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The Ways of Optimizing Treatment of the Patients with Comorbidity: Chronic Pancreatitis and Metabolic Syndrome

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We have examined 84 patients to study the clinical-functional peculiarities of combined courses of the chronic pancreatitis (CP) with metabolic syndrome (MS), lipid and carbohydrate exchange infringements efficiency of usage omega-3 polyunsaturated fatty acids (PFA). The results of research show positive influence omega-3 PFA (the indices of triacylglycerides (TG), cholesterol lipoproteins very low density has possibly decreased) and a carbohydrate exchange (index HOMA has possibly decreased) in patients with chronic pancreatitis and metabolic syndrome. This work is a new method of correction metabolic disoders in patients with comorbidity.

Keyword: Chronic Pancreatitis, Metabolic Syndrome, Dyslipidemia, Insulin resistance, Omega-3 PFA.

1. Introduction

In recent years, the increase of chronic pancreatitis and its severe complications, with serious social consequences is associated with concomitant metabolic syndrome [1,3,4,12]. Functional state of the pancreas has a significant share in the development of key components of the metabolic syndrome (hyperinsulinemia, insulin resistance, impaired glucose tolerance) and, conversely, the existing metabolic changes (obesity, atherogenic dyslipidemia) contribute to disorders of the endocrine and exocrine pancreatic function[11]. We could not find information on metabolic disorders in patients with chronic pancreatitis in combination with MS in scientific publications. Nowadays, there is strong evidence of the usage of drugs omega-3 PFAs in different fields of medicine [2, 7].

2. The aim of Research

study of the clinical efficacy of omega-3 PFA in the treatment of chronic pancreatitis in combination with metabolic syndrome on the base of study the dynamics of lipid and carbohydrate metabolism.

3. Material and Methods

The study involved 84 patients with chronic pancreatitis in combination with methabolic syndrome. Patients were examined in gastroenterological department in Clinical Hospital № 1 in Ivano-Frankivsk. 30 patients were men - (35.7%) and 54 patiens - women (64.2%). The age of the patients ranged from 20 to 61, and the average was 48,3±4,1 years. The patiens under examination were randomized by sex and age. All the patiens under examination were informed and signed the agreement. After they were taken into clinical and laboratory-instrumental examination. The diagnosis of CP was verified by clinical data (complaints, anamnesis, physical data) and laboratory and instrumental examination according to order of the Ministry of Health of Ukraine № 271 from

13.06.2005. MS diagnosis was verified according to the recommendations of the World Diabetes Federation (IDF)[8, 9]. Status of lipid metabolism was assessed by determining the level of serum total cholesterol (total cholesterol), triglycerides (TG), high-density lipoprotein cholesterol (HDL) photocolorimetric way through a set of reagents company «LACHEMA» (CZ) method Zlatiks-Zack[10]. Determination of LDL cholesterol (mmol / l) was performed by calculation method using the formula. LDL cholesterol = total cholesterol - (VLDL + LDL cholesterol HDL). The level of VLDL cholesterol (mmol/l) was determined by the ratio (TG * 2.29) / 5, provided that the concentration of TG did not exceed 4.5 mmol/l[6]. For a more accurate reflection of favorable and unfavorable combinations of different lipid metabolism in relation to the risk of atherosclerosis atherogenic index was calculated using the formula: SC = (total cholesterol - HDL cholesterol) / HDL cholesterol [6].

In the presence of elevated levels of glucose in the blood in patients was performed glucose test (GTT) by the standard method recommended by WHO and National Diabetes Data Group (1979). Determination of serum immunoreactive insulin was performed by enzyme immunoassay analyzer "Stat Fax 303 Plus" (USA) using ELISA reagent set firm "DRG". Calculation of indices of insulin resistance were carried out using formulas HOMA (Homeostasis Model Assessment) and Caro. HOMA-IR = (G × I)/22, 5, G - the level of fasting glucose (mmol / l), I - fasting insulin levels (mklOd / ml) 22.5 - factor[9]. Caro index was calculated by the formula: glucose (mmol/l)/ fasting blood insulin (mkOD/l)[9].

