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Clinical and metabolic results of fasting abbreviation with carbohydrates in coronary artery bypass graft surgery

Resultados clínicos e metabólicos da abreviação do jejum com carboidratos na revascularização cirúrgica do miocárdio

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Abstract

Introduction: **Limited information is available about preoperative fasting abbreviation with administration of liquid enriched with carboidrates (CHO) in cardiovascular surgeries.**

Objectives: **To assess clinical variables, security of the method and effects on the metabolism of patients undergoing fasting abbreviation in coronary artery bypass graft (CABG) surgery.**

Methods: **Forty patients undergoing CABG were randomized to receive 400ml (6h before) and 200ml (2h before) of maltodextrin at 12.5% (Group I, n=20) or only water (Group II, n=20) before anesthetic induction. Perioperative clinical variables were assessed. Insulin resistance (IR) was assessed by Homa-IR index and also by the need of exogenous insulin; pancreatic beta-cell excretory function by Homa-Beta index and glycemic control by tests of capillary glucose.**

Results: **Deaths, bronchoaspiration, mediastinitis, stroke and AMI did not occur. Atrial fibrillation occurred in two patients of each group and infectious complications did not differ among groups (*P*=0.611). Patients of Group I presented two days less of hospital stay (*P*=0.025) and one day less in the ICU (*P*<0.001). The length of time using dobutamine was shorter in Group I (*P*=0.034). Glycemic control in the first 6h after surgery was worse for Group II (*P*=0.012). IR was verified and did not differ among groups (*P*>0.05). A decline in the endogenous production of insulin was observed in both groups (*P*<0.001).**

Conclusion: **Preoperative fasting abbreviation with the administration of CHO in the CABG was safe. The glycemic control improved in the ICU; there was less time in the use of dobutamine and length of hospital and ICU stay was reduced. However, neither IR nor morbimortality during hospital phase were influenced.**

Descriptors: **Myocardial Revascularization. Perioperative Care. Insulin Resistance. Metabolism. Fasting.**

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Abbreviations, acronyms & symbols	
ACERTO	Accelerated Total Recovery Postoperative
ACTH	adrenocorticotropic hormone
CABG	coronary artery bypass graft
CVS	cardiovascular surgery
CPC	cardiopulmonary bypass
CHO	carbohydrate
CABG	coronary artery bypass graft
GERD	gastroesophageal reflux disease
AAF	acute atrial fibrillation
LVEF	Left ventricle ejection fraction
GH	growth hormone
Homa	Homeostatic model assessment
AMI	acute myocardial infarction
CAD	coronary artery disease
BMI	body mass index
PO	postoperative
IPO	postoperative period
IR	insuline resistance
SIRS	systemic inflammatory response syndrome
WIC	written informed consent
ICI	intensive care unit
PONV	posteoperative nausea and vomiting

Resumo

Introdução: **Existe pouca informação sobre abreviação do jejum pré-operatório com oferta de líquidos ricos em carboidratos (CHO) nas operações cardiovasculares.**

Objetivos: **Avaliar variáveis clínicas, segurança do método e efeitos no metabolismo de pacientes submetidos à abreviação do jejum na cirurgia de revascularização do miocárdio (CRVM).**

Métodos: **Quarenta pacientes submetidos à CRVM foram randomizados para receberem 400 ml (6 horas antes) e 200 ml (2 horas antes) de maltodextrina a 12,5% (Grupo I, n=20) ou apenas água (Grupo II, n=20) antes da indução anestésica. Foram avaliadas diversas variáveis clínicas no perioperatório e também a resistência insulínica (RI) pelo índice de Homa-IR e pela necessidade de insulina exógena; além da função excretora da célula beta pancreática pelo Homa-Beta e controle glicêmico por exames de glicemia capilar.**

Resultados: **Não ocorreram óbitos, broncoaspiração, mediastinite, infarto agudo do miocárdio ou acidente vascular encefálico perioperatórios. Fibrilação atrial ocorreu em dois pacientes de cada grupo e complicações infecciosas não diferiram entre os grupos (*P*=0,611). Pacientes do Grupo I apresentaram dois dias a menos de internação hospitalar (*P*=0,025) e um dia a menos na UTI (*P*<0,001). O tempo de uso de dobutamina foi menor no Grupo I (*P*=0,034). Houve pior controle glicêmico nas primeiras 6 horas de pós-operatório no Grupo II (*P*=0,012). RI foi constatada e não diferiu entre os grupos (*P*>0,05). Declínio da produção endógena de insulina ocorreu em ambos os grupos (*P*<0,001).**

Conclusão: **Abreviação do jejum pré-operatório com oferta de CHO na CRVM foi segura, melhorou o controle glicêmico na UTI, diminuiu tempo de uso de dobutamina, e de internação hospitalar e na UTI. Contudo, não influenciou a RI e morbimortalidade de fase hospitalar.**

Descritores: **Revascularização miocárdica. Assistência perioperatória. Resistência à insulina. Metabolismo. Jejum.**

INTRODUCTION

The traditional perioperative care has been questioned and evidence has shown that certain behaviors are obsolete and applied without scientific support. Thus, studies that discuss multimodal protocols of fast-track or ckecklist in surgical patients attempt to define perioperative care to involve themselves with less morbidity, lower costs and accelerate recovery. The implementation of these protocols with quality control in cardiovascular surgery (CVS) does not seem easy, but it is necessary, since the specialty needs to interact with several different areas of medicine and hospital sectors [1-6].

