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original article

Preoperative fasting - "nihil per os" a difficult myth to break down: a randomized controlled study

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SUMMARY: **Preoperative fasting - "nihil per os" a difficult myth to break down: a randomized controlled study.**

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Introduction. *For several years the scientific anaesthesia societies declared a preoperative fast of 6 hours for solid foods and 2 hours for clear liquids before elective surgical interventions to be sufficient. The aim of this study is to identify the extent of the gap that exists between the preoperative fasting time required and that actually encountered in operating rooms.*

Patients and methods. *The safety and clinical applicability of a reduction of the preoperative fasting time was investigated through the use of oral solutions enriched with maltodextrin and their effects on the pre- and postoperative well-being that this may have on patients who are candidates for elective abdominal surgery. The study was conducted in two successive phases (I and II) and patients divided into two groups (A and B).*

Discussion. *Clinical practice is slow to change, in fact, in our study the duration of fasting was an average of 19 hours for solids and 13 hours for liquids. The duration of the fasting did not show differences in the various surgical departments, demonstrating that it is a transversal practice and is not only limited to abdominal surgery in which the utility of fasting would theoretically be greater. Among Group patients A, the fasting time for liquids was about 9 hours. This shows that the time is certainly shorter but not much different when compared to the fasting time for liquids in group B which was on average 14 hours. It is important how difficult it is to achieve good compliance from patients when trying to reduce the time of preoperative fasting based on scientific evidence that is now well established.*

Conclusion. *The use of carbohydrate-enriched drinks up to 2 hours after induction of anaesthesia appears to be a safe procedure. The use of these solutions reduces the catabolic response to surgery and contributes to maintaining a pre-operative state of well-being by reducing feelings of hunger and thirst and the state of preoperative anxiety.*

KEY WORDS: Preoperative fasting - Surgery - Maltodextrin.

Introduction

The evolution of the ideas surrounding preoperative fasting refers to the recommendations of the British surgeon Sir Joseph Lister, who in 1883 considered it "desirable that ... it will be found very salutary to give a cup of tea or beef-tea about two hours before a surgical operation". For several years the scientific anaesthesia societies declared a preoperative fast of 6 hours for solid foods and 2 hours for clear liquids before elective surgical interventions (1) to be sufficient. However, in today's clinical practice, the times to which patients are subject are still significantly longer.

The aim of this study is to identify the extent of the gap that exists between the preoperative fasting time required and that actually encountered in our operating rooms.

Secondly, the safety and clinical applicability of a reduction of the preoperative fasting time was investigated through the use of oral solutions enriched with maltodextrin and their effects on the pre- and postoperative well-being that this may have on pa-

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tients who are candidates for elective abdominal surgery.

In fact, in several studies it has been shown that an intake of drinks enriched with carbohydrates up to two hours before an operation does not entail a greater risk of aspiration during the induction of anaesthesia (2-4) and maintaining oral feeding longer may reduce the organic response to surgical stress (5, 6), in particular by reducing postoperative insulin resistance levels (7-9). Added to this is the reduction of preoperative discomfort and postoperative nausea and vomiting (10, 11). These elements are often considered marginal although they play an important role in the evolution of fast track surgery and in Enhanced Recovery After Surgery protocols (12-14).

Patients and methods

The study was conducted in two successive phases:

- In phase I the duration of absolute preoperative fasting in current practice was evaluated in patients undergoing surgery in a range of fields.
- In phase II a randomized controlled open-label study limited to patients due to undergo elective abdominal surgery was proposed to evaluate the effects of the intake of fluids containing maltodextrin up to 2 hours before surgery.

The first objective was an analysis of fasting time in patients undergoing surgical procedures with an assessment of the overall restriction for solid and liquid foods in patients prescribed the traditional preoperative fasting from the night before the operation.

