there was no significant correlation between time of fasting and RGV. These data suggest that this type of nutritional supplement can safely be

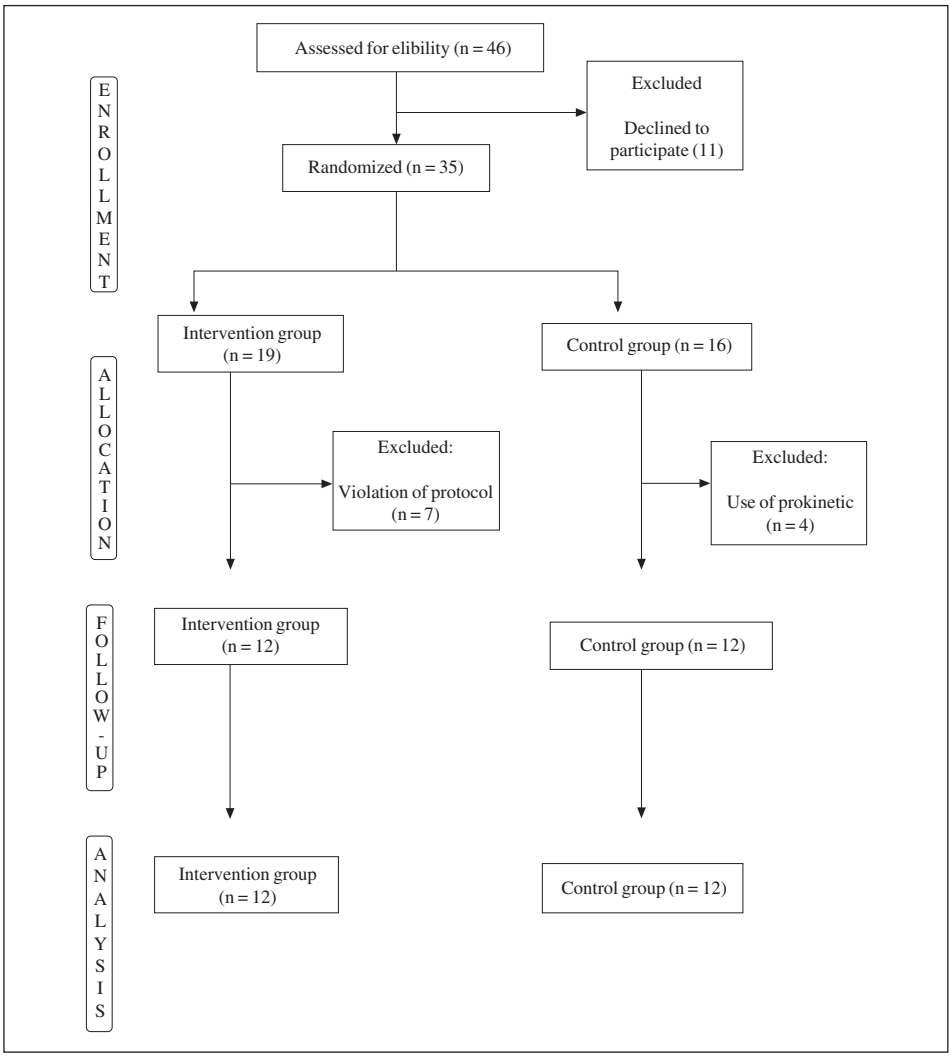


*Fig. 1.—Flowchart of the study.*

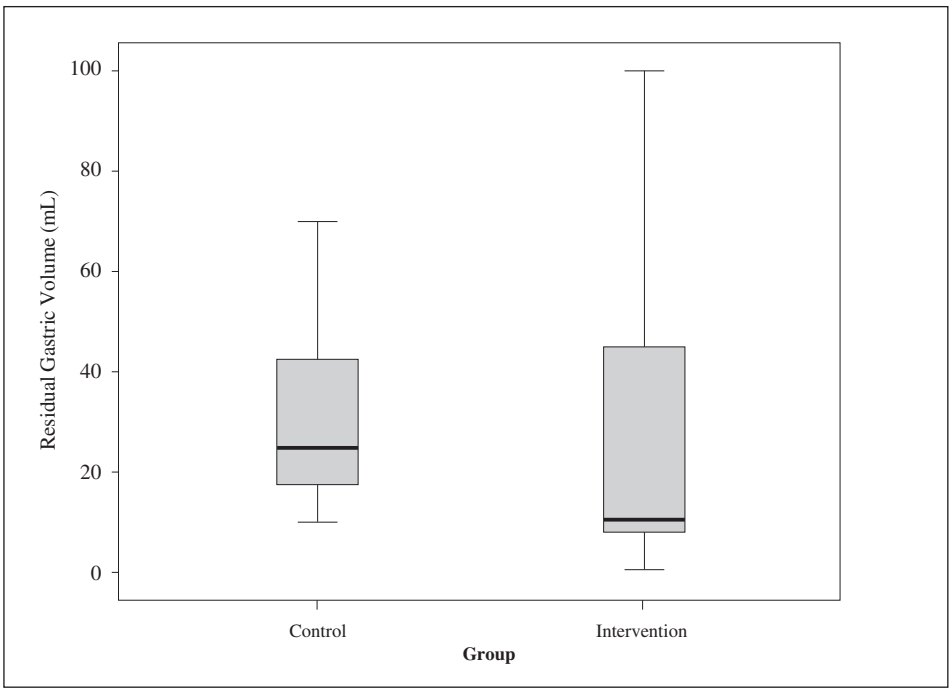


*Fig. 2.—Boxplot of the residual gastric volume found during upper digestive endoscopy in the two groups. Data are the median, interquartile range, and interval (P = 0.32).*

used to abbreviate fasting before anesthesia thus encouraging further studies.