Example of multimodal protocol questioning old paradigms is ACERTO (Accelerated Total Recovery Postoperative), with the main points of action: assessment and perioperative nutritional therapy, abbreviation of preoperative fasting with free liquid carbohydrate (CHO), both restriction of intravenous fluids and use of catheters and drains, feedback and early mobilization postoperatively (PO), reduction of length of stay in intensive care unit (ICU), among others. [7]

The prevalence of malnutrition in surgical patients ranges from 22% to 58% [8], and the the identification of these patients is the task of protocols applied to daily practice. In a multicenter national study [9], the prevalence of malnourished hospitalized patients was 48%. In all those who are screened as moderate to severe malnutrition, nutritional therapy is indicated for preoperative surgical outcomes and to improve healing, decrease complications, duration of mechanical ventilation in ICU, length of stay and hospital costs [10]. Malnourished patients undergoing CVS have higher mortality and incidence of mediastinitis, especially in patients with hypoalbuminemia preoperatively [11].

Another important aspect is the question of the time of preoperative fasting, which was established when the anesthetic techniques were rudimentary, to prevent pulmonary complications associated with aspiration of gastric contents (Mendelson's syndrome). In the early nineteenth century, it was allowed to drink a small cup of tea a few hours before the operation. After the questioning of Mendelson's syndrome, the guidelines for preoperative fasting have changed, adopting rules for fasting from midnight to patients who had their operation scheduled for the morning, and allowed light breakfast for those who underwent surgery in the afternoon. This position was put into practice because of its convenience. [12,13] However, current guidelines recommend clear liquids (water, tea and juices without waste) until two hours before surgery [14]. The benefits of fasting six to eight hours to prevent gastric aspiration have been questioned, and this practice is considered obsolete [14,15]. In general, patients with gastroesophageal reflux disease (GERD) and gastroparesis are susceptible to gastric aspiration.

The metabolic response to trauma is enhanced by prolonged fasting, and decreased insulin levels (single anabolic hormone in the acute phase of trauma response), however, there are increased levels of glucagon, causing rapid utilization of liver glycogen. Previously, gluconeogenesis is activated and the muscle protein starts providing glucose to tissues that depends on this exclusively as an energy source. This phenomenon has central regulation, also causing increased secretion of ACTH (adrenocorticotropic hormone) by the pituitary gland and increased secretion of cortisol by the adrenal gland. Serum levels of growth hormone (GH) rise when hypoglycemia or decreased circulating free fatty acids. Not only the cortisol, but also the decrease of insulin and the increased adrenergic hormones are responsible for catabolic reactions to provide amino acid to the circulatory system [16].

Within the metabolic response to trauma insulin resistance (IR) manifests, which can last up to three weeks after the holding of elective surgeries. This expression is more intense in the 1^{st} and 2^{nd} postoperative day and is directly proportional to the size of the surgery [17]. The prolonged preoperative fasting contributes to increase insulin resistance and hyperglycemia by increasing the metabolic stress of the surgery. The precise mechanisms of this manifestation has not been completely unraveled, and defects in transmembrane proteins (facilitative glucose transporter protein) seems to play an important role. The decrease of the signal from the insulin receptor and changes its structure biomolecular promote IR. This metabolic state is similar to type 2 diabetes, so the glucose uptake by the cells becomes diminished by the inability of the "GLUT-4" carrier to perform this action, resulting in decreased production of glycogen and increased endogenous glucose production, *gluconeogenesis* pathway [18].

Hyperglycemia is an independent factor of worse prognosis in CVS, because it increases infection rates, worsening wound healing and leads to increased morbidity and mortality. The negative influence of hyperglycemia is proven mainly in diabetics, but also in non-diabetic patients undergoing CABG, increasing platelet aggregation, inflammation postoperatively and hospital costs. Tight glucose control is associated with reduced complications and mortality in CABG [19]. Another aspect that corroborates the IR and hyperglycemia in CVS is the use of cardiopulmonary bypass (CPB); it has been proven that the CPB is responsible for the development of systemic inflammatory response, with the possibility of increased morbidity. However, this event nowadays is well understood and controlled [20].