The second objective was the verification of the safety, tolerability, patient compliance and effects on preoperative anxiety of a regimen that, as an alternative to the traditional 12-hour fast, provides for the administration of iso-osmolar drinks containing carbohydrates (maltodextrin) at a concentration of 12.5% up to 2 hours before surgery. Also of great importance was the taking into consideration of the recurrence of adverse events such as the appearance of nausea and vomiting, intolerance to the oral glucose load, gastric stagnation evaluated in ml in relation to the positioning of the nasogastric tube in the operating room and problems with the induction of anaesthesia. Secondary objectives included the evaluation of the applicability in clinical practice of a programme of reduction in the preoperative fasting period with the measurement of preoperative blood glucose, of the feeling of thirst and hunger in the preoperative period and of the duration of the passage time for gases and faeces during the hours under postoperative care.

In the first phase of the study a survey was conducted on the actual duration of fasting in a group of patients who were candidates for surgical procedures of a range of specialties and in different operating rooms of the University Hospital of Bari, SE Italy. This phase of the study was conducted with the collaboration of doctors undergoing specialized training in Anaesthesia and Intensive Care Unit who gathered the necessary information.

As is usually the case in our operating rooms, all patients had been instructed to follow an absolute fast starting at midnight. On the morning for which surgery was scheduled they were asked the time when they had consumed their last solid meal and what they had eaten and the time they drank liquids for the last time. Patients' personal information and the type of intervention were gathered together with the start time of the operation and recorded, from which it was possible to obtain the actual fasting time for solids and liquids for each patient.

In the second phase of the study a prospective randomized clinical trial was conducted in a sample of patients who were candidates for abdominal surgery in four consecutive months starting in September 2018. The aim of the study was to evaluate the safety, tolerability and adherence of patients to a pre-operative regimen that envisaged the use of carbohydrate-enriched drinks as an alternative to fasting from midnight. All the patients examined were subject to the traditional preoperative anaesthesia evaluation. The inclusion criteria were the following ones:

- Age between 18 and 85 years
- Class ASA I - III patients
- Patients who are candidates for elective abdominal surgery.

The exclusion criteria were as follows:

- BMI> 35
- ASA> 3
- Hospitalization in Day Surgery

- Presence of clinical or radiological signs of gastric neoplasms
- Hiatal hernia associated with gastro-oesophageal reflux syndrome
- Neurological and / or psychiatric diseases that prevent the following of the study protocol
- Diabetes
- Patient's lack of consent
- Lack of consent from the anaesthesiologist or surgeon of reference.

Patients due to be subjected to general anaesthesia with oro-tracheal intubation were studied for elective interventions of the median and major abdominal surgery (open or laparoscopic technique).

Patients were divided into two groups:

GROUP A: the evening before the operation, patients were given 800 ml of a drink (PreOp® - Nutricia) containing maltodextrin at a concentration of 12.5%. Table 1 shows the precise composition of the drink in use. An additional 400 ml of the same solution was taken on the morning of the operation up to 2 hours before it began.

GROUP B: the control group who followed the traditional fast from midnight on the day before surgery.

This study was carried out by open randomization since it was not possible, in consideration of its characteristics, to conduct it in a double-blind study. Each patient was presented with the aims and methods involved in the conduction of the study, after explaining all information needed and reading an information sheet and an informed consent form. Each patient was then randomly assigned to one of the two groups and after this assignment the preoperative regimen to be followed was known to the patient and the experimenters and consisted of either the administration of an oral solution containing carbohydrates or fasting from midnight. The personal data of each patient, the dates of entry and discharge, the diagnosis on admittance and the intervention performed were recorded. A brief pathological history for each patient was noted with particu-

TABLE 1 - PREOP® COMPOSITION.

