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POSTER PRESENTATION

The Effects of a Meldonium Pre-Treatment on the Sepsis-Induced Rat Heart Injury

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Abstract

Background: Sepsis is a life-threatening condition caused by the dysregulated and overwhelming response to infection, accompanied by exaggerated pro-inflammatory state and lipid metabolism disturbance leading to sequential organ failure.[1, 2] Meldonium is an anti-ischemic and anti-inflammatory agent, clinically used to treat myocardial ischemia.[3] By shifting energy production from fatty acid oxidation to glycolysis, as an oxygen less consuming pathway, meldonium interferes negatively with lipid metabolism.
Methods: Thus, we investigated the effects of a 4-week meldonium pre-treatment in 300 mg/kg b.m./day dosage on the course of the sepsis induced by a single intraperitoneal injection of faeces (0.5 g faeces/1 mL saline/100 g b.m.) in Sprague-Dawley male rats. The degree of the heart injury was evaluated by measuring tissue pro-apoptotic Bax and anti-apoptotic Bcl-2 ratio, tissue level of the necrotic marker - high mobility group box 1 protein level (HMGB1), together with the heart histology analysis. Sepsis-associated heart inflammation was assessed by measuring level of an activated form of NF-kB p65 (phospho-NF-κB p65).
Results: In the heart whole homogenates of the septic group of animals (S) HMGB1 level increased 1.7-fold, in comparison to control rats, while meldonium reduced sepsis-induced increase by 18 % (M+S). The underlying mechanism of the proinflammatory action of HMGB1 includes activation of NF-κB signalling pathways tissue, so the increased HMGB1 level was followed by a 1.4-fold increase of p-NF-κB p65 in the heart of the S group of rats and a 19 % decreased in the heart of M+S group. The apoptotic marker Bax/Bcl-2 ratio changed in the same manner: 1.4-fold increase in the heart of animals from the S group and a 32 % decrease in the heart of the M+S group. On the other hand, heart histology analysis shows that meldonium worsened the heart histological score, causing the severe and diffuse interstitial mononuclear infiltration along with a greater loss of myocytes and myofibrillar contraction band necrosis. The heart lipidomic analysis suggests that meldonium exhibits potentially harmful effects under septic condition due to the lipid-mobilization impairment.
Conclusion: Meldonium exerted anti-inflammatory, anti-apoptotic, and anti-necrotic effects, while it worsened the septic rat heart histology.

Key words: Sepsis; Heart; Inflammation; Lipidomics; Rat.

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