After an overnight fast, the gastric camera is almost never completely empty and the RGV in healthy volunteers can range from 0 to 120 ml with a mean ranging from 19-37 mL[20] because the stomach continuously secrete up to 50 ml/h of acidic fluid even in fasting patients[21]. Our findings are in accordance to the above figures. Gastric emptying can be assessed by various methods. Since the introduction of radionuclide gastric emptying tests, considerable improvement has been achieved in both methodology and operational equipment, and scintigraphy has become the 'gold standard' for measurements of gastric emptying in research and in the clinical setting[22]. Recently magnetic resonance image has been proved to be an excellent method[23]. All the above techniques are non-invasive which is very important to the comfort of the patients. Other studies however have reported the use of nasogastric intubation to collect gastric contents[16,23]. Although this method is useful at the surgical unit on the other hand it is comprehensible imprecise. We have assessed the gastric emptying by gastroscopy. Gastroscopy is not only reliable but effective because the gastroscopist can visualize the whole gastric camera and then suctioning all contents[24]. This method was recently used as gold standard to assay the efficacy of a mathematical model for ultrasound assessment of the RGV[25].

Another importance of these findings is that it keeps opened the gate for testing other proteins or amino acids in addition to carbohydrate-enriched drinks aiming to abbreviate the period of preoperative fasting. The use of whey protein in addition to carbohydrate beverage may theoretically benefit patients undergoing elective operation. Not only insulin resistance can be decreased but acute phase postoperative response can be diminished[15]. Insulin resistance is a mark of metabolic response to both prolonged fasting and trauma, and the intake of oral nutritional supplements containing either only carbohydrate or carbohydrate in addition to protein or aminoacids may promote additional benefits[9,13,15,16,23].

One methodological limitation of this trial is the small number of cases. However it was based on sample calculation with sufficient power analysis. In addition, the RGV was assessed by a direct and reliable technique and the study design was a randomized, double-blind controlled trial which increase the reliability for the results. Overall, the findings of this randomized trial indicate that this type of oral nutritional supplement is safe to be drunk up to 150 minutes before anesthesia. However, further studies are necessary to confirm these findings. The present findings allow us to conclude that the gastric empty 150-210 minutes after the ingestion of 200 mL of a carbohydrate plus whey protein enriched-drink is similar to an overnight fast. These data reinforces the idea of safety of such types of drinks 2-3 h before sedation or anesthesia.


## Acknowledgements

We thank Ms Neila Aparecida da Silva for helping us in the sequence alignment and randomization of the patients. We also thank BioMed Proofreading for the English copy editing of this manuscript, and Dr Alfredo Matos, MD for correction of the abstract in Spanish.

Conflict of interest: Jose Eduardo de Aguilar-Nascimento has received in the last 2 years travel reimbursement and honoraria from Fresenius-Kabi, Abbott, and Nestle for participation in Congresses.


