DE GRUYTER OPEN

ПРИЛОЗИ. Одд. за мед. науки, XXXVI 3, 2015 МАНУ
CONTRIBUTIONS. Sec. of Med. Sci., XXXVI 3, 2015 MASA

10.1515/prilozi-2015-0079 ISSN 1857-9345
UDC: 615.252.349.015.8:616-089

INSULIN RESISTANCE, GLYCEMIA AND CORTISOL LEVELS IN SURGICAL PATIENTS WHO HAD PREOPERATIVE CALORIC LOAD WITH AMINO ACIDS

Marija Jovanovski-Srceva[1], Biljana Kuzmanovska[1], Maja Mojsova[1], Andrijan Kartalov[1], Mirjana Shosholcheva[1], Marina Temelkovska-Stevanoska[1], Aleksandra Gavrilovska[1], Sotir Stavridis[2], Zoran Spirovski[3], Borislav Kondov[3], Anita Kokareva[1], Risto Todorov[4], Tatjana Spirovska[1]

[1] University Clinic for Anesthesia, Reanimation and Intensive care, Faculty of Medicine, University "Ss. Cyril and Methodius", Skopje, R. Macedonia
[2] University Clinic for Urology, Faculty of Medicine, University "Ss. Cyril and Methodius", Skopje, R. Macedonia
[3] University Clinic for Thoracic Surgery, Faculty of Medicine, University "Ss. Cyril and Methodius", Skopje, R. Macedonia
[4] University Clinic for General Surgery "St. Naum Ohridski" Faculty of Medicine, University "Ss. Cyril and Methodius", Skopje, R. Macedonia

Corresponding Author: Marija Jovanovski-Srceva, MD, MSc, Clinic for Anesthesia, Reanimation and Intensive Care, Faculty of Medicine, University "Ss. Cyril and Methodius", 1000, Skopje; Tel: + 389 (0)2 72 65 24 75;
E-mail: marijasrceva@gmail.com

Abstract

Introduction: Surgical stress response, results in elevated levels of anti-insulin hormones and reduced insulin secretion. This hormonal state may be detrimental for surgical patients due to the presence of insulin resistance and hyperglycemia. Additionally, pre-operative fasting favors this conditions. The aim of this study is to analyze the impact of pre-operative caloric load, with 440kJ from amino acid infusions on the levels of glucose, cortisol and insulin resistance in surgical patients.

Material and Methods: The study included 20 female patients scheduled for mastectomy, aged 30–60 years without diabetes and BMI < 30 m^2, divided into two groups. The study group A, the evening before the surgery, received 1000 ml amino acid infusions, while the control group B didn't receive any infusion. In both groups glucose, C-peptide and cortisol levels were determinate preoperatively and postoperatively. From the obtained C-peptide and glucose values, with the help of computer model (HOMA2*), the insulin resistance (IR), functionality of beta cells (BETA) and insulin sensitivity (IS) were calculated.

Results: Postoperative values of insulin resistance (0.94 ± 0.12 vs 1.13 ± 0.2; p = 0.02) and glucose (4.79 ± 0.5 vs 5.77 ± 0.6; p = 0.002) were lower in the study group compared to control group. Postoperative cortisol levels in both groups were higher than the preoperative, but no significant difference was found. The study group showed higher values for BETA and IS. Percentage changes between the groups were significant for all parameters.

Conclusion: Pre-operative caloric load (amino acids) reduces the level of insulin resistance and glucose in the presence of elevated cortisol levels.

Key words: Insulin resistance, blood glucose, cortisol, preoperative fasting, amino acid
*HOMA 2 model is available on www.OCDEM.ox.ac.uk

Introduction

Literature is decisive that stress response to a surgery and anesthesia affects glycemic homeostasis on many levels. The prototypical scenario in surgical patients (with or without diabetes) is: elevated levels of contra-regulatory hormones (catecholamines, glucagon and cortisol) which have various anti-insulin metabolic effects and promote increased net catabolic activity. On the other hand, due to the unexplained defect of the beta pancreatic cells, during surgery, plasma insulin levels fall and secretion of insulin in response to glucose becomes impaired. These hormonal and metabolic changes promote occurrence of hyperglycemia and insulin resistance in all surgical patients with or without diabetes [1–3].

Insulin resistance usually starts to develop during the surgery and is present for the period of 10 to 30 post-operative days, depending of the magnitude of the surgical trauma [4–6]. Gender, age and pre-operative levels of insulin (in the plasma) are not factors that correlate with its occurrence [7].

Increased levels of cortisol, developed insulin resistance and hyperglycemia have significant negative impact on the healing process and cause increased morbidity and mortality in surgical patients. When insulin resistance and hyperglycemia are present, cells (not dependent on insulin) are flooded with glucose and have alerted functionality [4–7].