Contents	Per 100 mL
Energy (kcal)	50
Protein (g)	0
Carbohydrates (g)	12.5
Polysaccharides (g)	10
Sugars (g)	2.1
Lactose (g)	0
Fats (g)	0
Fibers (g)	0
Minerals	
Sodium (mg)	50
Potassium (mg)	122
Chloride (mg)	6
Calcium (mg)	6
Phosphorus (mg)	1
Magnesium (mg)	1
Water (g)	92
Osmolarity (mOsm)	240
Osmolality (mOsm/H20)	260
pH	4.9

lar attention to previous surgery (especially gastric surgery) and other associated pathologies such as diabetes, neurological pathologies, psychiatric disorders, gastroesophageal diseases. On the morning of the surgery, each patient was asked how many bottles of the drink enriched with maltodextrin they had consumed and the time of the last intake. If the patient had fasted since midnight, the time of the last fluid intake was noted. Then each patient had to express their feelings of nausea and vomiting (yes/no), and of thirst and hunger (no/little/a lot). Preoperative blood glucose was measured and then the duration of the operation, the duration of the anaesthesia, the drugs administered as premedication and the drugs used for analgesia were recorded together with the volume of liquid collected by the nasogastric tube (if this had been placed) at the time of induction and at the end of anaesthesia. A gastric stagnation greater than 25 ml was considered pathological when positioning the tube. Finally, postoperative data was collected on the permanence of the nasogastric tube and the daily volume collected, on any episodes of vomiting after the removal of the NGT and whether its repositioning proved necessary. Finally, the recovery time of peristalsis, intestinal patency to flatulence and faeces (in hours) and the time taken to feed (liquid, semi-liquid and solid, in days) were noted.

Results

Phase I

For the evaluation of the total pre-operative fasting time, a sample of 163 patients who were candidates for elective surgery was considered. The cases examined came via the various operating rooms of general surgery (n=49), plastic surgery (n=5), thoracic surgery (n=1), vascular surgery (n=4), gynaecology and obstetrics (n=80), orthopaedics (n=11), urology (n=6) and ophthalmology (n=6) of the University Hospital of Bari.

The age of this patient group ranged from 14 to 90 years, with an average of 49.3 years (± SD 16). The interval between the last solid food intake and the beginning of an intervention was, on average, 19 hours (± 0.22 SD), with a minimum value of 5 hours and a maximum value of 46 hours. The time between the last fluid intake and the intervention was, on average, 13 hours (± SD 0.20) with a minimum value of 1 hour and a maximum value of 33 hours. In four cases the fasting time for liquids was less than or equal to 4 hours, it being 1 hour in a case of orthopaedic surgery (reduction and synthesis of a tibia fracture) and in a case of plastic surgery (the removal of a neuroma and its repair using a graft). It lasted 2 hours in a case of obstetric surgery (a caesarean section) and lasted 4 hours in the case of a case involving general surgery (a laterocervical lymph node biopsy). Table 2 shows the time intervals in hours between the last intake of solid foods and the beginning of the intervention of the individual surgical interventions. Table 3 shows the time intervals in hours between the last fluid intake and the start of the intervention in the individual surgical areas, there being no significant differences in the duration of fasting in relation to the different surgical fields.

Phase II

Phase II of the study was undertaken, however, to answer the question on the applicability, safety and tolerability of the use of oral carbohydrate-containing solutions as opposed to complete fasting ('nil per mouth') from midnight and was conducted only in patients admitted to the General Surgery Operative Unit. 40 patients were eligible for the study in the period under review. Of these only 20 gave their consent to be part of the study with 10 being randomized to group A (intake of carbohydrate-enriched drinks), 5 men and 5 women and 10 to group B (the control group), 7 men and 3 women. Twelve of the 20 patients who refused participation in the study consented only to the collection of data and therefore in the analysis of the results they were associated with the control group, having observed fasting from the evening before the operation. Overall 22 patients formed the control group B, made up of 14 men and 8 women.

