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Original

Safety of oral glutamine in the abbreviation of preoperative fasting; a double-blind, controlled, randomized clinical trial

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Abstract

Introduction: **No study so far has tested a beverage containing glutamine 2 h before anesthesia in patients undergoing surgery.**

Objectives: **The aim of the study was to investigate: 1) the safety of the abbreviation of preoperative fasting to 2 h with a carbohydrate-L-glutamine-rich drink; and 2) the residual gastric volume (RGV) measured after the induction of anesthesia for laparoscopic cholecystectomies.**

Methods: **Randomized controlled trial with 56 women (42 (17-65) years-old) submitted to elective laparoscopic cholecystectomy. Patients were randomized to receive either conventional preoperative fasting of 8 hours (fasted group, n = 12) or one of three different beverages drunk in the evening before surgery (400 mL) and 2 hours before the initiation of anesthesia (200 mL). The beverages were water (placebo group, n = 12), 12.5% (240 mOsm/L) maltodextrine (carbohydrate group, n = 12) or the latter in addition to 50 g (40 g in the evening drink and 10g in the morning drink) of L-glutamine (glutamine group, n = 14). A 20 F nasogastric tube was inserted immediately after the induction of general anesthesia to aspirate and measure the RGV.**

Results: **Fifty patients completed the study. None of the patients had either regurgitation during the induction of anesthesia or postoperative complications. The median (range) of RGV was 6 (0-80) mL. The RGV was similar (p = 0.29) between glutamine group (4.5 [0-15] mL), carbohydrate group (7.0 [0-80] mL), placebo group (8.5 [0-50] mL), and fasted group (5.0 [0-50] mL).**

Conclusion: **The abbreviation of preoperative fasting to 2 h with carbohydrate and L-glutamine is safe and does not increase the RGV during induction of anesthesia.**

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Key words: *Cholecystectomy. Preoperative fasting. Glutamine. Residual gastric volume. Randomized controlled study.*

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SEGURIDAD DE LA GLUTAMINA ORAL EN LA ABREVIACIÓN DEL AYUNO PREOPERATORIO; UN ENSAYO CLÍNICO DOBLE CIEGO, CONTROLADO, ALEATORIZADO

Resumen

Introducción: **Ningún estudio hasta el momento ha investigado una bebida que contiene glutamina 2 h antes de la anestesia en pacientes sometidos a cirugía.**

Objetivos: **El objetivo del estudio fue investigar: 1) la seguridad de la abreviación del ayuno preoperatorio para 2 h con una bebida conteniendo carbohidratos y L-glutamina, y 2) el volumen gástrico residual (RGV), medido después de la inducción de la anestesia en colecistectomías laparoscópicas.**

Métodos: **Ensayo controlado aleatorizado con 56 mujeres (42 (17-65) años) sometidas a colecistectomía laparoscópica electiva. Las pacientes fueron aleatorizadas para recibir ayuno preoperatorio convencional de 8 horas (grupo ayuno, n = 12) o una de tres bebidas diferentes tomadas la noche antes de la cirugía (400 ml) y también 2 horas antes del inicio de la anestesia (200 ml). Las bebidas eran agua (grupo placebo n = 12), 12,5% (240 mOsm/l) maltodextrina (grupo carbohidrato, n = 12) o carbohidrato además de 50 g (40 g la noche anterior y 10 g por la mañana) de L-glutamina (grupo glutamina, n = 14). Una sonda nasogástrica 20 F fue insertada inmediatamente después de la inducción de la anestesia general para aspirar y medir el RGV.**

Resultados: **Cincuenta pacientes completaron el estudio. Ninguno de los pacientes han presentado regurgitación durante la inducción de la anestesia ni complicaciones postoperatorias. La mediana (variación) del RGV fue de 6 (00-80) mL. El RGV fue similar (p = 0,29) entre el grupo glutamina (4,5 [0-15] mL), el grupo carbohidrato (7,0 [0,80] mL), grupo placebo (8,5 [0-50] mL), y grupo ayuno (5,0 [0-50] mL).**

Conclusión: **La abreviación del ayuno preoperatorio para 2 h con carbohidratos y L-glutamina es seguro y no aumenta el RGV durante la inducción de la anestesia.**

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Palabras clave: *Colecistectomía. Ayuno preoperatorio. Glutamina. Volumen gástrico residual. Estudio controlado aleatorizado.*

