Carbohydrate metabolism disorders in patients with chronic pancreatitis

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Introduction

Chronic pancreatitis (CP) is a chronic inflammatory-dystrophic disease of the pancreas, causing on the progression of the pathological process violation of its cross-duct sclerosis parenchyma.

In industrialized countries, the incidence of CP ranges from 49.5 to 73.4 cases per 100 thousand per year. At the same time, over the past 40 years there has been approximately double incidence of morbidity. According to the world statistics, CP in the structure of the digestive system disease ranges from 5.1 to 9%, and in the structure of the general clinical practice — from 0.2 to 0.6% [3, 4]. This is due not only to the improvement of methods of diagnosis of the disease, but also with an increase in alcohol consumption in some countries, increased exposure to adverse environmental factors.

It is well known that one of the complications of CP is a violation of both exocrine and endocrine pancreatic function. Transient hyperglycemia develops also an exacerbation of CP, which is associated with swelling of the pancreas and trypsin inhibitory effect (its content in the blood during acute pancreatitis and CP exacerbation increases) on insulin production. As pancreatic attack stops, blood glucose level becomes normal [2]. According to various authors, diabetes mellitus (DM) occurs in 10-90% of patients with CP, and in half the cases — DM type 1 [5, 6].

The aim of research is to study frequency of disorders of carbohydrate metabolism (CHM) in patients with chronic pancreatitis, depending on the duration of the disease.

Materials and methods

The work is based on the analysis of the results of monitoring 59 patients in outpatient and inpatient treatment in the Republican Specialized Science & Research Centre and Republican Specialized Centre of Surgery n. a. acad. V. Vakhidov.

Inclusion criteria: patients receiving conservative treatment for chronic pancreatitis attacks, without a history of diabetes.

Most of the patients were men — 32 (54.2%), women were 27 (45.8%). Patients' age ranged from 16 to 70 (mean age 43,30 ± 1,83 years). Body mass index (BMI) in patients averaged 25,70 ± 0,64 kg/m^2. Excess body weight is registered in 17 (28.8%) patients, obesity — in 13 (22.0%) patients. The main causative effect on the development of CP was the pathology of the biliary system in 27 (45.7%), alcoholic factor — in 21 (35.6%), violation of the diet — in 11 (18.6%). All patients were divided into 3 groups depending on the timing of chronic pancreatitis. The first group included 19 patients with pancreatitis over three years, the second group — 26 patients with disease duration from 3 to 5 years. The third group consisted of 14 patients with pancreatitis over 5 years or more. The control group consisted of 10 people, matched by sex and age, without disrupting glucose metabolism and pancreatic diseases (Table 1).

All patients were determined the level of immunoreactive insulin (IRI) using a radioimmunoassay method using standard kits of Immunotech (Czech Republic). Examination also included: measurement of growth, body weight and body mass index calculated by the formula:

$$BMI=BM(kg)/H\ (m)^2,$$

where BM — body mass, H — height.

The concentration of glucose in capillary blood was determined by glucose oxidase method fasting and 2 hours after the meal. The level of glycosylated hemoglobin (HbAlc) was determined by the colorimetric method of R. Flutchiger,

K.N. Winterhalter (1976), modified by E.S. Abraham et al. (1978). Changes in carbohydrate metabolism were evaluated based on the diagnostic criteria for diabetes and other disorders of carbohydrate metabolism (WHO, 1999). Glucose tolerance test was performed with 75 g glucose. Insulin resistance and functional activity of the pancreatic b-cells were assessed using HOMA-IR index and HOMA-FB, proposed by Matthews et al.

The calculation was performed using the following formulas:

HOMA-IR=insulin of blood serum fasting (mcU/ml) x glucose of blood serum fasting (mmol /l)/22,5

HOMA-FB=(20 x IRI (mcU/ml))/(glycemia fasting (mmol/l) — 3,5).

Statistical processing of the results of study was carried out using STATISTICA (version 6.0). Data are given as mean values and the arithmetic mean error (M ± SD), as well as Me [25; 75] (Me — median, interquartile values: 25 and 75 — percentile).