The average age of the sample was 59.79 years (± SD 12.84) in a range between 30 and 84 years. The average age of group A was 57.75 years (± SD 16.57), while the average age of group B was 59.19 (± SD 26.92). The interventions which patients in group A underwent were colorectal surgery (n=3), cholecystectomy (n=3), pancreatic surgery (n=2) and

TABLE 2 - TIME INTERVALS IN HOURS BETWEEN THE LAST INTAKE OF SOLID FOODS AND THE BEGINNING OF THE INTERVENTION OF THE INDIVIDUAL SURGICAL INTERVENTIONS.

Type of surgery	N	Average (h)	DS±
General surgery	49	18	0,19
Plastic surgery	5	17	0,34
Thoracic surgery	1	18	_
Vascular surgery	4	18	0,25
Gynaecology and Obstetrics	80	20	0,25
Orthopaedics	11	19	0,18
Urology	6	18	0,11
Ophthalmology	6	16	0,20

TABLE 3 - TIME INTERVALS IN HOURS BETWEEN THE LAST FLUID INTAKE AND THE START OF THE INTERVENTION IN THE INDIVIDUAL SURGICAL AREAS.

Type of surgery	N	Average (h)	DS±
General surgery	49	14	0,20
Plastic surgery	5	12	0,33
Thoracic surgery	1	16	_
Vascular surgery	4	12	0,13
Gynaecology and Obstetrics	80	13	0,21
Orthopaedics	11	13	0,27
Urology	6	16	0,14
Ophthalmology	6	13	0,13

gastrectomy (n=2). In group B the patients colorectal surgery (n=12), cholecystectomy (n=3), pancreatic surgery (n=2) and abdominal hernia surgery (n=5) were performed.

Among patients in group A, 5 patients (50%) took the entire 6 bottles of carbohydrate solution, 4 took 5 bottles while 1 took only 4. Only the first 5 patients drank the preop solution on the morning of

surgery, while the others took only the evening dose. All patients in group B followed the stricture of nil per mouth from midnight on the day before the operation. The average time interval between the last fluid intake and the induction of anaesthesia was 8 hours and 57 minutes (± 0.28 SD) in group A, with a minimum time of 3 hours and 10 minutes and a maximum time of 20 hours 35 minutes, while in group B the average was 14 hours 10 minutes (± SD 0.19), with a minimum of 8 hours 20 minutes and a maximum of 23 hours 15 minutes. The distribution of the patients in the two groups was on the basis of the fasting time for liquids.

With regard to glucose load tolerance, the preoperative blood glucose in group A (oral carbohydrate drink) was 100.63 mg/dl (± SD 23.73) compared to 92.53 mg dl (± SD 21.67) in group B (nil per mouth). No patient in either group suffered episodes of vomiting in association with surgery and only one patient in group A (10%) reported a feeling of nausea as against none from group B. Pre-operative thirst among patients in group A was null for 8 patients and a little for 2, while in group B it was null for 2 patients, a little for 14 and considerable for 6 patients. In addition, 7 patients in group A reported having no hunger and 3 patients reporting a little, while 2 patients in group B reported that they were not hungry, 17 had a little and 3 were very hungry. The following values were assigned in the distribution of patients for these two surveys: NO HUNGER = 0; LITTLE HUNGER = 1; VERY HUNGRY = 2.

A nasogastric tube was positioned in 50% of cases in group A (5/10) and in 59.1% of the cases in group B (13/22). No patient had pathological gastric stagnation at the time of NGT placement. Among the patients in group A the nasogastric tube was removed after 1 day in 2 cases, after 3 days in 2 cases and after 5 days in only one case. Among the patients in group B the removal took place after 1 day in 5 cases, after 2 days in 5 cases, after 3 days in 3 cases and after 5 days in only one case. Vomiting episodes occurred in one patient in group A (10%) and in two patients in group B (9.1%). The consumption of water took place after 2 days on average in group A and after 2.25 days in group B with the return to a free diet occurring on average on the fourth day postoperative in group A and on the fifth day postoperative in the group B. Postoperative hospital stay was on average 7.25 (± 5.75 SD) days in group A and 11.95 (± 15.16 SD) days in group B. Although the efficacy of the evaluation tests for assessing anxiety was certain, the analysis of the data collected in the two groups did not reach a sufficient number to be able to analyse the data in this phase of the study.

