was receiving placebo. Three patients stopped the treatment because of side effects while taking Seatone. One had headaches; one abdominal pain, diarrhoea, and headaches; and one constipation. Additional minor side effects were reported by two patients receiving Seatone and four receiving placebo. One patient was withdrawn from the study for reasons unrelated to treatment.

Comment

These results show clearly that a single course of Seatone was not superior to a fish extract in rheumatoid arthritis. Previous evidence for the effectiveness of Seatone is slender. The anti-inflammatory activity shown by Miller and Ormrod[1] was obtained by intraperitoneal and not oral administration. Intraperitoneal administration of chemicals may have a spurious anti-inflammatory effect and is therefore unreliable. The effects in patients shown by Gibson *et al*[2] were slight. Their study remained double-blind for only three months, during which time 10 out of 17 patients with rheumatoid arthritis receiving Seatone improved compared with three out of 11 receiving placebo. This difference is not statistically significant ($\chi^2=2{\cdot}67$, $p>0{\cdot}1$). The results of measurements of pain, stiffness, and articular index were not given for patients receiving placebo, and no other evidence was put forward to show that Seatone was superior to placebo.

A four-week course of Seatone does not appear to be worth while except for the very considerable placebo effect that any new treatment has in rheumatoid arthritis.

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Systemic side effects with eye drops

One advantage of topical preparations of drugs is the lack of systemic side effects. Ecothiopate eye drops are sometimes used in the treatment of glaucoma. Ecothiopate is an anticholinesterase, and systemic cholinergic effects may occur.

Case report

The patient, a 59-year-old man, presented in 1980 complaining of excessive sweating of increasing severity for two years, which was most troublesome after meals and during the night. He also complained of intermittent diarrhoea for 10 years. This had been investigated in 1974 and no definite cause found. It had been adequately controlled with codeine phosphate. He had also noticed muscle weakness and fatigue for two years. He was completely blind as a result of glaucoma, for which he had been using "eye drops" since the age of 29 years. Apart from blindness no abnormal physical signs were apparent on examination. The following investigations were performed and yielded normal results: full blood count and erythrocyte sedimentation rate, blood urea and electrolyte concentrations, glucose tolerance test, thyroid function tests, urinary 4-hydroxy-3-methoxymandelic acid, gastrointestinal hormone assays (vasoactive intestinal polypeptide, pancreatic polypeptide, gastrin, and glucagon), and barium meal and follow-through. He was treated with propantheline with minimal improvement.

Two months later it was suggested he stop using pilocarpine, one of his eye drops. He had no ill effects from this and so took it on himself to stop using his other eye drops—namely, Phospholine iodide 0·25% (ecothiopate). All his symptoms—the hyperhydrosis, muscle weakness, fatigue, and diarrhoea—resolved and he was able to stop taking the codeine phosphate. On reintroducing ecothiopate he noticed a return of postgustatory sweating; he stopped using these drops again and remained well and asymptomatic.

Comment

This case history emphasises the importance of a full drug history, including topical applications used, and full knowledge of the side effects of any such drugs. Such knowledge would have saved many years of symptoms and unnecessary investigations. Ecothiopate is an anticholinesterase, and symptoms of cholinergic overactivity have been reported.[1 2] These side effects may have potentially lethal implications in respect of surgery and anaesthesia, when muscle relaxants such as suxamethonium may be used. Gesztes[3] reported prolonged apnoea occurring after anaesthesia in a patient who underwent laparotomy for abdominal colic, vomiting, and diarrhoea. The patient had been using ecothiopate eye drops for seven years before this event.

I would hope that the above case history was unusual. There is a problem, however, when patients are treated simultaneously by diverse specialist departments. Side effects of some specialist treatments simulate other medical disorders and may lead to referral to further specialised departments unfamiliar with both the treatment already being received and its potential side effects.

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Tetracycline-induced oesophageal ulceration

Oesophageal ulceration associated with ingestion of tablets is being increasingly recognised. Drugs already well known to be implicated are emepronium bromide and slow-release potassium.[1] We report a case of oesophageal ulceration after ingestion of a tetracycline hydrochloride tablet.

Case report

A previously fit 24-year-old Iraqi man with no history of upper gastrointestinal disease or oesophageal motility disorder was given a seven-day course of tablets containing 250 mg tetracycline hydrochloride for a chest infection. He was taking no other medication. On one occasion he swallowed a single tablet without water at 1 am, after which he went immediately to bed and slept. He was awakened at 4 am with severe epigastric and lower retrosternal pain unrelieved by water, milk, or antacids. He took no further tetracycline tablets and presented to the casualty department eight hours later still complaining of pain and odynophagia. Examination revealed only epigastric tenderness. He was referred to a medical outpatient clinic and seen two days later, by which time the epigastric pain had settled but odynophagia continued. There were no abnormal physical signs.

Investigations showed haemoglobin concentration to be 14·4 g/dl; a chest x-ray film was normal. Fibreoptic endoscopy revealed localised ulceration of the left lateral oesophageal wall 28 cm from the incisors. Oesophageal mucosa above and below this lesion was normal, as were the stomach and duodenum. Biopsy specimens of the ulcer showed pyogenic granulation tissue consistent with an inflammatory ulcer. No specific treatment was given and repeat endoscopy three weeks later showed the lesion to have healed without stricture formation.

Comment

Tetracycline hydrochloride tablets have been cited as a cause of oesophageal ulceration in two American cases,[2] but both patients were young women and each had a hiatus hernia. No such hernia existed in our patient, but in all three cases the history was similar in that the offending tablet had been taken just before sleeping and the patient had awakened a few hours later with severe retrosternal pain.