Based on the aforementioned prolonged fasting, researchers have experimented with the use of clear liquids until two hours before surgery, to improve the metabolic response. A calorie content (pure CHO or with proteins) associated with the liquid proved to be beneficial for the reversal of IR related to surgical trauma in some types of surgeries, and also assessed in the CVS. Typically, it is used 12.5% maltodextrin (200-400 ml), two hours before surgery with safety. Studies have shown benefits in reducing the loss of muscle mass and strength, reduced anxiety, hunger and thirst, beyond the maintenance of immune function in the postoperative period [21-23]. Aguilar-Nascimento et al. [7] investigated the rate of postoperative nausea and vomiting (PONV) in surgical patients, and found a lower rate of these complications in those who used CHO solution preoperatively. Yagci et al. [24] demonstrated that CHO-rich liquid in the evening before surgery and two hours before induction of anesthesia does not alter the gastric pH and its contents, suggesting safety in terms of aspiration.

Within this context, the aim of this study was to investigate whether abbreviation of the preoperative fasting using CHO-content fluid, would improve clinical perioperative glycemic control and IR of nondiabetic patients undergoing elective CABG with CPB.

METHODS

Characterization of the study

This is a prospective, double-blind randomized controlled trial, with data collection performed from May 2010 to June 2011.

Ethical Considerations

The study was approved by the Ethics Committee in Research of Hospital Geral Universitário (Registration No. 053/CEP/UNIC; protocol 2010-048) and all patients signed a written informed consent (WIC).

Inclusion and exclusion criteria

The present study included patients with clinical diagnosis of coronary artery disease (CAD), with indication for elective CABG and accepted to participate in the study after a review of the informed consent, their understanding, agreement and signature.

We excluded patients under 18 or over 70 years, diabetics or those with fasting glucose above 110mg/dl; patients with gastroparesis or GERD; those who did not sign the WIC; who were in the chronic use of corticosteroids within six months before surgery; emergency surgery or combined (eg. CABG and valve replacement); previous cardiovascular surgeries (re-operations); those in the presence of acute coronary syndrome or mechanical complications of infarction and severe malnutrition requiring nutritional therapy.

Design by Groups, abbreviation of preoperative fasting

We included 40 consecutive patients, divided and randomized into two groups of 20 each (Group I – Intervention and Group II - Control), with the aid of GraphPad Software ™ (QuickCalcs).

Fasting for solids occurred at 22h the day before surgery. Abbreviation of fasting occurred as recommended by the ACERTO project [7]. It was offered CHO-rich liquid (12.5% maltodextrin) for patients randomized in the group I and water to patients in group II. The amount was 400 ml 6h and 200 ml 2h before induction of anesthesia for both groups.

Variables studied

Main outcome: Evaluation of IR by Homa-IR method [25] and the amount of exogenous insulin used to maintain blood glucose <150mg/dl in the operating room and in the first 6h of recovery in the ICU; glycemic control for capillary glucose tests and serial exams of blood glucose; incidence of mediastinitis, acute myocardial infarction (AMI), stroke and in-hospital mortality; length of hospital stay and ICU stay.

Secondary outcome: presence of thirst and discomfort preoperatively; presence of PONV in the postoperative recovery phase; assessment of excretory function of pancreatic beta-cell by Homa-Beta index [25]; incidence of bronchoaspiration during induction of anesthesia; need and duration of use of vasoactive drugs both in the operating room and ICU; duration of mechanical ventilation in the ICU and incidence of acute atrial fibrillation (AAF).

Anesthesia and surgical technique

The anesthetic technique used was the routine of the Service. Anesthesia was induced with midazolam infusion (0.1 mg/kg), fentanyl (2-5 mcg/kg) and pancuronium bromide (0.1 mg/kg) for muscle relaxation. Additional doses of these medications for maintenance of anesthesia were performed if necessary and every hour. Isoflurane was used by inhalation, in usual doses (0.5%-1.25%) for balanced general anesthesia. All patients were maintained on mechanical ventilation. The surgical approach was through median sternotomy with CPB to perform the allotted time. The oxygenator used was of membrane type, Braile Biomedica® (São José do Rio Preto/Brazil). As a method of myocardial protection was used hypothermic intermittent anterograde blood cardioplegia (every 15-20 min.) associated with mild systemic hypothermia (33°- 35°C).

Parameters analyzed - collection of blood samples and capillary blood glucose monitoring

In the preoperative phase, patients were assessed by a multidisciplinary team, and nutritional assessment was performed and collected anthropometric and clinical data of relevance. In the perioperative and recovery phase, in addition to serum elements object of this study, clinical data have been documented to answer the questions contained in the variables of study, in addition to the times of surgery, cardiopulmonary bypass and aortic clamping (AC).

