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Salbutamol Attenuates Diabetic Skeletal Muscle Atrophy by Reducing Oxidative Stress, Myostatin/GDF-8, and Pro-Inflammatory Cytokines in Rats

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Abstract: Type 2 diabetes is a metabolic disorder that leads to accelerated skeletal muscle atrophy. In this study, we aimed to evaluate the effect of salbutamol (SLB) on skeletal muscle atrophy in high-fat diet (HFD)/streptozotocin (STZ)-induced diabetic rats. Male Sprague Dawley rats were divided into four groups ($n = 6$): control, SLB, HFD/STZ, and HFD/STZ + SLB (6 mg/kg orally for four weeks). After the last dose of SLB, rats were assessed for muscle grip strength and muscle coordination (wire-hanging, rotarod, footprint, and actophotometer tests). Body composition was analyzed in live rats. After that, animals were sacrificed, and serum and gastrocnemius (GN) muscles were collected. Endpoints include myofibrillar protein content, muscle oxidative stress and antioxidants, serum pro-inflammatory cytokines (interleukin-1β, interleukin-2, and interleukin-6), serum muscle markers (myostatin, creatine kinase, and testosterone), histopathology, and muscle ^{1}H NMR metabolomics. Findings showed that SLB treatment significantly improved muscle strength and muscle coordination, as well as increased lean muscle mass in diabetic rats. Increased pro-inflammatory cytokines and muscle markers (myostatin, creatine kinase) indicate muscle deterioration in diabetic rats, while SLB intervention restored the same. Also, Feret's diameter and cross-sectional area of GN muscle were increased by SLB treatment, indicating the amelioration in diabetic rat muscle. Results of muscle metabolomics exhibit that SLB treatment resulted in the restoration of perturbed metabolites, including histidine-to-tyrosine, phenylalanine-to-tyrosine, and glutamate-to-glutamine ratios and succinate, sarcosine, and 3-hydroxybutyrate (3HB) in diabetic rats. These metabolites showed a pertinent role in muscle inflammation and oxidative stress in diabetic rats. In conclusion, findings showed that salbutamol could be explored as an intervention in diabetic-associated skeletal muscle atrophy.

Keywords: diabetes; salbutamol; skeletal muscle atrophy; sarcosine; metabolomics

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1. Introduction

Type 2 diabetes mellitus (T2DM) is a metabolic disorder that causes elevated blood glucose levels due to compromised insulin function and/or release [1]. Diabetes poses a