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Professional paper

Perioperative Management with Glucose Solution and Insulin

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A B S T R A C T

The objective of this study was to analyze how preoperative glucose treatment influences the blood glucose level as a measured exponent of surgical stress and to establish the best postoperative replacement considering glucose solutions and insulin. This prospective clinical trial involved 208 non-diabetic patients with normal glucose tolerance, who underwent major surgical procedures and needed 24 hours ICU monitoring postoperatively. Patients were randomly given 5% glucose solution (1000 mL) one day before surgery or after overnight fasting. Group A and group B were randomized to be given 5 different kinds of postoperative replacement with cristalloids and insulin. None of the patients from group A or group B were given glucose solutions during surgical procedures. Blood glucose levels were measured 14 times from the preoperative period until 24 hours after admission to the ICU and the main outcome measure was blood glucose level. All patients had a statistically significant increase in blood glucose levels in comparison to basal levels (p<0.05) in all measurements. All data were processed with descriptive statistics, chi-square test, parametric ANOVA test and ANOVA test with repeated measure, non parametric Kruskal-Wallis test and Mann-Whitney U-test. Statistically significant change was accepted with p<0.05. Preoperative glucose infusion decreased metabolic and endocrine response only during surgery; the smallest increase of postoperative blood glucose level was noticed after administering postoperative non-glucose crystalloid solutions; there is no clinical evidence that one specific postoperative replacement is better than the other; there is no clinical evidence that postoperative use of insulin can decrease or attenuate surgical induced insulin resistance.

***Key words:** glucose metabolism, postoperative insulin resistance, preoperative feeding, preoperative glucose infusion, surgical stress*

Introduction

Human metabolic and endocrine response to stress is the same as during an operative procedure[1]. One of the most important physiological tasks is to protect the blood glucose level, as the only energy source. Hyperglycaemic response is a common finding in all patients with polytrauma, patients who undergo major surgical procedures and usually occurs as a result of mobilization of energy stores after increases of cortisol and other regulative hormones[2,3].

Basal blood glucose levels are kept in a narrow range, mainly by food ingestion. During fasting, glucose reserves in the form of glucagon are expendable in 24 hours and every new stress is potentially dangerous. Such hypoglycaemia leads to metabolic disbalance and deterioration of the mental state, even in healthy individuals with intact regulatory mechanisms. To prevent mobilization of proteins and fat, regulatory mehanisms utilize all of the stored glucose with temporary hyperglycaemia as a consequence[4].

As a result of major surgical procedures glucose utilization on cell membrane occurs as a disorder of important metabolic functions. Surgically induced postoperative insulin resistance sometimes increases hyperglycaemia to pathological levels, even though temporarily high blood glucose levels serve as a defense mechanism.

Anaesthesia and analgesia decrease metabolic and endocrine responses to major surgical procedures, attenu-

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ate postoperative insulin resistance and improve glucose transport and utilization on cell membranes and stop the increase of blood glucose levels[5].

Infusion of glucose and other solutions are common and necessary procedures in patients who undergo surgery because of volume depletion and energy loss during the preoperative period and the surgical procedure itself[6]. The best way to prevent metabolic disturbances due to preoperative fasting and major surgical procedures as precipitants of major stress, is well planned perioperative administering of glucose solutions and insulin[7,8]. There is a lot of data about postoperative infusion of glucose solutions and insulin, but it still necessary to further ellucidate and explain their roles, especially the regulatory role of insulin in postoperative hyperglycemia[9,10].

The aim of the study

The aim of the study is to analyze the effect of preoperative glucose infusions on blood glucose levels as a measured exponent of surgical stress and to help answer the question of what is the best postoperative modality for the replacement of volume, electrolites, energy and insulin, to prevent surgically induced postoperative insulin resistance.