We collected blood samples at different stages: a first sample in the preoperative phase, 2nd and 3rd samples in the operating room, being the 2nd before induction of anesthesia and the 3rd at the end of CPB (post-CPB), from the 4th to 6th samples in the immediate postoperative period (IPO), being the 4th sample when reaching the ICU, the 5th with 6h of evolution and the 6th with 12h of postoperative evolution. Glucose and insulin were measured for calculation of the Homa index (IR and Beta) for each sample.

Two capillary blood glucose tests were performed in the operating room, and the 1st occurred immediately before entering CPB and the 2nd after 1h of infusion. Furthermore, six additional serial examinations were performed in the first 6h of recovery in the ICU at the bedside. It has been documented the amount of exogenous insulin used in these phases.

Statistical analysis

For values with Gaussian distribution we used parametric paired (or non-paired) t-tests, and analysis of variance. For values without Gaussian distribution we used nonparametric tests of Friedman, Wilcoxon and Mann-Whitney test. For qualitative variables we used chi-square and Fisher exact test. The descriptive analyzes were performed in Microsoft Office Excel 2007 and statistical analyzes in Stats Direct Statistical software (1.9.15).

Calculation of the sample was based on the premise of a two-day decrease in length of hospital stay. The significance level adopted was 5%, 80% power and two-tailed tests.

RESULTS

Clinical results of the preoperative phase

The demographic and clinical data, including analysis of risk factors for CAD, can be seen in Tables 1 and 2. In general, statistical analyzes revealed similarities between the groups (P> 0.05).

Analysis of patients revealed a mean left ventricular ejection fraction (LVEF) of 53.2 ± 11.9% for Group I and 49.8 ± 13.1% in Group II, what did not differ between groups (P=0.440).

The average time of fasting, in hours, for solids in Group I was 13.2 ± 2.8 h, as in Group II was 15.9 ± 4.1 h (*P*=0.020). Of the 40 patients assessed, only three patients in Group II reported discomfort and thirst preoperatively (*P*=0.115).

Clinical results of intraoperative phase

There were no cases of bronchoaspiration during anesthesia. No patient required the passage of a nasogastric tube for any reason. Gastric residue was not measured in this study.

The mean total surgery time was 237.2 ± 45.8 min. for Group I and 225 ± 46.4 min. For Group II (*P*=0.652). The mean CPB time was 73.6 ± 23.3 min. for Group I and 71.3 ± 25.1 for Group II (*P*=0.856). The mean AC time was 59.3 ± 20.2 min. in Group I and 58.9 ± 25.0 min. for Group II, with no significant difference between groups (*P*=0.835).

Regarding the need for vasoactive amines for weaning from CPB, four patients in Group I and ten patients of the Group II required dobutamine (positive inotropic drug), using as the standard an initial dose of 5 mcg/kg/min. This data denoted a reduced tendency to need the drug for Group I (*P*=0.057). No patient developed cardiogenic shock or vasoplegic syndrome. The mean LVEF of patients in Groups I and II who required dobutamine, compared to the other patients, did not differ statistically (*P*>0.05).

Clinical results of postoperative care unit (ICU and ward)

Incidence of PONV was assessed in the ICU. Six patients had nausea in Group I and eight patients in Group II (*P*=0.741); and three of these patients had at least one episode of emesis in Group I, while in Group II four patients experienced this manifestation. In the ward, three patients in Group I and five in Group II reported nausea (*P*=0.695), one patient in Group I presented vomiting, as in Group II, two patients presented emesis.

The duration of mechanical ventilation in the ICU, on average, was 373 ± 192.6 min. for Group I and 433.2 ± 185.3 min. for Group II (*P*=0.357).

There was no need for vasoconstrictors in the ICU and gradual weaning of the dobutamine introduced was only performed during recovery. When assessing over time (in

Table 1. Demographic and anthropometric data of 40 patients in the sample. Group I: patients undergoing fasting abbreviation with carbohydrate. Group II: patients undergoing fasting abbreviation with water to control.

	Group I (n=20) n(%) or mean±sd	Group II (n=20) n(%) or mean±sd	*P* Value
Age (years)	56.6 ± 6.56	60.5 ± 7.25	0.082
Male	14 (70)	12 (60)	0.530
White race, number	13 (65)	11 (55)	0.540
White race, number (kg)	71.1 ± 13.8	75.2 ± 11.6	0.312
Height (m)	1.65 ± 0.08	1.64 ± 0.07	0.739
BMI (kg/m2)	26.08 ± 3.27	28.00 ± 3.52	0.081
Waist Width (cm)	94.11 ± 9.07	99.6 ± 9.20	0.064
Hip width (cm)	96.52 ± 6.83	101.15 ± 8.08	0.058
Waist-hip ratio	0.95 ± 0.07	0.95 ± 0.05	0.224
SGAA	18 (90)	18 (90)	1.000
SGAB	2 (10)	2 (10)	1.000

SGA = Subjective Global Assessment, BMI = body mass index, SD = standard deviation, n = number of patients

Table 2. Clinical risk factors of the 40 patients of the sample. Group I: patients undergoing fasting abbreviation with carbohydrate. Group II: patients undergoing fasting abbreviation with water to control.

