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Effect of somatostatin on renal function

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Abstract

Somatostatin has profound effects on both splanchnic and portal vascular beds. The effects of intravenous somatostatin (100 μg/h) on urinary volume, effective renal plasma flow, and glomerular filtration rate were compared with the effects of a control infusion of physiological saline in six normal subjects. Renal plasma flow and glomerular filtration rate were measured by primed constant isotope infusions of iodine-125 iodohippurate and chromium-51 edetic acid. Urinary volume, renal plasma flow, and glomerular filtration rate were measured during 20 minute clearance periods. During the control infusion urinary volume, renal plasma flow, and glomerular filtration rate remained essentially unchanged at 254 (SEM 3) ml/20 min, 568 (5) ml/min/1·73 m², and 110 (2) ml/min/1·73 m² respectively. From similar basal values the infusion of somatostatin led to a rapid decrease in all three variables. After 120 minutes of infusion of somatostatin urinary volume, renal plasma flow, and glomerular filtration rate were reduced to 148 (17) ml/20 min ($p<0·01$), 422 (7) ml/min/1·73 m² ($p<0·001$), and 93 (3) ml/min/1·73 m² ($p<0·05$) respectively.

This effect on renal function should be borne in mind whenever somatostatin is used.

Introduction

Somatostatin (growth hormone release inhibiting factor), originally isolated from ovine hypothalamus, is widely distributed in the human body.[1,2] In addition to inhibiting several endocrine and exocrine secretions[2-4] supraphysiological concentrations of somatostatin reduce splanchnic, hepatic, and gastric mucosal blood flow.[5-7] Furthermore, recent studies have suggested that somatostatin has a direct intrarenal antidiuretic effect, resulting in a reduction in urine flow and free water clearance.[8]

We evaluated the acute effects of an intravenous infusion of somatostatin (100 μg/h) on the urinary volume, effective renal plasma flow, and glomerular filtration rate in normal healthy subjects.

Subjects and methods

Six normal healthy men (mean age 26·3 (SEM 2·3) years) were studied on two days seven to 10 days apart. They received, in a randomised order, a control infusion of physiological saline (0·15 mmol(mEq)/l) on one day and an infusion of somatostatin 100 μg/h (Bachem, USA) on the other. Investigations started at 0900 after an overnight fast. Intravenous cannulas (Vygon) were inserted in both arms and connected by a three way tap to a slow running infusion of physiological saline. Subjects remained supine throughout the study, standing up only to void urine. To promote diuresis they consumed 250 ml tap water every 20 minutes, starting one hour before the study and continuing throughout the clearance procedure, which lasted four hours. Renal plasma flow and glomerular filtration rate were measured by the isotope clearance method with a primed constant infusion of iodine-125 iodohippurate and chromium-51 edetic acid respectively (Amersham International, UK) delivered through one intravenous cannula.[9] Urinary volume, renal plasma flow, and glomerular filtration rate were measured during 20 minute periods throughout the four hour clearance procedure.

To achieve constant plasma isotope concentrations a one hour basal period was allowed after the start of the isotope infusion. Subjects then received an infusion of physiological saline for one hour. Thereafter the infusion was either changed to somatostatin (100 μg/h) or continued (control) for a further two hours. At the end of each clearance period heart rate and blood pressure were recorded and blood samples were obtained from the contralateral intravenous cannula. Aliquots of plasma in fluoride were used to estimate plasma glucose concentrations (Yellow Springs glucose analyser, Ohio, USA) and aliquots in heparin to determine immunoreactive insulin concentrations.[10]

Renal plasma flow and glomerular filtration rate were corrected for body surface area and expressed per 1·73 m². All results are expressed as means (SEM). Differences in mean values between the day of the control infusion and the day of the infusion with somatostatin were assessed by Student's paired t test. The study was approved by the area ethical committee, and subjects gave full informed consent.

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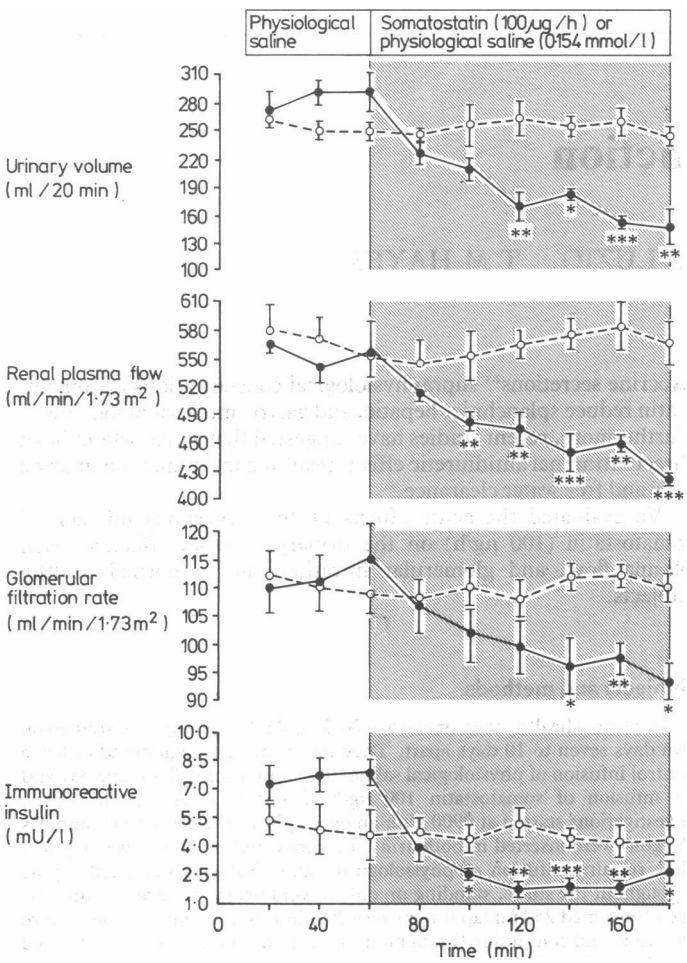
Results

