Statins and Insulin Resistance

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Statins are lipid-lowering drugs that are beneficial for the cardiovascular system. However, they are associated with skeletal muscle disorders and, recently, with insulin resistance and new-onset diabetes. To date, mechanisms underlying statin-induced insulin resistance are not fully elucidated.

The goals of the study were to characterise effects of simvastatin on glucose metabolism and processes leading to the induced insulin resistance in skeletal muscle cells and mice.

C2C12 skeletal myotubes were treated with simvastatin (10 µM) and/or insulin for 24 hours. Insulin receptor activation, GLUT4 translocation and glucose uptake were investigated. Male C57BL/6J mice were treated with water or 5 mg/kg/day simvastatin for 21 days. Basal glucose and insulin were measured in fasted mice. The ip glucose tolerance test (IGTT) and glucose uptake were performed and insulin concentrations were measured.

Simvastatin reduced activation of the insulin receptor in C2C12 and significantly decreased translocation of GLUT4 to the cell surface. Glucose uptake was reduced by half in simvastatin-treated myotubes and the absorption rate was restored with insulin. Simvastatin-treated mice had higher glucose plasma concentrations during the IGTT, higher insulin levels and higher HOMA-IR. Glucose uptake in their gastrocnemius was decreased.

Simvastatin induced insulin resistance in mice and impaired insulin signalling in C2C12 myotubes. In co-treatment, insulin prevented these adverse events. Future studies are needed to show if the identified processes contribute to diabetes in patients treated with statins. ■