	Group I (n=20) n(%)	Group II (n=20) n(%)	*P* Value
Smoking	12 (60)	10 (50)	0.660
Sedentarism	12 (60)	14 (70)	0.530
Dyslipidemia	16 (80)	16 (80)	1.000
Use of Statins	11 (55)	15 (75)	0.162
Use of Beta-blockers	15 (75)	18 (90)	0.327
Previous MI	13 (65)	11 (55)	0.743
Pre-CTA	4 (20)	5 (25)	0.657

CTA = Coronary Transluminal Angioplasty, AMI = Acute Myocardial Infarction, n = number of patients hours) of the use of dobutamine in the ICU, for Group I, the average was 12.1 ± 4.5 h, as in Group II was 15.9 ± 18.6 h, giving a statistical difference between groups (*P*=0.034).

Atrial fibrillation (AF) occurred in two patients in each group in the ICU. Infectious complications occurred in one patient in Group I and two patients in group II (*P*=0.611). Severe infections or mediastinitis did not occur, as there was no mortality during hospitalization and cases of perioperative stroke or MI.

As to the time of hospital stay (Figure 1), there was significant differences between groups. Patients in Group I remained, on average, 2.5 ± 0.5 days in the ICU, whereas patients in Group II remained 3.5 ± 1days (*P*<0.001). For the duration of hospital stay, patients in group I were hospitalized on average 7.8 ± 1.4 days, whereas patients in group II were 9.7 ± 3.1 days (*P*=0.025).

Results of glycemic control (blood glucose and tests of capillary glucose)

Two tests of capillary glucose tests were performed intraoperatively. In relation to the 1st test (before the start of CPB) there was no difference between groups (*P*=0.692), and in Group I, the average was 129.9 ± 38.4 mg/dl and in Group II was of 135.4 ± 40.5 mg/dl. For the 2nd examination (1h after initiation of CPB), the mean of Group I was 162.2 ± 46.6 mg/dl, as in Group II was 175.3 ± 31.7 mg/dl (*P*=0.274).

Six tests of capillary glucose time series were performed during the IPO, as part of the recovery protocol in the ICU (Figure 2). Statistical comparison was performed, and for Group I, there was no difference (*P*=0.497) between serial examinations (from 1st to 6th examination), even when assessed as paired data. In Group II, there was significant difference (*P*=0.012) between serial examinations, with a progressive increase in blood glucose values and worsening glycemic control in this group, evidenced by the paired analyzes.

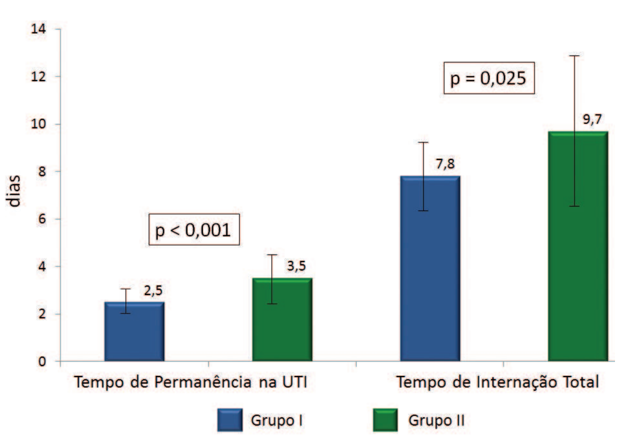

Fig. 1 - Comparison of mean time in days, with a standard deviation of ICU stay and total hospitalization for patients in groups I and II

Median blood glucose values preoperatively were similar between groups. When assessing the results of six blood glucose measured serially (preoperative, anesthetic induction, post-CPB, IPO, 6h and 12h PO), we observed a significant increase (*P*<0.001) of these values for both groups (Figure 3). However, the analyzes revealed no significant difference between groups (*P*>0.05).

Results from insulin resistance (Homa-IR and insulin requirements)

We observed a slight decline of the Homa-IR values of induction of anesthesia, for those of the preoperative phase in both groups. From induction to the post-CPB values, significant increase occurred in Group I (*P*=0.007) and Group II (*P*<0.001). The results of post-CPB measurements for the IPO, the opposite occurred, with a decline of these IPO values (4th measurement) for Group I (*P*=0.475) and group II (*P*=0.028). From the IPO in both groups a gradual increase of the index was observed, yielding an average of 11.2 ± 8.2 (median 8.9) for Group I and 11.6 ± 7.6 (median 9,2) for Group II in the last measurement (12h PO) (Figure 4). Between the groups, there was no significant difference in the assessment of the results (*P*>0.05).

