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Time Course of Malonic Dialdehyde and α-Tocopherol in Rat Pancreas during the First Hours of Acute Pancreatitis

N. V. Prokop'eva, L. F. Gulyaeva, and N. G. Kolosova

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Time course of malonic dialdehyde and α-tocopherol levels in rat pancreas during the first day of experimental pancreatitis indicates activation of lipid peroxidation and components of the antioxidant system in the involved organ.

Key Words: *acute pancreatitis; lipid peroxidation; a-tocopherol*

Acute pancreatitis (AP) is now responsible for up to 9% of acute and chronic diseases of the abdominal organs [6]. Some aspects of the pathogenesis of AP are little known. This diseases involves changes in lipid metabolism, *e. g.,* activation of lipid peroxidation (LPO) associated with enhanced proteolysis. Time course of LPO and activity of the antioxidant system in AP have been studied mainly by measuring their blood and plasma concentrations [4]. The data on LPO activity in the pancreas in this disease are scanty. There are no publications about the intensity of LPO and activity of the antioxidant system in the pancreas during the first hours of AP, which is so important for understanding the mechanisms of realization of toxic effect and activation of defense systems in the damaged organ.

We investigated the time course of malonic dialdehyde (MDA) and important lipophilic antioxidant α-tocopherol in rat pancreas during the first 24 h of experimental AP.

MATERIALS AND METHODS

Experiments were performed on 94 Wistar rats (200 g) under general halothane anesthesia under aseptic conditions. AP was induced as described previously [5] by damaging the pancreas without impairing its serous membrane. Sham-operated rats served as the control. LPO intensity was evaluated in pancreas homogenate 0.5, 1, 2, 3, 4, 6, 10, 15, and 20 h after AP induction (8-12 rats per point). After perfusion and washing from blood, the pancreas was homogenized in an isolation medium (0.1 M phosphate buffer, pH 7.4) at 1:10 tissue: medium ratio. Activity of LPO was evaluated by the content of LPO products reacting with thiobarbituric acid [9]; the level of α-tocopherol was measured fluorometrically [10] on an MPF-4 spectrofluorimeter (Hitachi) using d-l-α-tocopherol as the standard (Sigma). Experimental data were processed statistically by Student's *t* test using Statgraphics software.

RESULTS

The level of MDA increased 1.2 times as soon as 30 min after modeling of AP (Fig. 1), but by the end of the first hour it did not differ from the control. By the 2nd hour the content of MDA increased 1.5 times ($p<0.05$), and from the 3rd untill the end of 6th hour LPO intensity again virtually did not differ from the control. By the 10th hour of AP the content of LPO products increased 1.5 times compared to the control ($p<0.05$), and after 17 and 20 h it 1.5 and 4.3 times surpassed the control (Fig. 1).

Institute of Molecular Biology and Biophysics, Siberian Division of the Russian Academy of Medical Sciences; *Institute of Physiology, Siberian Division of the Russian Academy of Medical Sciences, Novosibirsk.
Address for correspondence: Kolosova@adapt.nsk.su. Kolosova N. G.

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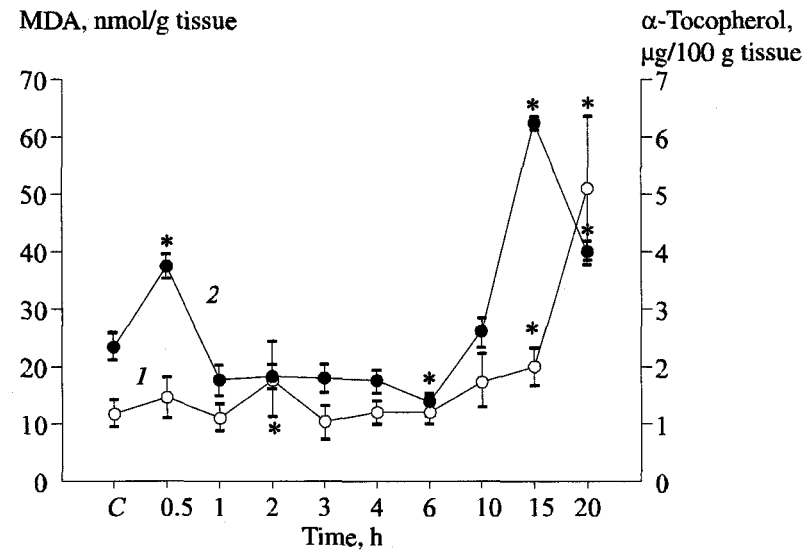

Fig. 1. Time course of malonic dialdehyde (*1*) and α-tocopherol (*2*) in the pancreas of rats with experimental acute pancreatitis. *$p<0.05$ *vs.* the control (*C*).

Thirty min after induction of AP the content of α-tocopherol 1.6-fold surpassed the control (Fig. 1), and then gradually decreased. The most significant (59%, $p<0.05$) decrease was observed by the 6th hour of the disease. Starting from the 10th hour the content of α-tocopherol increased 2.6 times ($p<0.05$), then again decreased, but by the 20th hour remained 1.7 times above the control ($p<0.05$).

Hence, we observed phasic changes in the content of LPO products and α-tocopherol in the pancreas during the first 24 h of AP. Activation of LPO after 2 h coincided with destruction of pancreatic acinar cells, which was confirmed by morphological findings [6]. Accumulation of LPO products led to activation of phospholipase A [11], the main pathochemical factor affecting cell membranes and responsible for autodestructive processes in the pancreas [7]. Subsequent stabilization of LPO can be due to stress activation of the antioxidant defense. This is confirmed by accumulation of α-tocopherol in the pancreas 0.5 h after induction of AP preceding the accumulation of LPO products. By the next rise of MDA (1.5 times by the 10th hour), numerous hemorrhages were seen in the pancreas and foci of round-cell, mostly neutrophil infiltration appeared in the interlobular connective tissue. Activated cells in the inflammation focus produced active oxygen forms and could induce hyperintensification of LPO, which was seen from 4-fold increase in MDA concentration by the 20th hour of the disease. Therefore, the time course of MDA concentrations in the pancreas during the first hours of AP is clear.

Time course of α-tocopherol content in the damaged organ was unexpected. An increase in α-tocopherol content in tissues in various diseases has been reported [8]. The 1.6 times increase in this parameter 30 min after the operation can be explained by compensatory mobilization and redistribution of α-tocopherol in the organism. During stress, mobilization of endogenous α-tocopherol is mediated by catecholamines [1,2]. The contents of catecholamines in AP markedly increased during the first hours of disease [1], but high expenditure of the antioxidant in the inflammation focus leads to its deficit: in our experiments the level of α-tocopherol during hours 2-6 of AP decreased in comparison with its level after 30 min and in comparison with the control. Starting from the 10th hour of disease the content of α-tocopherol gradually increases, which indicates redistribution of endogenous α-tocopherol. All this suggests that free-radical process are involved in the pathogenesis of AP. Intensification of LPO is not only an early nonspecific marker of AP, but also a mechanism triggering the restructuring of metabolism in the organ. Activation of LPO is paralleled by successive activation of antioxidant defense factors. Our findings suggest the necessity of correcting free-radical oxidation and normalizing LPO during combined therapy of AP.

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