KIDNEY FUNCTION IN NORMAL MAN
DURING SHORT-TERM GROWTH HORMONE INFUSION

By

ABSTRACT

Kidney function was studied in 9 normal males before and during a 2 h growth hormone (GH) infusion of 50 ng/kg/min. The following variables were measured during each 20 min clearance period: glomerular filtration rate, GFR, effective renal plasma flow, RPF (steady state infusion technique with urinary collections using $^{125}$Iiothalamate and $^{131}$Iiodohippurate), and urinary albumin and $\beta_2$-microglobulin excretion rates (radioimmunoassays).

The GH infusion resulted in a 10-fold increase in plasma GH concentration.

All the above mentioned variables remained practically unchanged during the infusion except for a small (~5%) but significant decrease in renal plasma flow ($P < 0.01$). Our negative results contrast to the findings of increased GFR and RPF during prolonged GH administration and suggest that GH requires several hours or days for its renal effects to become manifest.

It is well documented that functional alterations occur in the kidney in poorly controlled juvenile diabetics, viz. increased glomerular filtration rate (GFR), filtration fraction (FF) and urinary albumin and $\beta_2$-microglobulin excretion rate (Ditzel & Junker 1972; Mogensen 1972, 1976; Parving et al. 1976). The trigger mechanisms of these alterations are not known.

Mogensen (1972, 1976) suggested growth hormone (GH) as a factor of pathological importance.
In an attempt to evaluate this hypothesis the above-mentioned renal variables were determined before and during short-term growth hormone infusion in normal man. The GH infusion induced moderately elevated plasma levels, as typically found in poorly controlled juvenile diabetics.

**MATERIAL AND METHODS**

Nine healthy non-obese male medical students, aged 22–33 years, all of whom had been fully informed of the nature of the study before giving their consent, were investigated. None of the subjects were taking drugs.

The investigations were performed early in the morning in the fasting state. The subjects were supine during the investigation, standing up only during urinary voiding. To promote diuresis 250 ml tapwater was given every 20 min starting 1 h before the experiment and then continued throughout the clearance procedure. All the below-mentioned variables were measured in each 20 min clearance period.

GFR and RPF were measured using the classical steady state infusion technique with [125]iiodalatm and [131]iodohippurate, respectively (Mogensen 1972). Urinary albumin and β2-microglobulin were measured by radioimmunoassays (Miles et al. 1970; Evrin et al. 1971).

Plasma GH concentration was measured by radioimmunoassay (Hanssen 1973). Plasma glucose was measured by a glucose-oxidase method on an autoanalyzer. Blood pressure and pulse rate were determined at least 6 times during the investigation.

**Protocol**

After 40 min of constant infusion, 3 control clearance period of 20 min each were performed. Then a growth hormone (Nordisk Insulinlaboratorium, Copenhagen) infusion (50 ng/kg/min) was started and continued for 6 experimental clearance periods. Wilcoxon’s non-parametric test for paired comparison was used for statistical analysis, excluding the values for the transitional clearance period starting when the hormone infusion was initiated.

**RESULTS**

Fig. 1 demonstrates the changes in plasma GH and kidney function induced by the infusion of GH (50 ng/kg/min) in normal man. The infusion induced a 10-fold increase in plasma growth hormone concentration. All the renal variables remained nearly constant during the 60 min control period, except some minor insignificant variations in urinary albumin excretion and RPF. GFR was identical before and during the infusion, 130 ml/min. A slight, but statistically significant reduction in RPF occurred during the infusion, mean 558 ml/min compared with a control average of 586 ml/min (P < 0.01). Thus calculated filtration fraction \( \frac{\text{GFR}}{\text{RPF}} \) increased during infusion, mean 0.24, compared with a control mean of 0.22 (P < 0.01). Both urinary albumin and β2-microglobulin showed a slight, but statistically insignificant reduction.
Influence of physiological increments in plasma growth hormone on kidney function in 9 normal males, mean ± SEM. Except for a significant decrease in RPF and an increase in FF ($P < 0.001$), all the remaining renal variables were not significantly changed during the infusion.

(-18 %) during the infusion. There were no significant changes in blood pressure, pulse rate, plasma glucose and urinary output during the GH infusion. All subjects had urinary outputs greater than 10 ml/min.

**DISCUSSION**

The aim of the present study was to test the concept advocated by Mogensen (1972, 1976), and Mogensen & Andersen (1975) that plasma GH elevation in
poorly regulated juvenile diabetics may contribute to the increase in GFR and kidney size characteristic of this state. It is well known that GFR and RPF are increased to nearly the same extent (filtration fraction unchanged) in acromegaly. The increased kidney mass and the enlargement of extracellular volume have been suggested as the cause (Falkheden & Sjögren 1964). Conversely hypophysectomy decreases GFR, RPF and calculated kidney weight in long-term diabetics with severe retinopathy, acromegals as well as in patients with metastatic neoplastic disease (Falkheden & Wickbom 1965). But the reduction in GFR and RPF was found to occur at a much faster rate than the reduction in kidney mass suggesting that some of the changes are of functional nature rather than due to a reduced kidney mass (Falkheden & Wickbom 1965). Furthermore, daily im injections of 5 to 10 mg growth hormone for 4 days increase GFR and RPF about 15 % (filtration fraction unchanged) in normal man (Corvilain et al. 1962). Thus, the characteristic finding of an elevated filtration fraction and a normal RPF in untreated and treated juvenile diabetics (Mogensen 1976) can not be explained as a GH effect.

We studied the effect on kidney function of an 2 h continuous iv growth hormone infusion. The amount administered corresponds to approximately 5 mg growth hormone daily. The infusion induced a 10-fold increase in the plasma GH concentration, i.e. to levels found in poorly controlled juvenile diabetics (Hansen 1972). We did not find an elevated GFR and RPF. We have no explanation for the slight (−5 %) reduction in RPF observed during the GH infusion. Urinary albumin and β₂-microglobulin excretion rates are also augmented in poorly controlled juvenile diabetics, but it is not known whether or not long-term GH elevation has any influence on these variables. The present acute elevation of plasma GH concentration did not affect urinary albumin nor β₂-microglobulin excretion rates.

Our negative results contrast to the findings of increased GFR and RPF during prolonged GH administration and suggest that GH requires several hours or days for its renal effects to become manifest.

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