Methods

Subjects and design

After written consent and approval of the Hospital Ethical Committee, 220 nondiabetic patients who underwent major surgical procedures and needed ICU monitoring the following 24 hours or more, were included in this prospective study. The surgical procedures were major surgical procedures which lasted for more than 2 hours. There is no evidence of previously defective glucose tolerance in any of the patients included in our clinical trial. Patients were randomly given 5% glucose solutions (1000 mL) one day before the operation or after overnight fasting. Group A and group B were randomly given non-glucose crystalloid solutions, glucose solutions or glucose solutions with insulin postoperatively. None of the patients were given glucose solutions during the surgical procedure.

Randomization	group A – preoperative infusion of 5% glucose solution (1000 mL)	group B – preoperative overnight fasting
Subgroup I	normal saline, 1500 mL and Ringer's solution, 1000 mL	
Subgroup II	5% glucose solution, 1500 mL and Ringer's solution, 1000 mL	
Subgroup III	5% glucose solution + 8 IU of insulin per 500 mL of glucose solution, 1500 mL and Ringer's solution, 1000 mL	
Subgroup IV	10% glucose solution + 8 IU of insulin per 500 mL of glucose solution, 1500 mL and Ringer's solution, 1000 mL	

Clinical trial protocol:

Blood samples for laboratory testing of blood glucose levels were taken during:

1. anaesthesiologic examination
2. preoperatively, on the day of surgery
3. immediately after induction of anaesthesia before surgical incision
4. two hours after the begining of anaesthesia
5. at the end of the operation
6. 3 hours after admission to ICU
7. every 3rd hour during treatment in the ICU
8. 24 hours after admission to the ICU

All drugs for induction and anaesthesia maintenance (thiopental, propofol, midazolam, etomidate, leptosuccin, pancuronium bromide, fentanyl) and postoperative analgesia (tramadol) were used in all patients in the recommended doses per kg/body mass. The experimental procedure was interrupted on occurence of hypoglycemia (<3 mmol/L) or hyperglycaemia (>15 mmol/L).

Statistics

Twelve patients weren't included in statistical processing because they received extra doses of insulin for postoperative hyperglycaemia correction in the ICU, as the experimental protocol design proposed. Patients who had hyperglycemia higher than 15 mmol/L were included, but they did not receive extra doses of insulin because the anaesthesiologist in the ICU considered that at that time there was no danger to patients and such high blood glucose levels are temporary. Finally, statistical group A had 90 and group B 118 examinees. Every subgroup had more than 30 patients.

All data were processed with descriptive statistics and chi-square test between and within groups and subgroups. There were no significant differences found, so the findings were fully comparable. For further statistics, parametric ANOVA test and ANOVA test with repeated measure, non parametric Kruskal-Wallis test and Mann-Whitney U-test were used.. Statistically significant changes were accepted with $p<0.05$.

Results

All data are presented with tables and figures. The blood glucose data which was taken from blood samples and was calculated as a mean value from several measurements, has ordinal numbers which are used in tables and charts:

1. blood glucose level at anaesthesiologic examination
2. preoperative blood glucose level, on the day of surgery
3. blood glucose level immediately after induction of anaesthesia, before surgical incision

TABLE 1
GENERAL DATA

	Group A	Group B	All
Male	66 (42.04%)	91 (57.96%)	157
Female	24 (47.06%)	27 (52.94%)	51
All	90	118	208
Subgroup I	17	22	39
Subgroup II	18	19	37
Subgroup III	17	21	38
Subgroup IV	17	20	37
Subgroup V	21	36	57
All	90	118	208
Age	60.24 ± 11.92 godina	61.22 ± 10.57 godina	
Weight	73.15 ± 12.45 kg	75.38 ± 14.04 kg	
Height	170.46 ± 8.47 cm	171.45 ± 9.01 cm	

Basal blood glucose level is 5.5 mmol/L and the highest physiological blood glucose level is set according to the hospital biochemical laboratory.

