having increased activity of β-hydroxybutyrate dehydrogenase.

Aspartate aminotransferase activities <42 U/l were found in 84 patients who received streptokinase compared with 70 who received placebo. Similarly, alanine aminotransferase activities >50 U/l were found in 48 who received streptokinase compared with 35 who received placebo. Bilirubin concentrations were routinely measured, and increased concentrations were found in 10 of the patients with increased alanine aminotransferase activity who received streptokinase but none of those who received placebo. The activity of γ-glutamyltransferase was not routinely measured, but an increased activity (mean 176 U/l; normal range 11-55 U/l) was seen in six patients who received streptokinase who had an increased activity of alanine aminotransferase. Increased activity of aspartate aminotransferase with no other evidence of infarction occurred in 10 of 16 patients who received streptokinase and in eight of 21 who received placebo (mean activity 118 U/l and 57 U/l respectively). No patients with raised aminotransferase activities after treatment with streptokinase had necropsies.

Comment

Almost a quarter of patients treated with streptokinase developed activities of alanine aminotransferase exceeding twice the normal values. Some also showed an excessive rise in aspartate aminotransferase activity. This has obvious clinical implications. Firstly, the diagnostic value of standard biochemical testing may be reduced in patients with chest pain as the activity of aminotransferases may rise without other evidence of myocardial infarction.[2] Interpreting activities of aminotransferases is also made more difficult as early fibrinolytic treatment may abort acute infarction.[4] Secondly, the effects of streptokinase can mimic the biochemical characteristics of hepatobiliary disease. Unfortunately, the mechanism behind raised aminotransferase activity is unclear. The concomitant rise in γ-glutamyltransferase activity and bilirubin concentration suggests a hepatic source. These increases may be caused, however, by a reperfusion effect, as washout of cardiac enzymes can occur after successful thrombolysis in acute infarction and the activity of alanine aminotransferase is high in some hearts.[5] Whether other fibrinolytic treatments increase aminotransferase activities remains to be seen.

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(Accepted 15 May 1990)

Hyperthyroidism and eating disorders

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Br Med J 1990;**301**:322-3

Thyroid disease usually affects body weight. In patients with eating disorders (anorexia nervosa and bulimia) hyperthyroidism may cause difficulties in managing these conditions.[1,2]

Case reports

CASE 1

A 34 year old woman presented with diarrhoea and increased appetite. Her weight was 60 kg (height 165 cm). She was clinically hyperthyroid with a diffuse goitre. Her serum free thyroxine concentration was 120 pmol/l (normal range 8·8 to 23 pmol/l).

She had developed anorexia nervosa at the age of 18, which had been characterised by abstention from food, self induced vomiting, and amenorrhoea. Her weight had subsequently risen from 42 kg to 55 kg over three months in hospital. Psychiatric support had continued over the next five years. She then maintained a weight of 56 kg over the next 11 years and had normal menstrual periods. She occasionally felt the urge to induce vomiting but refrained from doing so and controlled her weight by dieting. Despite taking carbimazole 45 mg and propranolol 120 mg daily she remained hyperthyroid but refused surgery and treatment with radioactive iodine.

A month after she presented to us her weight rose to 62 kg. She admitted binge eating and vomiting and said that she had lost control over herself and was frightened of putting on weight. She was clinically hyperthyroid with a heart rate of 140 beats/min. With supervised drug treatment in hospital over two weeks her serum free thyroxine and free triiodothyronine concentrations fell to 11 pmol/l and 7·7 pmol/l respectively.

Three months later her weight increased to 70 kg and her serum free thyroxine concentration to 80 pmol/l despite treatment with carbimazole 30 mg daily. Despite being admitted to hospital she remained hyperthyroid, and self induced vomiting of her drugs was suspected. With continuous nursing supervision she became clinically euthyroid. She had a subtotal thyroidectomy, and postoperative hypothyroidism was treated with thyroxine. Her weight stabilised at around 60 kg, and she said that she felt more in control of her weight and life.

CASE 2

A 15 year old girl presented with irritability, increased appetite, and weight gain of 14 kg. She was clinically hyperthyroid with a goitre. Her serum concentration of protein bound iodine was 1·06 μmol/l (normal range 0·26 to 0·57 μmol/l), and uptake of radioactive iodine was 89%. She was treated with carbimazole 20 mg daily. Because of her increased appetite and fear of gaining weight she began dieting and lost 28 kg over six weeks; her periods stopped. Her behaviour became disturbed, and anorexia nervosa was diagnosed. After her admission her weight rose from 42 kg to 54 kg (height 170 cm), but after her discharge it fell again to 43 kg. Her hyperthyroidism was controlled with carbimazole. Anorexia, however, persisted and led to her suicide eight years later.

Comment

In both these patients hyperthyroidism resulted in weight gain. Hyperthyroidism occasionally causes weight gain by increasing the appetite and hence the intake of energy, which then exceeds the catabolic effect of the disease.[2] In case 1 anorexia nervosa was in remission, though the patient's fear of gaining weight persisted. The onset of hyperthyroidism led to the loss of her ability to control her weight by dieting, causing psychological distress. The increase in appetite may have unmasked a long suppressed tendency to bulimia.

