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Salbutamol ameliorates skeletal muscle wasting and inflammatory markers in streptozotocin (STZ)-induced diabetic rats

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ABSTRACT

Diabetes accelerates muscle atrophy, leading to the deterioration of skeletal muscles. This study aimed to assess the potential of the β2-adrenoceptor agonist, salbutamol (SLB), to alleviate muscle atrophy in streptozotocin (STZ)-induced diabetic rats. Male Sprague Dawley rats were randomized into four groups (n=6): control, SLB, STZ (55 mg/kg, single *i.p.*), and STZ + SLB (6 mg/kg, orally for 4 weeks). After the final SLB dose, animals underwent tests to evaluate muscle strength and coordination, including forelimb grip strength, wire-hanging, actophotometer, rotarod, and footprint assessments. Rats were then sacrificed, and serum and gastrocnemius (GN) muscles were collected for further analysis. Serum evaluations included proinflammatory markers (tumor necrosis factor α, interleukin-1β, interleukin-6), muscle markers (creatine kinase, myostatin), testosterone, and lipidemic markers. Muscle oxidative stress (malonaldehyde, protein carbonyl), antioxidants (glutathione, catalase, superoxide dismutase), and histology were also performed. Additionally, ^{1}H nuclear magnetic resonance serum profiling was conducted. SLB notably enhanced muscle grip strength, coordination, and antioxidant levels, while reduced proinflammatory markers and oxidative stress in STZ-induced diabetic rats. Reduced serum muscle biomarkers, increased testosterone, restored lipidemic levels, and improved muscle cellular architecture indicated SLB's positive effect on muscle condition in diabetic rats. Metabolomics profiling revealed that the STZ group significantly increased the phenylalanine-to-tyrosine ratio (PTR), lactate-to-pyruvate ratio (LPR), acetate, succinate, isobutyrate, and histidine. SLB administration restored these perturbed serum metabolites in the STZ-induced diabetic group. In conclusion, salbutamol significantly protected against skeletal muscle wasting in STZ-induced diabetic rats.

1. Introduction

Type 1 diabetes mellitus (T1DM) is linked to subsequent complications, encompassing retinopathy, nephropathy, cardiomyopathy, neuropathy, and myopathy [1,2]. Myopathy associated with diabetes is distinguished by the degradation of the structural arrangement of skeletal muscles, along with diminishing functional and metabolic capacities [3]. This progression ultimately leads to symptoms such as muscle pain, weakness, and muscle atrophy. Both experimental and clinical evidence have demonstrated that elevated blood glucose levels in both type 1 and type 2 diabetes contribute to a decline in muscle strength and muscle loss [4-6]. Nonetheless, this phenomenon can also arise due to a variety of other conditions, including cancer, AIDS, sepsis, burn injuries, organ malfunction, or respiratory and metabolic disorders [7]. Hyperglycemia undeniably plays a significant role in exacerbating muscle deterioration in diabetes. However, it's crucial to acknowledge the

Abbreviations: CK, creatine kinase; GDF-8, growth differentiation factor-8; LDL, low-density lipoprotein; MDA, malondialdehyde; SLB, salbutamol; SD, Sprague-Dawley rat; SOD, superoxide dismutase; STZ, streptozotocin; UPS, ubiquitin–proteasome system; TC, total cholesterol; TG, triglycerides; HDL, high-density lipoprotein; and T1DM, type 1 diabetes mellitus.

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