4. blood glucose level two hours after the begining of anaesthesia
5. mean blood glucose level during anaesthesia and surgical procedure
6. blood glucose level 3 hours after admission to the ICU
7. blood glucose level 6 hours after admission to the ICU
8. blood glucose level 9 hours after admission to the ICU
9. blood glucose level 12 hours after admission to the ICU
10. blood glucose level 15 hours after admission to the ICU
11. blood glucose level 18 hours after admission to the ICU
12. blood glucose level 21 hours after admission to the ICU
13. blood glucose level 24 hours after admission to the ICU
14. mean blood glucose level during treatment in the ICU

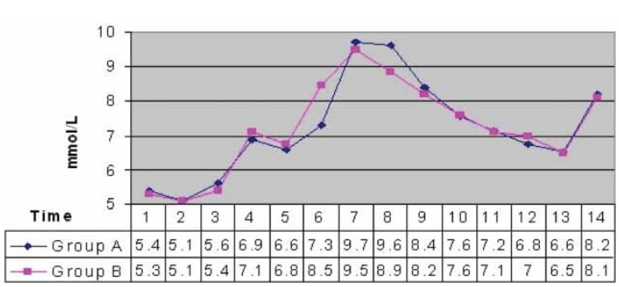

Fig. 1. Mean blood glucose level.

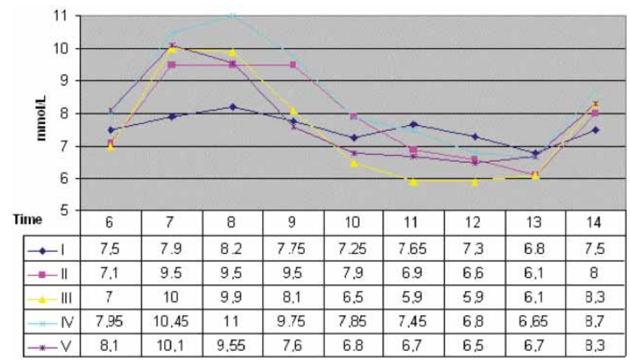

Fig. 2. Group A – mean blood glucose level in subgroups.

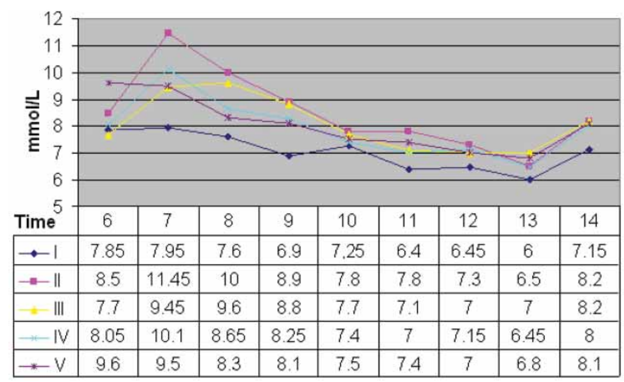

Fig. 3. Group B – mean blood glucose level in subgroups.

Discussion

Many studies have showed that the human organism responds in the same manner to immediate danger, trauma, stress or surgical procedure[11,12].Our study shows that one easily measured, but very sensitive mediator of homeostasis such as blood glucose level, can answer some questions and prevent some metabolic disturbances as negative consequences of surgical trauma.

All of our patients had statistically significant increases in blood glucose levels, in comparison to basal levels ($p<0.05$). Surgically induced hyperglycaemia occured as a consequence of cortisol activity and other regulatory hormones, as a protection mechanism of glucose reserves during surgical trauma, which correlates with other authors data[13]. Postoperative hyperglycaemia seems to be a result of insulin resistance more than the before mentioned protective mechanism[14,15]. Surgically induced insulin resistance was apparent after 24 hours from the beginning of our trial and persisted for 5 days, the blood glucose level was 23% higher than basal blood glucose levels, without respect to group or subgroup[16]. Previous data suggest that oscillations in insulin activity are not influenced only by increasing activity of stress hormones[17]. Volume, electrolites and energy reserves through infusion are necessary in every major surgical procedure, but there is still some doubt about perioperative use of glucose solutions[18,19].

