

**МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ  
ВИЩИЙ ДЕРЖАВНИЙ НАВЧАЛЬНИЙ ЗАКЛАД УКРАЇНИ  
«БУКОВИНСЬКИЙ ДЕРЖАВНИЙ МЕДИЧНИЙ УНІВЕРСИТЕТ»**



## **МАТЕРІАЛИ**

**101 – ї**

**підсумкової наукової конференції**

**професорсько-викладацького персоналу**

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## **THE SAFETY PROFILE OF PROTON-PUMP INHIBITORS: WHAT DO WE KNOW?**

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Proton-pump inhibitors (PPIs) are a group of medications whose main action is a pronounced and long-lasting reduction of stomach acid production. PPIs are among the most widely sold medications in the world, and the first one, omeprazole, is on the WHO Model List of Essential Medicines (World Health Organization, 2019). Their favorable safety profile has led to over-prescription by physicians, resulting in the fact that 44.9% of internal and 23.3% of surgical patients are already prescribed a PPI with hospital admission (Del Giorno, R. et al, 2018).

The view on PPI as harmless co-medication has increasingly been challenged by reports of potentially related complications, e.g., increased risk of osteoporotic fractures, pneumonia, and other, especially in long-term usage. PPI users have an increased risk of developing community-acquired enteric infections compared with nonusers. The meta-analysis showed (Hafiz R A et al., 2018) that PPI users have an increased risk of developing community-acquired enteric infection (pooled odds ratio [OR]=4.28; 95% CI=3.01-6.08). There was significant heterogeneity between the studies ( $I^2 = 85\%$ ;  $P < 0.001$ ), which was partly explained by type of microorganism. The strength of the association was similar for Salmonella (pooled OR=4.84; 95% CI=2.75-8.54;  $I^2 = 58.7\%$ ;  $P = 0.064$ ) and Campylobacter (pooled OR=5.09; 95% CI=3-8.64;  $I^2 = 81\%$ ;  $P < 0.001$ ) but lower for studies that combined all bacteria (pooled OR=2.42; 95% CI=0.96-6.14;  $I^2 = 94.3\%$ ;  $P < 0.001$ ).

A growing body of research is devoted to studying the effect of PPIs on the occurrence of allergy. Alongside the mucosa-protective attributes of gastric pH elevation, pH-dependent pepsin activation for protein digestion is impaired, subsequently also affecting pancreatic digestion (Pali-Scholl, I. & Jensen-Jarolim, E., 2011). On one side, PPIs enable the persistence of ingested epitopes and lead to antigen-specific Th2 type immune responses and allergic symptoms, on the other side, these drugs may promote cellular responses towards a Th2 bias. For instance, PPIs activate mast cells via AhR thereby synergizing with IgE-FcεRI signaling and enhancing release of human mast cell mediators and CD63 expression associated with allergic symptoms (Novotna, A. et al., 2014).

In population-based analysis, covering nearly all of Austria's population (8.2 million) between 2009 and 2013 (Galateja Jordakieva et al, 2019), there was found a high prevalence of anti-ulcer drug prescription associated with a highly significant subsequent prescription of anti-allergic medications. The rate ratios for anti-allergic following gastric acid-inhibiting drug prescriptions are 1.96 (95% CI:1.95–1.97) and 3.07 (95%-CI:2.89–3.27) in an overall and regional Austrian dataset. These findings are more prominent in women and occur for all assessed gastric acid-inhibiting substances. Rate ratios increase from 1.47 (95%CI:1.45–1.49) in subjects <20 years, to 5.20 (95%-CI:5.15–5.25) in >60 year olds.

Thus, proton-pump inhibitors provide important clinical benefits for many patients. PPIs are essential in managing gastroesophageal reflux disease, in treating patients with gastroduodenal ulceration, and in reducing the probability of upper gastrointestinal bleeding from aspirin or NSAIDs in high-risk patients. They have favorable safety profile, however, observational studies have suggested an association between PPI use and some adverse events. Of course, inappropriate use of PPIs should be avoided and physicians should be aware of the side effects of the drugs.

