Pancreatic polypeptide (PP) can be used as a marker for endocrine active tumors originating from the pancreas. After intravenous administration of secretin, individually divergent increases in plasma PP concentration can be observed hampering interpretation of the stimulation test. Under certain circumstances elevated basal PP concentrations can be observed. Besides age, renal insufficiency and diabetes, hypoglycemia can cause high PP levels. We therefore inquired whether in patients with atypically high increase of PP after secretin this increase could be caused by hypoglycemia during the secretin stimulation test. In order to test this hypothesis we prospectively determined the plasma glucose and insulin concentrations in addition to the routinely measured gastro-intestinal hormones in 19 patients referred for secretin provocation test. In the 16 patients in whom the increase of PP was not due to an endocrine active tumor or renal insufficiency, PP rose to 170 +/- 57 pmol/l (+/- SEM) 2 minutes after secretin administration. In parallel, plasma insulin concentration increased to 365 +/- 51 pmol/l 2 minutes after secretin. The maximal insulin concentrations correlated significantly with the PP concentrations observed at the same time (R = 0.73, p < 0.01). The mean glucose concentration, however, remained constantly between 4.8 +/- 0.3 and 5.2 +/- 0.3 mmol/l and there was no correlation between the peak plasma PP concentrations after secretin and the plasma glucose concentrations (R = 0.07). The minimal glucose concentrations observed were 3.3 mmol/l in three patients (30 minutes after secretin in 2 patients and 45 minutes after secretin in one). The mean plasma glucagon concentration rose to 22.5 +/- 4.1 pmol/l 10 minutes after secretin.