sentinel disease in patients in the United States.[3] A paraneoplastic syndrome has been postulated, since direct tumour infiltration is not responsible for the generalised osteoclast activity seen in these cases.[3]

There are no epidemiological data on the prevalence of HTLV infection in Nigeria. Recently, however, HTLV antibodies were found in the sera of people from several African countries, reflecting varying levels of HTLV infection in these populations (C Saxinger *et al*, paper submitted for publication). Thus the pattern of clustering of adult T cell leukaemia in areas of endemic HTLV infection[3] is likely to prevail in Nigeria.

The two cases of HTLV associated lymphoproliferative disorders were identified during a two month prospective search at a major referral hospital for patients with clinical features of adult T cell leukaemia.[3] This suggests that this type of disease may not be rare in some areas of Nigeria. Hence the recent report that about 70% of cases of non-Hodgkin's lymphoma in Jamaica with clinically aggressive features were seropositive for HTLV infection[4] appears to be of particular relevance, since reports also indicate a similar clinical pattern of non-Hodgkin's lymphoma in Ibadan, Nigeria.[5] The unusually aggressive nature of chronic lymphocytic leukaemia in Nigeria, especially when it occurs after 50 years, has been reported[5] and a virus link to similar cases in Jamaica postulated.[4] Thus, although it is clearly too early to conclude that Nigeria represents another cluster area for HTLV associated disease, these preliminary findings are suggestive and warrant thorough follow up studies.

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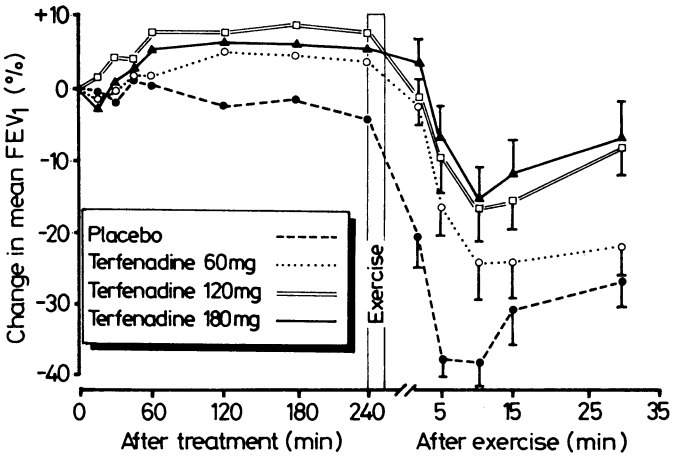
Terfenadine in exercise induced asthma

The release of histamine in exercise induced asthma remains controversial and it is also still not clear whether the raised plasma histamine concentrations observed by some workers are derived from the lung mast cells or from circulating basophils.[1] Nevertheless, asthmatic patients are well known to be hyperreactive to histamine. Histamine acts directly on H_1 histamine receptors on the bronchial smooth muscle or through stimulation of afferent vagal receptors to cause subsequent reflex bronchoconstriction. The failure of antihistamines to modify exercise induced asthma in previous studies may have resulted from inadequate blockade of H_1 histamine receptors of the airways; larger doses could not be given because of the central nervous system side effects observed with conventional antihistamines.[2 3] Terfenadine is a potent H_1 histamine receptor antagonist and as it does not cross the blood brain barrier it is devoid of major central nervous system side effects. To examine a dose response effect of antihistamines I compared the effect of placebo with that of terfenadine 60 mg, 120 mg, and 180 mg given orally to 10 patients with exercise induced asthma in a double blind study.

