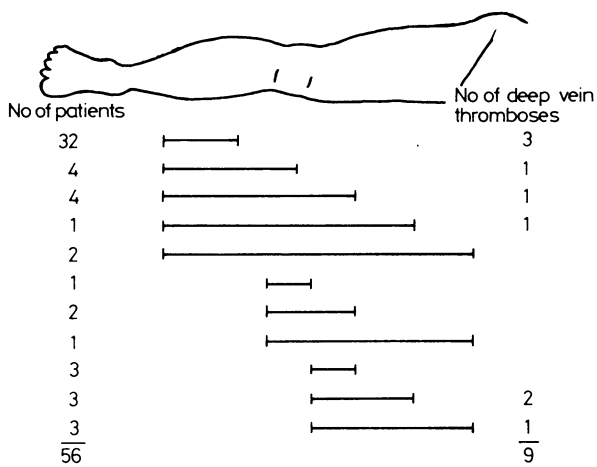
thrombosis. All phlebograms were interpreted by the same radiologist, and recent thrombosis was diagnosed when there were direct signs of thrombus tap. Such signs were present in all patients but one, in whom the diagnosis was based on indirect signs.

All patients were from Malmö, and at follow up after three to five years the local tumour register was checked to establish whether any patients had developed malignant diseases.

Results

At diagnosis the median duration of symptoms was three days (range one day to six months; one patient had had symptoms for six months, all the others for under one week). The figure shows the site of the lesions, most being below the knee. Four were of the migrating type, and all were in the great saphenous vein. Left sided thrombophlebitis was present in 40 patients and right sided in 16 ($p<0.05$). Thirty eight patients had varicose veins of different extension and severity. The patients with varicose veins had a median age of 58 (range 29-78) years and the patients without 65·5 (26-83) years. A history of thromboembolism was established in 19 (50%) with varicose veins and six (33%) without.



Anatomical site of superficial thrombophlebitis and distribution of deep vein thrombosis.

Phlebographic acute deep vein thrombosis was seen in nine patients, of whom eight did not have varicose veins. Thus the prevalence of deep vein thrombosis in patients without varicose veins was 44%, compared with 2·6% in those with ($p<0.01$). The site of the thrombophlebitis did not influence the presence or absence of deep vein thrombosis (figure). There were no pulmonary emboli. None of the patients with varicose veins had developed malignant disease at follow up, whereas two (11%) of the patients without varicose veins had (one mammary cancer and one polycythaemia vera) ($p<0.05$). Both the patients with malignancy had had deep vein thrombosis of the whole leg on phlebography initially.

Comment

This study was undertaken to establish the prevalence of deep vein thrombosis in patients presenting with symptoms and signs of superficial thrombophlebitis. In patients with varicose veins this combination is rare, but in patients without varicosities deep vein thrombosis is so common that phlebography should be strongly recommended. Thus about a quarter of patients with thrombophlebitis should undergo phlebography. Our patient with varicose veins and deep vein thrombosis had had deep vein thrombosis previously. The site of thrombophlebitis does not indicate whether deep vein thrombosis should be suspected. Thrombophlebitis of the migrating type was present in 7% of patients, none of whom had deep vein thrombosis.

The common occurrence of varicose veins in patients with superficial thrombophlebitis has been pointed out previously.[3,4] Edwards discussed the association between migrating thrombophlebitis and carcinoma on the basis of 23 published cases and six of his own.[5] As superficial thrombophlebitis is now considered to be part of a paraneoplastic syndrome our patients were followed up for three to five years: two of the 18 patients without varicosities, both of whom had deep vein thrombosis, developed malignancies. The possibility of malignancy must therefore be kept in mind, at least when superficial thrombophlebitis is combined with deep vein thrombosis.

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Restless leg syndrome and rheumatoid arthritis

The restless leg syndrome is an unpleasant, often distressing, dysaesthesia of the legs brought on by inactivity and temporarily relieved by movement.[1] Symptoms may be effectively treated with clonazepam.[2] We assessed the prevalence of the restless leg syndrome in patients with rheumatoid arthritis, patients with osteoarthritis, and healthy controls.

Subjects, methods, and results

We studied three groups of subjects: 70 consecutive patients admitted to hospital with classical or definite rheumatoid arthritis (mean age 59 years, range 21-81; 10 men, 60 women); 30 patients in hospital with osteoarthritis, matched as far as possible for immobility and predominantly suffering from osteoarthritis of the knees or hips, or both (mean age 68 years, range 30-83; four men, 26 women); and 70 normal controls from the general population matched for age and sex with the group with rheumatoid arthritis.

A standard questionnaire was used to assess dysaesthetic symptoms, and all subjects with such symptoms were examined to exclude clinically apparent polyneuropathy. Assessments were made independently by two observers. As the restless leg syndrome is a periodic condition, the presence of any symptoms in the preceding year was ascertained. In the group with rheumatoid disease activity was investigated by assessing morning stiffness, the number of inflamed joints, and the acute phase response to inflammation (erythrocyte sedimentation rate and C reactive protein concentration). Results were analysed by Student's t test or χ^2 test with Yates's correction. The prevalence of the restless leg syndrome was significantly higher in the group with rheumatoid arthritis compared with the group with osteoarthritis and the control group (table). No significant difference was observed between the group with osteoarthritis and the controls. Two patients with rheumatoid arthritis were excluded as the assessors disagreed over whether their symptoms were characteristic of the syndrome.