On the other hand, preoperative fasting (minimum 6 hours before surgical intervention) in order to reduce the risk of pulmonary aspiration, is a routine for surgical patients. The literature is precise that any starvation longer than 4 hours leads to a change of the insulin / glucagon ratio. This feature can further emphasize organic stress response to surgical trauma and has big impact on the glycemic control and insulin resistance [8, 9].

In the recent decades, it has been often debated that reduced preoperative fasting time (and / or pre-operative support of the body with nutrients) has positive impact on the levels of contra-regulatory hormones, insulin resistance and glycaemia [9–11].

The idea for this study rose as a result of two inspirational studies. The first study by Thorell A [12] and co-workers, who published results, shows that insulin resistance occurs without elevated levels of anti-insulin hormones (cortisol, catecholamines, and glucagon), in surgical patients who received pre-operative nutrient (glucose). The second study, although endocrinologic, by Luc van Loon [13], provides information that the ingestion of the amino acids in patients with type 2 diabetes increases the secretion of insulin and promotes better glycemic control.

From these studies, it seemed logical to hypothesize that the preoperative intake of amino acids might stimulate insulin secretion, might change the level of cortisol and all this will affect the level of postoperative insulin resistance.

Purpose

The objective of this research was to analyze the effects of pre-operative change of the state from "hungry" to "fed", with 440 kJ (from amino acids infusions), at the level of postoperative blood glucose, cortisol and insulin resistance in surgical patients.

Material and methods

This randomized prospective clinical study was performed at the Clinic for Traumatology, Orthopedic diseases, Anesthesia, Reanimation and Intensive Care Skopje, from January to October 2015. The study was conducted after the approval by the ethical committee and the signed information consent by every patient.

The study included 20 female patients, scheduled for elective radical mastectomy under general endotracheal anesthesia, aged 30–60 years, without personal or family history of diabetes, with pre-operative values of HgA1C< 5.7%, glucose < 6.1 mmol / l, BMI < of 30 m^2 and under physiological score for preoperative assessment of health – ASA (American Society of Anesthesiologists) 1 and 2.

The study excluded all patients with endocrine disorders, patients who had corticosteroid therapy (in any form) and patients who had weight loss greater than 7 kg (in the last two months).

From the commenced study, the patients in whom surgery lasted more than 2 hours and the patients who required administration of corticosteroids, vasopressors or glucose solutions at any time during the per-operative period were additionally excluded.

The patients were randomly assigned into two groups. The patients in the study group (group A, n = 10), the evening before surgery (at 22:00h), received 1000 ml of amino acids solutions with energy value of 440 kJ. The composition of the amino acids was as follows: alanine 15 gr, 5.10 gr phenylalanine, leucine 7.4 gr, proline 15 gr, arginin 12 g, 6.6 gr lysine, isoleucine 5 gr, threonine 4.4 gr, 14 g of glycine, histidine 3 gr, 4.3 gr methionine, valine to total 6.2 gr. In the control group (group B, n = 10), no infusion was administrated on the evening before surgery.

All patients underwent standard pre-operative protocol for nothing per mouth (for 6 hours) and premedication with oral Diazepam 5 mg.

The standardized intravenous anesthesia protocol was commenced for both groups. The induction was accomplished with fentanil (3 μg/kg) and propofol (2 mg/kg). The intubation was facilitated with rokuronium bromid 0.5 mg/kg. The anesthesia was maintained with continuous infusion of propofol 6 mg/kg /h. The patients were mechanically ventilated with inhaled fraction with a mixture of O_2 (50%) and air (50%).

In both groups the levels of insulin (C-peptide), glycaemia and cortisol were determined preoperatively (before the induction of anesthesia) and 24 hours postoperatively.

C-peptide or proinsulin is located in the secretory granules and is released into the blood in equimolar amounts to insulin. C-peptide is a substitute for the function of the beta cells and is often used in the classification of diabetes [14].

The concentration of C-peptide (referent values: 0.53–2.9 $ng.ml^{-1}$) and cortisol (referent values: 55–690 nmol/l) were determined by hemi-luminescence ECLIA (ELIKSIR 2010 – Roshe), while the glucose was determined by the glucose-oxidize method (Randoks, UK) with reference values 3.3–6.6 mmol / l.

From the determined levels of C-peptide and glucose, the levels of IR (Insulin Resistance), functionality of Beta cells (BETA) and IS (Insulin Sensitivity) were calculated with the HOMA (Homeostasis Model Assessment) method.