TABLE 2
BLOOD GLUCOSE LEVELS AT THE TIME OF MEASUREMENT

Time	Group A			Group B		
	Min	median	max	min	median	max
1	3.7	5.4	8.5	3.7	5.3	7.8
2	3.6	5.1	7.6	3.2	5.1	14.4
3	2.9	5.6	15.4	2.9	5.4	12.7
4	4.1	6.9	15.4	4.8	7.1	20.3
5	4.1	6.6	15.4	4.8	6.75	17.6
6	4.1	7.3	14.3	4.6	8.45	21
7	4.4	9.7	19.6	5.3	9.5	22
8	4.1	9.6	18.4	4.6	8.85	24
9	2.5	8.4	24.1	3.1	8.2	30
10	3.8	7.55	19.3	2.1	7.6	27.8
11	3.7	7.15	16.2	3	7.1	30.5
12	2.3	6.75	12.3	4.1	7	21.8
13	3.3	6.55	11.5	4.1	6.5	14.2
14	4.7	8.2	12.5	5.1	8.1	19.7

There is no clinical evidence from large and meta studies that would support the fact that intraoperative infusion of glucose would be more harmful than other crystalloid non-glucose solutions, but following the rule »primum non nocere«, all clinicians administer non-glucose infusions during surgical procedures[20,21]. Preoperative fasting, without glucose infusions during long operations and different approaches to postoperative glucose compensation cause metabolic and immune disturbances in many patients and this problem challenges investigators to find a way to decrease these negative manifestations. Preoperative treatment with glucose infusions showed some clinical benefits for patients who underwent major surgery[22].

In Table 2. are shown the mean, minimal and maximal blood glucose values during our experiment. In group B, the amplitude of glucose values shows more variations than in group A and that finding supports the hypothesis of stabilizing blood glucose levels with preoperative glucose infusions[23]. Patients in group B have a much higher increase in blood glucose levels only during the surgical procedure and with a statistical significance compared to group A ($p<0.05$). We concluded that preoperative glucose treatment attenuated metabolic and endocrine human responses during major surgery[24].

We did not include the changes in postoperative insulin resistance as an observed parameter in our clinical trial. Some authors show that it exists but besides clinical parameters, they used psychological, social and medico-economic parameters (discomfort, length of stay in the ICU and the hospital, the outcome) in their survey[25]. Some findings in postoperative measurements (Table 3.) can be misleading. From our data, we concluded that statistically significant differences between groups with respect to subgroups, which is seen in some postoperative measurements, is influenced by inadequate analgesia and does not correlate to preoperative glucose infusions[26]. We are convinced that our statement is valid because the significant difference in blood glucose levels occured in the first measurements taken in the ICU at time when intraoperative analgesia is reduced and postoperative is not adequately managed. Significant differences in increase occured in both groups, which proves that preoperative glucose infusion is not responsible for these changes. For all patients in subgroups II and III, preoperative glucose usage evidently produced a statistically significant difference in blood glucose levels with respect to subgroup I in which for postoperative compensation, patients only had non-glucose crystalloid solutions. Statistically significant difference in blood glucose level between subgroups is seen in group A, in every subgroup which, for postoperative replacement, has a glucose solution (subgroup II) and glucose solution with insulin (subgroup III,IV,V). The data are presented in Table 4. There are no significant differences in group B, which suggests that postoperative glucose can be utilized only if a sufficient dose of insulin exists. That correlates with the findings in literature that surgically induced insulin resistance is, mediated through interference with glucose utilization on cell membranes and fat and protein metabolism as the main reasons of postoperative hyperglycaemia[27]. Previous data shows that an 8 times higher insulin dose is necessary to maintain postoperative glycaemia

