Oxidative and nitrosative stress — the leading mechanisms of chronic pancreatitis and chronic obstructive pulmonary disease interaction and inducers of their progression

Abstract. Background. The frequency of chronic pancreatitis (CP) comorbidity with chronic obstructive pulmonary disease (COPD) has significantly increased recently. It may be accompanied by changes in oxidant-antioxidant homeostasis and activates a cascade of reactions of mutual burdening of these pathologies. The purpose of the current research was to evaluate the intensity of lipid peroxidation, oxidative modification of proteins and the state of individual factors of the antioxidant defense system in the development and course of CP, depending on the comorbid COPD. Materials and methods. Three hundred and seventeen patients were examined, including 62 patients with CP alone (group 1), 132 CP patients with comorbid COPD (group 2), 123 patients with COPD alone (group 3). The content in blood of isolated double bonds in compounds, conjugated dienes, ketodienes and conjugated trienes, malonic aldehyde, nitrites/nitrates, reduced glutathione, the activity of catalase, glutathione-S-transferase, glutathione peroxidase were evaluated in all patients. Results. In CP patients with comorbid COPD, the maximum oxidative stress intensity among the compared groups was registered. There was a reliable increase in the content of malonic aldehyde — by 2.0 times (p < 0.05), isolated double bonds — by 2.2 times (p < 0.05), conjugated dienes — by 1.9 times (p < 0.05), ketodienes and conjugated trienes — by 1.9 times (p < 0.05), nitrites/nitrates — by 2.6 times (p < 0.05). A reliable decrease in reduced glutathione content of erythrocytes was detected: in group 1 — by 1.5 times, in group 2 — by 1.9 times (p < 0.05), in group 3 — by 1.2 times (p < 0.05). The compensatory increase in the activity of glutathione-S-transferase, glutathione peroxidase and blood catalase was revealed: in group 1 — by 1.3, 1.2 and 1.5 times (p < 0.05); in group 2 — by 1.5, 1.3 and 1.8 times (p < 0.05), in group 3 — by 1.2, 1.2 and 1.4 times, respectively (p < 0.05). Conclusions. The comorbid course of CP and COPD is accompanied by the maximum intensity of oxidative and nitrosative stress compared to the isolated course of the disease. An increase was detected in intermediate and final metabolites of peroxide oxidation in the blood, oxidative modification of proteins, nitrites/nitrates in the blood against the background of a deep imbalance of antioxidant defense factors, an increase in ceruloplasmin content in the blood, which requires the administration of antioxidant agents to correct detected disorders and prevent the progression of both comorbid diseases.

Keywords: chronic pancreatitis; chronic obstructive pulmonary disease; oxidative and nitrosative stress
The frequency of CP comorbidity with chronic obstructive pulmonary disease (COPD) has significantly increased recently, and it may be accompanied by changes in oxidant–antioxidant homeostasis and activate a cascade of reactions of mutual burdening of these pathologies [1, 2]. This study is dedicated to this issue, since the established phenomena of intense OS and NS require the doctor to correct the standard treatment for the underlying and comorbid diseases, taking into account the established changes. At the same time, the mechanisms of the relationship between the degree of LPO processes activation and the characteristics of biochemical markers of inflammation in patients with CP with comorbidity with COPD, the development of exocrine pancreatic insufficiency, the degree of bronchial obstructive syndrome, and the phase of the disease remain unclear.

**The purpose** of the current research was to establish the state of oxidant–antioxidant homeostasis by studying the intensity of lipid peroxidation, oxidative modification of proteins (OMP) and the state of individual factors of the AOD system in the development and course of CP, depending on the comorbid COPD presence, its stage according to GOLD, availability of exacerbation, as well as the degree of exocrine pancreatic insufficiency.

**Materials and methods**

317 patients were examined, including 62 patients with isolated CP of mixed etiology in the acute phase of moderate severity (group 1), 132 CP patients with comorbid COPD (GOLD 2B, 3E) (group 2). The control group (group 3) for comparison consisted of 123 patients with isolated COPD (GOLD 2B, 3E). The average age of the patients was (58.3 ± 4.3) years. 89 women (28.1 %) and 228 men (71.9 %) were under supervision. The comparison group consisted of 30 practically healthy persons of the corresponding age and gender. The duration of CP was in the range of 7–15 years, while COPD duration — from 4 to 12 years.

