

Changes in insulin resistance after ileoduodenoplasty performing

The aim of the work: to analyze own experience of IR changes in the course of performing metabolic correction in original way of ileac shift by stomach with duodenum exclusion from food passage.

Materials and Methods. Insulin resistance (IR) was studied in 15 patients with body mass index (BMI) within 20.3–58.3 kg/m². Surgery consists of ileoduodenoplasty (IDP) performing by the way of duodenal and ileac transection and ileac shift by stomach with duodenum exclusion from food passage. In all patients fasting blood glucose, insulin and c-peptide levels were measured before surgery and 7–21 days by surgery.

According to blood level of insulin and c-peptide before surgery all cases may be differentiated into three groups.

Results and Discussion. Three weeks after surgery only in four patients of group 1 insulin content was on the upper level of norm or slightly higher of it while became, respectively, 59.1 %, and 32.8 %, and 42.2 %, and 34.7 % from preoperative indication. In two patients of group 2 insulin level falls into the range of norm, while in one it left slightly higher of those and, respectively, became 49.7 %, 34.7 %, and 21.0 % from those of pre-operation. Three patients (group 3) with insulin level withing normal range while c-peptide level was higher than range of norm.

It is not understandable at the time why c-peptide level at three weeks after surgery changes differently in all groups.

In all cases IR, which was regarded as higher than normal insulin or c-peptide level, disappear within three weeks after surgery.

Obtained data elucidate the difference in the IR origin. It is of interest the similar level of insulin in IR despite different concentration of c-peptide.

Also, it is of interest elevation of c-peptide level after surgery while IR disappear. Reasons of such reaction need further research.

Key words: insulin resistance; surgery; ileoduodenoplasty; diabetes mellitus; obesity; c-peptide; glucose; insulin.

Introduction. Gastrointestinal surgery has emerged as the most effective option for the treatment of obesity and diabetes, with level-1 evidence of diabetes remission [1].

As mechanism of insulin resistance (IR) is not fully clear it may be of interest our observations on it changes in response to gastrointestinal surgery.

The aim of the work: to analyze own experience of IR changes in the course of performing metabolic correction in original way of ileac shift by stomach with duodenum exclusion from food passage.

Materials and Methods. In all cases IR was regarded as higher than normal insulin or c-peptide level.

Changing of IR as the result of surgery was studied. All patients give an informed consent in writing prior to inclusion in the study. Results of 15 patients examining are analyzed. There were 8 men, 7 women 31–72 years old, mean age (M±σ) (54.7±13.8) years. Type 2 diabetes mellitus was in 8 patients. 5 patients received pill diabetes treatment, insulin – 3 patients. Body mass index (BMI) was within (20.3–58.3) kg/m² (Table 1).

Table 1. Patients BMI and diabetes characteristic

Patient	BMI, kg/m ²	Diabetes type 2	Diabetes treatment	
			pills	insulin
1	2	3	4	5
1	27.2	yes	no	insulin 60 units/day
2	58.3	no	no	no
3	45.3	no	no	no
4	26.6	yes	glibomed 2 tab/day	no
5	37.4	no	no	no

1	2	3	4	5
6	45.6	no	no	no
7	49.7	no	no	no
8	47.1	no	no	no
9	27.7	yes	glibenclamid 10 mg/day	no
10	20.3	yes	amaril 1,5 mg/day metformin 3000 mg/day	no
11	47.7	yes	siofor 3000 mg/day	no
12	52.7	yes	siofor 500 mg/day	no
13	25.1	yes	no	insulin 65 units/day
14	57.2	no	no	no
15	33.4	yes	no	insulin 66 units/day

Ileoduodenoplasty was performed by the way of duodenal and ileac transection and ileac shift by stomach with duodenum exclusion from food passage (Fig. 1).

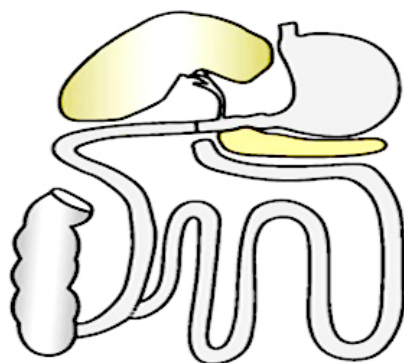


Fig. 1. Ileoduodenoplasty scheme

In all patients fasting blood glucose, insulin and c-peptide levels were measured before surgery and 7-21 days by surgery.

Insulin and c-peptide level had been estimated by radioimmunoassay with EC & G Berthold LB 2111 (USA) apparatus and Institute of Izotopes (Hungary) kits.

Glucose concentration had been measured by Enzymatic/PAP-End Point method and Selectra PRO XL apparatus using GLUCOSE PAP SL, ELITech Clinical Systems SAS (France) set.

Results and Discussion. Metabolic syndrome (MS) represents a cluster of metabolic abnormalities

that include hypertension, central obesity, IR, and atherogenic dyslipidemia [2]. Persons with MS have higher mortality rate when compared with people without MS, primarily caused by progressive atherosclerosis, accelerated by pro-inflammatory and pro-coagulation components of MS [3].