– Basics for use of HOMA (Homeostasis Model Assessment) in calculating IR, BETA and IS:

Insulin resistance (IR) can be calculated by various methods. The golden standard is hyperinsulinemic-euglycemic clamp. This presents a complex stress test, with hyper optimal doses of insulin and glucose that does not justify its use. In contrast, HOMA is a mathematical model which can noninvasively determine insulin resistance, functional capacity of the beta cells (BETA) and the sensitivity of the peripheral tissues to insulin (IS). It is based on the interaction between glucose and insulin levels, hepatic glucose production (dependent of the level of insulin released) and the ability of insulin to bind to glucose in the blood. Equations used are as follows:

HOMA-IR = PI* x PG** / 22.5;

HOMA-BETA = 20xPI / PG -3.5); where *PI is Plasma Insulin and **PG is plasma glucose

The calculated values of BETA and IS calculated with the HOMA method significantly correlate with the physiological insulin sensitivity and functionality [15].

In our study we used the computer program HOMA 2 (computer calculated equations) model. It is a purified HOMA method, which has integrated formulas that take into consideration the variations in the hepatic and peripheral insulin resistance. (HOMA 2 model is available on www.OCDEM.ox.ac.uk).

In healthy people without pancreatic diseases and normal body weight the normal functionality of the beta cells (BETA) is approximately 100% and the insulin sensitivity (IS) should be near the range of 90–100%, whereas the indication of insulin resistance is any value above 2 U.

Statistical Analysis

The databases were created with the help of computer programs, the processing of which is made with the standard descriptive and analytical bivariant methods. The attributive and numerical data were analyzed using the odds relations, proportions or the measure of the central tendency. The statistical significance was tested with the Mann-Whitney U Test, Student t-test. The significance is indicated when $p < 0.05$.

Results

In accordance with the including criteria, the study enrolled twenty patients randomized in two groups.

Among both groups of patients, there were no statistically significant differences in the baseline demographics characteristics (ethnicity, age, weight, height, BMI, ASA). The baseline demographics and the clinical characteristics of the patients are shown in Table 1.

In both groups, the largest number of patients had left side radical mastectomy. None of the patients had anesthetic or surgical complications in the first 24 hours.

The pre-operative values of blood glucose (5.37 ± 0.72 SD versus 5.21 ± 0.62 SD), insulin resistance (1.1 ± 0.26 SD versus 0.97 ± 0.3 SD) and C-peptide (1.48 ± 0.38 SD vs. 1.33 ± 0.37 SD) were not significantly different between the groups.

Table 1

Demographic and clinical characteristics (Mean ± SD)

Parameters	**Group A n = 10**	**Group B n = 10**	**p**
Age	45 ± 10.0SD	45 ± 9.74SD	NS
BMI(m^2)	25.5 ± 4.14SD	25.8 ± 2.4SD	NS
ASA 1/2	 5/5	 5/5	 NS
Blood glucose	5.37 ± 0.72SD	5.21 ± 0.62SD	NS
Laboratory findings: WBC/RBC/Hb/PLT Urea/Creatinine	Mean 7.8/4.6/132/250 5/66	Mean 7.4/4.5/134/250 4.7/58.5	 NS NS

Abbreviations: BMI-Body Mass Index; ASA- American Society of Anesthesiologist; WBC-White Blood Cells; RBC-Red Blood Cells; PLT-Platels; NS-Not significant (p > 0.05)

In the study group, the postoperative mean values of blood glucose (Mann-Whitney U test: Z = 1.98 p = 0.04) and insulin resistance (Z = 2.0 p = 0.04) were significantly lower than the pre-operative. In the same group, the postoperative values of C-peptide (Mann-Whitney U test: Z = 0.64 p = 0.5), BETA (Z = -0.45 p = 0.6) and insulin sensitivity (Z = -1.6 p = 0.09) were not statistically significantly different than the pre-operative ones.

Between the groups, the mean postoperative values for blood glucose (Mann-Whitney U test: Z = -3.02372 p = 0.002497) showed statistically significant differences.

The comparison of the average postoperative values for blood glucose, insulin resistance and C-peptide, between the groups is shown in Table 2.

Table 2

Average postoperative values of blood glucose, insulin resistance and C-peptide (Mean ± SD)

	Group A n = 10	**Group B n = 10**	**p**
Blood glucose (mmol/l)	4.79 ± 0.52 SD	5.77 ± 0.6 SD	p = 0.002
C-peptide (ng.ml-1)	1.37 ± 0.25 SD	1.47 ± 0.3 SD	p = 0.3
Insulin resistance (mU/l)	0.93 ± 0.12 SD	1.13 ± 0.23 SD	p = 0.02

The pre-operative values for the functionnality of the pancreatic beta cells and the insulin sensitivity, were not significantly different between the two groups.