## References


1. Mendelson CL. The aspiration of stomach contents into the lungs during obstetric anesthesia. *Am J Obst Gynecol* 1946; 52: 191-205.
2. Erskine L, Hunt JN. The gastric emptying of small volumes given in quick succession. *J Physiol* 1981; 313: 335-41.
3. Brener W, Hendrix TR, McHugh PR. Regulation of the gastric emptying of glucose. *Gastroenterology* 1983; 85: 76-82.
4. Phillips S, Hutchinson S, Davidson T. Preoperative drinking does not affect gastric contents. *Br J Anaesth* 1993; 70: 6-9.
5. Aguilar-Nascimento JE, Dock-Nascimento DB. Reducing preoperative fasting time: a trend based on evidence. *World J Gastrointest Surg* 2010; 2: 57-60.
6. Maltby JR, Lewis P, Martin A, Sutherland LR. Gastric fluid volume and pH in elective patients following unrestricted oral fluid until three hours before surgery. *Can J Anaesth* 1991; 38: 425-9.
7. Brady M, Kinn S, Stuart P. Preoperative fasting for adults to prevent perioperative complications. *Cochrane Database Syst Rev* 2003; (4): CD004423.
8. 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. *Br J Surg* 2005; 92: 415-21.
9. Faria MS, Aguilar-NascimentoJE, Pimenta OS, Alvarenga Jr LC, Dock-Nascimento DB, Slhessarenko N. Preoperative fasting of 2 hours minimizes insulin resistance and organic response to trauma after video-cholecystectomy: A randomized, controlled, clinical trial. *World J Surg* 2009; 33: 1158-64.
10. Graf S, Egert S, Heer M. Effects of whey protein supplements on metabolism: evidence from human intervention studies. *Curr Opin Clin Nutr Metab Care* 2011; 14: 569-80.
11. de Aguilar-Nascimento JE, Prado Silveira BR, Dock-Nascimento DB. Early enteral nutrition with whey protein or casein in elderly patients with acute ischemic stroke: a double-blind randomized trial. *Nutrition* 2011; 27: 440-4.
12. Sheikholeslami Vatani D, Ahmadi Kani Golzar F. Changes in antioxidant status and cardiovascular risk factors of overweight young men after six weeks supplementation of whey protein isolate and resistance training. *Appetite* 2012; 59: 673-8.
13. Borges Dock-Nascimento D, Aguilar-Nascimento JE, Caporossi C, Sepulveda Magalhães Faria M, Bragagnolo R, Caporossi FS, Linetzky Waitzberg D. Safety of oral glutamine in the abbreviation of preoperative fasting: a double-blind, controlled, randomized clinical trial. *Nutr Hosp*. 2011; 26: 86-90. [PMID: 21519733 ]
14. Awad S, Blackshaw PE, Wright JW, Macdonald IA, Perkins AC, Lobo DN. A randomized crossover study of the effects of glutamine and lipid on the gastric emptying time of a preoperative carbohydrate drink. *Clin Nutr* 2011; 30: 165-71.
15. Perrone F, da-Silva-Filho AC, Adôrno IF, Anabuki NT, Leal FS, Colombo T, da Silva BD, Dock-Nascimento DB, Damião A, de Aguilar-Nascimento JE. Effects of preoperative feeding with a whey protein plus carbohydrate drink on the acute phase response and insulin resistance. A randomized trial. *Nutr J* 2011; 10: 66 .

16. Henriksen MG, Hessov I, Dela F, Vind 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 Anaesthesiol Scand* 2003; 47: 191-9.
17. Smith I, Kranke P, Murat I, Smith A, O'Sullivan G, Søreide E, Spies C, in't Veld B; European Society of Anaesthesiology. Perioperative fasting in adults and children: guidelines from the European Society of Anaesthesiology. *Eur J Anaesthesiol* 2011; 28 (8): 556-69.
18. Gustafsson UO, Scott MJ, Schwenk W, Demartines N, Roulin D, Francis N, McNaught CE, MacFie J, Liberman AS, Soop M, Hill A, Kennedy RH, Lobo DN, Fearon K, Ljungqvist O; Enhanced Recovery After Surgery Society. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations. *Clin Nutr* 2012; 31 (6): 783-800.
19. Weimann A, Braga M, Harsanyi L, Laviano A, Ljungqvist O, Soeters P; DGEM (German Society for Nutritional Medicine), Jauch KW, Kemen M, Hiesmayr JM, Horbach T, Kuse ER, Vestweber KH; ESPEN (European Society for Parenteral and Enteral Nutrition). ESPEN Guidelines on Enteral Nutrition: Surgery including organ transplantation. *Clin Nutr* 2006; 25 (2): 224-44.
20. Maltby JR. Fasting from midnight—the history behind the dogma. *Best Pract Res Clin Anaesth* 2006; 20: 363-78.
21. Greenfield SM, Webster GJ, Brar AS, Ah Mun K, Beck ER, Vicary FR. Assessment of residual gastric volume and thirst in patients who drink before gastroscopy. *Gut* 1996; 39: 360-2. Maurer AH. Advancing gastric emptying studies: standardization and new parameters to assess gastric motility and function. Semin Nucl Med. 2012; 42:101-12.
22. Lobo DN, Hendry PO, Rodrigues G, Marciani L, Totman JJ, Wright JW, Preston T, Gowland P, Spiller RC, Fearon KC. Gastric emptying of three liquid oral preoperative metabolic preconditioning regimens measured by magnetic resonance imaging in healthy adult volunteers: A randomized double-blind, crossover study. *Clin Nutr* 2009; 28: 636-41.
23. Dock-Nascimento DB, de Aguilar-Nascimento JE, Magalhaes Faria 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. *JPEN J Parenter Enteral Nutr* 2012; 36: 43-52.
24. Attila T, Hellman RS, Krasnow AZ, Hofmann CL, Saeian K, Dua KS, Binion DG, Shaker R. Feasibility and safety of endoscopic evaluation of gastric emptying. *Endoscopy* 2005; 37: 240-3.
25. Perlas A, Mitsakakis N, Liu L, Cino M, Haldipur N, Davis L, Cubillos J, Chan V. Validation of a mathematical model for ultrasound assessment of gastric volume by gastroscopic examination. *Anesth Analg* 2013; 116: 357-63.
26. Awad S, Varadhan KK, Ljungqvist O, Lobo DN. A meta-analysis of randomized controlled trials on preoperative oral carbohydrate treatment in elective surgery. *Clin Nutr* 2013; 32: 34-44.