METFORMIN ROLE ON PRO-INFLAMMATORY PATHWAY IN SKELETAL MUSCLE

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Introduction and Objectives: Excessive cytokine production is associated with diabetes and worsen glucose uptake in peripheral tissues. Increase of tumor necrosis factor-α (TNF-α) induce insulin resistance by activator of nuclear transcription factor-κβ (NF-κβ), c-Jun-N-terminal kinase (p-JNK), and insulin receptor substrate (IRS1-ser). Evidence suggest that metformin decrease TNF-α via AMP-activated protein kinase (AMPK) activation and inhibition of NF-κβ and inhibitor kinase β (Ikβ) degradation. Thus, this study investigated the molecular mechanism of the metformin on pro-inflammatory pathway for glucose uptake in the skeletal muscle of diabetic rats. Materials and Methods: The diabetes was induced by intraperitoneal injection of streptozotocin (45 mg/kg) and the diabetics animals were divided into three groups: untreated (D), treated with insulin (D+I) and metformin (D+M) beyond the group non diabetic (ND). After seven days of treatment the glycemia was measured and the rats were sacrificed by sodium thiopental injection (80 mg/kg). The gastrocnemius muscle was collected, homogenized and probe to anti-GLUT4, anti-CAMKKβ, anti-CAMKKβ phosphorylate, anti-IRS1 tyrosine, anti-AMPK, anti-AMPK phosphorylate, anti-myosinV, anti-NF-κβ, anti-Iκβ, anti-JNK phosphorylate by ELISA and Western blotting methods beyond TNF-α and insulin level by ELISA. Results and conclusions: Metformin treatment decrease TNF-α, remained NFκβ/Iκβ complex, decrease p-JNK and activate both AMPK and CAMKKβ in hypoinsulinemic rats compared to untreated diabetic group. This drug inactives the NF-κβ signal pathway and induces both AMPK and CAMKKβ activity in skeletal muscle improving the peripheral glucose uptake. Our findings suggest that metformin improves glucose uptake in skeletal muscle by maintenance of NF-κβ/Iκβ complex and activation both of CAMKKβ and AMPK.

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Key words: diabetes, glucose uptake, insulin sensitivity.