The postoperative, average values for the functionality of the beta cells in the groups were not significantly different compared to the pre-operative ones. On contrary, the postoperative values of insulin resistance (Mann-Whitney U test Z = -2.19219 p = 0.028366) and insulin sensitivity (Z = 1.96542 p = 0.0049367) were significantly different between the groups (Table 3).

The coefficient of variations, was higher in the control group for insulin resistance

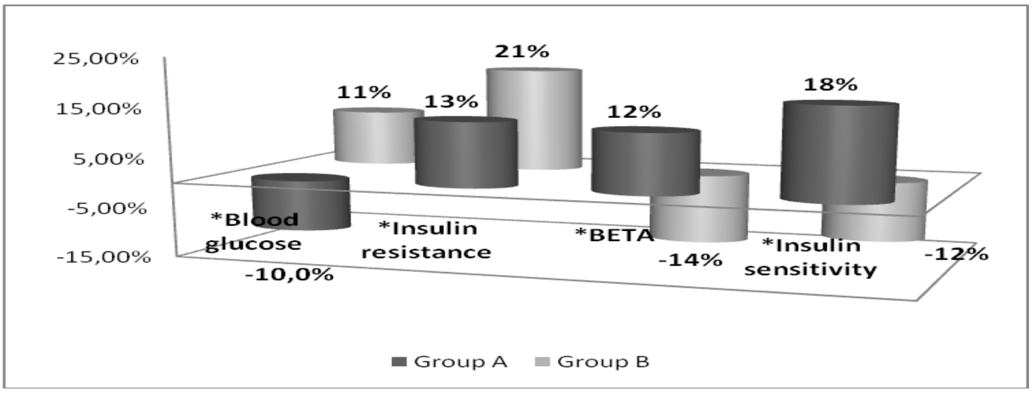
(18.2%) and insulin sensitivity (22.6%), whereas in the study group it was higher for C-peptide (30.8%) and functionality of beta cells (29.7%).

Table 3

Average values and changes of insulin sensitivity (IS) and functionality of beta cells (BETA) between the groups

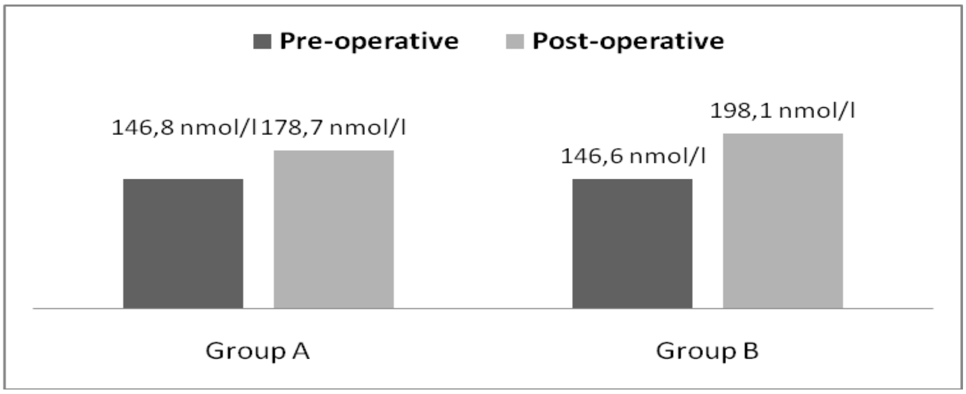
	Group A n = 10	Group B n = 10	p
BETA (%)	Mean (Min; Max)	Mean (Min;Max)	
Pre-operative	97 (51.5; 191)	89.6(129.6; 55.8)	p = 0.09
Post-operative	101.6 (149.2; 65.3)	73.61 (83.8; 45.6)	p = 0.08
Change	0,11 (0,5; -0.25)	-0.13(0.25; -0.4)	p = 0.04
Insulin sensitivity (%)			
Pre-operative	94.8 (130.5; 62.7)	108.23(146.1;64.7)	p = 0.1
Post-operative	108.29 (124; 84,2)	93.36(137.3; 63.4)	p = 0.04
Change	0.17(0.55; -0.04)	-0.12(0.002; -0.35)	p = 0.001

With regard to the changes expressed in percentages for the pre-operative and post-operative values for blood glucose, insulin resistance, functionality of beta cells and insulin sensitivity, significant difference was found between the groups (Graph 1).



