Beneficial effect of diazoxide in obese hyperinsulinemic adults.


Source

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Abstract

Hyperinsulinemia, insulin resistance, and increased adipose tissue are hallmarks of the obesity state in both humans and experimental animals. The role of hyperinsulinemia as a possible preceding event in the development of obesity has been proposed. We previously demonstrated that administration of diazoxide (DZ), an inhibitor of insulin secretion, to obese hyperinsulinemic Zucker rats resulted in less weight gain, enhanced insulin sensitivity, and improved glucose tolerance. Assuming that hyperinsulinemia plays a major role in the development of human obesity, then its reversal should have therapeutic potential. To test this hypothesis, we conducted a randomized placebo-controlled trial in 24 hyperinsulinemic adults [body mass index (BMI) > 30 kg/m2]. All subjects were placed on a low-calorie (1260 for females and 1570 for males) Optifast
(Sandoz, Minneapolis, MN) diet. After an initial 1-week lead-in period, 12 subjects (mean +/- SE for age and BMI, 31 +/- 1 and 40 +/- 2, respectively) received DZ (2 mg/kg BW.day; maximum, 200 mg/day, divided into 3 doses) for 8 weeks; and 12 subjects (mean +/- SE for age an BMI, 28 +/- 1 and 43 +/- 1, respectively) received placebo. Compared with the placebo group, DZ subjects had greater weight loss (9.5 +/- 0.69% vs. 4.6 +/- 0.61%, P < 0.001), greater decrease in body fat (P < 0.01), greater increase in fat-free mass to body fat ratio (P < 0.01), and greater attenuation of acute insulin response to glucose (P < 0.01). However, there was no significant difference in insulin sensitivity and glucose effectiveness, as determined by the insulin-modified i.v. glucose tolerance test (Bergman's minimal model) and no significant difference in glycohemoglobin values. CONCLUSION: 8 weeks treatment with DZ had a significant antiobesity effect in hyperinsulinemic obese adults without inducing hyperglycemia.

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