Results and discussion

Studies have shown that upon comparing the HOMA-IR index in the general group (i.e. generally those with disorders of CHM, and without it) was significantly higher in all groups as comparing to the control. HOMA-FB is lower than in the control group, but not significantly (Table 2).

For a more detailed study, we divided all three groups into sub-groups: those with and without violation of CHM disorders (Table 3).

We found that patients with CP duration >5 years with impaired CHM, IRI contents and HOMA-IR index were significantly higher, while the functional activity of b-cells (HOMA-FB) was uncertain, but lower than in patients without disorders of carbohydrate metabolism.

According to the world data, impaired carbohydrate tolerance usually develops at an early stage of CP. Sustainable glucose dysregulation occurs in an average in 5 years after the onset of the underlying disease, but diabetes can also be formed in the early clinical manifestations of CP. Further, the incidence of diabetes in CP assumes a linear dependence on time [1].

Table 1

Distribution of patients with CP depending on age, sex, BMI and duration of disease

Groups (CP duration)	BMI, kg/m^2	Male, n=32		Female, n=27		Age, years
		Abs.	%	Abs.	%	
1–3 years, n=19	24,90±1,16	14	73,7	5	26,3	44,60±3,38
3–5 years, n=26	26,60±0,88	8	30,8	18	69,2	45,00±2,56
5 years and more, n=14	25,00±1,47	10	71,4	4	28,6	38,50±3,96
Control, n=10	23,20±1,01	6	60,0	4	40,0	39,70±3,55

Table 2

CHM indices depending on CP duration in the common group

Indices	Group 1 n=19	Group 2 n=26	Group 3 n=14	Control n=10
Glycemia fasting, mmol/l	5,15 + 0,14 5,1 [4,8; 5,7]	5,31±0,23 5,2 [4,7; 5,7]	5,78 + 0,46 5,1 [4,7; 6,7]	4,76±0,14 4,6 [4,5; 5,1]
Glycemia in 2 hours after meal or GTT, mmol/l	5,64 + 0,27 5,3 [5,1; 5,9]	7,13±0,63 5,8 [5,1; 7,8]	7,85±1,05* 5,8 [5,0; 10,8]	5,05 + 0,12 4,9 [4,7; 5,4]
HbAlc, %	5,44±0,09 5,5 [5,3; 5,7]	5,94±0,15* 5,8 [5,3; 6,5]	6,14±0,28* 6,3 [5,3; 6,8]	5,38 + 0,06 5,4 [5,2; 5,5]
IRI, mU/ml	15,50±1,40 10,6 [9,0; 19,8]	16,80±1,52 13,2 [9,8; 19,5]	12,70+1,40 10,2 [4,5; 17,6]	8,85±1,14 9,9 [5,5; 11,3]
HOMA-IR	3,57±0,59* 1,87 [2,5; 4,3]	3,96±0,55* 2,97 [2,1; 4,4]	4,43±1,04* 2,76 [1,6; 4,0]	1,84±0,22 2,1 [1,1; 2,3]
HOMA-FB	216,1 +34,0 94,1 [200; 310,7]	175,5±43,4 126 [92; 198]	167,3 + 33,5 124 [103; 262]	250,5±35,5 170,4 [115; 380]

Note: * — p<0,05, significance relative to control; Me [25; 75] (Me — median; interquartile values: 25 и 75 — percentile).

Table 3

CHM indices, HOMA-IR and HOMA-FB indices in persons with or without CHM disorders depending on CP duration

Groups		Group 1	Group 2	Group 3
		Without CHM disorders (n= 14), With CHM disorders (n=5)	Without CHM disorders (n= 16), With CHM disorders (n=10)	Without CHM disorders (n=7), With CHM disorders (n=7)
Glycemia fasting, mmol/l	Without CHM	4,87±0,12	4,71±0,12	5,68±0,14