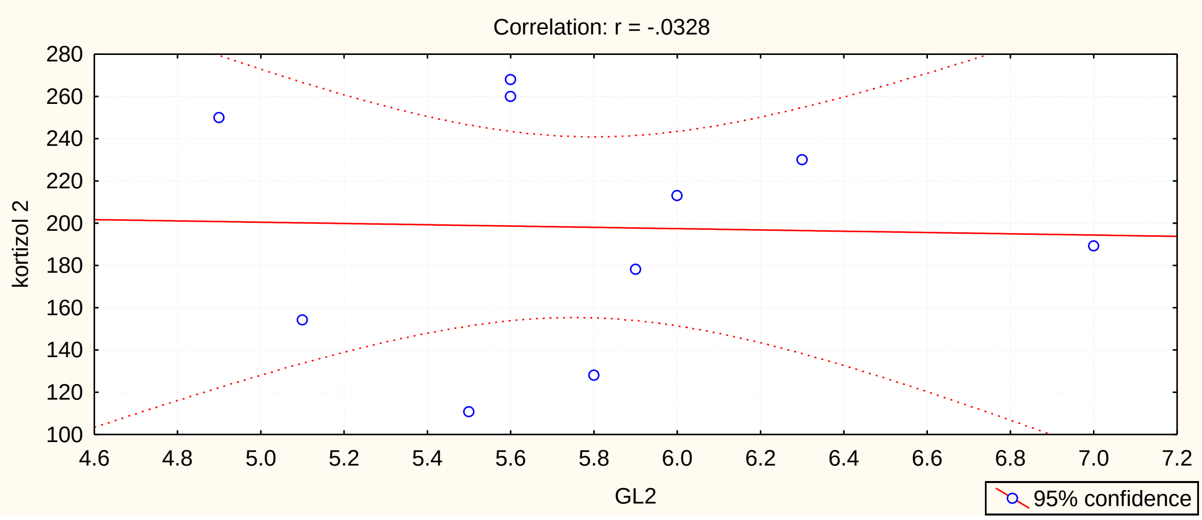
*Graph 1 – Changes expressed in percentage between the groups (*p < 0.05)*

The values of the cortisol showed an increase postoperatively (from 146.7 ± 56.5 SD to 178 ± 36.1SD, p > 0.05) for group A and (from 146.6 ± 76.9SD vs. 198.1 ± 55.3SD, p > 0.05) for group B. The average postoperative values of cortisol between the two groups were not significantly different.



Graph 2 – Change of the average values of cortisol in the groups

Between the postoperative values of cortisol and blood glucose insignificant negative correlation was found (r = -0.3238) (Graph No 3).



Graph 3 – Correlation of postoperative cortisol levels and blood glucose

Discussion

The presented study was conducted as pilot study and showed how in clinical practice it is possible to influence the levels of postoperative insulin resistance and blood glucose in surgical patients in the presence of elevated levels of cortisol.

Insulin resistance develops during the surgery and is present for long time in the postoperative period. Historically, the occurrence of insulin resistance was considered to be a clinical feature reserved only for diabetic patients with major surgical trauma [7]. Nowadays, it has been confirmed that postoperative insulin resistance is present in all surgical patients [8, 11, 12].

Resent clinical randomized studies showed results that preoperative consuming of nutritional solutions improves glycol-regulation and reduces insulin resistance, which was confirmed in our study [8–13, 16–18].

In our study, post-operative insulin resistance decreased for 13% (compared to preoperative values) in the group which had caloric intake. Contrary, in the control group, post-operative insulin resistance showed increase for 21%. Changes in the groups and between the groups were statistically significant. A significant reduction in insulin resistance was also observed by Perrone et al. [11] in patients scheduled for inguinal hernia repair and cholecystectomy. In his study similar to ours, in all patients 3 hours before the intervention, a nutritional support with carbohydrates and protein combined solutions was obtainned. The authors Nygren A., Thoreell A and Ljungqvist O. [12] published astonishing results and confirmed that shorter pre-operative fasting time, significantly reduced insulin resistance in surgical patients with major surgical trauma.

The values higher than 2U are an indication of insulin resistance. In our study, the values higher than 2 U were not registered in any patient. The differences in the results of the above-cited authors [11, 12] and our study are due to the inclusion criteria. In our study, the inclusion criteria was the level of HgA1c < 5.7%. This reliably rules out diabetes and prediabetes in patients. Therefore we can say that the results from our study are precise because all the patients in this study had intact pancreatic function.

Literature agrees on the fact that insulin resistance in the early post-operative period is located in peripheral tissues, predominantly muscles. In these tissues the intercellular activity of the proteins responsible for glucose transport is malfunctioning [9]. On the other hand there is a strong evidence that different types of amino acids in different extent improve glucose utilization by muscles which improves glucose oxidation [19]. These results are giving priority to the protein solutions over other solutions in surgical patients. Amino acids solutions as protein sparing therapy in surgical patients are reserved for the post-operative period. Maybe it is time to change the usual clinical practice.

