DISTURBANCES OF BRAIN SEROTONIN METABOLISM AFFECT THE BIOMECHANICAL PROPERTIES OF FEMORAL DIAPHYSIS IN RATS WITH EXPERIMENTAL CHRONIC RENAL FAILURE

VI Środkowo Europejski Kongres Osteoporozy i Osteoartrozy oraz XVII Zjazd Polskiego Towarzystwa Osteoartrologii i Polskiej Fundacji Osteoporozy, Kraków 25-26.09.2015

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Key words: *chronic renal failure, brain serotonin, bone biomechanical properties*

Objectives. Patients with chronic kidney disease (CKD) are at risk of developing CKD-mineral bone disorder (CKD–MBD). Bone loss occurs even in early stages of CKD, and worsens as renal function declines. Decrease in bone strength, which clinical manifestation is tendency to fractures, has been recognizes as an important component of CKD-MBD. Serotonin (5-HT) is a bioamine regulating bone mass accrual depending on its site of synthesis – it decreases accrual when synthesized in the gut, and increases it when synthesized in the brain. Brain 5-HT, by binding to its receptor 5-HT_{2c} on hypothalamic neurons, decreases sympathetic activity and favors bone mass accrual.

Aim. We used the experimental 5/6 nephrectomy model of chronic renal failure (CRF) to perform the study explaining the impact of the hypothalamic serotonin on the biomechanical

properties of femoral diaphysis in rat.

Material and methods. Forty 4 weeks-old Wistar male rats were randomly allocated to sham-operation (Controls, n=16) or 5/6 nephrectomy (CRF, n=24). After one (CRF1) and three months (CRF3) of CFR development the animals were sacrificed, their femurs were excised for three-point bending test and hypothalamic tryptophan and 5-HT levels were determined by high pressure liquid chromatography (HPLC).

Results. Hypothalamic TRP concentrations were significantly lower in CRF in comparison with controls after 1 month ($p<0.001$) and 3 months ($p<0.01$) of CRF development. 5HT/TRP ratio, reflecting serotoninergic pathway activation, was 6 times higher in CRF1 than in respective controls. 5HT levels were only slightly reduced in CRF1 compared to controls ($p<0.05$), whereas there was no difference between this hypothalamic monoamine levels between CRF3 and respective controls. However, the age-dependent decrease in serotonin concentrations were observed in CRF as well as in controls. Yield load (F_y) has been significantly decreased, whereas work to failure (W) and yield stress (σ_y) were increased in the femurs of CRF rats compared to controls. Serotonin and 5HT/TRP ratio were inversely associated with F_y and stiffness, whereas they were positively related to displacement at fracture (dl F_u) and ultimate stress (σ_u). Moreover, 5HT was positively associated with Young modulus of elasticity (E) in rats with CRF.

Conclusions. Despite the reduced TRP concentration, the synthesis of hypothalamic serotonin is strongly activated in animals with early stage of CRF. Brain serotonin seems to improved the material properties and bone plasticity, whereas it reduces the stiffness of femoral diaphysis in rats with CRF.

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WPŁYW ZABURZEŃ OŚRODKOWEGO METABOLIZMU SEROTONINY NA BIOMECHANICZNE WŁAŚCIWOŚCI KOŚCI UDOWEJ U SZCZURÓW Z DOŚWIADCZALNĄ PRZEWLEKŁĄ NIEWYDOLNOŚCIĄ NEREK

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Słowa kluczowe: *przewlekła niewydolność nerek, serotonina w mózgu, właściwości biomechaniczne kości*