TABLE 3
BLOOD GLUCOSE LEVEL AND STATISTICAL SIGNIFICANCE BETWEEN GROUPS

	Group A	Group B	p – level
Time 4	6.9 mmol/L	7.1 mmol/L	0.0224
Subgroup I			
Time 12	7.3	6.45	0.0471
Time 13	6.8	6	0.0269
Subgroup II			
Time 6	7.1	8.5	0.0252
Subgroup IV			
Time 8	11	8.65	0.0434
Subgroup V			
Time 8	9.55	8.3	0.0345

TABLE 4
STATISTICAL SIGNIFICANCE OF INCREASING BLOOD GLUCOSE LEVEL BETWEEN SUBGROUPS

Subgroups	p-level		
	A + B	Group A	Group B
I :II	0.0356	0.0132	NS
I : III	0.0109	0.0087	NS
I : IV	NS	0.0252	NS
I : V	NS	0.0116	NS

NS – non-sprecific

at preoperative values, that glucose utilization is 100% and all of the mentioned strongly proves that postoperative insulin doses used in our clinical trial are insufficient and inadequately regulated and do not influence surgically induced insulin ineffectivness[28]. Some other studies show that perioperative infusion of glucose and insulin can diminish surgical stress and future investigations have to answer which is the adequate dose[29].

Conclusion

The results of our clinical trial were thoroughly compared with available data from literature and we concluded that use of preoperative glucose infusion is beneficial to patients because it decreases metabolic and endocrine responses and maintains blood glucose levels in narrow limits, especially during surgery; use of non-glucose crystalloid solutions is the best way for postoperative volume, electrolite and energy replacement because the smallest increase of blood glucose levels is seen with such infusions; there is no clinical evidence that some specific replacement is better for patients than another; there is no clinical evidence that postoperative use of insulin can decrease or attenuate surgically induced insulin resistance and ineffectivness; postoperative pain must be carefully monitored and adequately treated in order to prevent the aggravation of consequences from surgical trauma.

