Changes in amylin and amylin-like peptide concentrations and beta-cell function in response to sulfonylurea or insulin therapy in NIDDM.

Rachman,J; Payne,MJ; Levy,JC; Barrow,BA; Holman,RR; Turner,RC

Diabetes Care. 1998 May; 21(5): 810-6.

OBJECTIVE: Amylin, a secretory peptide of beta-cells, is the constituent peptide of islet amyloid, which is characteristic of NIDDM, and changes in amylin secretion in response to therapies may influence the rate of production of islet amyloid. The primary objective of this study was to determine whether therapy with sulfonylurea or basal insulin in NIDDM would alter amylin secretion in a way that might affect the formation of islet amyloid. RESEARCH DESIGN AND METHODS: In a randomized crossover design, eight subjects with NIDDM underwent three 8-week periods of therapy with diet alone, sulfonylurea, or exogenous basal insulin, with evaluation of amylin, amylin-like peptide (ALP), and glucose and C-peptide concentrations, both during fasting and after a standard breakfast. Changes in beta-cell function (% beta) were assessed, in the basal state by homeostasis model assessment (HOMA) and in the stimulated state by hyperglycemic clamps. Seven nondiabetic control subjects each underwent a meal profile and hyperglycemic clamp. RESULTS: Both sulfonylurea and insulin therapy reduced basal glucose concentrations compared with diet alone, but neither reduced the increased postprandial glucose increments. Both sulfonylurea and insulin therapy increased basal % beta, assessed by HOMA, but only sulfonylurea increased the second-phase C-peptide responses to the hyperglycemic clamp. Sulfonylurea increased time-averaged mean postprandial amylin and ALP concentrations compared with diet alone (geometric mean [1-SD range] for amylin, 4.9 [2.0-11.8] vs. 3.0 [1.4-6.2] pmol/l, P = 0.003; for ALP, 16.4 [8.5-31.7] vs. 10.1 [4.9-20.8] pmol/l, P = 0.001). Insulin therapy reduced basal ALP concentrations compared with diet alone (2.9 [1.5-5.6] vs. 6.0 [2.6-13.6] pmol/l, P = 0.03), but had no effect on postprandial concentrations of amylin (3.0 [1.3-6.5] pmol/l) or ALP (10.0 [5.5-18.1] pmol/l). CONCLUSIONS: By increasing postprandial concentrations of the constituent peptides of islet amyloid, sulfonylurea therapy might increase the rate of deposition of islet amyloid and thereby accelerate the decline of % beta in NIDDM, compared with diet therapy alone.