Article 4

Telmisartan versus metformin in downregulating myostatin gene expression and enhancing insulin sensitivity in the skeletal muscles of type 2 diabetic rat model

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Abstract:

Objective: Telmisartan is an angiotensin receptor blocker (ARB) that specifically blocks angiotensin II type-1 receptors (AT1R). Telmisartan has been proven to have antidiabetic effects via a variety of mechanisms, and it can be utilized in some diabetic patients due to its dual benefit for hypertensive patients with type 2 DM (T2DM) and when the other oral antidiabetic medications are intolerable or contraindicated. However, its precise underlying hypoglycemic mechanism is still obscure.

Aim of work: We sought to establish a link between telmisartan administration and myostatin expression in skeletal muscles of T2DM rat model as a potential hypoglycemic mechanism of telmisartan. Materials and Methods: 32 male albino rats were included in the study; 8 rats served as controls (group I). T2DM was inducted in the other 24 rats, which were then randomly subdivided into 3 groups (8 in each): (group II) the Diabetic group and (groups III and IV) which were treated with either telmisartan (8 mg/kg/day) or metformin (250 mg/kg/day) respectively via oral gavage for a 4-week period.

Results: Telmisartan administration resulted in a significant improvement in OGTT, HOMA-IR, glucose uptake, and muscle mass/body ratios in Telmisartan group as compared to Diabetic group ($p < 0.05$). Additionally, telmisartan induced a significant boost in adiponectin and IL-10 serum levels with a substantial drop in TNF-α and IL-6 levels in Telmisartan group compared to diabetic rats ($p < 0.05$). Moreover, telmisartan significantly boosted SOD and GSH, and decreased MDA levels in the skeletal muscles of telmisartan group. Furthermore, a significant downregulation of myostatin and upregulation of insulin receptor, IRS-1, and IRS 3 genes in the skeletal muscles of Telmisartan group were also detected. Histologically, telmisartan attenuated the morphological damage in the skeletal muscle fibers compared to diabetic rats, as evidenced by a considerable decrease in the collagen deposition area percentage and a reduction in NF-kB expression in the muscle tissues of group III.

Conclusion: Telmisartan administration dramatically reduced myostatin and NF-kB expressions in skeletal muscles, which improved insulin resistance and glucose uptake in these muscles, highlighting a novel antidiabetic mechanism of telmisartan in treating T2DM.