Exercise training and the antioxidant alpha-lipoic acid in the treatment of insulin resistance and type 2 diabetes.

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One hallmark of the insulin-resistant state of prediabetes and overt type 2 diabetes is an impaired ability of insulin to activate glucose transport in skeletal muscle, due to defects in IRS-1-dependent signaling. An emerging body of evidence indicates that one potential factor in the multifactorial etiology of skeletal muscle insulin resistance is oxidative stress, an imbalance between the cellular exposure to an oxidant stress and the cellular antioxidant defenses. Exposure of skeletal muscle to an oxidant stress leads to impaired insulin signaling and subsequently to reduced glucose transport activity. Numerous studies have demonstrated that treatment of insulin-resistant animals and type 2 diabetic humans with antioxidants, including alpha-lipoic acid (ALA), is associated with improvements in skeletal muscle glucose transport activity and whole-body glucose tolerance. An additional intervention that is effective in ameliorating the skeletal muscle insulin resistance of prediabetes and type 2 diabetes is endurance exercise training. Recent investigations have demonstrated that the combination of exercise training and antioxidant treatment using ALA in an animal model of obesity-associated insulin resistance provides a unique interactive effect resulting in a greater improvement in insulin action on skeletal muscle glucose transport than either intervention individually. Moreover, this interactive effect of exercise training and ALA is due in part to improvements in IRS-1-dependent insulin signaling. These studies highlight the effectiveness of combining endurance exercise training and antioxidants in beneficially modulating the molecular defects in insulin action observed in insulin-resistant skeletal muscle.

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