All 3 groups were examined. Group N=I included 42 patients with chronic pancreatitis in combination with MS, the components of which were abdominal obesity, high blood pressure (BP) higher than 130/85 mm Hg (or the presence of diagnosed hypertension), fasting hyperglycemia over 5,6 mmol/l (or verified diabetes mellitus (DM)). Patients of group N= II were 42 patients with chronic pancreatitis in combination with MS, whose components were dyslipidemia, abdominal obesity, high blood pressure above 130/85 mm Hg (or the presence of diagnosed hypertension), fasting hyperglycemia over 5,6 mmol/l (or verified DM). A control group included 20 healthy persons. Patients Groups N=I and N=II in accordance with the applicable treatment were divided into two subgroups: IA, IIA (subgroup comparisons) - subgroup received basic therapy, patients IB and IIB (sub monitor) - subgroups received basic therapy in combination with omega-3 PFA. As omega-3 PUFAs used epadol domestic product in an amount of 2 g / day (Kyiv Vitamin Plant). As a basic treatment used medical complex: diet number 5, antispasmodics (Nospanum 2 mL of 2% w/m, papaverine hydrochloride 2% 2 mL d/s), analgesics (spazmalhon 5.0 d/c), enzymes (pancreatin 10 thousand units 3 times a day during meals) acidlowers (omeprazole 40 mg 1 time per day) were administered as needed antibiotics (ceftriaxone 1.0 A/m 2 g/d) infusion therapy. In the presence of hypertension they got mullion antihypertensive (amlodipine 5 mg/day, further dose was titrated based on the effect of antihypertensive therapy). In the presence of carbohydrate metabolism patients with impaired carbohydrate tolerance, fasting glucose were appointed diet number 9, patients with verified diabetes - diet number 9, SIOFOR hypoglycemic drug, the dose which ranged from 1000 to 2000 mg/day. In the presence of dyslipidemia prescribed lipid-lowering drug simvastatin 20 mg/day in the evening.

Clinical, instrumental and laboratory studies were conducted in all patients before treatment, after 3 weeks and 3 months after the prescribed treatment. Statistical analysis of the results of research

conducted through programs «Statistica for Windows v. 7.1". Probability differences of quantitative indicators were determined by Student's t-test. The differences between the figures considered statistically significant at $p < 0,05$. To investigate the relationship between indicators that are analyzed, correlation analysis with calculation of Pearson's correlation coefficient pair (r).

4. Results and Discussion

Pain of weak and moderate intensity was detected in 80% of patients, subgroups of comparison and 78,5% of sub observation. Dyspeptic syndrome (nausea, burping air, vomiting, bloating, diarrhea) was noted in all patients. In patients supervision group was noted more rapid relief of pain: on 2nd-3rd day - in 30,23% of patients, on 4th - 5th in 53%, on 6th - 7th days - 12% of patients in the course of treatment. Dyspeptic syndrome disappeared in most patients of this group (93,4%) on 8th - 9th days. In comparisons subgroup disappearance of pain occurred on 2nd - 3rd day in 13,4% of patients, on 4th - 5th day - in 33,4%, on 6th - 7th days 40%, on 8th - 9th day - in 6,6%, on 10th - 11th day - in 6,6% of patients. Dyspeptic syndrome completely disappeared on 14th - 16th day of treatment in 60% of patients on 29th - 30th days - 30% persisted after treatment in 10% of patients subgroup comparisons.