The CP was diagnosed based on complaints, anamnesic data, the results of clinical, laboratory and instrumental examinations were carried out in accordance with the Ministry of Health of Ukraine order No. 638 of September 10, 2014 [16]. The International Statistical Classification of Diseases and Related Health Problems, 10 revision (K86.1 Chronic pancreatitis) was used for classification and headings of CP cases. The study design included clinical, laboratory, biochemical blood tests (α-amylase activity in the blood), enzyme immunoassay (ELISA) (focal analysis for elastase-1 content), biochemical analysis of duodenal content (pancreatic enzyme activity), coprogram, ultrasonographic examination of the pancreas. The analysis of clinical, ultrasonographic manifestations of CP, biochemical (blood α-amylase), laboratory parameters of the functional state of the pancreas was carried out according to generally accepted methods. The comprehensive ultrasonographic study was performed using the AU-4 Idea ultrasound scanner (Biomedica, Italy) using a convex transducer with 3.5 MHz frequency. The content of C-reactive protein in blood serum was determined by the latex method using the NVL Granum Kit (Ukraine). The parameters of fecal pancreatic elastase-1 in patients were studied by ELISA using the LabSystems Multiskan MS (Netherlands) enzyme immunoassay analyzer.

The COPD diagnostics and treatment was made out in accordance with the recommendations of clinical guidelines (Order of the Ministry of Health No. 555 of June 27, 2013, taking into account the recommendations of GOLD, 2023) [17–20].

The content of molecular products of lipid peroxidation (LPO) in blood — isolated double bonds (IDB) in compounds, conjugate dienes (CD), ketodienes and conjugate trienes (KD & CT) was studied according to O.A. Volchhorsky et al., malonic aldehyde (MA) in blood plasma and erythrocytes Y.A. Vladymyrov, A.I. Archakov [3]. The intensity OMP was determined by the content of aldehydes and keto dinitrophenyl hydrazones of the basic (AKDNPH MN) and neutral nature (AKDNPH NN) in the blood serum according to the method developed by O.Ye. Dubinina, I.F. Meshchyshen (1998) [3]. The content of NO metabolites: nitrates/nitrates in the blood was studied according to the method of Green L.C. et al. [3]. The content of reduced glutathione (RG) in the blood was determined by the titration method according to O.V. Travina in the modification of I.F. Meshchyshen, I.V. Petrova. The activity of the enzyme of the AOD system — catalase was studied using the method introduced by M.A. Koroliuk et al., the activity of glutathione-S-transferase (GT), glutathione peroxidase (GP) was studied using I.F. Meshchyshen method [3].

The normality of the distribution of values in randomized samples was analyzed by determining the skewness and kurtosis coefficients using the Shapiro-Wilk’s criterion before checking the statistical hypotheses. The significance of changes in the variations in the treatment dynamics with normal distribution in the samples was determined by the paired Student’s-t-test, in other cases, by the non-parametric paired Wilcoxon test. Mathematical processing of the obtained data was made using the computer-based AMD Athlon 64 processor using the Primer of Biostatistics Version 4.03 software.

**Results**

The results showed that in CP patients with an isolated course, reliable activation of LPO processes was registered against the background of the AOD factors of the body system imbalance (Table 1). This point of view is supported by the increase of LPO finish products content in the blood, namely, in observation group 1, the reliable increase of MA plasma and erythrocytes 1.7 times (p < 0.05), as well as the increase of IDB content in the blood 1.8 times compared to AHP (apparently healthy persons) (p < 0.05) (Table 1). Therefore, the results of the analysis of the content of the LPO final metabolites indicate significant metabolic intoxication in the group of patients with CP in the acute phase.

When assessing the content of LPO intermediate molecular products in the blood, the reliable increase in the content of CD and KD & CT in the blood in group 1, respectively, by 1.7 times (p < 0.05) and by 1.6 times (p < 0.05), was revealed.

The significant increase in the OMP intensity was established along with the LPO intensification in CP, in particular, the content of AKDNPH MN in the blood was 2.3 times (p < 0.05) higher than in the AHP, as well as a significant increase in the intensity of NS (according to the nitrates/nitrates content in blood): 1.5 times (p < 0.05) (Table 1).
The significant OS intensity was registered with the increase of end and intermediate molecular LPO products content in the blood of COPD (2B, 3E) patients with an isolated course in the entire group, in particular, in group 3, a reliable increase (1.3 and 1.2 times) in the content of MA plasma and erythrocyte levels, respectively (p < 0.05), was revealed as well as the 1.5–time increase of the IDB, CD, and KD & CT content in the blood compared to the AHP (p < 0.05) (Table 1). It should be noted that the results of the content analysis of intermediate and final metabolites of LPO in COPD patients in the acute phase also indicate the OS significant intensity, however, the level of its activation was probably lower than in patients with CP with an isolated course (p < 0.05). At the same time, the OS effect in terms of the OMP processes intensity (the content of AKDNPH NS in the blood) in COPD patients, when compared to the indicator in CP patients, was probably higher both from the AHP indicator (2.6 times) and from the indicator in CP patients with the isolated course (p < 0.05). The significant increase of the NS intensity (2.2 times; p < 0.05) was also established in isolated COPD patients compared to CP (Table 1).

