

Abstract

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Effect of thiol antioxidant on body fat and insulin reactivity.

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BACKGROUND: Insulin signaling is enhanced by moderate concentrations of reactive oxygen species (ROS) and suppressed by persistent exposure to ROS. Diabetic patients show abnormally high ROS levels and a decrease in insulin reactivity which is ameliorated by antioxidants, such as N-acetylcysteine (NAC). A similar effect of NAC has not been reported for non-diabetic subjects.

RESULTS: We now show that the insulin receptor (IR) kinase is inhibited in cell culture by physiologic concentrations of cysteine. In two double-blind trials involving a total of 140 non-diabetic subjects we found furthermore that NAC increased the HOMA-R index (derived from the fasting insulin and glucose concentrations) in smokers and obese patients, but not in nonobese non-smokers. In obese patients NAC also caused a decrease in glucose tolerance and body fat mass. Simultaneous treatment with creatine, a metabolite utilized by skeletal muscle and brain for the interconversion of ADP and ATP, reversed the NAC-mediated increase in HOMA-R index and the decrease in glucose tolerance without preventing the decrease in body fat.

CONCLUSIONS: As the obese and hyperlipidemic patients had lower plasma thiol concentrations than the normolipidemic subjects, our results suggest that low thiol levels facilitate the development of obesity. Supplementation of thiols plus creatine may reduce body fat without compromising glucose tolerance.

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