**Pavliukovych N.D.**

## **ERYTHROCYTE MEMBRANE MORPHOLOGY OF PATIENTS WITH CHRONIC HEART FAILURE AND DIABETES MELLITUS**

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Blood rheological properties changes are one of the crucial points in the pathogenesis of most diseases, especially in case of comorbidity. Research aimed at investigation of possible



structural changes of erythrocytes membranes (EM) in patients with chronic heart failure (CHF) and diabetes mellitus type 2 (DM). Methods of the optical physics reveal and objectify structural changes of EM, which can expand the arsenal of diagnostic methods of rheological disorders detection due to various pathological conditions.

60 patients with CHF (I group) and 55 patients with CHF with comorbid DM (II group) were included in the study. For objective assessment of functional state of EM laser polarimetry of the red cell suspension smear was applied.

Intensity distribution of histogram of Fourier spectrum of erythrocytes suspension smear had symmetrical “bell-like” appearance. Unlike this, intensity distribution of Fourier spectrum of erythrocytes suspension smear of patients of II group was uneven, and histogram transformed into asymmetric dependence. Revealed fact indicates growth of anisotropic component of EM, conditioned primarily by conformational changes of the protein structure of EM due to chronic hyperglycemia (activation of the peroxic oxidation of the biopolymers and lipids, protein molecules glycolization, and, as a result, change of the conformational and spatial orientation of the protein fibrils, including integrated, of the erythrocyte membrane), accompanied by worsening of morphological features of EM. Correlation analysis showed statistically significant direct relationship between level of fasting glucose and anisotropy degree of the red blood cells suspension of patients of CHF and DM.

Thus, methods of the laser polarimetry of the EM may be used for early diagnosis of structural changes of erythrocytes in patients with CHF and DM.

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## **ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH CHRONIC CHOLECYSTITIS AND HYPOTHYROIDISM**

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Much attention is paid to the role of endothelial dysfunction and mechanisms of cytokine regulation in pathological changes of different organs during hypothyroidism. Increased vascular endothelial growth factor (VEGF) plasma level is characterized for the development of endothelial dysfunction, which promotes the development of nitrogen monoxide and prostacyclin stimulating vasodilation. Violation of the endothelium functional state and cytokine-mediated mechanisms of inflammation are important components in the pathogenesis of chronic cholecystitis (CC). The abovementioned indicates the need for timely detection of endothelial disorders in patients with CC and hypothyroidism for their further therapeutical corrections.

The objective of the study was to investigate activity of the markers of endothelial dysfunction in patients with chronic cholecystitis and hypothyroidism.

The study involved 72 patients with CC and hypothyroidism (main group). 30 patients with CC with normal functional activity of the thyroid gland (comparison group) were examined to establish the possible effect of hypothyroidism on the CC course. Control group included 20 healthy individuals. The average age of patients of main group was  $42,3 \pm 2,6$  years, comparison group— $46,0 \pm 1,6$  years, control group— $40,1 \pm 2,9$  years. Biochemical studies were performed on the blood biochemical analyzer "Accent-200" ("Cormay SA", Poland). The biochemical blood analysis included: total bilirubin and its fractions concentrations, albumin level, plasma enzyme activity (aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), alkaline phosphatase (AP), gamma-glutamyl transferase (GGT)).

Endothelial function was investigated by measuring VEGF blood level with the help of immunoassay method. The quantity of circulating desquamated endothelial cells was calculated by J. Hladovec method in N.N. Petrishchev et al. modification.

Patients of both groups showed an increased AST activity as compared to healthy individuals. It was significant only for patients with CC and hypothyroidism, in which the activity of this enzyme by 18,2% ( $p=0,004$ ) prevailed control indicators. ALT activity was significantly