The OS intensity analysis according to the above indicators in comorbid CP patients with COPD in the acute phase of both diseases indicates the maximum OS intensity among the compared groups, namely, the reliable increase of MA plasma and erythrocyte levels by 1.9 and 2.0 times, respectively (p < 0.05), as well as the 2.2–time increase of the IDB content in the blood compared to AHP (p < 0.05) (Table 1). The more intensive increase of the intermediate LPO product level in group 3 was also established: CD and KD & CT — 1.9 times, which indicates decomposition of LPO processes in patients with comorbidity, and probably exceeds the figures in groups with isolated CP and COPD courses (p < 0.05). Markers of the OMP intensity significant increase were established in group 2 patients: AKDNPH NS exceeded the indicator in the AHP 2.7 times (p < 0.05), that is, the maximum among the comparison groups. The OMP affects structural and transport proteins, receptors, enzymes and, as a result, a violation of their functional activity in metabolic processes, an increase in the permeability of cell membranes, an acceleration of their apoptosis and the development of cytolysis is formed. In the group of patients with comorbidity, the intensity of NS also increased significantly — 2.6 times (p < 0.05), which exceeded the damaging effect of nitrates, nitrites, as well as peroxynitrites, which are formed in increased amounts during inflammation, hypoxia during COPD and CP with isolated course.

The assessment of the AOD factors state in the examined groups of patients revealed a reliable decrease in the RG content of erythrocytes in group 1 — 1.5 times, in group 2 — 1.9 times (p < 0.05), in group 3 — 1.2 times (p < 0.05) compared to the AHP indicators. The indicators in group 2 were probably lower compared to the indicators obtained in groups 1 and 3 (p < 0.05). Against the background of the obtained changes, a compensatory increase in the activity of GT, GP and blood catalase was revealed in group 1 — 1.3, 1.2 and 1.5 times, respectively (p < 0.05), in group 2 — 1.5, 1.3 and 1.8 times, respectively (p < 0.05), in group 3 — 1.2, 1.2 and 1.4 times, respectively (p < 0.05) compared to the AHP indicators. The maximum increase of the GT; GP and blood catalase activity was found in the group of patients with comorbid pathology, compared with groups 1 and 3 (p < 0.05). The body’s compensatory response to OS and NS activation can explain the increased activity of glutathione enzymes. The compensatory increase of the ceruloplasmin content in the blood of group 1 patients — 1.5 times, in group 2 — 2.6 times and in group 3 — 2.2 times (p < 0.05) can be explained as a peculiar response to OS and NS. The maximum depletion of glutathione content in erythrocytes was found in group 2 patients, in which the maximum tension and hyperactivation of the antioxidant defense enzymes of the glutathione system are simultaneously observed according to the obtained data.

### Table 1 — Indicators of the intensity of lipid peroxidation, oxidative modification of proteins and the state of antioxidant protection in patients with CP with comorbidity with COPD (M ± m)

