been reported cytologically as non-neoplastic the cytological specimens were reviewed. In one case from the first year of the study a retrospective cytological diagnosis of papillary carcinoma was made, but in all other cases there were no cytological features suggesting neoplasia, although in two cases the specimens would now be classed as unsatisfactory.

Aspiration cytology is an adjunct to the management of thyroid swellings but is not a definitive diagnostic test and, in particular, negative results do not exclude neoplastic disease. Definition of an optimum management policy depends on further study, which should include the financial and psychological implications of repeated clinic attendances and of repeated aspiration, which may culminate in delayed surgical treatment.

We gratefully acknowledge financial support from the Scottish Hospitals Endowment Research Trust and the assistance of the Aberdeen University Computing Centre.

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(Accepted 15 June 1990)

Activities of aminotransferases after treatment with streptokinase for acute myocardial infarction

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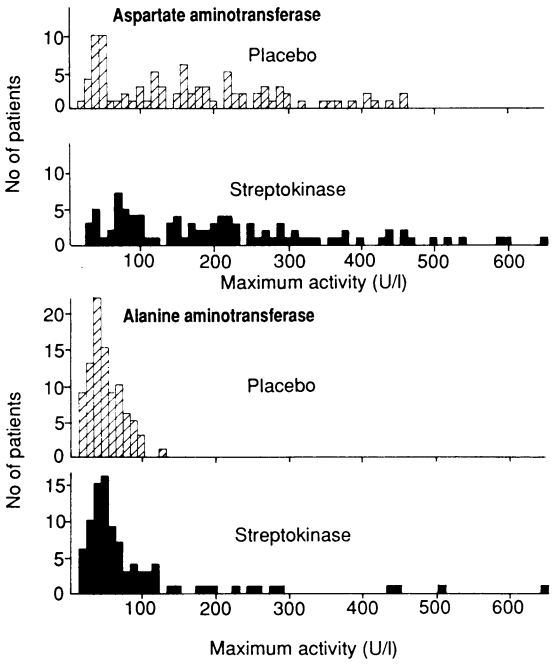
Br Med J 1990;**301**:321-2

Treatment with streptokinase can increase the serum activities of aspartate aminotransferase and alanine aminotransferase.[1,2] We examined the activities of aminotransferases in patients who had been treated with streptokinase for acute myocardial infarction to determine the incidence and clinical relevance of this drug reaction.

Subjects, methods, and results

We examined the case records of 189 patients from Dumfries and Galloway Royal Infirmary who had been entered into the second international study of infarction (ISIS 2)—a placebo controlled trial of streptokinase and aspirin in patients who had had a suspected acute myocardial infarction.[3] Of our patients, 95 (64 men, 31 women; mean age 58·9 (SD 8·38) years) had received streptokinase and 94 (71 men, 23 women; mean age 56·8 (8·52) years) had received placebo. Venous blood had been taken for assay of enzyme activity on admission to hospital and then once daily for 72 hours.

The figure shows the distribution of the peak activities of aminotransferases as determined from the case records (normal range: aspartate aminotransferase 13-42 U/l, alanine aminotransferase 11-50 U/l). The geometric mean of the peak activity of aspartate aminotransferase was 157 U/l for patients who received streptokinase and 120 U/l for those who received placebo ($p<0·05$; ratio 1·31, 95% confidence interval 1·02 to 1·66). The corresponding values for alanine aminotransferase were 60 U/l and 43 U/l ($p<0·05$; 1·40, 1·15 to 1·76). There was no significant difference in enzyme activity between men and women given streptokinase or between patients given aspirin and those given placebo for aspirin. (Patients in the streptokinase and placebo groups had also been randomised to receive aspirin or a placebo for aspirin.) Of the patients who received streptokinase, 79 had had myocardial infarctions, with 66 showing typical changes on electrocardiography and 71 having increased activity of β-hydroxybutyrate dehydrogenase. Of the patients who received the placebo for streptokinase, 73 had had infarcts, with 61 showing changes on electrocardiography and 64



Distribution of maximum enzyme activities after treatment with streptokinase or placebo

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.