Insulin resistance by itself or accompanied by elevated blood sugar leads to increased morbidity and mortality. In this study, changes of the insulin resistance were followed by significant changes in blood glucose. In our study, the postoperative blood glucose values were increased in the control group (from 5.21 mmol/l to 5.77 mmol / l), while in the study group were decreased (from 5.39 mmol / l to 4.79 mmol/l). Maitra et al. [20], Zong et al. [21] and Srceva et al. [22] argue that the administration of different fluids in the pre-operative period differently affect the blood sugar levels. From this study and the studies of Srceva [22] and Zong [21] we can clearly conclude that pre-operatively given amino acids has strong positive impact on the postoperative blood glucose levels.

From the large number of endocrine studies it is known that protein intake triggers increased protein anabolism and increased insulin secretion [13].

In our study, insulin levels (expressed by C-peptide) did not show significant change between the groups. Anyhow, worth to note is the fact that postoperative values of insulin were lower in the control group compared to the study group (1.37 ng / ml versus 1.47 ng / ml). Similar to this, Perrone et al. [11] observed a significant drop in insulin levels and insulin resistance in patients who received combined carbohydrate-protein solution pre-operatively. In contrast, Srceva [22] although working by different protocol, has proved a strong insulin-tropic effect of the amino acids given preoperatively to patients with minor surgical trauma. The differences in the two studies may be due to several factors. In the study of Srceva [22], baseline C-peptide was determined before the intervention with amino acids and the volume of the given amino acids was assessed by body weight. It seems that caloric intake of 440 kJ (although with energy value equal to a small meal) is hypo caloric to stimulate the secretion of large amounts of insulin.

Isolated discussing of the insulin resistance, insulin and blood glucose is possible but is not adequate due to the wide range of factors involved in its determination. In patients with diabetes, insulin resistance is correlated with the plasmatic insulin and glucose concentrations. Decreased insulin levels are proportional to insulin resistance [11].

In surgical patients, the shift from anabolism to catabolism promotes glycemic deregulation and insulin resistance. For our study, the postoperative cortisol levels in both groups showed significant increase. Although the changes were not significantly different between the groups, it shows that in patients who undergo radical mastectomy the stress response and catabolism are activated. The elevated levels in one of the anti-insulogenic hormones (cortisol) in our study did not correlate with the increased insulin resistance in patients who received preoperative calories. The study of Thorell A and coworkers [12], confirms insulin resistance in the absence of elevated cortisol levels. Kee et al. [23] argue that the parenteral administration of amino acids enhances the whole anabolic function of the body. From here it is confirmed that pre-operative fasting and low calories nutrition is a strange way of preparing the body for stress.

Insulin resistance is mathematical obtainned product from the levels of C-peptide and glucose. The advantage of the mathematical calculation is in the parallel with the calculated functionality of the pancreatic beta cells and the sensitivity of the cells to insulin.

Literature is rich in studies that debate about the isolated insulin resistance, but there is a lack of studies which cover the overall picture of glycemic response in correlation with resistance, sensitivity and beta cell functionnality.

During stress, the pancreatic cells have compromised functionality. Prisseig [24] proved their limited ability to adapt to newly occurred changes under these conditions. The mathematical calculation model for the functionality of the beta cells, reflects their activity, but not their pathological condition. In patients without diabetes, the functionality of the beta cells would normally be about 100%. In this study, the pre-operative values of the beta cells functionality in both groups were close to normal. On the contrary, the postoperative beta cell functionality was reduced in the control group compared to the group with caloric load (73.61 ± 11.3 SD versus 101.64 ± 30.2 SD). This means that patients who are "hungry" pre-operatively, show decreased beta cell ability to secrete "enough good" insulin for reversion of the extra glucose (product of the stress response) postoperatively. At the same time, in this group, the reduced sensitivity of the peripheral tissues to insulin is noticed (to 93% compared to 108% which occurs in the examined group). Although these figures are rough surrogate of the glyco-methabolic response and their interpretation can hardly be isolated, it is clearly apparent that "hungry" patients behave like being "diabetic" in the postoperative period. This means that the body is overloaded with endogenous glucose in the presence of elevated levels of insulin and peripheral tissues inability to use it.

Conclusion

From the above, we can conclude that pre-operative intake of amino acids in surgical patients scheduled for radical mastectomy, reduces the occurrence of insulin resistance and hyperglycemia, and improves the functionality of the beta cells in the presence of increased cortisol levels.