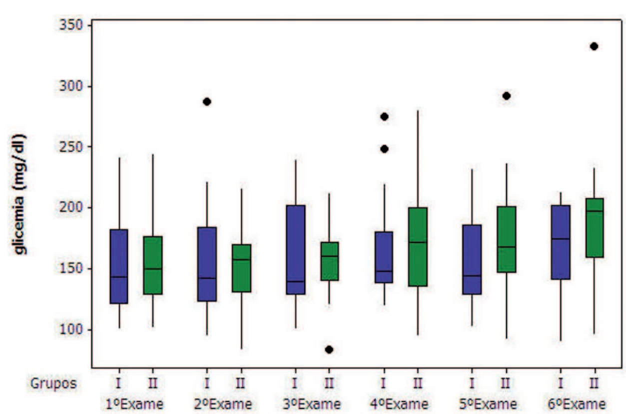

Fig. 2 - Box plot showing the results of capillary blood glucose serial testing for patients in groups I and II, in the first six hours of recovery in the ICU.

The mean use of exogenous insulin in the operating room, for Group I was 5.9 ± 5.7 IU, whereas in Group II was 7.5 ± 5.0 IU (*P*=0.321). Seven patients in Group I and three Group II did not require exogenous insulin at this stage (*P*=0.679). In the ICU and for Group I, the mean utilization was 18.5 ± 13.4 IU; in Group II was 21.1 ± 11.5 IU (*P*=0.424). One patient in Group I and two in Group II did not require insulin in the ICU (*P*=0.892).

Results of the excretory function of pancreatic beta cell (Homa-Beta)

As for the Homa-Beta index (Figure 5) in both groups there was a progressive decline of the median values found in the various phases measured (*P*<0.001), indicating decrease of the function of endogenous insulin-producing cell, with gradual return (rise of values) during recovery in the ICU, more precisely the values of IPO until 12h postoperatively. For the paired assessments of the Homa-Beta index results between the groups, there were no significant differences (*P*>0.05).

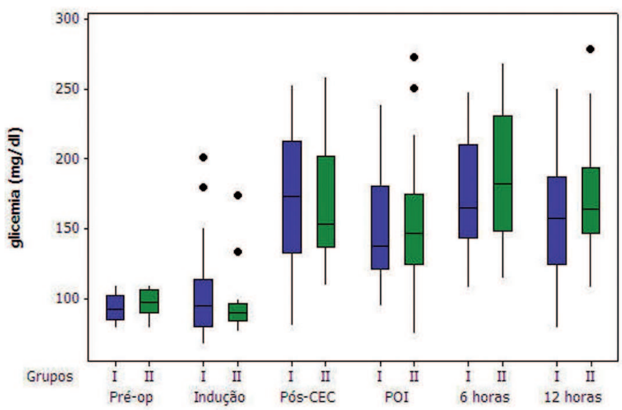

Fig. 3 - Box plot showing the results of blood glucose testing for patients in groups I and II, in the different periods collected for analysis. Pre-op = Preoperative; CPB = cardiopulmonary bypass; IPO = Immediate Postoperative

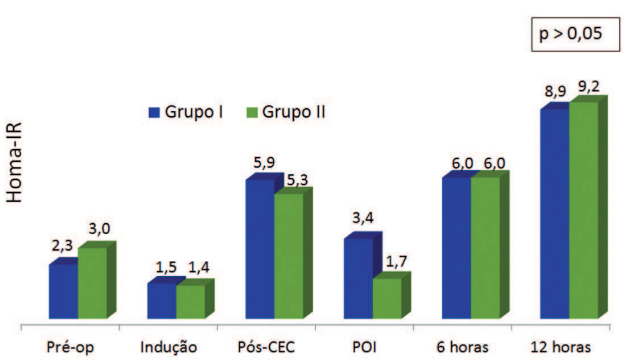

Fig. 4 - Comparison of the results of the median values of Homa-IR index to patients in groups I and II, in different periods. Pre-op= Preoperative; CPB = cardiopulmonary bypass; IPO = Immediate Postoperative

DISCUSSION

The groups were homogeneous. Discomfort and thirst in the preoperative phase were reported by only three patients of all sampling. We considered this as satisfactory and relevant to the purpose of multimodal protocols, but it deals with a subjective matter. The method of fasting abbreviation used was considered safe and there was no *bronchoaspiration* nor increased morbidity. Death, MI, stroke or mediastinitis did not occur in this study.

