Cimetidine and renal failure

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Abstract
A patient is described who developed reversible renal failure while taking cimetidine.

Introduction
Cimetidine is a recently introduced but widely used histamine H2-antagonist. It is known to produce significant increases in plasma creatinine in normal people but the increased values usually remain in the normal range (Burland and Simkins, 1977). In clinical trials a tendency for plasma creatinine to rise, particularly in patients treated with high doses of cimetidine, was found but with continued treatment values generally remained steady or fell (Haggie, Fermont and Wyllie, 1976; Blackwood et al., 1976). McElligott (1978) reported a patient who had a reversible deterioration in renal function during cimetidine therapy and a further case is now reported where a rapid resolution of symptoms and improvement in renal function followed cessation of cimetidine.

Case report
A 72-year-old man who had previously enjoyed good health suffered an episode of melaena in 1974 when a duodenal ulcer was discovered. Subsequently he had rare mild dyspepsia with complete remissions of up to one year, for which he took an occasional tablet of a magnesium antacid. On a recent occasion he was prescribed cimetidine (1 g/day). He continued on this dosage for approximately one month when he began to experience an unpleasant taste, dry tongue, and loss of appetite. Two weeks later he was advised to stop the drug but after 3 days he recommenced treatment in the same dose. Symptoms continued and he noticed, in addition, some thirst and polyuria. He lost approximately 6 kg in weight during this period and he was referred for investigation.

On examination his BP was 172/90 mmHg. There was mild hepatomegaly and he had a small amount of oedema of the ankles to which he had been accustomed for 30 years, associated with obvious varicose veins. There was mild smooth enlargement of the prostate, but he denied symptoms of prostatic obstruction and intravenous urography was normal. Urine analysis revealed only a trace of proteinuria and no haematuria. His Hb was 10.8 g/dl and his blood urea was elevated at 26.5 mmol/l (160 mg/dl) with a serum creatinine of 375 μmol/l (4.2 mg/dl), serum sodium: 140 mmol/l (mEq/l), potassium: 3.5 mmol/l (mEq/l), bicarbonate: 15 mmol/l (mEq/l). Liver function tests normal. Serum albumin 32 to 35 g/l (3.2-3.5 g/dl). Serum

![Graph showing Urea and Creatinine levels over time](http://pmj.bmj.com/)

Fig. 1. Conversion s.i. to traditional units – Urea: 1 mmol/l = 6.02 mg/dl. Creatinine: 1 μmol/l = 0.01 mg/dl.

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electrophoresis showed a slight increase of $\alpha_2$-globulin. Immunoglobulins were normal. Serum calcium: 2.12 mmol/l (8.5 mg/dl), phosphate: 1.68 mmol/l (5.2 mg/dl). Three faecal specimens tested for occult blood were negative.

Cimetidine was stopped and he was encouraged to take a high fluid intake. He continued to take an occasional tablet of magnesium antacid if he experienced dyspepsia but this was rare. His urine output was satisfactory and his blood urea and serum creatinine fell rapidly so that one week later his blood urea was 14 mmol/l (84 mg/dl) with a creatinine of 228 $\mu$mol/l (2.6 mg/dl).

His electrolytes remained normal and his Hb was steady at approximately 10.3 g/dl (Fig. 1).

Six weeks after the cessation of cimetidine his blood urea and serum creatinine were normal. A barium meal showed gross deformity of the duodenal cap but he declined endoscopy. Chest X-ray was normal.

Discussion

It seems highly probable that cimetidine was the cause of renal failure in this man, although the mechanism is not clear. The presence of only a trace of protein in the urine makes a glomerular lesion unlikely, but a reversible effect on tubular function might be a possibility. Five possible cases of interstitial nephritis, some proved by renal biopsy, including one with recurrence of renal failure following re-challenge with cimetidine, have been reported from the U.S.A. (Smith, Kline and French Ltd, 1979). This rare occurrence has been mentioned in the recently revised pharmaceutical data sheet for cimetidine.

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References

SMITH, KLINE & FRENCH LTD (1979) on the file.