<table>
<thead>
<tr>
<th>Indicator, units of measurement</th>
<th>PHI, n = 30</th>
<th>Groups of examined patients</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>COPD (group 3), n = 123</td>
<td>CP (group 1), n = 62</td>
</tr>
<tr>
<td>MA in plasma, μmol/l</td>
<td>2.51 ± 0.03</td>
<td>3.37 ± 0.06**</td>
</tr>
<tr>
<td>MA in erythrocytes, μmol/l</td>
<td>8.08 ± 0.11</td>
<td>9.45 ± 0.15**</td>
</tr>
<tr>
<td>IDB, Е220/ml of blood</td>
<td>2.93 ± 0.13</td>
<td>4.35 ± 0.08**</td>
</tr>
<tr>
<td>CD, Е232/ml of blood</td>
<td>1.54 ± 0.11</td>
<td>2.36 ± 0.11**</td>
</tr>
<tr>
<td>KD &amp; CT, Е278/ml of blood</td>
<td>0.76 ± 0.02</td>
<td>1.11 ± 0.02**</td>
</tr>
<tr>
<td>AKDNPH MN, μmol/l of protein</td>
<td>1.35 ± 0.02</td>
<td>3.45 ± 0.09**</td>
</tr>
<tr>
<td>RG, μmol/l</td>
<td>0.92 ± 0.02</td>
<td>0.74 ± 0.03*</td>
</tr>
<tr>
<td>GT, mmol RG per 1 min/g Hb</td>
<td>110.90 ± 1.51</td>
<td>132.45 ± 1.61**</td>
</tr>
<tr>
<td>GP, mmol RG per 1 min/g Hb</td>
<td>145.71 ± 1.63</td>
<td>171.31 ± 3.22*</td>
</tr>
<tr>
<td>Catalase, mmol/1 min/g Hb</td>
<td>14.45 ± 0.11</td>
<td>20.91 ± 0.34*</td>
</tr>
<tr>
<td>Ceruloplasmin, mmol/l</td>
<td>12.63 ± 0.12</td>
<td>19.87 ± 0.73*</td>
</tr>
<tr>
<td>Nitrites/nitrates, mmol/l</td>
<td>15.52 ± 1.45</td>
<td>33.58 ± 1.23*</td>
</tr>
</tbody>
</table>

Notes: * — reliable changes compared to indices in AHP (p < 0.05); ** — reliable changes compared to indices of group 3 patients (p < 0.05); * — reliable changes compared to indices of group 1 patients (p < 0.05).
We performed a binary correlation analysis to confirm the role of the imbalance of indicators of the oxidant-antioxidant system in patients with CP and COPD. The direct correlation was established between the blood MA plasma content and markers of hyperenzymemia (α-amylase \( r = 0.52; p < 0.05 \), C-reactive protein content in the blood \( r = 0.51; p < 0.05 \), blood levels of IDB and α-amylase \( r = 0.45; p < 0.05 \), AKDNPH MN and α-amylase \( r = 0.47; p < 0.05 \), nitrite/nitrate content and α-amylase \( r = 0.42; p < 0.05 \), activity of catalase and α-amylase \( r = 0.51; p < 0.05 \), content of RG and elastase-1 in erythrocytes \( r = 0.62; p < 0.05 \) in feces, as well as an inverse correlation was established between the content of RG in the blood and the activity of α-amylase \( r = -0.43; p < 0.05 \), the content of RG in erythrocytes with the content C-reactive protein \( r = -0.47; p < 0.05 \), MA content in plasma and elastase-1 in feces \( r = -0.59; p < 0.05 \), ceruloplasmin content in blood and elastase-1 in feces \( r = -0.51; p < 0.05 \), RG content in erythrocytes and nitrite/nitrate content in blood \( r = -0.54; p < 0.05 \)). At the same time, a linear regression relationship was established between LPO intensity indicators (MA, IDB, AKDNPH MN, ceruloplasmin) and the degree of broncho-obstructive syndrome (FEV1 \((\text{within } r = -0.44{-}0.63; p < 0.05)\)) as well as a direct linear relationship between the antioxidant protection factor (RG) and FEV1 \((r = 0.59; p < 0.05)\).

**Discussion**

The activation of the LPO, OMP with a simultaneous imbalance in the activity of AOD factors, which forms the so-called “insidious cycle” of the CP development and progression, plays an important role in the CP progression [3, 4, 7]. In the case of primary damage to pancreatocytes by a number of etiological factors the generation of a large amount of AOS due to a respiratory burst by phagocytes of the inflammatory infiltrate, which enhance the LPO processes, OMP of membranes and lead to increase in their permeability [21], induce apoptosis of the damaged pancreatic acinar epithelium [7, 12], activate intraductal pancreatic enzymes, as well as contribute to the syndrome of deviation of pancreatic enzymes into the blood [3]. In this context, organelle-specific autophagy, including mitophagy, pexophagy, reticulophagy (endoplasmic reticulum), ribophagy, lysophagy, and nucleophagy, is a proven phenomenon [15, 22]. These types of organelle-specific autophagy are the adaptive response of the body to the cell aging control, as well as to inflammatory disorders, implemented by eliminating damaged organelles and maintaining homeostasis [22].