Discussion

The present study is set within the wide debate on preoperative fasting, which finds evidence for its reduction in length in the literature, but which, even after more than 20 years, is often discounted and with a poor application in clinical practice.

The many publications of Ljungqvist (7, 9), Nygren (3, 5), Hausel (11) and De Aguilar-Nascimento (15, 16) have certainly convinced the scientific community, and especially numerous Scientific Societies of Anaesthesiologists, that prolonged fasting is not only unnecessary but, on the contrary, actually harmful (17, 18). In patients without known risk factors, the guidelines recommend the intake of clear fluids (including water, pulp-free juice and tea or coffee without milk) for up to 2 h while avoiding solid food for at least 6 h before elective surgery (19).

The metabolic response to long fasting leads to an intensification of the organic response occurring after trauma, which is mainly manifested as increased insulin resistance, and loss of lean body mass. Clinical studies have consistently shown that 50-100 g of carbohydrates (usually 12.5% maltodextrin with or without additives) solution given the night before and additional 25-50 g given 2-4 hours before elective surgical procedures may attenuate the development of postoperative insulin resistance. Prolonged pre-operative fasting may lead to an increase in the inflammatory markers of the acute phase response after surgery, and carbohydrate-rich oral supplements 2-3 hours before surgery attenuate this response (20, 21). The levels of HLA-DR expression on monocytes in patients receiving carbohydrates increased with respect to that of fasting patients. This is particularly important because immunodepression and the resulting increased rate of

infections were associated with the duration of preoperative fasting.

Finally, the findings of a meta-analysis by Awad et al. showed that oral administration of CHO-rich fluids to patients undergoing major abdominal surgery reduced the postoperative length of stay by 1 day (22).

Drinking carbohydrate-rich fluids, such as Nutricia Preop before surgery was found to reduce thirst, anxiety, hunger and especially reduces postoperative insulin resistance (23).

Studies attempting to find out the ideal composition to use before surgery instead of fasting, show that a carbohydrate such as maltodextrin performs better than glucose.

Maltodextrin, frequently used in these preparations (Nutricia Preop), is a polymer and provides energy gradually without causing a hypoglycaemic insulin reaction and has a lower osmolality compared to glucose or other monomers (3). The rate of gastric emptying for maltodextrin is greater than simple glucose. This is due to its lower osmolality and with a consequent reduced gastric secretion, caused by a lower activation of the stomach's osmoreceptors,

New preparations containing protein hydrolysates, such as the Oral Nutrition Supplement (ONS300 and ONS400) which contains glutamine (15 grams) and antioxidants in addition to carbohydrates, have been compared to beverages containing only carbohydrates. The intake of this type of solution requires more time for the stomach to return to a basal volume: 180 minutes versus the 120 minutes necessary for the complete passage of drinks containing only carbohydrates. Because of this, the use of solutions containing hydrolyzed proteins requires a fasting time of 3 hours to be considered safe (24). Nevertheless, these drinks represent the basis for the future of the preoperative treatment of a surgical patient.

Many studies have showed that general discomfort, including malaise, thirst, hunger and weakness, postoperative nausea and vomiting can be reduced before and after surgery by patients receiving oral carbohydrate-rich fluids compared with control patients undergoing standard fasting. Given that preoperative fasting is still the rule (25) rather than the exception and the time of surgery is not always respected, this leads to even greater levels of unnecessary fasting.

There was no significant difference in age, gender, ethnicity and educational level between the patients who knew the correct reason for preoperative fasting and those who did not. Furthermore, it did not make a significant difference in fasting compliance whether the patients were told of the need to fast by doctors, nurses, or both doctors and nurses. Fasting compliance was also observed not to be significantly affected by whether patients had previously undergone surgery and whether they had received written instructions regarding fasting before surgery (26).