Limitations and recommendations

This study has several shortcomings. The number of respondents is small. Age inclusion criteria (30–60 years) is a heterogeneous age group, but the literature is determined that age does not have impact on the insulin resistance [7]. A second drawback is that the caloric load with 440kJ was used in all patients regardless the body weight. The reliability of the study would be higher if it demonstrated the impact of the pre-operative support with different nutrients divided in several groups. The data derived from the mathematical model (HOMA 2) would be much more reliable if being compared with the clinical model of euglycemic-hyperglycemic clamp.

Although small, from our study we can draw back several recommendations. This study opened the door for a larger study to access the problem of preoperative nutrition and glycemic response. Rough surrogate figures shown from the mathematical model (HOMA2) can be discussed through clinical vocabulary and should be used in larger number of clinical studies. If the results of this study are confirmed in large clinical study, the applicability of the method can be used in daily surgical practice especially in patients with diabetes.

Conflict of Interest: There is no conflict of interest.

Acknowledgments

The authors would like to express their gratitude to Borka Kocevska and Slavica Shurbevska from the University Clinic of Endocrinology, Skopje for their contribution and consultation for the laboratory findings. We would also like to give gratitude to Goran Kondov from The University Clinic for Thoracic Surgery, Skopje and Rozalinda Isijanovska for their help in recruiting patients and statistical support.

REFERENCES

1. Desborough JP. The stress response to surgery. Br J Anaesth. 2000; 85: 109–17.
2. Blebuyck JJ. The Metabolic Response to stress. An overview and update. Anesthesiology. 1990; 73: 308–27.
3. Burton D, Nicholson G, Hall G. Endocrine and metabolic response to surgery. Critical Care & Pain. 2004; 4: 144–147.
4. Black PR, Brooks DC, Beasey PQ at al. Mechanisms of insulin resistance following injury. Ann Surg. 1984; 196: 420–435.
5. Umpierrez GE, Isaacs SD, Bazargan N at al. Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. J Clin Endocrinol Metab. 2002; 87: 978–982.
6. Pomposelli JJ, Baxter JK III, Babineau TJ, et al. Early postoperative glucose control predicts nosocomial infection rate in diabetic patients. JPEN J Parenter Enteral Nutr. 1998; 22: 77–81.
7. Thorell A, Ljungqvist O, Efendic S, et al. Development of postoperative insulin resistance is associated with the magnitude of operation. Eur J Surg. 1993; 159: 593–599.
8. Ljunqvist O. To fast or not to fast? Metabolic preparation for elective surgery. Scandinavian Journal of Nutrition. 2004; 48(2): 77–82.
9. Ljunqvist O. Modulating postoperative insulin resistance by preoperative carbohydrate loading.Best Practice &Research Clinical Anesthesiology. 2003; 23: 401–409.
10. Faria MS, de Aguilar-Nuscimento JE, et al. Preoperative fasting of 2 hours minimizes insulin resistance and organic response to trauma after video-chole-

cystectomy: randomized, controlled, clinical trial. World J Surg. 2009; 33: 1158–1164.
11. Perrone F, da-Silva-Filho AC, Adôrno IF, et al. Effects of preoperative feeding with a whey protein plus carbohydrate drink on the acute phase response and insulin resistance. A randomized trial. Nutrition journal 2011; 10: 2–68.
12. Thorell A, Ljungqvist O Nygren N. Insulin resistance: a marker of surgical stress. Curr Opin Clin Nutr Metab Care. 1999; 2(1): 69–78.
13. Van Loon Lj et al. Amino acid ingestion strongly enhances insulin secretion in patients with long-term type 2 diabetes. Diabetes Care. 2003; 26 (3): 625–30.
14. Wright-Pascoe R, Mills J, Choo-Kang E, Morrison EY. The role of C-peptide in the classification of diabetes mellitus. West Indian Med J. 2000; 49(2): 138–42.
15. Wallace MT, Levy JC, Mathews DR. Use and abuse of HOMA modeling. Diabetes Care. 2004; 27(6): 1487–495.
16. Nygren JO, Thorell A, Soop M, et al. Perioperative insulin and glucose infusion maintains normal insulin sensitivity after surgery. Am J Physiol. 1998; 275: 140–8.
17. Svanfeldt M, Thorell A, Hausel J, Soop M, Nygren J, Ljungqvist O: Effect of "preoperative" oral carbohydrate treatment on insulin action- a randomised cross-over unblinded study in healthy subjects. Clin Nutr. 2005; 24: 815–821.
18. Wallin M, Selldén1 E, Eksborg S, et al. Amino acid infusion during anesthesia attenuates the surgery induced decline in IGF-1 and diminishes the "diabetes of injury". Nutrition & Metabolism. 2007; 4: 86–9.
19. Jingyi l et al.Insulin resistance and metabolism of branched–chain amino acid. Front. Med. 2013; 7; 53–59.
20. Maitra S, Kirtania J et al: Intraoperative blood glucose levels in non-diabetic patients undergoing elective major surgery under general anesthesia receiving different crystalloid solutions for maintenance fluid. Anesthesia Essays and Researches. 2013: 7(2): 183–188.
21. Zhong J. Effects of intraoperative amino acid infusion on blood glucose under general anesthesia combined with epidural block. Ann Nutr Metab. 2012; 61: 1–6
22. Srceva M et al. Effects of preoperatively given amino acid infusion on blood glucose and C-peptide levels in surgical patients. Physioacta. 2015; 9(1): 131–141.
23. Kee J, Baxter R, Smith R. Parenteral amino acid promotes anabolic action in rats. Amer.Journ of Physy. 1999: 277: 63–72.
24. Preisssig CM, Hansen I, Roerig P, et al. A protocolised approach to identify and manage hyperglycemia in a pediatric critical care. Pediatr Crit Care Med. 2008; 9: 582–8.