	disorders			
	With CHM disorders	5,94±0,09***	6,28±0,42***	7,06±0,6***
Glycemia in 2 hours after meal or GTT, mmol/l	Without CHM disorders	5,16±0,10	5,25±0,11	5,36 + 0,10
	With CHM disorders	7,00±0,73***	10,20+1,10***	10,80±1,42***
HbAlc, %	Without CHM disorders	5,34±0,10	5,62±0,16	5,94±0,40
	With CHM disorders	5,72±0,12*	6,47±0,22**	6,73±0,24*
IRI, mU/ml	Without CHM disorders	15,50±1,21	16,30±1,23	8,45±1,28
	With CHM disorders	15,60+1,86	17,50±1,97	25,00±1,73***
HOMA-IR	Without CHM disorders	3,39±0,50	3,46±0,51	1,72±0,47
	With CHM disorders	4,07±0,71	4,75±0,64	7,13±1,65***
HOMA-FB	Without CHM disorders	236,4±37,9	223,2±40,8	212,2±36,9
	With CHM disorders	201,1±31,4	131,7 + 46,5	123,7±30,8

Note: * — p<0,05; ** — p<0,01; *** — p<0,0001, достоверность по отношению к группе без НУО.

Malka D. et a1. [7] found out that in the debut of CP diabetes is diagnosed in 10% of cases, among which 2% are cases of DM type 1. In 10 and 25 years from the start of the main disease diabetes is detected respectively in 50 and 83% of cases, and DM type 1 is detected respectively in 26 and 53% of cases. The authors believe that the likelihood of developing diabetes in CP is 3.5%, and DM type 1 — 2.2% annually. Consequently, almost 80-90% of patients with CP are likely to have diabetes in 25 years from onset of the disease.

In our study, CHM disorders in patients with CP duration of up to three years are observed in 26.4% of cases, mainly in the form of impaired glucose fasting (15.8%). In the group of patients with CP duration of three to five years, CHM disorders occur in 38.5% of cases and manifest itself mainly as impaired glucose tolerance (19.3%). The proportion of patients with diabetes (21.4%) is higher among patients with CP >5 years than upon the shorter CP duration (Fig. 1).

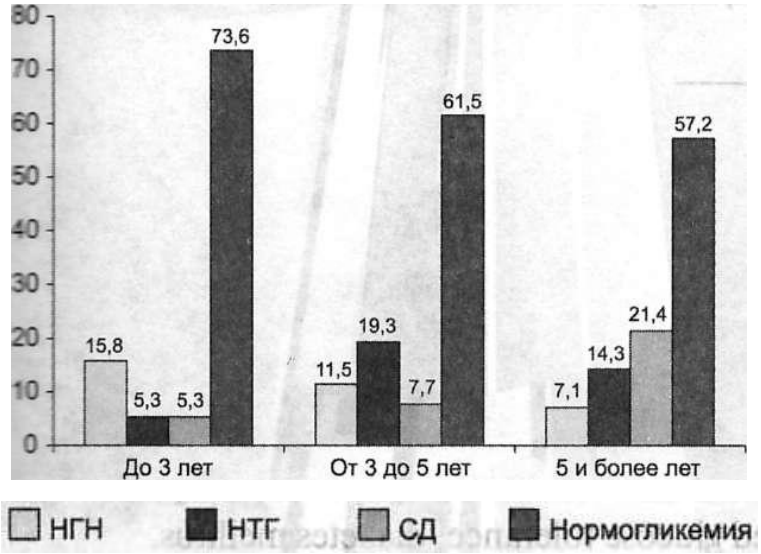

Fig. 1. Occurrence of CHM metabolism disorders depending on CP duration.

Conclusions

1. Pathology of the biliary system (45.7%) and alcohol abuse (35.6%) are the main risk factors for pancreatitis.
2. Persons with the duration of CP >5 years with impaired CHM have higher IRI level and HOMA-IR index, and lower HOMA-FB index than that of patients without CHM disorders.
3. Patients with the disease duration of up to three years predominantly have impaired fasting glucose, with the duration of chronic pancreatitis from three to five years there is an impaired glucose tolerance, while in individuals with a course of disease for more than 5 years diabetes mellitus is more common.

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This article deals with dependence of the carbohydrate metabolism disorders on the duration of disease in patients with non-destructive chronic pancreatitis. Patients with the disease duration of up to three years predominantly have impaired fasting glucose, with the duration of chronic pancreatitis from three to five years there is an impaired glucose tolerance, while in individuals with a course of disease for more than 5 years diabetes mellitus is more common.