Elevated proinsulin but not islet amyloid polypeptide accompanies declining β-cell function in type 2 diabetes.

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Islet amyloid formation could result from raised secretion of islet amyloid polypeptide (IAPP) and contribute to declining β-cell function leading to insulin therapy in type 2 diabetes. Raised proinsulin (PI) concentrations have been detected in subjects before onset of diabetes. The aims of this study were to determine if plasma IAPP and PI concentrations are elevated in patients with glucose intolerance or with diabetes. One-hour infusion of glucose test (l80mg/m^2/min) was used in 19 non-diabetic subjects, 58 non-diabetic 1st-degree relatives of type 2 diabetics and 39 type 2 diabetic subjects; blood samples were collected at time zero and at 1-hour. The nondiabetic and control subjects (ND) were stratified in three groups based on fasting glucose; Normal (N); fpg<5.5mmol/l, n=52*,* Intermediate glucose (IG); fpg>5.5<6.l mmol/l, n=14, Impaired Fasting Glucose (IFG); fpg> 6.1 mmol/l, n=11. There was no significant differences in gender or BMI in the ND groups but the IFG subjects were significantly older (N,48y; IG,46y, IFG,59y, p<0.05*).* The diabetics (D) were stratified according to treatment with insulin treated group being older than diet or oral treatment (p<0.05). C-peptide (CP), IAPP and P1 concentrations were increased in IFG group compared to N (p<0.05). PI/CP% and IAPP/CP% were not different in ND groups, indicating proportional changes with increased fpg. In the diet and oral treated D, fasting CP and IAPP were similar to those in IFG but were lower (p<0.000l) in insulin treated group. However, fasting PI was elevated in all groups of diabetics (p<0.00l) and PI/CP% was elevated in insulin treated group (p<0.001). Conclusions: IAPP and PI secretion rises significantly and in proportion to CP with deteriorating glucose tolerance in nondiabetic subjects; there was no evidence of disproportionately increased IAPP production at any stage. Disproportionately increased PI occurred in diabetic subjects in contrast to a decline in CP and IAPP