According to Table 1, the content of total cholesterol, triglycerides, LDL cholesterol in patients I and II groups compared with the control was increased, whereas HDL cholesterol content was reduced. Our results consonant with the literature data on the presence of dyslipidemia in the metabolic syndrome, which is characterized of triglycerydemia and hypercholesterolemia [4,9,11,12]. In patients I and II groups showed changes in blood glucose and insulin levels on carbohydrate metabolism (Table 1). In the examined groups of patients with fasting glucose exceeded 30% of the control group values. The presence of IR in both groups confirmed the performance HOMA-IR and Caro. The changes of carbohydrate and lipid metabolism in patients after an exchange rate of three basic treatment are shown in Table 1. According to Table 1 positive effect of the basic treatment that consisted of authentic ($p<0,05$) decrease in serum glucose, immunoreactive insulin, index HOMA-IR, total cholesterol, triglycerides, LDL cholesterol, VLDL cholesterol, AF in patients IA and IIA subgroups. However, the data stored difference ($p<0,05$) with indicators of healthy individuals, indicating a lack of effect of basic treatment and requires the inclusion of a comprehensive drug therapy that can effectively influence violations. The indices of carbohydrate and lipid metabolism after treatment using the drug omega-3 PFA are presented in Table 2.

Analyzing the dynamic parameters of carbohydrate and lipid metabolism (Table 2), three months after combined treatment with the inclusion of the drug omega-3 PFA we showed a significant ($p<0,05$) decrease in serum insulin and HOMA-IR index and approximation values to those of healthy people. In particular, insulin levels significantly decreased in 1,5 and 1,6 ($p<0,05$) times index HOMA-IR - in 1,7 and 1,8 ($p<0,05$) in patients IB subgroup and IIB subgroups accordingly. Index Caro significantly increased by 23,3% in IB and 17,8% in IIB in the groups treated with omega-3 PFA. The difference between performance in comparison to groups treated with basic therapy was proved unreliable ($p>0, 05$). In patients IIB subgroup a significant reduction in serum triglycerides at 25,2% ($p<0,05$) was showed, compared with the group only basic treatment took, where the figure fell by 5,37 % ($p<0,05$)) after a three-month course of treatment. VLDL and LDL was significantly decreased by 9,75% ($p<0,05$) in patients IIB subgroups. We found probable difference between this indicator and IIA IIB subgroups: subgroup of patients IIB LDL, VLDL was significantly lower ($p<0,05$). Also, we showed a significant ($p<0,05$) increase HDL cholesterol, lower levels of total cholesterol, LDL cholesterol, AF IIB subgroup of patients but the difference between performance and IIA IIB subgroups was proved unreliable ($p>0,05$).

According to the correlation analysis revealed statistically significant correlation relationships usually mean force between the degree of insulin resistance, which was defined by HOMA-IR, and total cholesterol ($r=0$ 34, $p=0,007$) and TG ($r=0,72$, $p=0,0001$), anthropometric indicators that reflect abdominal obesity: OT ($r=0,37$, $p=0,003$). The presence of correlation relationships between an index of insulin resistance and lipid metabolism suggesting their involvement in the development and progression of chronic pancreatitis against MS[9].

5. Conclusion

Application of this treatment method with the inclusion in the complex therapy of omega-3 polyunsaturated fatty acids results in more effective correction of lipid and carbohydrate metabolism, which is authentic lowering TG and VLDL cholesterol and certifies clinical and laboratory efficacy treatment programme for patients with chronic pancreatitis in combination with MS.

Table1: Dynamics of carbohydrate and lipid metabolism in patients with chronic pancreatitis in combination with metabolic syndrome it after a course of basic therapy

