Streptokinase-induced jaundice

Sir,

Streptokinase is widely used to treat myocardial infarction. It can cause abnormal liver function but rarely jaundice. We describe the case of a patient who developed jaundice following streptokinase infusion for acute myocardial infarction.

A 43 year old male was admitted with an acute myocardial infarction. He took atenolol 50 mg daily for hypertension, smoked 20 cigarettes each day and drank 2 pints of beer a week. He had no history of gallstones, foreign travel, contact with hepatitis, previous blood transfusion or intravenous drug abuse. He received 300 mg aspirin and an infusion of 1.5 MU streptokinase. Pain and nausea were relieved by intravenous dimorphine and metoclopramide.

The following day he was jaundiced. Urinalysis showed blood and bilirubin. His full blood count remained stable, and plasma electrolytes and clotting screen were normal. Liver function tests (normal on admission) showed: plasma bilirubin 133 IU/l (NR < 17), aspartate amino-transferase 140 IU/l (NR 6–38), alanine amino-transferase 143 IU/l (NR 4–40) and alkaline phosphatase 117 IU/l (NR 30–130). Abdominal ultrasound showed no evidence of intra- or extrahaepatic biliary dilatation or biliary calculi. Markers for hepatitis A and B, cytomegalovirus and Epstein–Barr virus were negative. The jaundice subsided and liver function tests returned to normal over the next 3 days. In the absence of any other explanation, the jaundice was attributed to streptokinase.

Four weeks later he was readmitted with chest pain and left ventricular failure. Serial electrocardiogram and cardiac enzymes confirmed extension of the original myocardial infarction. He did not receive further thrombolysis.

The Committee on Safety of Medicines has received 22 reports of liver complications with streptokinase (July 1963 – April 1993): four with abnormal liver function, 15 with jaundice and four with hepatocellular damage. Yet, despite its widespread use in acute myocardial infarction, only three cases of jaundice have been reported in this context in the literature.1,2 Jaundice has been reported after streptokinase infusion for extensive deep venous thrombosis, settling when the infusion was discontinued, but recurring when rechallenged.3

The pathophysiology of streptokinase-induced jaundice is not known. Animal studies show a rise in liver enzymes following infusion with streptokinase, thought to be due to proteases reaching liver tissue.4 Normally proteases are rapidly inactivated by plasma protein binding to alpha 2 plasmin and alpha 2 macroglobulin, before being metabolized by the liver. Streptokinase causes generalized fibrinolysis which may overwhelm this protective mechanism in susceptible individuals.

When this patient presented with further myocardial infarction, we considered additional thrombolytic treatment but were apprehensive about subsequent reaction. It is possible that alteplase, being clot specific, so causing less plasmam formation, could have been given with impunity.

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Massive rectal bleeding due to ileocaecal tuberculosis (conservative approach)

Sir,

Torrential bleeding due to ileocaecal tuberculosis is a rare manifestation. The traditional method of treatment has been surgical resection of the affected part. We report a case managed conservatively with complete recovery.

A 27 year old female was admitted with continuous fever and weakness for about 2½ months. On physical examination she was emaciated, febrile, pale and toxic. There was icterus, tachycardia and mild pallor. The liver was 1 cm below the subcostal arch, with a firm mass in the right iliac fossa. Next day she had 250 ml of reddish bleeding per rectum. Her general condition deteriorated and she continued to bleed for one week.

Her haemoglobin was 7.8 g/dl which dropped down to 4.5 g/dl. Chest X-ray revealed a non-homogeneous opacity in the left upper zone consistent with active tuberculosis. Colonoscopy showed an oozing nodular.
fibrosing ulcer in the caecum and terminal ileum, brushings from which showed for acid-fast bacilli. Biopsy revealed a chronic inflammatory granulomatous disease. She required 10 units of blood transfusion with antitubercular treatment and had an uneventful recovery.

Review of the literature for the past 22 years revealed 13 cases of colonic tuberculosis which presented with massive rectal bleeding.\(^1\)\(^-\)\(^4\) Intestinal tuberculosis is associated with increased capillary vascularity and oblitative endarteritis which makes bleeding uncommon. All the reported cases required intestinal resection except one which was managed with transcatheter embolization.\(^5\)

The reported case was managed conservatively as she was not willing for surgery and to our surprise she made a complete recovery.

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References

Bradycardia associated with fluoxetine in an elderly patient with sick sinus syndrome

Sir,

Selective serotonin re-uptake inhibitors (SSRIs) are a relatively recent class of drug introduced for treatment of depression and promoted as being largely free of serious side effects. In particular they do not have the quinidine-like activity of tricyclic anti-depressants.\(^1\)

However, a clinically non-significant slowing of pulse rate is recorded with SSRIs,\(^2\) and instances of cardiac side effects in patients with underlying cardiac disease have been reported.\(^3\)\(^-\)\(^5\) We report a patient who developed bradycardia whilst taking fluoxetine (Prozac) and who was subsequently found to suffer from sick sinus syndrome.

A previously fit 89 year old woman who had been started on fluoxetine 20 mg/day for depression 18 months previously, presented with dizzy spells and falls. Other medication was a small dose of amitriptyline of 25 mg/day and occasional temazepam 10 mg nocte for insomnia. Both latter drugs had been taken for several years. There was no past history of cardiac disease.

Examination revealed a regular pulse of 44/minute, blood pressure 140/80 mmHg and a grade 2/6 ejection systolic murmur was heard over the left sternal edge. Central nervous system examination was unremarkable. Electrocardiogram (ECG) revealed sinus bradycardia at a rate of 40/minute, a chest radiograph was within normal limits.

All her medications were stopped and her pulse rate rose to 72/minute within 24 hours of admission. Her symptoms disappeared and she became independently mobile. An ambulatory 24 hour ECG recording was performed and showed features of sick sinus syndrome with pauses of over 3 seconds duration. A permanent pacemaker was therefore inserted prior to discharge home.

Although not absolutely proven since re-challenge was not considered ethical, we feel it is likely that fluoxetine contributed to the bradycardia and symptoms in this patient. The low dosage and longer duration of use of other medication makes their contribution unlikely and the prompt resolution of the bradycardia on stopping medication suggests that the sick sinus syndrome alone was not responsible. It is also of interest that, although slowing of cardiac conduction is apparently a feature of all the SSRIs, previous case reports have implicated fluoxetine where cardiac side effects have occurred,\(^3\)\(^-\)\(^5\) as was the case with our patient.

We therefore suggest that SSRIs do carry a risk of cardiac side effects, particularly where cardiac disease and/or conduction defects are present. Awareness of this and appropriate assessment is therefore advisable before prescribing SSRIs, including ECG examination. This is especially important in the elderly where occult cardiac disease and conduction abnormalities are relatively common.

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Massive rectal bleeding due to ileocaecal tuberculosis (conservative approach)

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