Oesophageal hold-up of tablets taken without water has been shown radiologically and is particularly likely if gastro-oesophageal reflux or hiatus hernia is present and the patient assumes a supine posture immediately after ingestion.[3] Anatomically the oesophagus is indented by the aortic arch and the left main bronchus at about 24 and 28 cm respectively from the incisor teeth. In 18 cases reviewed by Collins *et al*[1] in which the ulceration was probably due to direct contact between the tablet and mucosa and in which the site of the lesion was specified, the ulcer occurred in mid-oesophagus in 12 patients. It would seem reasonable to suggest that this site is vulnerable because of the anatomy of the area. With regard to tetracycline hydrochloride tablets in particular, the likelihood of mucosal damage is enhanced by the fact that these tablets dissolve in water to produce a highly acidic solution with pH as low as 2·3.[2]

We believe that the oesophageal ulceration in our patient was caused by a direct irritant effect from prolonged contact between oesophageal mucosa and a tetracycline hydrochloride tablet at about the level at which the left main bronchus crosses the oesophagus. It is advisable for patients using this antibiotic to take the evening dose some time before retiring and with adequate volumes of fluid.

We thank Professor J M Evanson for permission to report this case.

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Severe hypoglycaemia during physical exercise and treatment with beta-blockers

Despite important metabolic effects beta-blocking agents are usually well tolerated, but during metabolic stress important perturbations may occur. For instance, treatment with a non-selective beta-blocker leads to a slower rate of recovery from insulin-induced hypoglycaemia.[1] Similarly, blood glucose concentrations are more rapidly reduced during prolonged physical exercise during treatment with a beta-blocker.[2] Serious hypoglycaemia has occurred during prolonged exercise in patients receiving treatment with propranolol[3] and pindolol.[4]

We report on a patient treated with alprenolol, a non-selective beta-blocker with intrinsic sympathomimetic activity, who developed serious hypoglycaemia during endurance exercise.

Case report

The patient was a previously healthy 61-year-old man who was accustomed to jogging for one to two hours several times a week. Hypertension had been detected six years previously and the treatment finally adjusted to alprenolol 100 mg twice daily and hydrallazine 25 mg twice daily, with which his blood pressure was well regulated. He received no other medication and did not abuse alcohol. No diabetes was known in his family.

In 1979 he went cycling for about 1½-2 hours. He became increasingly fatigued and eventually lost consciousness. He recovered slowly on the way to a local hospital, where he was given glucose with immediate improvement.

Later in 1979 he went jogging after having had only a light lunch. After about 1-2 hours he felt increasing weakness and unsteadiness and then fell and could not rise. He was found unresponsive on the ground and brought to hospital. He had sinus bradycardia with a heart rate of around 30 beat/min. Blood pressure was190/110 mm Hg. Blood glucose concentration was 1·9 mmol/l (34 mg/100 ml). He was given intravenous glucose with immediate improvement: he became orientated and gave adequate answers though could not remember what had happened after he had fallen. Heart rate stabilised around 60 beats/min and blood pressure around 160/90 mm Hg. Subsequent electrocardiography showed sinus rhythm with slightly raised ST intervals. Serum aspartate transaminase activity was slightly raised but then normalised; serum alanine transaminase activity remained normal. Lactate dehydrogenase isoenzyme electrophoresis showed increases in isoenzymes of myocardial origin. These enzyme changes combined with the discrete electrocardiographic changes suggest the possibility of a myocardial infarction, which might have developed during the hypoglycaemia. He had not felt any chest pain while jogging.

Fasting blood glucose concentrations while he was in hospital were all in the normal range (around 4·2 mmol/l (76 mg/100 ml)) as was the fasting insulin concentration (3·0 mU/l).

He was subsequently discharged from hospital taking metoprolol (a cardioselective $beta_1$-blocking agent) 100 mg twice daily and hydrallazine 25 mg twice daily. He was told to eat regularly, particularly when taking exercise. He remained well and resumed his previous level of physical activity.

Comment

In this patient one suspected and one verified episode of severe, symptomatic hypoglycaemia occurred in association with prolonged exercise. There was no evidence of an insulinoma or any other known cause of hypoglycaemia apart from the endurance exercise.

During prolonged, submaximal exercise glucose and free fatty acids are mainly taken up from the blood stream and used by the working muscles.[5] Splanchnic glucose production cannot keep pace with the increased rate of use, leading to a fall in blood glucose concentrations.[5] With beta-blockade, particularly with non-selective agents, this fall occurs more rapidly,[2] probably because of impaired glucose production in the liver and a greater dependency on glucose as substrate since the release of free fatty acids from the adipose tissue is impaired by these agents.[1]

The haemodynamic pattern in our patient (bradycardia and raised blood pressure) was similar to that reported previously in patients with hypoglycaemia receiving concomitant treatment with a non-selective beta-blocker.[1] Thus a potentially serious reaction may occur during prolonged physical exercise and concomitant beta-blockade. Patients treated with beta-blockers should be particularly careful to ingest suitable energy-giving food when participating in endurance exercise.

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Educational value of printed information for patients with hypertension

Printed information booklets are widely used to inform patients about their condition. We investigated the educational value of one such booklet among patients with high blood pressure.

Patients, methods, and results

One hundred consecutive patients attending a blood pressure clinic were randomised into two groups, one of which received a booklet about hypertension[1] and the other attended the clinic as before. The booklet explained the reasons for controlling high blood pressure, the need for continuous treatment even in the absence of symptoms, the importance of cardiovascular