

PANCREATIC BETA CELL FUNCTION IN NON DIABETIC PATIENTS WITH RENAL FAILURE

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Summary

Pancreatic beta cell secretory function was evaluated in non diabetic patients with renal failure. Beta cell activity was measured by the insulin and C-peptide response to intravenous glucagon. Continuous ambulatory peritoneal dialysis, haemodialysis and non-dialysed uraemic patients were studied. Basal and peak serum insulin concentrations were normal in all groups and a significant increment occurred after glucagon. Basal and peak plasma C-peptide concentrations were raised in all uraemic groups but all had a significant rise to pancreatic stimulation. We conclude that uraemia, and in particular continuous ambulatory peritoneal dialysis, has no adverse effect on beta cell secretory capacity.

Introduction

The effect of continuous ambulatory peritoneal dialysis (CAPD) on pancreatic beta cell secretory function is unknown. The continuous glucose absorption from dialysate could possibly affect insulin release from the pancreas with profound consequences on glucose, lipid and aminoacid metabolism. Continuous glucose administration may exhaust beta cells as seen in maturity onset diabetics [1]. Alternatively, continuous stimulation of the beta cells may augment serum insulin which could further impair carbohydrate tolerance by increasing the insulin resistance that is common in uraemia [2]. This study evaluates beta cell activity in chronic renal failure with emphasis on CAPD, by measuring the beta cell peptides response to glucagon [3]. Insulin and C-peptide concentrations can be elevated in renal failure due to impaired peptide degradation [4] and therefore to assess the specific effect of CAPD we compared different groups of both dialysed and non-dialysed uraemic patients.

Methods

Forty uraemic patients were grouped as chronic renal failure (CRF on conservative management), haemodialysis, new CAPD (duration of dialysis less than six months) and chronic CAPD (duration of dialysis more than one year). Eight healthy subjects with normal renal function were controls. All patients were non diabetic. Haemodialysis patients were studied on their interdialysis day and CAPD patients omitted the overnight dialysis cycle prior to the study. No patients were taking beta blockers, steroids or drugs known to interfere with carbohydrate metabolism.

After a 10 hour overnight fast, 1mg glucagon (Novo) was given by intravenous bolus and serial blood samples were taken at 0, 5, 10, 15, 20, 30, 45 and 60 minutes post injection for glucose, insulin and C-peptide. Blood glucose was measured by the glucose oxidase method [5], serum insulin by double antibody radioimmunoassay [6] and plasma C-peptide by radioimmunoassay with ethanol precipitation [7]. Statistical analysis was by analysis of variance to compare data between the groups and paired 't' test to measure change within each group.

Results

Age, serum creatinine and duration of dialysis (mean \pm SD) are given in Table I for each group. Figure 1 shows basal and peak responses (mean \pm SEM) of glucose, insulin and C-peptide to intravenous glucagon. All groups had a similar basal (fasting) and peak blood glucose with no significant difference between the groups. However, the glucose increment from basal to peak within each group was highly significant ($p < 0.001$). Basal serum insulin was similar in all uraemic

TABLE I. Patient data

	Controls	CRF	HD	New CAPD	Chronic CAPD
Subjects M	3	5	7	5	4
F	5	5	3	5	6
Age (years)	42 \pm 11.5	61 \pm 5.5	50 \pm 12.4	54 \pm 12	59 \pm 4.7
Serum Creatinine (μ mol/L)	89 \pm 16	779 \pm 257	889 \pm 145	951 \pm 238	1118 \pm 189
Duration of dialysis (months)	—	—	24 \pm 32.3	3.6 \pm 2	35.4 \pm 13.5

CRF = chronic renal failure; HD = haemodialysis; New CAPD = New continuous ambulatory peritoneal dialysis; Chronic CAPD = Chronic continuous ambulatory peritoneal dialysis

groups and did not differ from controls. Peak insulin levels were also similar between all groups ($p>0.5$). The insulin change from basal to peak was highly significant in all groups. Fasting and peak C-peptide concentrations were significantly higher in all uraemic groups compared to controls ($p<0.01$), but within the four groups with renal failure there was no significant difference between basal levels or between peak responses. The C-peptide increment from basal to peak in all groups was highly significant ($p<0.001$).