In case 2 hyperthyroidism caused an increase in appetite, and loss of control over the patient's eating behaviour may have precipitated the onset of anorexia nervosa.

Thyroid hormones may be misused by obese patients and occasionally by anorectic patients in an attempt to lose weight. Factitious hyperthyroidism was excluded in our patients by the increased uptake of radioactive iodine by the thyroid. A lack of response to carbimazole is usually due to poor compliance, which in case 1 was compounded by self induced vomiting. Uncontrolled hyperthyroidism leading to cardiac failure has been reported in a patient who refused treatment because hyperthyroidism helped her to lose weight.[3]

Eating disorders are common in young women with diabetes, in whom weight loss may precipitate diabetic complications.[4] Medical advice may draw the patient's attention to body weight and diet, precipitating anorexia nervosa.

We conclude that hyperthyroidism in patients with eating disorders may lead to psychiatric distress because of loss of control over body weight. Self induced vomiting may cause apparent failure to respond to drug treatment.

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(Accepted 6 June 1990)

Recurrent acute hypersensitivity to quinine

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Br Med J 1990;**301**:323

We report on a woman who developed acute renal failure on three separate occasions over 20 years after taking various substances that contained quinine. Our report highlights the potential hazards of hypersensitivity to quinine.

Case report

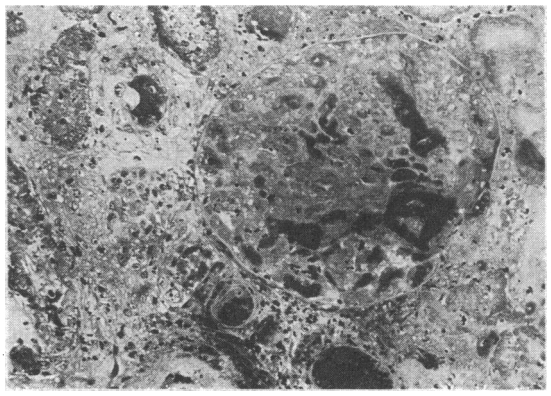
A 63 year old woman presented in December 1987 with a 72 hour history of anuria. She had developed shivering and had felt generally unwell after drinking tonic water, which contains quinine. By 36 hours anuria, generalised itching, and spontaneous bruising had developed. Her recent general health had been good. In 1965 she had required dialysis after taking a sedative that contained quinine. In 1981 she had again developed acute renal impairment with evidence of disseminated intravascular coagulation shortly after drinking bitter lemon, which contains a small amount of quinine; her renal function had improved after treatment.

On admission in 1987 the patient had renal failure (urea concentration 40·1 mmol/l, creatinine concentration 1540 μmol/l). Her haemoglobin concentration fell from 122 g/l to 54 g/l with a platelet count of 64×10^9/l. Ultrasound scanning showed a small left kidney but a normal sized right kidney. A screen of coagulation factors showed a raised concentration of fibrin degradation products (32 mg/l). Renal biopsy showed extensive cortical necrosis, red cells and fibrin in the glomeruli, and fibrin in the walls of the arterioles (figure). Glomeruli that were not necrotic showed segmental sclerosis. These findings were thought to be due to severe recurrent hypersensitivity.

After haemodialysis she gradually improved but nine months later had permanent renal impairment (urea concentration 16·6 mmol/l, creatinine concentration 363 μmol/l). She was given a list of foods and compounds that contain quinine, which she was told to avoid, and two years later she remained well.

Comment

This patient's history suggests a diagnosis of recurrent hypersensitivity to quinine resulting in disseminated intravascular coagulation with secondary thrombocytopenia. Biopsy showed that the acute uraemic crises were caused by cortical ischaemia with intravascular coagulation and deposition of fibrin; the cortical necrosis shows the severity and permanence of the renal damage. Between 1981 and 1988 the patient's left kidney shrank considerably, probably because of chronic vascular insufficiency.



Renal biopsy specimen stained with Masson trichrome showing necrotic glomerulus containing clumps of darkly staining fibrin

Hypersensitivity to quinine, rather than direct toxicity, has been reported many times; manifestations include purpura,[1] thrombocytopenia,[2] disseminated intravascular coagulation,[2] haemolysis,[3] haemoglobinuria,[4] and acute renal failure.[5] Our case supports the theory that in acute renal failure of this type intravascular coagulation is a more important factor than haemolysis.[5]

Hypersensitivity to quinine is rare but potentially fatal. Small amounts of quinine are found in many medicines, tonics, drinks, and dietary items. All substances containing quinine should be clearly labelled, and all patients starting treatment with quinine should be questioned for evidence of hypersensitivity. A comprehensive list of substances that contain quinine should be available for hypersensitive people.

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(Accepted 23 May 1990)