At the same time, the OS induction by reactive oxygen species with the formation of extremely toxic intermediate and final metabolites of LPO, OMP, hydroperoxides, aldehydes, and ketones contributes to the depletion of AOD factors under the condition of inflammation [21]. First of all, we are talking about the glutathione system that performs the function of not only a powerful antioxidant redox system, but glutathione itself is an active agent of the detoxification second phase [3, 21]. Our studies have shown that CP exacerbation is characterized by a significant depletion of the glutathione system in erythrocytes, which is a reflection of RG deficiency and is inversely proportional to the intensity of pancreatic endotoxicosis and hyperenzymemia. We also registered a significant increase in the activity of glutathione-dependent enzymes: glutathione peroxidase, glutathione-S-transferase, as well as other AOD factors: catalase and ceruloplasmin, which is due to a compensatory reaction with tension in the AOD system under conditions of enhanced OS and endotoxicosis [3].

The inflammation in the pancreatic tissue also induces the expression and liberation of inducible NO synthase (iNOS) by the monocyte-macrophage system, resulting in a local and later systemic increase in the amount of stable NO metabolites — nitrites/nitrates, which, when exposed to AOS, turn into peroxynitrite — extremely toxic and a highly reactive compound that induces NS [3, 4, 7, 23]. Both LPO and OMP are natural processes of control and regulation of cell aging and their utilization by apoptosis [3]. At the same time, a significant intensity of OS and NS belongs to the category of damaging factors, which, under certain conditions, increase in intensity over time and lead to a cascade of already irreversible reactions [3, 23]. Among these reactions, we can mention the induction of fibrosing reactions under the influence of OS and NS in the pancreas, progressive exocrine insufficiency of the pancreas due to a decrease in the acinar epithelium functioning, the formation of pancreaticogenic insulin-dependent diabetes mellitus due to damage to β-cells of the islets of Langerhans, etc. [2–4, 12, 15]. The LPO initiation is accompanied by damage to the lipid bilayer of membranes not only in the pancreas, but also in the epithelium of the bronchi and alveolocytes in the lungs in the comorbid course of CP and COPD [6, 8, 10, 24]. Confirmation is our data on the maximum increase in the content of MA, IDB, CD, and KD & CT in CP and COPD \((p < 0.05)\) patients among the comparison groups, which probably differed from the indicators in groups with both CP and COPD \((p < 0.05)\) isolated course. The reliable increase in intermediate and final forms of LPO, OMP, nitrites-nitrates indicates the deep OS against the background of metabolic intoxication, decomposition of LPO in CP patients with COPD comorbidity [1, 2, 13, 14, 23]. The imbalance was formed in the system of antioxidant homeostasis simultaneously with the activation of lipid peroxidation processes, and it was accompanied by the increase of the catalase, ceruloplasmin, glutathione-dependent enzymes activity against the background of significant depletion of the reduced glutathione itself. The most intense changes were observed in CP patients with COPD comorbidity \((p < 0.05)\). It is likely that catalase activity is stimulated compensatory in response to the presence of free superoxide ion-radicals, which indicates the AOD mechanism activation, while the depletion of RG is probably due to an increase in the cytotoxic load and the initiation of the P450 cytochrome system, the use of the RG pool for conjugation of toxic molecules and released AOS, which enhances OS and NS [3, 25]. The AOD activity also decreases during inflammatory processes [23], in our case, in CP and COPD, phospholipase is activated, through which free fatty acids (FFA) are released from phospholipids and oxidized. Oxidized FFA activate LPO, which leads to the development of mitochondrial dysfunction and cell death by apoptosis or ferroptosis [5]. The mitochondrial matrix is characterized by a high concentration of RG, which plays an important role in protecting mitochondria from free radi-
cal aggression and regulating the lifespan of erythrocytes in hypoxia [10]. Therefore, a decrease in RG is not only a marker of the AOD system depletion, but also indicates the development of endotoxiosis due to the depression of the detoxification processes of endogenous toxins and mitochondrial dysfunction, which, under conditions of comorbidity with COPD, can lead to the death of pancreatic cells by increasing apoptosis and ferroptosis. Confirmation of the role of disorders in the system of oxidants-antioxidants in the pathogenesis of mutual aggravation of CP and COPD are the established correlation relationships of medium strength between the intensity of LPO, OMP, NS and markers of hyperenzymazemia in CP (u-amylase), markers of inflammation of the pancreas (CRP), degree of exocrine insufficiency of pancreas (fetal elastase-1), as well as degree of broncho-obstructive syndrome (FEV 1) (p < 0.05).

The established profound imbalances in the oxidant-antioxidant system require the prescription of not only the basic treatment in accordance with current patient management protocols for patients with comorbid CP and COPD in the acute phase, but also additional antioxidant agents to correct the established disorders and prevent the progression of both.

