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POLYMORPHISM N34S OF THE SPINK1 GENE IN UKRAINIAN PATIENTS WITH DIFFERENT FORMS OF ACUTE PANCREATITIS

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Introduction. The course of acute pancreatitis, whose onset is stipulated by one and the same factor, may be of quite an opposite nature in different patients - from the edematous form to pancreatonecrosis. It directly depends on the marked character of the aggressive influence of activated aggressive enzymes on the pancreas and its surrounding tissues (9). Here, an important role is played by genetically determined defense mechanisms aimed at preventing an intrapancreatic activation of enzymes (1-10). One of the such fundamental mechanisms is the neutralizing effect of the secretory pancreatic trypsin inhibitor (the serine protease inhibitor of Kazal's type I - SPINK1).

The aim of the work. The presence of this genetic defect is accompanied with the incapability of one of the chief mechanisms of neutralizing trypsin, and may lead to an excessive uncontrolled intra acinar activation of this enzyme. This, in our opinion, can significantly affect the nature of the course of acute pancreatitis, determining the expediency of carrying out such studies.

Material and methods. The research involved 37 people with different forms of acute pancreatitis. Among them: 25 (67.6%) men and 12 (34.2%) women. The average age of the patients was 48 ± 14,4 years. The patients were divided into 2 groups. The first group consisted of 17 patients with acute edematous pancreatitis. The second group comprised 20 patients with acute necrotizing pancreatitis.

The presence of the favorable "wild - type" N - allele ("wild - type", Wt) - 73,0% (27) of the people was detected in the majority of the subjects. The pathological "mutant" S – variant was identified in 27,0% (10) of the people. Hereat, there were 45.9% (17) of the cases of homozygous carriers of the "wild" NN - genotype (N34), NS - heterozygotes (N34S) - 51,4% (19) of the cases. One (2,7%) patient was a homozygous carrier of the mutant S - allele (SS - genotype, 34S). A distribution of the genotypes according to the polymorphic N34S variant of the SPINK1 gene among the examinees corresponded to expected Hardy – Weinberg's equilibrium ($p > 0,05$).

On distributing all the patients according to the etiological agent it was found out that the frequency of the NN - and NS - genotypes in patients with biliary pancreatitis made up 52,6% (10) and 47,7% (9), respectively and did not differ statistically from that in patients with pancreatitis of nonbiliary genesis – 33,3% (6) and 61,1% (11) respectively ($\chi2 = 0,003$, $p = 0,95$ and $\chi2 = 0,68$, $p = 0,4$ respectively).

Results. While analyzing the group of patients with acute edematous biliary pancreatitis, it was established that the homozygous carriers of the favorable "wild" N - allele and heterozygotes occurred with the same frequency - 50% (5) and 50% (5), respectively.

In patients with acute destructive pancreatitis of biliary and nonbiliary genesis the frequency of detecting genotypes NN - (N34) and NS - (N34S) did not differ significantly: 55,5% (5) and 44,5% (4) versus 45,5% (5) and 45,5% (5) respectively ($\chi2 = 0,001$, $p = 0,97$ and $\chi2 = 0,114$, $p = 0,74$ respectively).

The homozygous mutation SS - genotype was detected in one person of the group mentioned. It should be noted that the initiation of the disease was associated with the nonbiliary factor in a female patient with the SS - genotype. The course of the disease was characterized by particular "aggressiveness" with the development of acute suppurative subtotal pancreatonecrosis which became complicated by the formation of abscesses of the omental bursa and the right subdiaphragmatic space, retroperitoneal phlegmon, external pancreatic and duodenal fistulae, left - side exudative pleurisy and toxic bacterial shock. The length of the hospital staying of the patient made up 118 bed days 10 step – by - step surgical interferences, having been performed during this period. The development of the painful form of chronic pancreatitis with a predisposition to frequent recurrence was certified in the said patient in the process of a follow - up. Taking into account the adduced analysis of the patient's case history with the SS-genotype, as well as the nonbiliary and nonalcoholic etiology of the disease, we rightfully consider, that one of the principal

causes of such a severe clinical course of acute pancreatitis in a specific case was its hereditary character.

Conclusions. Thus, the frequency of the NN - and NS - genotypes of the SPINK1 gene in the patients examined by us, did not differ significantly from the patients with various forms of acute pancreatitis. The carriage of the unfavorable SS - genotype, in our opinion, may be a contributory factor for the onset of the disease and a potentiation of its further progression, as well as a prognostic marker of a severe clinical course of acute pancreatitis with the development of necrotic lesions of the pancreas.

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ACUTE PERITONITIS AS AN URGENT PROBLEM OF MODERN SURGERY

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Introduction. Over the past decades, in connection with the active introduction of new technologies, methods of diagnosis and treatment of acute peritonitis (AP), in particular, the improvement of the technique of surgical interventions, the expansion of the possibilities of drug therapy, as well as the development of complex measures before and during surgical intervention and in the postoperative period, there is a positive trend in the results of the treatment of this pathology. However, the mortality due to AP remains high, varying, depending on the form and prevalence, from 16 to 80% and has no significant downward trend. One of the reasons for the high mortality rate is the lack of in-depth knowledge of the pathogenesis of AP in connection with the incomplete elucidation of the mechanisms of the initiation of the inflammatory process, as well as the factors supporting it, contribute to its progression and spread throughout the peritoneal cavity. This primarily concerns cytokines, especially interleukin 1β (IL-1β), which plays an important role in the regulation of various inflammatory mechanisms. The study of these factors, in our opinion, will make it possible not only to diagnose the presence of peritonitis reliably, but also to predict the nature of its course.

The aim of the study. Study of factors that make it possible to predict and diagnose the course of acute peritonitis

Materials and methods. A comprehensive examination of 115 patients admitted to the hospital with the signs of diffuse peritonitis was conducted. The diagnosis was confirmed surgically. All the patients underwent examination of the variants of IL1β -511C/T gene polymorphism. The material for molecular-genetic examination was DNA isolated from the lymphocytes of the peripheral venous blood of patients by means of the set of reagents «DNA-sorb-B». Polymerase chain reaction (PCR) was conducted using TaqDNA-polymerase and specific primers. The alleles were discriminated by means of specific endonucleases of AVAI and AVAII restriction («Fermentas», Lithuania) in hydrolysis reaction. PCR restriction products were divided by means of electrophoresis in 2% agarous gel with tris borate buffer (TBB) concentrated with ethidium bromide for 30-45 minutes: “mutant” AVAII-resistance Tallele was divided into “wild” C-allele [1]. The fragments were visualized by means of transilluminator with the molecular mass marker available 100-1000 bp. The level of cytokines in the blood serum was evaluated by means of immunoenzyme method on the analyzer STAT-Fax Plus-303 (USA); test systems DIACLON were used (France), DRG (Germany).

Results. It is known that the activity of cytokines is genetically determined. Different versions of the modification of the IL-1β gene (-511C/T), which encodes its synthesis, lead to differences in the nature of the inflammatory process, changes in the parameters of nonspecific resistance and reactivity, which can contribute to the cascade progression of the mechanisms of damage to organs and structures, and disruption of homeostasis. 115 patients undergoing inpatient treatment of various forms of acute peritonitis, which complicated the course of various acute surgical diseases, were studied, and the IL-1β level and the IL-1β -511C/T gene polymorphism were determined.