Patients, methods, and results

I studied 10 patients aged 16-50 years with extrinsic and reproducible exercise-induced asthma. Patients taking oral or aerosol corticosteroids were excluded. Sodium cromoglycate and bronchodilator drugs were discontinued for 24 hours before each test. Forced expiratory volume in one second (FEV_1) was recorded on a dry wedge spirometer (Vitalograph). Exercise testing consisted of steady state running on an inclined treadmill (10°) for up to eight minutes. Speed was adjusted so that the pulse rate at the end of exercise was at least 170-180/min. The same setting and duration were used for each test in any one patient. Room temperature on study days varied from 20 to 22°C and the relative humidity from 40 to 60%. The study was carried out in a random double blind fashion using placebo and terfenadine 60 mg, 120 mg, and 180 mg given orally. Spirometry was repeated 30, 45, 60, 120, 180, and 240 minutes after treatments, then at 2, 5, 10, 15, and 30 minutes after exercise. The exercise tests were performed four hours after treatment as plasma concentrations of terfenadine reach a peak at this time. The results of the tests were expressed as mean percentage fall in FEV_1 from the baseline at 240 minutes after treatment and analysed with Student's *t* test.



The effect of placebo and terfenadine on the mean baseline FEV_1 (SEM) and mean percentage falls in FEV_1 after exercise in 10 patients with asthma.

The mean baseline values of FEV_1 (SEM) before treatments on four days of testing were: 3·16 (0·26) l, 3·20 (0·26) l, 3·08 (0·28) l, and 3·09 (0·23) l and no statistical difference was noted. Although terfenadine produced a small bronchodilator effect this did not reach statistical significance with any of the doses used. After exercise the mean maximal percentage falls in FEV_1 (SEM) after placebo and terfenadine 60 mg, 120 mg, and 180 mg were 32·9 (4·8)%, 27·6 (5·0)%, 22·8 (4·1)%, and 21·2 (4·6)% respectively 10 minutes after exercise (see figure). Terfenadine at 120 mg ($p < 0·02$) and 180 mg ($p < 0·01$) offered significant protection compared with placebo. There was considerable variation in response to terfenadine between patients: three patients had good protection, four showed partial protection, and in three terfenadine had no effect at any of the doses. The non-responders were all over the age of 40. The only side effect observed was dryness of mouth. None of the patients complained of drowsiness or tiredness.

Comment

Terfenadine given orally in a single dose of 120 mg and 180 mg offered significant protection against exercise induced asthma in the patients studied, whereas 60 mg of terfenadine showed no significant inhibition. Terfenadine is a potent antagonist of histamine H_1 receptor mediated responses both in vitro and in vivo and does not possess anticholinergic, antiserotonin, or antiadrenergic properties. It antagonises histamine in two ways: by competitive blockade at low concentrations and by a non-equilibrium blockade at higher con-

centrations.[4] The inhibitory effect of terfenadine in this study is consistent with observations reported with the inhaled antihistamine clemastine in exercise induced asthma.[5] Obviously more detailed experimental and clinical studies will be required before terfenadine can be recommended for management of asthmatic patients.

I thank Mrs Rita Jack for technical help and Dr J D F Lockhart of Merrell Pharmaceuticals Limited for supplies of the drug for the study.

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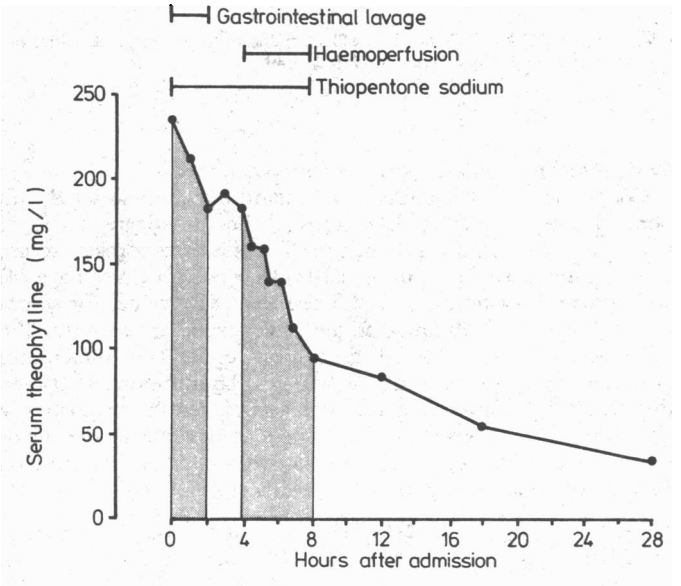
Treatment of severe poisoning with slow release theophylline

Treatment of severe poisoning with slow release theophylline remains a problem clinically, as fatal concentrations of theophylline may occur several hours after oral ingestion[1] and continuing absorption of the drug causes a secondary rise in concentrations of theophylline even after effective haemoperfusion has been performed.[2] We report on a patient treated with gastrointestinal lavage and haemoperfusion.



