

Streszczenie w języku angielskim

Ticks living in the human environment, can carry various pathogens, including tick-borne encephalitis virus (TBE) and bacteria (*Borrelia burgdorferi* and *Anaplasma phagocytophilum*). Due to climate change favoring an increasing number of ticks in the human environment, more and more infections and co-infections caused by these microorganisms are observed, which poses both diagnostic and therapeutic problems.

Consequently, the purpose of this study was to determine changes in oxidation-antioxidant balance and inflammation, and to evaluate metabolic disturbances at the lipid and protein levels, with a special focus on biologically active products of lipid metabolism in patients infected with TBEV and patients with bacterial co-infections caused by *Borrelia burgdorferi* and *Anaplasma phagocytophilum*. Approval for the study was granted by the Bioethics Committee of the Medical University of Białystok (No. R-I-002/169/2018).

The study enrolled tick-bitten individuals, with 40 patients diagnosed with tick-borne encephalitis (TBE), including 14 women and 26 men, and 6 patients with TBE and co-infections, caused by the bacteria *Borrelia burgdorferi* (Lyme borreliosis - LB) and *Anaplasma phagocytophilum* (human granulocytic anaplasmosis - HGA), 4 women and 2 men, treated at the Department of Infectious Diseases and Neuroinfections at the Medical University of Białystok. Plasma and blood granulocytes and lymphocytes from patients with TBE and co-infections (TBE+Borreliosis/anaplasmosis) and age- and sex-matched control subjects (20) were used for the study. Patients' blood was collected upon arrival at the hospital and at the end of treatment.

Results were obtained by standard methods used in biochemical studies, including: Elisa technique for protein levels determination, spectrophotometric methods for enzymes activity assessing, GC/FID/GCMS/LCMS for phospholipid and free PUFAs as well as lipid peroxidation products level examination and LCMS for products of PUFAs enzymatic metabolism (endocannabinoids and eicosanoids) determination.

It was found that TBE and bacterial co-infections promote increased production of ROS and decreased antioxidant defense, especially with regard to system components glutathione and thioredoxin in plasma, despite increased efficiency of transcription factor Nrf2 in granulocytes. The observed oxidative stress promotes oxidative modifications of phospholipids with significantly increased levels of lipid peroxidation products (4-HNE, MDA, 8-isoPGF₂ α , neuroprostanes), as well as protein modifications assessed as 4-HNE-protein adducts, carbonyl groups and dityrosine, and a decrease in tryptophan levels, which may promote structural and functional modification of transcription factors: Nrf2 and NF- κ B. At the same time, there is a decrease in the levels of phospholipid and free polyunsaturated fatty acids (LA, AA, EPA). The results indicate the potential possibility of using the evaluated metabolic parameters to introduce targeted pharmacotherapy in cases of bacterial infections/co-infections. Increased activity of enzymes that metabolize phospholipids and free PUFAs (PLA₂, COX 1/2, NOX5) contributes to increased levels of endocannabinoids and eicosanoids (13-HODE, 15-HETE, LTB₄) with decreased anti-inflammatory 15-PGJ₂, which was accompanied by activation of granulocyte receptors (CB₁, CB₂, TRPV₁, PPAR γ) before pharmacotherapy and showed only a tendency to normalize after treatment.

The results confirm the therapeutic problems for tick-borne diseases. This is evidenced by relatively small differences in the values of metabolic parameters in both groups of patients, both before and after pharmacotherapy. It can be suggested that only a partial reduction in lesions after classical pharmacotherapy indicates only a reversal of the disease process, and not a return of the body to a physiological state. Therefore, taking into account the presented results and the fact that impaired phospholipid metabolism is generally associated with oxidative stress, one can suggest the introduction of antioxidants especially lipophilic into the classical pharmacotherapy of TBE infection, especially in the case of bacterial co-infections.