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Effect of Pioglitazone on Intracellular Na+ Homeostasis in Metabolic Syndrome-Induced Cardiomyopathy in Male Rats

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Abstract : Metabolic syndrome, is associated impaired blood glucose level, insulin resistance, dyslipidemia caused by abdominal obesity. Also, it is related with cardiovascular risk accumulation and cardiomyopathy. The hypothesis of this study was to examine the effect of thiazolidinediones such as pioglitazone which is widely used insulin-sensitizing agents that improve glycemic control, on intracellular Na+ homeostasis in metabolic syndrome-induced cardiomyopathy in male rats. Male Wistar-Albino rats were randomly divided into three groups, namely control (Con, n=7), metabolic syndrome (MetS, n=7) and pioglitazone treated metabolic syndrome group (MetS+PGZ, n=7). Metabolic syndrome was induced by providing drinking water that was 32% sucrose, for 18 weeks. All of the animals were exposed to a 12 h light – 12 h dark cycle. Abdominal obesity and glucose intolerance had measured as a marker of metabolic syndrome. Intracellular Na+ ([Na+]i) is an important modulator of excitation–contraction coupling in heart. [Na+]i at rest and [Na+]i during pacing with electrical field stimulation in 0.2 Hz, 0.8 Hz, 2.0 Hz stimulation frequency were recorded in cardiomyocytes. Also, Na+ channel current (INa) density and I-V curve were measured to understand [Na+]i homeostasis. In results, high sucrose intake, as well as the normal daily diet, significantly increased body mass and blood glucose level of the rats in the metabolic syndrome group as compared with the non-treated control group. In MetS+PZG group, the blood glucose level and body inclined to decrease to the Con group. There was a decrease in INa density and there was a shift both activation and inactivation curve of INa. Pioglitazone reversed the shift to the control side. Basal [Na+]i either MetS and Con group were not significantly different, but there was a significantly increase in [Na+]i in stimulated cardiomyocytes in MetS group. Furthermore, pioglitazone had not effect on basal [Na+]i but it reversed the increase in [Na+]i in stimulated cardiomyocytes to the that of Con group. Results of the present study suggest that pioglitazone has a significant effect on the Na+ homeostasis in the metabolic syndrome induced cardiomyopathy in rats. All animal procedures and experiments were approved by the Animal Ethics Committee of Ankara University Faculty of Medicine (2015-2-37).

Keywords : insulin resistance, intracellular sodium, metabolic syndrome, sodium current
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