Coma (grade)	III	III	II	I	I	0	0	0
Convulsions	+++	+	0	0	0	0	0	0
Ectopic beats	+++	+	0	0	0	0	0	0
Heart rate (beats/min)	180	144	145	156	135	126	125	120
Cardiac output (l/min)		8·6	10·2	8·9	8·6	8·8	8·5	8·0

Serum theophylline concentrations and response to treatment in 20 year old woman with severe poisoning with slow release theophylline.

Case report

A healthy 20 year old woman was admitted to hospital 12 hours after taking 100 capsules each containing 250 mg anhydrous theophylline as a slow release preparation in micropellets. On admission she was comatose and had non-purposive protective reflexes (grade III coma). Vomiting, generalised seizures, and ventricular ectopic beats were also present. Laboratory investigation gave normal results apart from mild hypokalaemia (serum potassium concentration 3·4 mmol(mEq)/l) and moderate rhabdomyolysis (creatine phosphokinase activity 4·95 IU/l), which was probably due to the convulsions. After oral intubation a double lumen gastric tube was inserted and gastrointestinal lavage performed with 4 l iso-osmotic lavage fluid containing 2 g activated charcoal/l.[3] Gastrointestinal lavage was stopped after two hours, when theophylline micropellets were found in a stool. Her convulsions were treated by a continuous infusion of thiopentone sodium at an infusion rate of 200 mg/h. Four hours after her admission haemoperfusion with activated charcoal was started, and this continued until her clinical condition had improved four hours later. Neurological examination showed grade II coma with purposive protective reflexes. The seizures and ventricular ectopic beats had resolved. After 20 hours she was well and cooperative, and extubation was performed without any problems. After five days she was discharged from hospital.

Serum theophylline concentrations were analysed retrospectively by high performance liquid chromatography using the method described by Naish.[4] The figure shows that her serum theophylline concentration was 236 mg/l on admission and 182 mg/l after gastrointestinal lavage. It increased slightly to 189·7 mg/l and after haemoperfusion had fallen to 94·6 mg/l. Thereafter it decreased to 26·4 mg/l 28 hours after admission. The estimated theophylline half life was 3¾ hours during gastrointestinal lavage, 3½ hours during haemoperfusion, and 13½ hours after haemoperfusion. The efficacy of haemoperfusion was estimated by measuring theophylline concentrations in samples taken before (arterial) and after (venous) blood had been passed through the charcoal column. Samples were obtained every 30 minutes. The extraction rate ((arterial-venous)/arterial) ranged from 0·77 to 0·97, which indicated an excellent clearance of theophylline during haemoperfusion.

Comment

Serum theophylline concentrations fell continuously during gastrointestinal lavage and haemoperfusion, indicating that both procedures were effective in protecting the patient from fatal concentrations of theophylline and a secondary rise in concentrations of theophylline after haemoperfusion. No electrolyte disturbances were seen during gastrointestinal lavage. Although we did not measure the theophylline content of the micropellets in the stool, we assume that considerable amounts were removed by gastrointestinal lavage as after this procedure no appreciable secondary rise in serum theophylline concentration occurred. Haemoperfusion gave an excellent rate of extraction of theophylline, and there were no side effects apart from mild haemolysis and a slight fall in the platelet count. We therefore conclude that gastrointestinal lavage and haemoperfusion are effective in treating severe poisoning with slow release theophylline.

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