REFERENCES

1. LONGARELA A, OLARRA J, SUAREZ L, GARCIA DE LORENZO A, Nutr Hosp, 15 (2000) 275. — 2. ENGIN A, BOZKURT BS, ERSOY E, OGUZ M, GOKCORA N, Surg Laparosc Endosc, 8 (1998) 435. — 3. LANG CH, Shock, 1 (1994)36. — 4. FELIG P, WAHREN J, SHERWIN R, HENDLER R, Diabetes, 25 (1976) 1091. — 5. SCHRICKER T, LATTERMANN R, FISET P, WYKES L, CARLI F, J Appl Physiol, 91 (2001) 2523. — 6. ROYALL D, FAIRHOLM L, PETERS WJ, JEEJEEBHOY KN, ALLARD JP, Crit Care Med, 22 (1994) 399. — 7. NYGREN J, SOOP M, THORELL A, EFENDIC S, NAIR KS, LJUNGQVIST O, Clin Nutr, 17 (1998) 65. — 8. HAUSEL J, NYGREN J, LAGERKRANSER M, HELLSTROM PM, HAMMARQVIST F, ALMSTROM C, LINDH A, THORELL A, LJUNGQVIST O, Anesth Analg, 93 (2001) 1344. — 9. NELSON KM, LONG CL, BAILEY R, SMITH RJ, LAWS HL, BLAKEMORE WS, Metabolism, 41 (1992) 68. — 10. GILON P, RAVIER MA, JONAS JC, HENQUIN JC, Diabetes, 51 (2002) 144. — 11. THORELL A, NYGREN J, LJUNGQVIST O, Curr Opin Clin Nutr Metab Care, 2 (1999) 69. — 12. NYGREN JO, THORELL A, SOOP M, EFENDIC S, BRISMAR K, KARPE F, NAIR KS, LJUNGQVIST O, Am J Physiol, 275 (1998) 140. — 13. BREUER JP, VON DOSSOW V, VON HEYMANN C, GRIESBACH M, VON SCHICKFUS M, MACKH E, HACKER C, ELGETI U, KONERTZ W, WERNECKE KD, SPIES CD, Anesth Analg,103 (2006) 1099. — 14. BRANDI LS, SANTORO D, NATALI A, ALTOMONTE F, BALDI S, FRASCERRA S, FERRANNINI E, Clin Sci (Lond), 85 (1993) 525. — 15. NORDENSTROM J, SONNENFELD T, ARNER P, Surgery 105 (1989) 28. — 16. THORELL A, EFENDIC S, GUTNIAK M, HAGGMARK T, LJUNGQVIST O, Br J Surg, 81 (1994) 59. — 17. THORELL A, EFENDIC S, GUTNIAK M, HAGGMARK T, LJUNGQVIST O, Eur J Surg, 159 (1993) 593. — 18. BRUEMMER-SMITH S, AVIDAN MS, HARRIS B, SUDAN S, SHERWOOD R, DESAI JB, SUTHERLAND F, PONTE J, Br J Anaesth, 88 (2002) 489. — 19. LELL WA, NIELSEN VG, MCGIFFIN DC, SCHMIDT FE JR, KIRKLIN JK, STANLEY AW JR, Ann Thorac Surg, 73 (2002) 1246. — 20. BERLEUR MP, DAHAN A, MURAT I, HAZEBROUCQ G, J Clin Pharm Ther, 28 (2003) 31. — 21. HAUSEL J, NYGREN J, THORELL A, LAGERKRANSER M, LJUNGQVIST O, Br J Surg, 92 (2005) 415. — 22. GIDDINGS AE, MANGNALL D, ROWLANDS BJ, CLARK RG, Ann Surg, 186 (1977) 681. — 23. SOOP M, NYGREN J, MYRENFORS P, THORELL A, LJUNGQVIST O, Am J Physiol Endocrinol Metab, 280 (2001) 576. — 24. NYGREN J, THORELL A, LJUNGQVIST O, Curr Opin Clin Nutr Metab Care, 4 (2001) 255. — 25. LJUNGQVIST O, NYGREN J, THORELL A, Proc Nutr Soc, 61 (2002) 329. — 26. SCHRICKER T, CARLI F, SCHREIBER M, WACHTER U, GEISSER W, LATTERMANN R, GEORGIEFF M, Anesth Analg, 90 (2000) 450. — 27. THORELL A, NYGREN J, HIRSHMAN MF, HAYASHI T, NAIR KS, HORTON ES, GOODYEAR LJ, LJUNGQVIST O, Am J Physiol, 276 (1999) 754. — 28. BRANDI LS, FREDIANI M, OLEGGINI M, MOSCA F, CERRI M, BONI C, PECORI N, BUZZIGOLI G, FERRANNINI E, Clin Sci (Lond), 79 (1990) 443. — 29. NYGREN JO, THORELL A, SOOP M, EFENDIC S, BRISMAR K, KARPE F, NAIR KS, LJUNGQVIST O, Am J Physiol, 275 (1998) 140.

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PERIOPERATIVNA PRIPREMA GLUKOZOM I INZULINOM

SAŽETAK

Razina glukoze u krvi je važan pokazatelj stresnog odgovora tijekom i nakon operacije. Istraživanje je provedeno na 208 pacijenata koji su nakon velike operacije zahtijevali 24 satni boravak u jedinici intenzivnog liječenja. Prije i poslije operacije ispitanicima su slučajnim odabirom davane otopine 5% glukoze ili kristaloidne otopine. Razina glukoze u krvi mjerena je prije, tijekom i poslije operacije. Pokazali smo da je prijeoperacijski davanje glukoze korisno u smislu smanjenja metaboličkog i endokrinog stresnog odgovora te održavanja razine šećera u krvi u uskim granicama. Nema dokaza da poslijeoperacijsko davanje otopina glukoze uz inzulin smanjuju kirurški uzrokovanu poslijeoperacijsku inzulinsku rezistenciju.