Effect of Phenylbutyrate on Skeletal Muscle Atrophy induced by Hindlimb Unloading in Wistar Rat

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Abstract

Background: Mechanical unloading in the hindlimb negatively affects skeletal muscle and also alter the gut microbiota that recently been recognized as a major contributor(s) in disrupted metabolism and physiology. Present study aimed to investigate the potential role of phenylbutyrate (PB) on skeletal muscle atrophy and colon induced by hindlimb unloading (HLU) in rats.

Methods: All rats were allocated into three groups *viz* control, hindlimb unloaded (HLU) (for 2 weeks,) and HLU+PB (for 300mg/kg orally for 14 days). All rats were sacrificed, and serum, colon and gastrocnemius (GN) muscles were collected for further endpoints. Various motor coordination activities, serum creatinine level, colon, and GN muscle oxidative stress levels, and histopathology were performed.

Results: The findings showed that phenylbutyrate treatment significantly improved muscle coordination in hind limb unloading rats. Further, results showed the restoration of the levels of creatinine, oxidative stress, and antioxidants in the HLU+PB rats. Furthermore, histological results confirmed that phenylbutyrate treatment significantly improved the GN muscle and colonic histological architecture in HLU rats.

Conclusions: These findings suggested that phenylbutyrate ameliorates muscle coordination, colon, and skeletal muscle cellular architecture in the HLU-induced rat model. Phenylbutyrate significantly restored the antioxidant and oxidative stress levels in HLU-treated rats. In conclusion, phenylbutyrate may be an effective intervention against colon and skeletal muscle loss in the hind limb unloading model.

Keywords: Skeletal muscle atrophy, phenylbutyrate, hindlimb unloading, colon, oxidative stress

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Introduction

Mechanical unloading of skeletal muscles leads to progressive loss of muscle mass and negatively affects several physiological functions of the body, including liver and gut microorganisms. Study shows that dysbiosis, as well as the loss of microbiota, causes significant changes in skeletal muscle metabolism (Grosicki et al., 2018). This illness is relevant in a variety of settings, ranging from prolonged bed rest in chronic pathology patients to microgravity during space flights (Fitts et al., 2010). Several interventions have been used to reduce disuse muscle atrophy such as supplements, passive muscle contraction, electrical stimulation, and exercise) (Cava et al., 2017).However, a handful of therapies and pharmacological interventions are available to increase muscle mass and gut microbiota during prolonged inactivity. The hindlimb unloading (HLU) experimental rodent model reproduces several aspects of mechanical unloading, such as muscle atrophy and alteration in gut microbiota, and is an excellent model for testing potential pharmacological interventions (Grosicki et al., 2018). However, no effective drug therapy exists to prevent/treat muscle atrophy and lot of research are going on to explore the molecular

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