Introduction

The main reason for traditional 8 hours of preoperative fasting 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] in adults scheduled for elective surgery 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-rich beverage in the immediate preoperative period is not only safe, but may also reduce the catabolic stress response to surgery and thus enhance postoperative recovery.[8,9] The use of additional metabolic conditioning agents such as glutamine may be of potential benefit to patients undergoing surgery. Glutamine is a conditionally essential amino acid, which improves both gastrointestinal perfusion and immune function,[10] and possesses a multiple beneficial systemic function.[11] A beverage containing glutamine in addition to carbohydrate may, therefore, provide additional benefits to surgical patients, beyond carbohydrate loading alone. One study has shown that gastric emptying time for beverages containing glutamine is approximately 160 minutes in healthy volunteers.[12] However no study so far has tested this solution in patients undergoing surgery offered two hours before anesthesia. The aim of the study was to investigate: 1) the safety of the abbreviation of preoperative fasting to 2 h with a carbohydrate-L-glutamine-rich drink; and 2) the residual gastric volume (RGV) measured after the induction of anesthesia for laparoscopic cholecystectomies.

Materials and methods

A group of 56 adult women (median age = 42 (17-65) years-old) scheduled to undergoing elective laparoscopic cholecystectomy at Santa Rosa Hospital, Cuiabá, Brazil were eligible for inclusion in this trial. Exclusion criteria were: American Society of Anesthesiologists (ASA) score above II, diabetes mellitus, pregnancy, age above 65 years old, renal or hepatic failure, gastroesophageal reflux, acute cholecystitis, use of corticosteroids up to 6 months previously, and any noncompliance or violation on the assigned protocol of preoperative fasting. The local ethics committee approved the study, and all patients gave written informed consent before randomization.

Three patients were excluded before randomization due to refusal to participate (1) or age above 65 years-old (2). Patients were randomized to receive either conventional preoperative fasting of 8 hours (fasted group, n =12) or one of three different beverages to be drunk in the evening before surgery (400 mL) and 2 hours before the initiation of anesthesia (200 mL). The beverages were water (placebo group, n = 14), 12.5% (240 mOsm/L) maltodextrine (Nidéx®, Nestlé, São Paulo, Brazil) (carbohydrate group, n = 12) or the latter in addition to 50 grams (40 g in the evening drink and 10 g in the morning drink 2 hours before the induction of anesthesia) of L-glutamine (Resource Glutamine®, Nestlé, São Paulo Brazil (glutamine group, n = 15). Osmolarity of the beverage containing L-glutamine was either 639.2 mOsm/L (evening drink, 400 mL) or 219.8 mOsm/L (morning drink, 200 mL).

Preoperative protocol

All patients received both oral and written information about the protocol at the outpatient clinic. The assignment was done by randomized numbers arranged by a computer. Operations were scheduled to begin at 7:00 AM The evening before operation patients were free to ingest solid food until 11:00 PM. The patients belonging to the three groups of abbreviation of fasting were told to ingest the beverage at 11:00 PM (400 mL) and at 5:00 AM (200 mL), and be at the hospital admission unit at 6:00 AM.

Intraoperative protocol

A 20 F nasogastric tube was inserted immediately after the induction of anesthesia to aspirate and measure the gastric contents. Placement of the nasogastric tube was checked by a stethoscope positioned over the epigastric region followed by a bolus injection of 10-20 cc of air. Patients were submitted to general anesthesia without epidural blockage and received a single dose of 1 g of intravenous cefazolin.

Outcome variable and statistical analysis

Sample size was calculated supposing a mean difference of 3 mL (based on a pilot study) in the RGV and with a standard deviation of 2 mL. Therefore a number of 11 cases per group were estimated to attain 80% power. The main endpoint of the study was the RGV. Gastric contents regurgitation during induction of anesthesia was a secondary endpoint. Comparison of RGV among groups was done by Kruskal-Wallis test. A 5% level was adopted for significance. Data were presented as either median (range) or mean ± SD as appropriate. All analysis were done by SPSS statistical software v 10.0.