Clinical practice is slow to change, in fact, in our study the duration of fasting was an average of 19 hours for solids and 13 hours for liquids. The duration of the fasting did not show differences in the various surgical departments, demonstrating that it is a transversal practice and is not only limited to abdominal surgery in which the utility of fasting would theoretically be greater.

In the second phase of the study, among Group patients A, the fasting time for liquids was about 9 hours. This shows that the time is certainly shorter but not much different when compared to the fasting time for liquids in group B which was on average 14 hours.

It is important and, in some ways, surprising to note how difficult it is to achieve good compliance from patients when trying to reduce the time of preoperative fasting based on scientific evidence that is now well established. In fact, 50% of the patients enrolled in phase II of the study did not give their consent to participation. This protocol was proposed to them as "new" and this probably compromised their rates of accession to the trial. In most cases the patient refused, opting to do "as always", based on previous surgical experiences. In fact, 9 of the patients who did not agree to participate in the study, had previously undergone other surgical procedures. A poor understanding of the potential benefits of preoperative fasting has was encountered, while for many patients it is extremely important to respect the tradition of preoperative fasting with them believing that this is essential in preventing any postoperative complications.

These data agree with that which emerged from a

study conducted by a group of researchers in Singapore (27): 93.8% of patients believed that it was extremely important to continue to fast before surgery while 80.5% thought this was essential to avoid major complications. This common idea is confirmed by the fact that even among the patients in Group A who were asked to drink the Preop up to 2 hours before the surgery, not all of them adhered exactly to the instructions and only 50% of these drank 800 ml in the evening before and continued to take the remaining 400 ml of the solution on the morning of surgery.

An important aspect involves organization of the patient's pre-, peri and post-operative time and the difficulty of correctly guaranteeing the times in the operating theatre, especially as regards the afternoon interventions which are characterized by longer periods of preoperative fasting that can reach and sometimes exceed 24 hours. This prolongation of fasting can prove particularly dangerous for diabetic patients, who risk arriving on the operating table with major glycaemic imbalances. In our study, diabetic patients were excluded in order to avoid important contraindicative factors. There is sufficient evidence in the literature that preoperative supplementation with drinks containing carbohydrates is not harmful and that it is not associated with increased gastric stagnation. In fact, several studies show that especially in the inadequately compensated patient, while there may be a delay in gastric emptying for solid foods, the emptying times for clear liquids are similar to those for non-diabetics.

Many patients making preoperative use of CHO-drinks also understood how these might benefit their surgical outcome but, when interviewed, reported that these drinks do not were not to their liking and that they would not use them postoperatively, perhaps out of fear of incidents of nausea and vomiting.

This study supports the need for the provision of more information and more clarity by doctors and nurses in order to achieve good uptake by patients who can thus feel actively involved in their recovery path.

In 2014, a Cochrane group review (28), collected and compared the data obtained in 27 trials from around the world comparing groups that followed fasting (nil per mouth) from midnight, groups that were administered a placebo and groups to which carbohydrate-enriched drinks were given up to 2 hours post-surgery.

Data analysis leaves no doubt about the safety of the administration of carbohydrate-enriched solutions in the preoperative phase. With regard to the much-cited risk of pulmonary aspiration, it was observed that no pathological gastric stagnation was encountered in any patient undergoing anaesthesia and only one patient in group A experienced preoperative nausea and an episode of vomiting in the postoperative period. With regard to the risk of possible imbalances in the glucose regulatory system, in our experience no pathological glucose values were encountered prior to the surgical intervention. The results, though preliminary, are in line with the evidence in the literature and confirm that the intake of liquids containing maltodextrin contributes to improving patient well-being in the preoperative phase, reducing feelings of hunger and thirst especially when compared to patients subject to prolonged fasting and probably also reducing the inevitable state of anxiety that characterizes the wait for surgical intervention.