It was found (see Table 1) that among our patients with BMI within ambit of 20.3–37.4 kg/m² there were 3 who received insulin, and 3 on pill as antidiabetic treatment, and 1 without diabetes. At the same time among patients with BMI 45.3 kg/m² and higher there were 6 without diabetes, and 2 on pill diabetic control. Thus, the genesis of IR cannot be blamed neither on diabetes severity nor on BMI.

According to blood level of insulin and c-peptide before surgery all cases may be differentiated into three groups.

Blood insulin level was significantly greater of normal level in 9 patients (1 group) (Table 2).

Extremely high patients' mean insulin and c-peptide level (54.1±20.7) mkIU/ml and 3203.9±1862.1 pmol/l respectively before surgery may be qualified as real IR.

At the same time, we've seen in 3 patients (group 2) high insulin level correspondent to IR simultaneously with c-peptide within normal range (Table 2).

While mean insulin level before surgery in group 2 was not significantly different from those in group 1, namely, (50.6±15.4) mkIU/ml, mean c-peptide content differs gradually, (605.9±168.8) pmol/l. This data raise question about not only mechanism but also functional significance of such situation. We cannot assess at the moment whether it is harmful impact by itself or it is the compensatory result of some pathological changes.

Table 2. Insulin and c-peptide level in group 1

Patient	Glucose mMol/l		Insulin*		C-peptide**	
	before	1-3 weeks by	before	1-3 weeks by	before	1-3 weeks by
2	5.4	4.9	43.5	25.7	3122.8	1950.3
3	10.7	6.4	102.4	16.2	6347.0	2530.4
4	4.4	5.1	42.3	13.9	4094.7	1478.1
5	7.3	4.9	44.9	16.5	2824.9	1426.8
6	6.2	5.9	71.1	23.3	4691.0	2356.9
7	6.1	4.6	52.8	19.4	1605.2	1199.1
8	7.6	4.9	39.6	19.2	2494.7	2023.9
11	11.2	7.5	52.1	22.0	1663.2	2384,53
12	6.0	5.9	37.9	18.8	1992.0	1409,31
М			54.1	19.4	3203.9	1862.1
Б			20.7	3.7	1578.6	497.5

Примітка: * – normal range 5.9–22.5 mкIU/ml; ** – normal range 295–1165 pmol/l

There were also, three patients (group 3) with insulin level within normal range while c-peptide level was higher than range of norm (table 3). Whether mentioned patients are really those who has IR or not may be discussed. Despite insulin level wasn't extremely high it is of interest mechanism and implication of so high concentration of c-peptide in this situation.

Most impressive impact of surgery on IR was in group 1 (see Table 2). Three weeks after surgery only in four patients, 2, 6, 12, and 14, insulin content was on the upper level of norm or slightly higher of it while became, respectively, 59.1 %, and 32.8 %, and 42.2 %, and 34.7 % from preoperative indication.

Same changes happened to patients of group 2. In two of them insulin level falls into the range of norm,

while in one it left slightly higher of those and, respectively, became 49.7 %, 34.7 %, and 21.0 % from those of pre operation. Roslin et al. noticed a much lower rise in 1-h insulin, with this difference being statistically significant at $p < 0.05$ and as a result a less abrupt reduction in blood glucose at 6 months following duodenal switch surgery, in comparison with other types of metabolic surgery [4].

It is not understandable at the time why c-peptide level at three weeks after surgery changes differently in all groups.

In group 1 it was typical lowering of c-peptide level, find out in 8 of 9 patients, while in one patient it raised up to 143.4 % while insulin content dropped to 42.3 % from initial.

Table 3. Insulin and c-peptide level in group 2

Patient	Glucose mMol/l		Insulin*		C-peptide**	
	before	1-3 weeks by	before	1-3 weeks by	before	1-3 weeks by
1	12.5	6.4	37.9	18.9	788.6	1403.4
13	9.8	5.3	67.7	23.5	455.8	688.6
15	8.8	6.0	46.2	9.7	573.2	918.5
М			50.6	17.4	605.9	1003.5
Б			15.4	7.0	168.8	364.9

Table 4. Insulin and c-peptide level in group 3

Patient	Glucose mMol/l		insulin*		c-peptide**	
	before	1–3 weeks by	before	1–3 weeks by	before	1–3 weeks by
9	16.9	18.1	14.33	5.4	1269.3	930.0
10	13.3	4.9	17.61	9.1	1472.9	501.1
14	5.8	5.2	20.44	7.7	1571.5	584.1
M			17.7	7.4	1437.9	671.7
Б			3.1	1.9	154.1	227.5

At the time in group 2 c-peptide level raised in all three patients though only in one of them higher than norm. It is remarkable that preoperative median insulin level in this group was similar to those in group 1 and the scale of it lowering in both groups are analogous. This suggested different pathogenetic mechanism of diabetes in some cases.

While no one patient in group 3 is regarded as those with IR, their c-peptide level was higher than norm and lowered gradually into the normal boundaries after surgery. This reflect the core effect of such kind of surgery.