Indices	Healthy persons(n=20)	IA subgroup (n=42)			IIA subgroup (n=42)		
		Before treatment	On 3 weeks	On 3 month	Before treatment	On 3 weeks	On 3 month
Glucose, mmol/ml	4,39± 0,09	5,98±0,14 э	5,68±0,14*э	5,53±0,12*э	6,4±0,19 э	5,8±0,1*э	5,52±0,*э
Immunureactive insulin, mkОд/l	8,21± 0,33	27,84±1,57 э	24,11±1,01*э	20,48±0,99*э	30,32±1,7 э	27,28± 1,3 э	24,33±1,19*э
HOMA-IR	2,21± 0,09	7,36±0,44 э	5,6±0,21*э	4,9±0,2*э	8,56±0,58 э	7,24±0,29 *э	6,8±0,3*э
Caro	0,34± 0,03	0,23±0,01 э	0,23±0,01 э	0,27±0,01 э	0,23±0,01	0,20±0,009	0,26±0,01 э
Total cholesterol, mmol/ml	4,28± 0,14	4,36±0,07	4,34±0,05	4,35±0,07	5,39±0,1 э	5,21±0,07 э	5,13±0,09*э
Triacilglycerides, mkod/l	1,4± 0,03	1,5±0,02	1,48±0,02	1,47±0,02	1,86±0,03 э	1,81±0,03 э	1,76±0,02*э
HDL, mmol/l	1,51±0,07	1,44±0,05	1,45±0,04	1,41±0,04	1,09±0,03 э	1,11±0,02 э	1,11±0,03 э
LDL, mmol/l	2,65± 0,09	2,77±0,07	2,77±0,07	2,76±0,04	3,46±0,12 э	3,28±0,06*э	3,18±0,09*э
VLDL, mmol/l	0,71± 0,02	0,72±0,01	0,68±0,01	0,68±0,01	0,82±0,02 э	0,83±0,01 э	0,8±0,0*э
AF	2,48± 0,02	2,51±0,08	2,58±0,03	2,61±0,08	4,08±0,16 э	3,72±0,13 э	3,66±0,13*э

Notes * - differences in probability before and after treatment ($p<0,05$), э - differences in probability compared of healthy persons ($p<0,05$).

Table2: Dynamics of carbohydrate and lipid metabolism in patients with chronic pancreatitis in combination with metabolic syndrome after a course of treatment with omega-3 PFA

Indices	Healthy persons (n=20)	I Б subgroup (n=42)			II Б subgroup (n=42)		
		Before treatment	On 3 weeks	On 3 month	Before treatment	On 3 weeks	On 3 month
Glucose, mmol/ml,	4,39± 0,09	5,92±0,14 э	5,41±0,14*● э	5,4±0,11*э	6,38±0,19 э	5,48±0,12*● э	5,37±0,07*● э
Immunureactive insulin, mkОд/l	8,21± 0,33	27,8± 1,57 э	24,7±0,93	17,93±0,79*● э	30,3± 1,7 э	20,68±0,56*● э	19,42±1,06*● э
HOMA-IR	2,21± 0,09	7,32± 0,44 э	4,82±0,19*● э	4,36±0,11*● э	8,53± 0,58 э	5,01±0,19*● э	4,64±0,2*● э
Caro	0,34± 0,03	0,22± 0,01 э	0,26±0,01э	0,3±0,01	0,23±0,01	0,23±0,008 э	0,28±0,008 э
Total cholesterol, mmol/ml	4,28± 0,14	4,71±0,07 э	4,88±0,04 э	4,86±0,05 э	5,36±0,1э	5,21±0,07 э	5,12±0,08*э
Triacilglycerides, mkod/l	1,4± 0,03	1,56± 0,02	1,53± 0,02 э	1,48±0,06	1,84± 0,03 э	1,81±0,03 э	1,39±0,04*●
HDL, mmol/l	1,51± 0,07	1,27±0,05	1,38±0,03 э	1,34±0,03 э	1,09± 0,03 э	1,11±0,02 э	1,17± 0,03*э
LDL, mmol/l	2,65± 0,09	2,77±0,07	2,65±0,07	2,66±0,07	3,45±0,12 э	3,22± 0,13 э	3,16± 0,13*э
VLDL, mmol/l	0,71± 0,02	0,71±0,01	0,69±0,01	0,68±0,01	0,81± 0,02	0,78± 0,01*	0,74±0,01*● э
AF	2,48± 0,17	2,96±0,18 э	2,88±0,08 э	2,86±0,08 э	4,07± 0,16 э	3,62± 0,13 э	3,43±0,14*э

Notes: * - differences in probability before and after treatment ($p<0,05$), ● - differences in probability compared of basic therapy ($p<0,05$), э - differences in probability compared of healthy persons ($p<0,05$).

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