Conclusions

The most recent studies are unanimous in proposing a reduction in the duration of preoperative fasting as this is not associated with an increased risk of aspiration pneumonia. Therefore the use of carbohydrate-enriched drinks up to 2 hours after induction of anaesthesia appears to be a safe procedure. The use of these solutions reduces the catabolic response to surgery and contributes to maintaining a pre-operative state of well-being by reducing feelings of hunger and thirst and the state of preoperative anxiety. Further research in this area aims to extend the applicability of preoperative support with this type of carbohydrated-based solution to diabetic patients as well and to verify the safety and efficacy of solutions containing proteic hydrolysates in addition to carbohydrates. All of this should be seen in a process of greater attention to increasingly minute aspects in the care of surgical patients, as required by the philosophy of the Enhanced Recovery After Surgery but in the face of overcoming traditional

edicts as well as economic and organizational obstacles.

Disclosures

Drs A. Panebianco, R. Laforgia, A. Volpi, C. Punzo, G. Vacca, M. Minafra, M. Di Salvo, A. Pezzolla have no conflicts of interest or financial ties to disclose. All Authors have no financial relationships with any pharmaceutical or device company. No funds were involved in raising money for profit.

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References

1. Maltby RJ. Fasting from midnight - the history behind the dogma. Best Practice & Research Clinical Anaesthesiology. 2006;20(3):363-378.
2. Soreide E, Eriksson LI, Hirlekar G, Eriksson H, Henneberg SV, Sandin R, Reader J. Pre-operative fasting guidelines: an update. Acta Anaesthesiologica Scandinavica. 2005;n. 49:1041-1047.
3. Nygren J, Thorell A, Jacobsson H, Ljungqvist O. Preoperative Gastric Emptying - Effect of Anxiety and Oral Carbohydrate Administration. Annals of Surgery. 1995;222(6):728-734.
4. Scarr M, Maltby JR, Jani K, Sutherland LR. Volume and acidity of residual gastric fluid after oral fluid ingestion before elective ambulatory surgery. CMAJ. 1989;vol. 141.
5. Nygren J. The metabolic effect of fasting and surgery. Best Practice & Research Clinical Anaesthesiology. 2006;20(3):429-438.
6. Kaška M, Grosmanová T, Havel E, Hyšpler R, Petrová Z, Brtko M, Bareš P, Bareš D, Schusterová B, Pyszková L, Tošnerová V, Sluka M. The impact and safety of preoperative oral or intravenous carbohydrate administration versus fasting in colorectal surgery - a randomized controlled trial. Wiener klinische Wochenschrift. 2010;n. 122:23-30.
7. Ljungqvist O, Soreide E. Preoperative fasting. British Journal of Surgery. 2003;n. 90:400-406.
8. Thorell A, Loftenius A, Sndersson B, Ljungqvist O. Postoperative insulin resistance and circulating concentrations of stress hormones ad cytokines. Clinical Nutrition. 1996;n. 15:75-79.
9. Ljungqvist O. Modulating postoperative insulin resistance by preoperative carbohydrate loading. Best Practice & Research Clinical Anaesthesiology. 2009;n. 23:401-409.
10. Bopp C, Hofer S, Klein A, Weigand MA, Martin E, Gust R. A liberal preoperative fasting regimen improves patient comfort and satisfaction with anesthesia care in day-stay minor surgery. Minerva Anestesiologica. 2011;77(Luglio):680-686.
11. Hausel J, Nygren J, et al. A Carbohydrate-Rich Drink Reduces Preoperative Discomfort in Elective Surgery Patients. Anesth Analg. 2001;n. 93:1344-1350.