Literature data on morbidity and mortality during hospitalization for patients with clinical features similar to this sample, who underwent elective CABG with CPB show frequency of occurrence between 1.4% to 3.8% for perioperative stroke, 27% to 40% occurrence of the AF; 1% to 2% for MI or in-hospital phase mediastinitis, in addition to overall mortality rate of 1% to 2% in patients with preserved LVEF [26].

Time in ICU and hospital stay was lower in group I (intervention) (*P*<0.05), from, in part, the tendency to lower use of inotropic dobutamine in patients in this group (*P*=0.057) during perioperative phase, as well as by the short time of use (weaning) of the drug in the ICU (*P*=0.034). This data indicates the benefit obtained with the abbreviation of fasting and CHO delivery. However, the assertion that there was a protective effect to the heart by less need for inotropic agents should be careful. The inference allows only indirect analysis of the finding, considering that perioperative ventricular performance depends on multiple clinical variables, LVEF and the associated surgery.

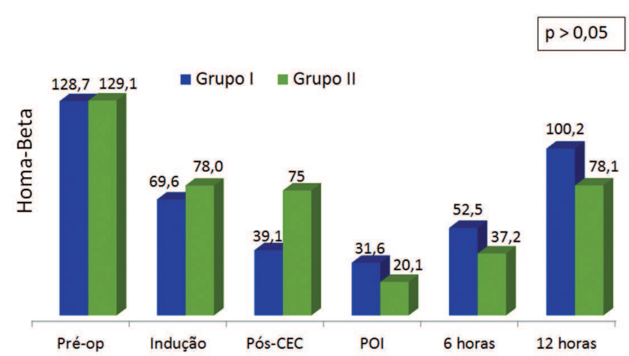

Fig. 5 - Comparison of the results of the median values of the Homa-Beta index for patients in groups I and II, in different periods. Pre-op = Preoperative; CPB = cardiopulmonary bypass; IPO = Immediate Postoperative

Experimental models in rats undergone prolonged fasting or adequate nutrition before stress (hemorrhage induced hypotension and ischemia/reperfusion) were tested in order to establish possible improvements in cardiac function and obtained favorable results for rats previously fed. [27] Studies administering CHO in the preoperative phase of CVS, data on pure formulation or associated with intravenous lipids, or with concomitant infusion of a solution containing glucose-insulin-potassium, showed benefits on cardiac performance, decreased need for inotropes, incidence of AF and acute ventricular failure. [28-30].

Multimodal protocols belong to the reality of CVS, also being recommended in guideline for CABG [2-6,26]. De Vries et al. [6] compared 3760 patients who underwent CVS before implementation of a protocol checklist, with 3820 patients operated after implementation. The number of complications per 100 patients decreased from 27.3 (25.9 to 28.7, 95% CI) to 16.7 (15.6 to 17.9, 95% CI). The percentage of patients with complications decreased from 15.4% to 10.6% (P<0.001). In Brazil, reference centers in CVS have been concerned with the creation and deployment of multimodal protocols, with the proposition of risk scores for patients undergoing CABG and maintaining databases in order to assess the results and adoption of impact measures for improvements [2-5,31-34]. Atik et al. [5] showed that after adoption of the organizational model, there was a reduction in hospital mortality (from 12% to 3.6%, RR=0.3, P=0.003), as well as adverse events combined (22% to 15%, RR=0.68, P=0.011).

As for the results of glucose, because only nondiabetic patients participated in this study, the median values found for blood glucose tests and blood were <200 mg/dl at all stages measured. The results of blood glucose between groups showed no significant difference (P>0.05). However, glycemic control for testing blood glucose in the initial 6h of the IPO was worse in Group II (P=0.012). This information is relevant and shows another beneficial effect obtained with the abbreviation of fasting and CHO delivery.

Metabolic control in CVS is of fundamental importance for improvements in morbidity, reducing the exacerbation of neurological damage and specific mortality [35]. McAlister et al. [36] assessed the rates of glucose in the first postoperative day of CABG, showing 17% increase in adverse events (stroke, MI, arrhythmias, sepsis and death) for each 1 mmol/L (18 mg/dl) surplus 6.1 mmol/L (110 mg/dl) of glucose in blood samples. Furnay et al. [37] studied 4864 patients who underwent CVS, and perioperative hyperglycemia was associated with higher rates of mediastinitis, higher hospital costs and prolonged hospitalization. In a multicenter study, Székely et al. [38] assessed the relationship between perioperative hyperglycemia and mortality in 5050 patients undergoing CABG. Mortality was higher in diabetic patients (4.2% versus 2.95%, P=0.02), however, this population was not associated with hyperglycemia mortality. However, in non-diabetic the glucose levels in the PO phase between 250 and 300 mg/dl (OR 2.56, 95% CI, 1.18 to 5.57, P=0.02), patients who had blood glucose 300 mg/dl or more (OR 2.74, 95% CI, 1.22 to 6.16, P=0.01) and intensive insulin therapy (OR 4.2, 95% CI, 1.12-3.70, P=0.01) were considered independent risk factors for hospital mortality. Several authors are emphatic in stating the treatment of hyperglycemia with schemes of continuous infusion of insulin [36-38].