Р е з и м е

НИВО НА ИНСУЛИНСКА РЕЗИСТЕНЦИЈА, ГЛИКЕМИЈА И КОРТИЗОЛ КАЈ ХИРУРШКИ ПАЦИЕНТИ ПО КАЛОРИСКО ВНЕСУВАЊЕ АМИНОКИСЕЛИНИ

Марија Јовановски-Срцева[1], Билјана Кузмановска[1], Маја Мојсова[1], Андријан Карталов[1], Мирјана Шошолчева[1], Марина Темелковска-Стеваноска[1], Александра Гавриловска[1], Сотир Ставридис[2], Зоран Спировски[3], Борислав Кондов[3], Анита Кокарева[1], Ристо Тодоров[4]

[1] Клиника за анестезија, реанимација и интензивно лекување, Медицински факултет, Универзитет „Св. Кирил и Методиј“, Скопје, Р. Македонија
[2] Клиника за урологија, Медицински факултет, Универзитет „Св. Кирил и Методиј“, Скопје, Р. Македонија
[3] Клиника за тораковаскуларна хирургија, Медицински факултет, Универзитет „Св. Кирил и Методиј“, Скопје, Р. Македонија

Вовед: Оперативниот стрес-одговор резултира со зголемено ниво на антиинсулогени хормони и намалена секреција на инсулин. Ваквото хормонско миле го зголемува морбидитетот кај хируршките пациенти поради појава на хипергликемија и инсулинска резистенција. Литературата вели дека предоперативното гладување кај хируршки пациенти е дополнителен промотор на инсулинска резистенција. Цел на ова истражување е да се анализира влијанието на предоперативното калориско внесување од 440 кЈ врз нивото на кортизол, инсулинската резистенција и функционалноста на бета-клетките кај хируршките пациенти.

Материјал и метод: Студијата вклучува 20 пациентки на кои им е закажана радикална мастектомија, на возраст 30–60 години, без лична анамнеза за дијабетес и BMI < 30 m^2 поделени во две групи. Испитуваната група А, вечерта пред оперативната интервенција, доби интравенски 1000 ml аминокиселини, додека контролната група Б не доби никаква инфузија. Кај двете групи пациенти, гликемија, С-пептид и кортизол се одредуваа предоперативно и 24 часа постоперативно. Од добиените вредности за С-пептид и гликемија, со компјутерскиот модел (*HOMA2) се пресметуваа вредностите за инсулинска резистенција (ИР), функционалноста на бета-клетките (Бета) и инсулинска сензитивност (ИС).

Резултати: Постоперативните вредности на инсулинска резистенција (0.94 ± 0.12 vs1.13 ± 0.2; p = 0.03) и гликемија (4.79 ± 0.5 vs 5.77 ± 0.6; p = 0.001) беа пониски во испитуваната група споредено со контролната група. Постоперативните вредности на кортизол во двете групи беа значително повисоки споредено со предоперативните (p = 0.005 и p = 0.001), но не беа значително различни меѓу себе. Испитуваната група покажа повисоки вредности за Бета и ИС. Процентуалните промени меѓу групите беа сигнификантни (p < 0.05) за ИР, ИС, Бета и гликемија.

Заклучок: Предоперативното калориско внесување влијае на намалување на инсулинската резистенција и гликемија во услови на покачено ниво на кортизол.

Клучни зборови: инсулинска резистенција, кортизол, аминокиселини, хируршки пациенти

*HOMA 2 моделот е достапен на www.OCDEM.ox.ac.uk