Effect of bromocriptine on plasma growth hormone and glucose tolerance in chronic renal failure

Chronic renal failure is associated with high circulating levels of growth hormone (GH) which are not affected by stimuli such as glucose loading.¹ They may be due to delayed degradation, excessive secretion, or both. Secretion of GH seems to be increased by catecholamines.² Bromocriptine (2-brom-alpha-ergocryptine; CB 154), an ergot alkaloid with dopaminergic activity, suppresses abnormal GH secretion in patients with acromegaly³ but not in normal subjects or in patients with diabetes mellitus.⁴ We therefore assessed the effects of bromocriptine on abnormal GH secretion in response to glucose loading in patients with chronic renal failure.

Patients, methods, and results

Four well-nourished patients treated with chronic intermittent haemodialysis (18 h/week, Kiil multipoint) were studied. After an overnight fast and with the patient resting in bed an intravenous glucose tolerance test was done about 14 hours after the previous haemodialysis. Venous samples were collected with an indwelling catheter. After a fasting specimen of blood had been obtained 140 mmol glucose (as a 2.78 mmol/l aqueous solution) was given intravenously over two minutes into the opposite arm. Thereafter samples were withdrawn 3, 6, 10, 15, 30, and 60 minutes after the start of the infusion.

The patients were then given bromocriptine 2.5 mg daily with food. The dose was increased by 2.5 mg every second day until the daily dose was 10 mg (2.5 mg 6-hourly). When this dose had been taken for two days a second intravenous glucose tolerance test was performed at a similar time relative to dialysis.

Plasma GH and insulin were estimated by radioimmunoassay, and blood glucose by a glucose oxidase method.

One patient had persistent hypotension when taking the full dose of bromocriptine (10 mg/day). A fasting sample of blood was taken but a second glucose tolerance test was not done. Another patient noted transient nausea and hypotension. Before treatment glucose tolerance was normal ($k = 2.87\%$ /min). Fasting levels of GH were raised in 3 of the 4 patients (mean ($\pm$ SEM) $3.8 \pm 1.4 \mu\text{g/l}$) and in all patients paradoxical rises of GH were seen (fig).

Mean ($\pm$ SEM) responses of blood glucose, plasma insulin, and growth hormone to intravenous glucose in dialysed patients with chronic renal failure before and after treatment with bromocriptine.

Treatment with bromocriptine did not affect glucose tolerance or insulin response. Fasting levels of GH were consistently higher after treatment (mean $8.5 \pm 1.5 \mu\text{g/l}$) than before treatment ($P < 0.01$). The nature of the GH response to glucose remained abnormal after treatment.

Discussion

In contrast to its effect in acromegaly,³ treatment with bromocriptine 10 mg/day in patients with renal failure neither suppressed

the fasting levels of GH nor altered paradoxical secretion of GH after administration of glucose. This suggests that dopaminergic receptors in the hypothalamic region of patients with chronic renal failure function normally and that the paradoxical secretion of GH after the administration of glucose is mediated by mechanisms which differ from those in acromegaly.

Despite the rise of fasting levels of GH no changes were noted in glucose tolerance or insulin response. Therefore GH levels are probably not a major factor in the abnormal carbohydrate tolerance of chronic renal failure.

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¹ Samaan, N A, and Freeman, R M, *Metabolism*, 1970, **19**, 102.

² Martin, J B, *New England Journal of Medicine*, 1973, **288**, 1384.

³ Thorner, M O, et al, *British Medical Journal*, 1975, **1**, 299.

⁴ Cassar, J, et al, *Lancet*, 1975, **2**, 181.

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Hazards of monocomponent insulins

Conventional insulins are being replaced by the new monocomponent insulins (Actrapid MC, Semitard, and Monotard), which are claimed to be more beneficial.¹ The following report, however, shows that dosage requirements in individual patients may be much smaller than with standard insulins, and thus more warning of the changeover should be given.

Case report

A 15-year-old boy who had been diabetic for three years was stabilised initially on twice daily soluble insulin with transfer for a few months to insulin lente once daily. The only complication of his diabetes had been severe renal glycosuria, though in April 1974 he had had an episode of diabetic ketoacidosis caused by a dental abscess. His insulin requirements, always rather high, then began to increase, and by November he was taking up to 280 units of ordinary (beef) soluble insulin daily. He was admitted to hospital for transfer to neutral soluble insulin (Actrapid). Initially his insulin requirement fell by 23% (see fig) but it rapidly rose again, and by May 1975

Sequential change in minimum insulin requirement. 1=Episode of ketoacidosis. 2=Change to neutral soluble (pork) insulin (Actrapid). 3=Change to monocomponent insulin (Actrapid MC).