12. Gustafsson U, Scott M, Schwenk W, Demartines N, Roulin D, Francis N, McNaught C, MacFie J, Liberman A, Soop M, Hill A, Kennedy R, Lobom D, Fearon K, Ljungqvist O. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS) Society recommendations. Clinical Nutrition. 2012;n. 31:783-800.
13. Bona S, Molteni M, Rosati R, Elmore U, Bagnoli P, Monzani R, Caravaca M, Montorsi M. Introducing an enhanced recovery after surgery program in colorectal surgery: A single center experience. World Journal of Gastroenterology. 2014;20 (46):17578-17587.
14. Fearon K, Ljungqvist O, Meyenfeldt MV, et al. Enhanced recovery after surgery: A consensus review of clinical care for patients undergoing colonic resection. Clinical Nutrition. 2005;n. 24:466-477.
15. De Aguilar-Nascimento JE, Dock-Nascimento DB. Reducing preoperative fasting time: A trend based on evidence. World Journal of Gastrointestinal Surgery. 2010;2(Marzo):57-60.
16. Pimenta GP, Aguilar-Nascimento JE. Prolonged Preoperative Fasting in Elective Surgical Patients: Why should we reduce it? Nutrition in Clinical Practice. 2014;29(1):22-28.
17. Bilku D, Dennison A, Hall T, Metcalfe M, Garcea G. Role of preoperative carbohydrate loading: a systematic review. Ann R Coll Surg Engl. 2014;n. 96:15-22.
18. Sada F, Krasniqi A, Hamza A, Gecaj-Gashi A, Bicaj B, Kavaja F. A randomized trial of preoperative oral carbohydrates in abdominal surgery. BMC Anesthesiology. 2014;14(93).
19. Smith I, Kranke P, Murat I, Smith A, O'Sullivan G, Soreide E, Spies C. Perioperative fasting in adults and children: guidelines from the European Society of Anaesthesiology. European Journal of Anaesthesiology. 2011;n. 28:556-569.
20. Pexe-Machado PA, de Oliveira BD, Dock-Nascimento DB, de Aguilar-Nascimento JE. Shrinking preoperative fast time with maltodextrin and protein hydrolysate in gastrointestinal resection due to cancer. Nutrition. 2013;n. 29:1054-1059.
21. Ravanini GdAG, Filho PEP, Luna RA, Oliveira aVAd. Organic inflammatory response to reduced preoperative fasting time, with a carbohydrate and protein enriched solution; a randomized trial. Nutriciòn Hospitalaria. 2015;n. 2:957-957.
22. Awad S, Varadhan KK, Ljungqvist O, Lobo DN. A meta-analysis of randomised controlled trials on preoperative oral carbohydrate treatment in elective surgery. Clinical Nutrition. 2013;n. 34:34-44.
23. Ljungqvist O, Nygren J, Thorell A, Brodin U, Efendic S. Preoperative nutrition- elective surgery in the fed or the overnight fasted state. Clinical Nutrition. 2001;n. 20 (Supplement 1):167-171.
24. Lobo DN, Hendry PO, Rodrigues G, Marciani L, Totman J, 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 randomised double-blind, crossover study. Clinical Nutrition. 2009;n. 28:636-641.

25. De Aguilar-Nascimento J, De Almeida Dias A, Dock-Nascimento D, Correia MI, Campos A, Eder Portari-Filho P, Olivera S. Actual preoperative fasting time in Brazilian hospitals: the Bigfast multicenter study. Terapeutics and Clinical Risk Management. 2014;10:107-112.
26. Short V, Atkinson C, Ness AR, Thomas S, Burden S, Sutton E. Patient experiences of perioperative nutrition within an Enhanced Recovery After Surgery programme for colorectal surgery: a qualitative study. Colorectal Disease. 2015;n. 18:74-80.
27. Lim HJ, Lee H, Kah L. An audit of preoperative fasting compliance at a major tertiary referral hospital in Singapore. Singapore Med J. 2014;n. 55(1):18-23.
28. Smith MD, McCall J, Plank L, Herbison GP, Soop M, Nygren J. Preoperative carbohydrate treatment for enhancing recovery after elective surgery. The Cochrane Library. 2014;n. 8.