## Streszczenie w języku angielskim

### 10.1 Introduction

Major Depressive Disorder (MDD) is one of the most common mental disorders in the world. The etiopathogenesis of depression is complex and still not fully understood. Among the biological factors involved in depression, genetic predisposition, disturbances of monoaminergic transmission, dysregulation of the stress axis (hypothalamic – pituitary – adrenal glands) and the state of imbalance between inflammatory and anti-inflammatory processes should be mentioned. Oxidative and nitrosative stress (O&NS) is also considered as one of the key biological factors involved in depression pathogenesis. Oxidative and nitrosative stress is a measure of the effect of reactive oxygen (ROS) and nitrogen (RNS) species on the body. Under physiological conditions, ROS and RNS are neutralized by the body in several ways. One of them is the so-called free radicals scavenging, e.g. through reduced glutathione. Another is enzymatic inactivation, e.g. by superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT). When oxidative processes are not sufficiently balanced by antioxidant systems, ROS and RNS damage cellular macromolecules such as proteins, lipids and deoxyribonucleic acid (DNA), increasing inflammation and causing further damage.

There is a close connection between O&NS and the neurodegenerative processes that are characteristic of neurodegenerative diseases such as Alzheimer's disease. Research suggests that depression can be considered as a neurodegenerative disease. In the population of depressive patients, especially in the elderly, altered levels of β-amyloid deposits in the cerebral cortex have been noted.

Contemporary research in the field of psychiatry focuses, among others, on on the search for biomarkers of mental disorders. A growing body of scientific evidence points to the existence of a number of biochemical markers of MDD that can be used to distinguish depressed patients from the healthy population. Markers of the severity of oxidative and nitrosative stress may be of interest in the context of diagnosing and treating depression as well as a deeper understanding of the pathogenetic mechanisms responsible for the manifestation of the disorder. Urine biomarkers are an interesting alternative to blood biomarkers due to the simple and non-invasive way of sample collection and the fact that the concentration of biomarkers in the urine may at least partially reflect their concentration in the blood.

## 10.2 Aim of the study

The aim of the study was to search for potential peripheral biomarkers of depression.

## 10.3 Material and Methods

29 patients diagnosed with MDD and 30 healthy volunteers were recruited for the study. The diagnosis of depression (i.e. a depressive episode or recurrent depressive disorder) was based on the International Classification of Diseases, 11th edition (ICD-11) criteria and confirmed by an experienced psychiatrist. A Structured Interview Questionnaire (MINI) was used to exclude other potential psychiatric entities. Study participants were assessed using psychometric scales – the Beck depression inventory 1 (BDI), the Hamilton depression scale (HAM-D) and the Hamilton anxiety scale (HAM-A). The duration of illness was measured as the number of years from the onset of the first depressive episode.

Basic blood tests – blood count, potassium, sodium, creatinine, alanine transaminase (ALT), aspartate aminotransferase (AST), C-reactive protein (CRP), thyroid-stimulating hormone (TSH), total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL) concentration – were performed in each study participant.

Urine samples were collected and the following parameters were assessed: total antioxidant capacity (TAC), CAT, GPx, SOD, reduced glutathione (GSH), total oxidative status (TOS), 3-nitrotyrosine (3-NT), advanced glycation end-products (AGE), advanced protein oxidation products (AOPP), N-formylkynurenine (NFKN), kynurenine (KN), tryptophan (TRY) and β-amyloid.

## 10.4 Results

The group of patients with depression was characterized by higher mean concentrations of TGA in the serum, higher SOD, 3-NT, CAT, GSH and TRY in the urine, and lower concentrations of HDL in the serum.

The results of the HAM-A, HAM-D and BDI psychometric scales as well as the disease duration factor showed significant associations with serum HDL and TGA concentrations as well as SOD, 3-NT, CAT and TRY concentrations in urine. GSH concentration in the urine correlated with the HAM-A score.

A negative correlation with HDL was observed – a higher scale score, as well as a longer duration of the disease, correlated with a decrease in HDL concentrations. The increase in the

scores of psychometric scales and the longer duration of the disease correlated with the increase in the level of TGA, SOD, 3-NT, CAT, TRY and GSH.

An increase in HDL of 1.00 mg/dl reduced the log odds ratio for depression by 0.07, assuming other predictors were controlled for. Increasing the 3-NT concentration by 1.00 nmol/mg protein increased the log odds ratio of depression by 15.52. The analyzed data show that patients with HDL concentration < 40 mg/dl and 3-NT concentration > 0.3 nmol/mg protein were more prone to depression, while patients with HDL concentration > 80 mg/dl and 3-NT concentration < 0.15 nmol/mg protein were less likely to develop depression.

## 10.5 Conclusions

1. The population of depressive patients is characterized by a higher intensity of oxidative and nitrosative stress compared to the healthy population.

2. Nitrosative stress marker – 3-nitrotyrosine (3-NT) – determined in the urine, in combination with high-density lipoprotein (HDL) determined in the blood, may be a potential biomarker of depression.