Evaluating the Effect of Acarbose Treatment on Insulin Secretion and Sensitivity in Early Diabetes Using a Novel Interpretation of the Disposition Index Equation

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Background and Hypothesis:

In pathologic states such as obesity and insulin resistance, there is a progressive decline in insulin sensitivity requiring greater insulin secretion to maintain normoglycemia. The inverse relationship between insulin sensitivity and secretion is mathematically defined by the Disposition Index (DI), a measure of β-cell function adjusted for insulin sensitivity. We are working to generalize the DI equation to allow direct physiologic interpretation of the DI term, and of the slope relating insulin secretion with insulin sensitivity. We tested study treatment effects hypotheses using these new analytic methods.

Experimental Design or Project Methods:

We used data from hyperglycemic clamp procedures and from standardized oral glucose tolerance testing performed in the Early Diabetes Intervention Program, a randomized controlled study evaluating the effects of acarbose, an alpha-glucosidase inhibitor, on β-cell function. We applied our novel analytic method to 1-year treatment data comparing acarbose versus placebo effects on DI, secretion-sensitivity coupling slopes, and the joint change in secretion and sensitivity with intervention. Multiviarate analysis of variation was the primary statistical approach to evaluate joint changes in secretion and sensitivity; ANOVA was used to compare DI terms.

Results:

These analyses revealed statistically significant 1-year changes in DI, in secretion-sensitivity coupling slopes, and in the joint changes in secretion and sensitivity. However, these treatment effects did not differ by randomized treatment group, suggesting an on-study effect beyond the randomized treatments.

Conclusion and Potential Impact:

We have applied a novel analytic approach to evaluate the secretion-sensitivity relationship modeled by the disposition index equation to investigate the effect of randomized therapy on β-cell function in a placebo-controlled randomized clinical trial. These analyses revealed study effects on the secretion-sensitivity relationship that have not been previously described, suggesting that this novel approach will have value in clinical studies of β-cell dysfunction and treatment effects.