Discussion

Carbohydrate intolerance is common in uraemia [2] but the impact of dialysis is still debatable with reports of both improvement [8] and deterioration [9]. No further deterioration in glucose tolerance has been reported in the short-term on CAPD [10]. In this study non-dialysis, haemodialysis and peritoneal dialysis patients showed a significant increase in both serum insulin and plasma C-peptide in response to glucagon. Glucagon stimulation is a dynamic test of residual beta cell secretory function [3] and all uraemic patients responded in a physiological manner. New and chronic CAPD patients showed that beta cell integrity was intact and that no exhaustion or hypersecretion of peptide occurred. Basal and peak insulin levels were similar in all groups and did not differ significantly from controls, but both basal and peak C-peptide concentrations were significantly elevated in all uraemic groups. Raised C-peptide levels due to impaired degradation have been confirmed by others [4] but we found no difference within the uraemic groups, particularly between haemodialysis and CAPD patients. Thus despite continuous glucose absorption patients established on CAPD for up to five years, as well as other uraemics, were able to produce a significant rise in insulin and C-peptide in response to glucagon indicating normal pancreatic beta cell secretory function.

Acknowledgments

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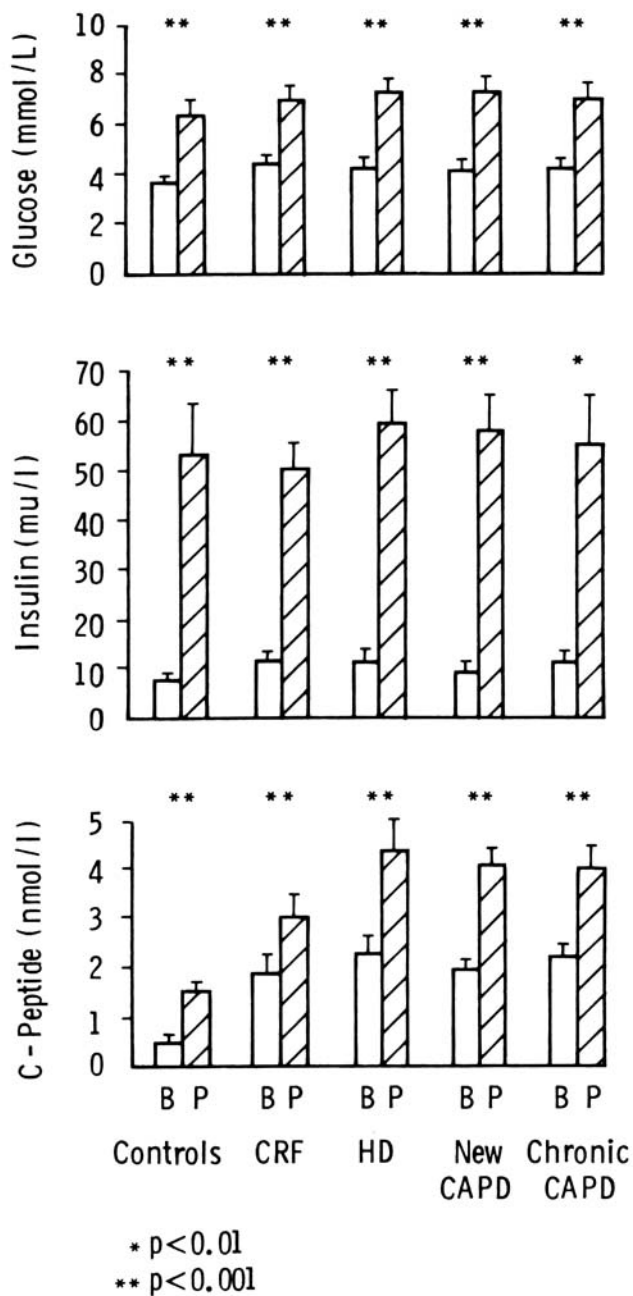


Figure 1. Basal (B) and peak (P) responses to intravenous glucagon