Patients, methods, and results

Peripheral venous blood samples were collected from 23 epileptic women of reproductive age who were otherwise healthy and using no other medication than that for epilepsy. Blood was collected at their routine visits at the department of neurology. The plasma SHBG concentration was determined by the method of Rosner² and phenytoin concentrations by the method of Norell *et al.*³

The figure shows the SHBG and the phenytoin concentrations in each subject. The distribution of SHBG in a reference group of 68 fertile, healthy women using intrauterine devices for contraception is indicated by the horizontal lines. Only three of the epileptic women had an SHBG concentration at or below the mean for the reference group. Another five had concentrations within the upper half of the reference range and 15 women had concentrations over two standard deviations above the reference values. A weak correlation ($r = 0.40$; $P < 0.05$) existed between the phenytoin concentration and the plasma SHBG concentration. In a woman who had recently discontinued her phenytoin we found an SHBG concentration of 144 nmol/l (41.8 μ g/l) at a phenytoin concentration of only 18 μ mol/l (4.5 μ g/l). Four months later, without medication, her SHBG concentration was normal at 35 nmol/l (10 μ g/l).

Plasma SHBG and phenytoin concentrations in 23 women treated with phenytoin for epilepsy. Horizontal lines indicate mean and ± 2 SD of a reference distribution of SHBG in fertile women.

Conversion: SI to traditional units: SHBG: 1 nmol dihydrotestosterone bound/l ≈ 0.29 μ g/l. Phenytoin: 1 μ mol/l ≈ 0.25 μ g/ml.

Comment

To our knowledge no one has reported an effect by antiepileptic drugs on SHBG concentration. Our finding obviously represents another effect of phenytoin on hepatic metabolism, but the further implications can only be hypothetical. It is well known that antiepileptic treatment induces steroid-metabolising enzymes, which alter the effects of both endogenous and exogenous steroids.⁴ Occasional pregnancies in women on oral contraceptives and the lack of therapeutic effect of corticosteroids in epileptics with asthma have both been blamed on this enzyme induction. The induction of SHBG, and possibly of other high-affinity carrier proteins for steroids and other substances, may play a further part in reducing the effects of steroids and possibly vitamins in epileptics by changing the proportion of free and biologically available compound.

Because it is easy to measure, the SHBG concentration may be useful as a measure of enzyme induction in patients treated with antiepileptic medication.

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⁴ Richens, A, in *Anticonvulsant Drugs and Enzyme Induction*, ed A Richens, p 3. Amsterdam, Elsevier, 1976.

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St Anthony's fire and pseudochronic renal failure

St Anthony's fire, due to consumption of rye bread contaminated with *Claviceps purpurea*, was endemic in Europe in the Middle Ages. Most modern cases are iatrogenic, caused by prescribed ergot derivatives. We report here a case of acute renal failure, presenting clinically as chronic renal failure, associated with ergotamine overdose.

Case report

A 42-year-old housewife presented with a two-week history of headaches, vomiting, debility, confusion, and cold, painful hands. She suffered migraine, and had taken 10 1-mg dihydroergotamine tablets daily for two weeks, and 20 tablets the day before admission. She was pale, confused, with pigmented excoriating skin, white nails, but no oedema. Blood pressure was 145/75 mm Hg and central venous pressure $+ 3.5$ cm H₂O. Urine output was 3 l/24 h, with no history of antecedent oliguria.

Investigations showed: plasma urea 70 mmol/l (422 mg/100 ml), creatinine 2750 μ mol/l (31 mg/100 ml), sodium 126 mmol(mEq)/l, potassium 4.8 mmol(mEq)/l; urinary urea 140 mmol/l (843 mg/100 ml), creatinine 6.8 μ mol/l (0.08 mg/100 ml), sodium 48 mmol/l, potassium 25 mmol/l; creatinine clearance 3 ml/min; serum calcium 2.3 mmol/l (9.2 mg/100 ml), phosphate 4.8 mmol/l (15 mg/100 ml), urate 1.02 mmol/l (17.2 mg/100 ml); haemoglobin 8.4 g/dl, normochromic normocytic film, white cell count 8.4×10^9 /l (8400/mm³). High-dose intravenous urography (IVU) gave an instant dense persistent nephrogram with normal-sized kidneys but no pyelogram.

She was managed conservatively with fluid and dietary control. Plasma urea fell spontaneously. Urine output remained high, and sodium and potassium supplements were required initially. Three weeks later clinical recovery was complete, plasma urea and creatinine were normal, and creatinine clearance was 54 ml/min. Three months later creatinine clearance was 59 ml/min, renal tubular function was normal, and haemoglobin was 13.4 g/dl. A repeat IVU was normal.

Comment

Our patient presented with many features of chronic renal failure¹: pigmented excoriating skin, white nails, severe normochromic normocytic anaemia, extremely high plasma creatinine, normal serum calcium, and high urine output (over 2.5 l/24h is unusual in established acute renal failure). Her recovery and subsequent investigation led to a diagnosis of acute renal failure, possibly already in the diuretic phase.

Peripheral arteriospasm is a well-recognised complication of ergotamine treatment.² Ergotism is usually due to overdose but may occur after small doses in sensitive individuals.³ It has followed administration by injection, by suppository, and by mouth.⁴ Ergotamine may cause reversible renal arterial spasm,⁵ and patients with ergotism may have a reduced creatinine clearance.^{3,5} We have found no reports of acute renal failure in ergotism. Prolonged renal arteriospasm, due to ingestion of high doses of ergotamine, may have caused the condition in this case. No other causal factor was apparent. Vomiting late in the illness may have prevented absorption of some ergotamine, allowing recovery of peripheral and renal arteriospasm, but it did not cause significant salt and water depletion.

Our case illustrates the occasional difficulty in differentiating between acute and chronic renal failure. We believe that ergotamine caused this patient's renal failure, and that monitoring of renal function is advisable in individuals taking high doses of ergot alkaloids.

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⁵ Fedotin, M S, and Hartman, C, *New England Journal of Medicine*, 1970, **283**, 519.

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