Obtained results pointed out different genesis of hyperinsulinemia, hyper-c-peptidemia, and IR.

In patients of group 1 there is high insulin secretion what is the reflection of tissue IR. High c-peptide output is the reason of hyperinsulinemia. By the surgery IR disappear what lead to insulin and c-peptide level lowering to norm.

Patients of group 2 before surgery represents high insulin blood level with c-peptide rate within normal range. We can suggest the mechanism of such discordance in normal insulin secretion with suppressed insulin assimilation in liver. By the surgery suppression is canceled what lead to blood insulin level lowering simultaneously with the higher c-peptide and insulin production. Such suggestion should be verified.

It had been established rapid improving of glycemia in obese patients after bariatric surgery which purportedly caused by exclusion of part of small bowel from the transit of food and depend on length of excluded loop [1]. May be the reason lies not in the loop length but its microbiota contains [5]. Reis and co-authors pointed out that the mechanisms used by antimicrobials that could lead to the improvement of insulin sensitivity are dependent on the modulation of

the intestinal microbiota. In addition, the secretion of glucagon-like peptide-1 would be modulated by metabolites produced by the intestinal microbiota, such as secondary bile acids and short-chain fatty acids [6]. Napoleao et al. show calorie restriction boosts exercise insulin sensitivity response [7].

Two major theories have been advocated to explain the early remission of type 2 diabetes mellitus following Roux-en-Y gastric bypass or biliopancreatic diversion before a meaningful weight loss takes place, the foregut and the hindgut hypotheses. The former holds that the bypass of the proximal intestine, i.e. duodenum and jejunum, prevents the secretion of signals – including nervous transmitters and hormones – promoting insulin resistance, the latter instead states that the delivery of nutrients directly into the ileum stimulates the secretion of hormones improving glucose disposal [8, 9, 10].

Conclusions. We found dramatic changes and almost disappearance of IR within first three weeks after metabolic surgery in form of ileoduodenoplasty though mechanism of such transformation is not clear.

Obtained data elucidate the difference in IR origin without direct connection to BMI, diabetes presence/absence or way of glycemia correction. It is of interest the similar level of insulin in blood despite different mechanism of it.

Also, it is of interest elevation of c-peptide level post-surgery while IR disappear. Causes of such reaction need further research.

Our conclusions have limitations because of small quantity of observations. No doubt further data amounting needed.

There is no conflict of interest among authors.

LITERATURE

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Електронна адреса для листування: sepodpryatov@yahoo.com

С. Є. ПОДПРЯТОВ, С. С. ПОДПРЯТОВ, О. В. ІВАНЬКО, В. П. КОРЧАК, О. В. ЛЕВИЦЬКА, І. В. САЦЮК

Київська міська клінічна лікарня № 1

ЗМІНИ ІНСУЛІНОРЕЗИСТЕНТНОСТІ ПІСЛЯ ІЛЕОДУОДЕНОПЛАСТИКИ

Мета роботи: дослідити зміни інсулінорезистентності в процесі корекції метаболізму шляхом виконання оригінального втручання з шунтуванням шлунка у здухвинну кишку з виключенням дванадцятипалої кишки від проходження їжі.

Матеріали і методи. Досліджено інсулінорезистентність у 15 пацієнтів з індексом маси тіла у межах 20,3 – 58,3 кг/м². Хірургічне втручання полягало у виконанні ілеодуоденопластики шляхом перетину дванадцятипалої та клубової кишки та зміщення клубової кишки шлунком з виключенням дванадцятипалої кишки з проходження їжі. У всіх пацієнтів натщесерце вимірювали рівень глюкози в крові, інсуліну та с-пептиду до операції та через 7–21 день після операції.

Залежно від рівня інсуліну і с-пептиду в крові до операції всіх пацієнтів було розділено на три групи.

Результати досліджень та їх обговорення. У чотирьох хворих 1-ї групи лише через 3 тижні після операції вміст інсуліну був на верхньому рівні норми або дещо перевищував його, становлячи відповідно 59,1 % та 32,8 % та 42,2 % та 34,7 % від доопераційних показників. У двох хворих 2-ї групи рівень інсуліну був у межах норми, а в одного – дещо вищий і, відповідно, становив 49,7 %, 34,7 % і 21,0 % від доопераційного. У трьох пацієнтів (група 3) рівень інсуліну був у межах норми, а рівень с-пептиду вище норми.

Наразі незрозуміло, чому рівень с-пептиду через три тижні після операції змінюється по-різному в усіх групах. У всіх випадках ІР, які вважалися вищими від нормального рівня інсуліну або с-пептиду, зникали протягом трьох тижнів після операції.

Отримані дані з'ясовують різницю в походженні ІР. Викликає інтерес подібний рівень інсуліну в ІР, незважаючи на різну концентрацію с-пептиду.

Також цікавим є підвищення рівня с-пептиду після операції при зникненні ІР. Причини такої реакції потребують подальших досліджень.

Ключові слова: інсулінорезистентність; хірургія; ілеодуоденопластика; цукровий діабет; ожиріння; с-пептид; глюкоза; інсулін.