On the day of the control infusion urinary volume remained unchanged at 254 (3) ml/20 min. Similarly, renal plasma flow and glomerular filtration rate remained essentially unchanged at 568 (5) ml/min and 110 (2) ml/min respectively (figure). In contrast, the infusion of somatostatin resulted in a prompt and rapid fall in urinary volume from a basal volume of 285 (20) ml/20 min to 170 (14) ml/20 min after 60 minutes ($p<0.01$) and 148 (17) ml/20 min after 120 minutes ($p<0.01$). A decrease in renal plasma flow, from 552 (16) ml/min before the infusion of somatostatin to 476 (19) ml/min after 60 minutes ($p<0.01$) and 422 (7) ml/min after 120 minutes ($p<0.001$) of the infusion, was also noted. Glomerular filtration rate was 112 (5) ml/min before the infusion, decreasing to 96 (5) ml/min after 80 minutes ($p<0.01$) and 93 (3) ml/min after 120 minutes ($p<0.05$) of infusion.



Urinary volume, renal plasma flow, glomerular filtration rate, and immunoreactive insulin concentration during somatostatin and control infusions.
*$p<0.05$, **$p<0.01$, ***$p<0.001$.

Heart rate and blood pressure did not alter during either infusion. Subjects did not experience any untoward side effects during the infusion of somatostatin. A small decrease was found in plasma immunoreactive insulin concentration, from 5·0 (0·2) mU/l to 4·8 (0·2) mU/l (figure), on the day of the control infusion, but the infusion of somatostatin led to a rapid and prompt decrease in plasma insulin concentration, from 7·7 (0·2) mU/l to 2·0 (0·5) mU/l at 80 minutes ($p<0.001$) and 2·7 (0·6) mU/l at 120 minutes ($p<0.05$). Plasma glucose concentrations, however, did not change during the infusion of somatostatin, being 4·8 (0·2) mmol/l (84 (4) mg/100 ml) before and 4·7 (0·2) mmol/l (87 (4) mg/100 ml) during the infusion.

Discussion

Since its discovery many endocrine and exocrine properties have been attributed to somatostatin. Among these is the reduction of gastric acid secretion,[3,4] which, together with a reduction of gastric mucosal, hepatic, and splanchnic blood flow,[5-7] seems to make somatostatin suitable in the management of gastrointestinal bleeding. Preliminary studies suggest that it may be effective in the treatment of bleeding peptic ulcers resistant to cimetidine and oesophageal varices.[11,12]

An appreciable and prompt decrease in effective renal plasma flow and consequently in glomerular filtration rate was detected during the infusion of somatostatin. The dose of somatostatin in this study was 100 μg/h, lower than that in studies assessing its role in the management of gastrointestinal haemorrhage. A decrease in urinary volume, as noted by Walker *et al*, was confirmed.[8] Walker *et al* reported a decrease in urinary flow and an increase in urinary osmolality without simultaneous change in plasma arginine vasopressin concentrations. The results of our study suggest that the rapid reduction in urinary flow is due to an appreciable decrease in the effective renal plasma flow.

The precise mechanism of this effect of somatostatin on the kidney and other vascular tissues remains unknown, particularly as systemic haemodynamics do not seem to be influenced.[13] The rapid onset of these effects suggests that somatostatin acts directly on the vascular smooth muscle. The reduction in renal plasma flow witnessed during the infusion of somatostatin may be secondary to the inhibition of glucagon secretion, as short term infusions of glucagon at supraphysiological concentrations have been reported to increase renal plasma flow and glomerular filtration rate.[14] This explanation of the vascular effect of somatostatin, however, is unlikely, as glucagon at physiological concentrations has been noted not to have any effect on splanchnic blood flow in man.[15]

This study clearly shows that somatostatin has a profound early effect on renal plasma flow. As somatostatin has recently been advocated in the management of patients with gastrointestinal tract haemorrhage these results emphasise the need for frequent monitoring of renal function.

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