Results

The flowchart of the randomized trial is presented in figure 1. Three patients were excluded due to either

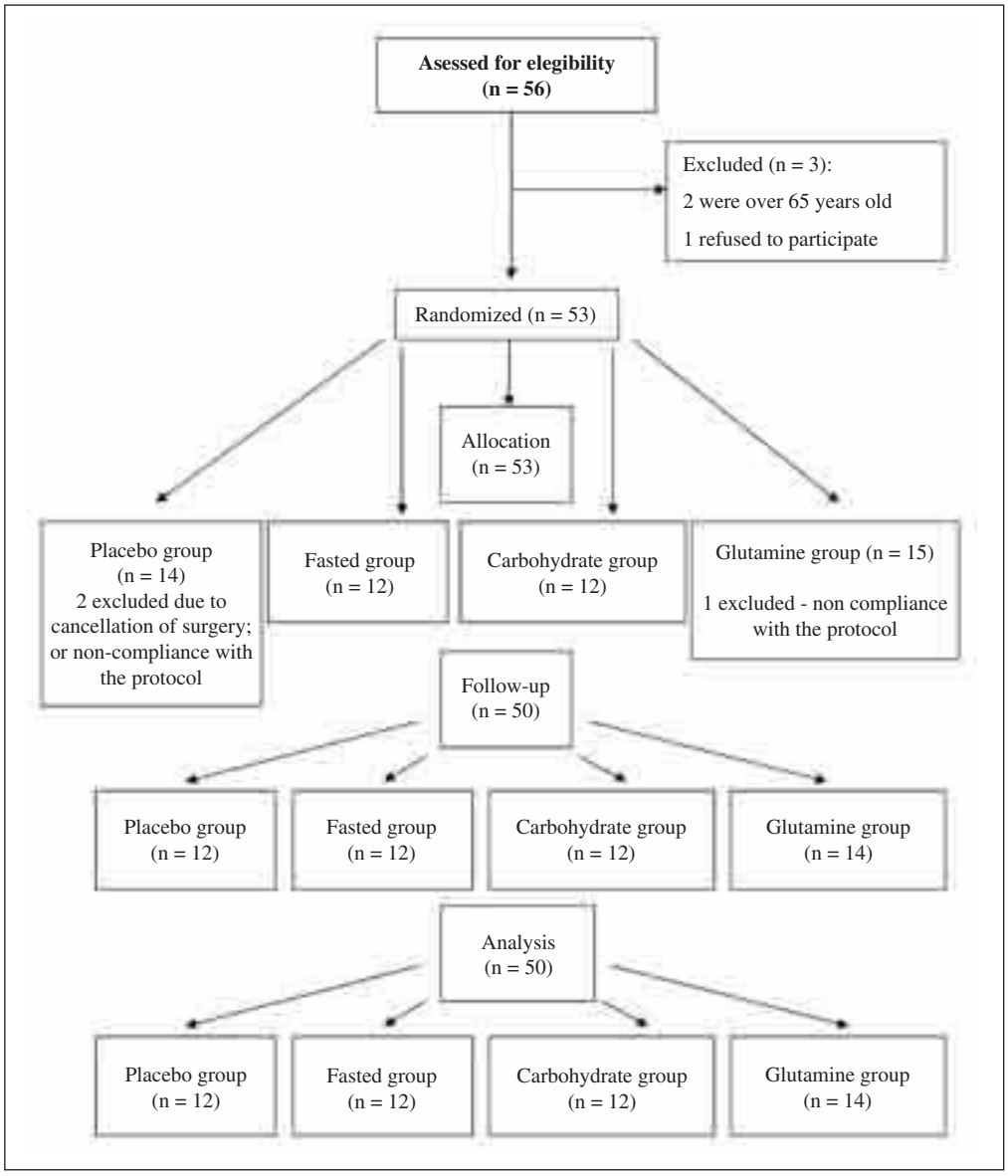

Fig. 1.—Flowchart of the randomization.

being aged (2) or refused to participate (1). After randomization three others were ruled out due to either have not correctly ingested the beverage (one in glutamine group and one in placebo group) or cancellation of the surgery (one case in placebo group). Therefore, 50 patients completed the study. There was no difference in demographic and biochemical data between groups (table I). None of the patients had regurgitation during the induction of anesthesia. There were neither deaths nor postoperative complications.

The median (range) of RGV was 6 (0-80) (mean = 10.6) mL. Comparisons showed that the RGV was similar (p = 0.29) between glutamine group (median = 4.5 [0-15], mean = 4.9) mL), carbohydrate group (median = 7.0 [0-80], mean = 12.6 mL), placebo group (media = 8.5 [0-50], mean = 12.9 mL), and fasted group (median 5.0 [0-50], mean = 12.1 mL). This can be seen in figure 2.