In recent years there has been growing interest in measuring the degree of IR in clinical practice, and the Homa method (Homeostatic model assessment) as one of the most used [25]. It is a mathematical model that predicts insulin sensitivity by measuring the blood glucose and insulin, it is easy to perform, low cost and requires short time to get the result, in addition to have validated relationship with follow-up and prognosis of cardiovascular disease [39,40]. The model has positive correlation with the hyperinsulinemic euglycemic clamp method [41], considered the gold standard, however more difficult to reproduce, being costly and time consuming. From the Homa method are extracted the Homa-IR and Homa-Beta index, that aim to translate the insulin sensitivity and secretory capacity of pancreatic beta cells.

The Homa method is used and validated in several studies that discuss the IR, however, the value of the cutoff point for the index is still subject to controversy [42]. To define the cutoff point in the present study we use the Guidelines of the Brazilian Society of Diabetes [43] being considered a criterion for IR, Homa-IR values >3.6 when occurring BMI >27.5 kg/m^2 or simply Homa-IR >4.65. For the Homa-Beta index, there were no differences in the literature, and the values were considered normal when between 167-175 or 100% activity of pancreatic beta cells [38].

IR was observed in this study and differed little between groups, despite the intervention (P>0.05). The increase in IR occurred mainly after the end of CPB and during recovery in the ICU, with increasing values until 12h postoperatively. The Homa-Beta index measured in the groups showed a reduction in pancreatic beta cell function, seen from the preoperative values (P<0.001). This data denoted a decrease in endogenous production of insulin in the perioperative period, which may favor the loss of glycemic control. These changes are due to CPB use, hypothermia related to the technique, electrolyte abnormalities related to the potassium and increased secretion of adrenaline, which in turn are characteristic of this type of surgery and interfere with the function of the endocrine pancreas [44].

The use of CPB may worse IR; Lehot et al. [45] showed that during hypothermic CPB, blood glucose levels tend to increase, while insulin levels tend to decline. During rewarming, however, insulin levels have a strong fluctuation and may increase substantially, associated with increased catecholamines, cytokines, cortisol and GH. Therefore, there would be an interposition of factors associated with the trauma and the increased secretion of pro-inflammatory hormones could worsen the IR. Knapik et al. [46] showed that CPB increases blood glucose levels, and promote IR in diabetic and nondiabetic patients undergoing CABG. Part of the explanation of these findings comes from the systemic inflammatory response syndrome (SIRS) and activation of the complement system [20]. The blood contact with non-biocompatible surfaces of CPB, surgical trauma and reperfusion injury imposed by the method have been considered precise mechanisms for this event [47].

Contemporary evidence for improvement in metabolic control with CHO delivery preoperatively and abbreviation fasting is concise, even for highly complex procedures [48]. Breuer et al. [21] studied 188 patients who underwent CVS, being performed abbreviated fasting with CHO or placebo in two different groups and conventional fasting in another group. It was supplied with 800 ml drink the night before surgery and 200 ml 2h before induction of anesthesia. Need for exogenous insulin to maintain glucose levels <180 mg/dl was used as a marker of IR and did not differ between groups (*P*>0.05). Comfort preoperatively and absense of thirst were better for groups on which fasting was abbreviated (*P*<0.01), there was no case of bronchoaspiration and the need for dobutamine was lower in the CHO group (*P*<0.05). Jarvela et al. [49] studied 101 patients, and fasting was abbreviated with 400 ml of CHO-rich liquid, 2h before CABG or conventional fasting as a control. There was no difference between glucose levels, IR or need for exogenous insulin, but, unexpectedly, the group that received the intervention obtained higher rates of nausea, compared to controls (*P*=0.04).

Therefore, it is clear that in the CVS, unlike some areas of general surgery, IR is present manifestation, unwieldy and sometimes exaggerated. Studies of abbreviation fasting and CHO supply should be performed to substantiate the findings of this study, as well as to examine possible protective effects to the heart, effects on IR and inflammatory responses arising from the use of CPB.

A sample of 40 patients was considered a limiting factor, although sample size calculation was performed in this study for the application of appropriate statistical methodology.

CONCLUSION

Abbreviation of preoperative fasting in CHO delivery in CABG was safe and may be practiced. It improved glycemic control in the first six hours of recovery in the ICU, decreased hospital and ICU stay and provided less time for the use of dobutamine. However, neither IR nor morbimortality during hospital phase were influenced.

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