Conclusions

1. The isolated course of chronic pancreatitis in the exacerbation phase is accompanied by the significant intensity of oxidative and nitrosative stress with an increase of intermediate and final metabolites of lipid peroxidation (within 1.6–1.8 times) in the blood, oxidative modification of proteins, nitrites/nitrates (1.5 times) (p < 0.05) against the background of a significant imbalance of AOD factors (glutathione deficiency — 1.5 times), activation of glutathione-dependent enzymes and catalase (1.2–1.4 times), the increase of ceruloplasmin content in the blood (1.9 times) (p < 0.05).

2. The isolated course of COPD (2B, 3E) in the exacerbation phase is accompanied by the lower intensity of oxidative stress due to a slight reliable increase of intermediate and final metabolites of lipid peroxidation (1.2–1.5 times) in the blood, but the OS higher intensity due to the activation of oxidative modification of proteins (2.6 times) and NS: increase of the content of nitrites/nitrates in the blood (2.2 times) (p < 0.05) against the background of the imbalance of AOD factors (glutathione deficiency — 1.2 times, activation of glutathione-dependent enzymes and catalase — 1.2–1.4 times), increase of ceruloplasmin content in the blood (1.6 times) (p < 0.05).

3. The comorbid course of chronic pancreatitis as well as the COPD (2B, 3E) in the acute phase is accompanied by the maximum intensity of oxidative and nitrosative stress compared with the isolated course of the disease — with the increase of intermediate and final metabolites of peroxide oxidation (1.9–2.2 times) in the blood, oxidative modification of proteins (2.7 times), nitrites/nitrates (2.6 times) (p < 0.05) in the blood against the background of AOD factors deep imbalance (glutathione deficiency — 1.9 times, activation of glutathione-dependent enzymes, catalase — 1.3–1.8 times), an increase of ceruloplasmin content in the blood (2.3 times) (p < 0.05), which requires the appointment of antioxidant agents to correct established disorders and prevent the progression of both comorbid diseases.

References


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Статистичний анализ

Оксидативний і нітрозативний стрес — провідні механізми взаємодії хронічного панкреатиту й хронічного обструктивного захворювання легень та індуktörів їх прогресування

Резюме. Актуальність. Останнім часом значно зросла частота коморбідності хронічного панкреатиту (ХП) із хронічним обструктивним захворюванням легень (ХОЗЛ), що може супроводжуватися змінами оксидантно-антioxидантного гомеостазу та активувати каскад реакцій взаємобтягення, супроводжуватися змінами оксидантно-антioxidантного балансу.

Мета дослідження: оцінити інтенсивність певних індикаторів, пов'язаних з оксидативним стресом при розвитку та перебігу ХП залежно від наявності коморбідності.

Матеріали та методи. Обстежено 317 пацієнтів: 62 з ізольованим ХП (1 група), 132 з ХП та коморбідним ХОЗЛ (2 група), 123 особи із ізольованим ХОЗЛ (3 група). У всіх хворих оцінювали вміст у крові оксидантів: глутатіону, активність каталази, глутатіон-S-трансферази, трієнів — у 1,9 раза (p < 0,05), нітритів/нітратів — у 2,6 раза (p < 0,05). Установлено вірогідне зниження рівнів відновленого глутатіону в еритроцитах: в 1,5 раза — у 1 групі, в 1,9 раза (p < 0,05) — у 2 групі, в 1,2 раза (p < 0,05) — у 3 групі. Виявлено компенсаторне підвищення активності глутатіон-S-трансферази, глутатіонпероксидази та каталази крові: у 1 групі — відповідно в 1,3; 1,2 та 1,5 раза (p < 0,05), у 2 групі — у 1,5 та 1,8 раза (p < 0,05), у 3 групі — у 1,2; 1,2 та 1,4 раза (p < 0,05).

Висновки. Коморбідний ХП та ХОЗЛ супроводжується максимальною інтенсивністю оксидативного та нітрозативного стресу відповідно з ізольованим перебігом хвороби. Зафіксовано зростання вмісту в крові проміжних та кінцевих метаболітів перекисного окиснення ліпідів, оксидативної модифікації білків, концентрації нітритів/нітратів на тлі зниження рівня глутатіону, що вимагає призначення засобів антиоксидантного захисту.

Ключові слова: хронічний панкреатит; хронічне обструктивне захворювання легень; оксидативний та нітрозативний стрес...