Discussion

The findings showed that the abbreviation of preoperative fasting for 2 hours with carbohydrate and L-glutamine-rich drink was safe and was not associated with complications during the induction of anesthesia. Furthermore the RGV was similar in either fasted patients or in groups treated with abbreviation of preoperative fasting to 2 h. This is most relevant since this is the first study in the surgical setting that compared RGV with a group drinking a beverage containing glutamine 2 h before anesthesia. The data suggest that this new ingredient to abbreviate preoperative fasting is safe thus encouraging further studies.

After an overnight fast, the stomach is almost never completely empty and the RGV in healthy volunteers can range from 0 to 95ml with a mean of 27 mL.[12] Various techniques are available to study gastric emptying,

Table I
Demographic and biochemical data of the study population

	Group				
Variable	*Fasted*	*Placebo*	*Carbohydrate*	*Glutamine*	*p*
Age (years)†	42 (19-65)	44 (17-63)	34 (17-62)	45 (22-65)	0.46
BMI (kg/m²)†	26.5 (20.4-31.2)	27 (20.4-33.3)	24.7 (23.3-29.1)	22.8 (19.2-29.1)	0.10
*Serum glucose (mg/dl)**	88.1 ± 4.9	82.6 ± 8.4	83.8 ± 10.8	85.5 ± 11.5	0.75
*Hemoglobin (g/dl)**	13.6 ± 1.1	12.4 ± 0.9	12.4 ± 1.0	13.2 ± 1.3	0.10
*Creatinine (mg/dl)**	0.64 ± 0.84	0.69 ± 0.21	0.73 ± 0.23	0.67 ± 0.98	0.72
*SGOT (u/l)**	17.3 ± 5.0	23.8 ± 9.6	20.8 ± 4.1	17.5 ± 3.6	0.31
*SGPT (u/l)**	19 ± 55	23.6 ± 9.3	22.8 ± 12.2	16.3 ± 4.3	0.27
ASA (n; %)					
I	8 (66.6)	7 (58.3)	8 (72.7)	8 (57.1)	0.84
II	4 (33.3)	5 (41.6)	3 (27.2)	6 (42.8)	

* = Mean ± SD.
† = Median (range).
SGOT: serum glutamic-oxalacetic transaminase.
SGPT: serum glutamic-pyruvate transaminase.
ASA: American Society of Anesthesiologists score.

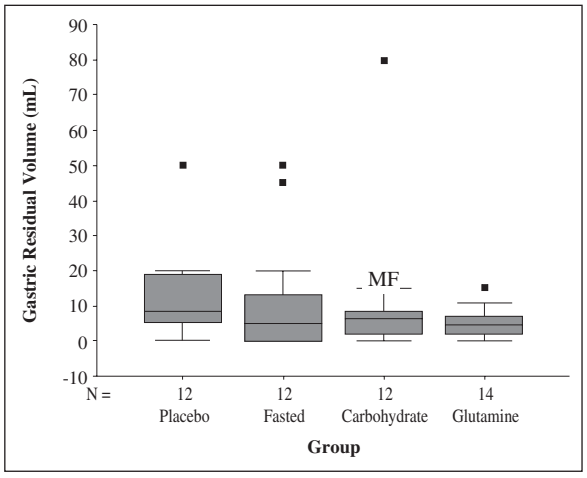

Fig. 2.—Gastric residual volume in the four groups. Data express the median, variation, and interquartile range (p = 0.29). Black dots are outliers.

all of them having specific advantages and disadvantages. 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.[13] Recently magnetic resonance image has been also used.[12] While room to criticism may exist in connection with the accuracy of this method, other studies have also reported its useful application at the surgical unit.[14,15] Moreover, the data showed that all groups including glutamine group had similar RGV at induction of anesthesia.

Another importance of these findings is that it keeps opened the gate for testing other nutrients for abbreviation of preoperative fasting in addition of carbohydrate-rich beverages. The use of L-glutamine associated with carbohydrate beverage may theoretically accelerate postoperative recovery by improving glucose metabolism and insulin requirements,[16] reduce anti-oxidative and anti-inflammatory response,[17] and as a result reduce postoperative complications[11,18] and mortality.[11] Insulin resistance as a result of prolonged fasting may be also reduced. Insulin resistance is a mark of metabolic response to both prolonged fasting and trauma.[9] Further studies are necessary to confirm all these benefits associated to the abbreviation of preoperative fasting with beverages containing L-glutamine.

The present findings allow us to conclude that the abbreviation of preoperative fasting to 2 h with carbohydrate and L-glutamine is safe and does not increase the RGV during induction of anesthesia.

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