All subjects with symptoms of the restless leg syndrome were women. The age distribution of these patients in the group with rheumatoid arthritis closely followed that of the group as a whole. In eight patients symptoms were sufficiently severe for them to lose more than an hour's sleep regularly. Fourteen patients had sought a medical opinion about their dysaesthesia, but in no case was an explanation or treatment given. Within the group with rheumatoid arthritis there was no association between the presence of symptoms at the time of questioning, or within the preceding year, and any clinical or laboratory index of disease activity. In addition, all the patients with rheumatoid arthritis with the restless leg syndrome could dissociate their dysaesthesia from joint stiffness and pain and had not observed a worsening of their dysaesthesia in relation to temporary flares of synovitis.

Comment

The prevalence of the restless leg syndrome among patients with rheumatoid arthritis in hospital is high (30%) and significantly different

Prevalence of dysaesthetic symptoms characteristic of the restless leg syndrome

	Dysaesthesia		
	Present*	Absent	Prevalence (%)
Rheumatoid arthritis (n=70)	21	49	30
Osteoarthritis (n=30)	1	29	3
Controls (n=70)	4	66	6

*Defined as present if patient had had characteristic symptoms in previous year.
Significance: rheumatoid arthritic *v* controls, $p<0.01$; rheumatoid arthritic *v* osteoarthritis, $p<0.01$; oesteoarthritis *v* controls, NS.

from that among normal controls and patients with osteoarthritis. Immobility per se does not seem to be a primary factor as the patients with osteoarthritis did not show an increased prevalence compared with the control group.

Certain medical conditions, including pure iron deficiency, uraemia, pregnancy, gastrectomy, and carcinoma, are associated with the syndrome, providing potential clues about its mechanism.[3] Interestingly, these conditions lead to either pure iron deficiency or anaemia of chronic disease, and anaemic patients experience more severe symptoms.[4] As patients with rheumatoid arthritis characteristically develop the anaemia of chronic disease the increased prevalence of the syndrome observed in the group with rheumatoid arthritis may relate to this secondary complication.[5]

The combination of the restless leg syndrome and rheumatoid arthritis contributes considerably to discomfort and anxiety, and in our experience few doctors are aware of this condition.

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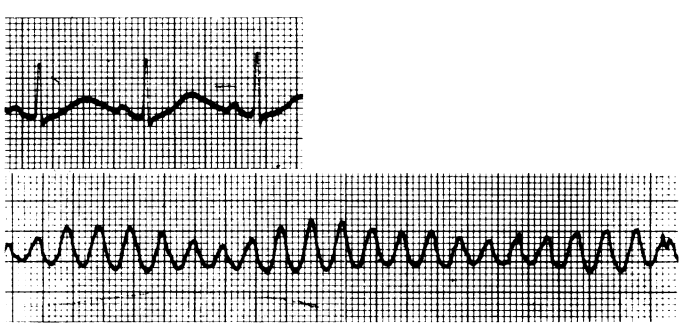
Torsade de pointes after astemizole overdose

Astemizole is a comparatively new long acting antihistamine (H_1) preparation. Histamine receptors are present in the heart, though their function is not clear.[1] No case of self poisoning with astemizole has been recorded. I report a case of acute ventricular arrhythmia that occurred after astemizole overdose.

Case report

A 16 year old girl presented to the accident and emergency department five hours after swallowing 20 tablets of astemizole (total dose 200 mg), which had been prescribed for allergic rhinitis (10 mg daily). She had vomited several times and claimed not to have taken any other medication or substance. Examination showed nothing abnormal. As she was still vomiting gastric lavage was not performed and she was admitted to the ward for overnight observation.

Seven hours after the overdose she suddenly became unconscious and was found to have no palpable cardiac output. A sharp blow to the sternum restored output and the electrocardiogram monitor confirmed sinus rhythm. She regained consciousness and was transferred to the intensive therapy unit. Pulse was 80/min and regular and blood pressure 100/60 mm Hg supine. There were no signs of cardiac failure or decompensation. One hour later she developed a spontaneous ventricular tachyarrhythmia requiring DC cardioversion with 150 J. Bolus intravenous lignocaine (100 mg) was given and an intravenous infusion of lignocaine begun at 4 mg/min for 20 minutes, reduced in steps of 1 mg/min every 40 minutes.



TOP: Standard lead II of a 12 lead electrocardiogram recorded on admission to intensive therapy unit showing Q-T_c interval 0·65 s (paper speed 25 mm/s). BOTTOM: Strip of ventricular tachyarrhythmia characteristic of torsade de pointes (paper speed 25 mm/s).

Investigation showed a haemoglobin concentration of 134 g/l and a normal white cell count. Serum biochemical values were normal, in particular potassium 4·0 mmol(mEq)/l, corrected calcium concentration 2·7 mmol/l (10·8 mg/100 ml), and albumin 43 g/l. Blood and urine sent for analysis to both the poisons unit at New Cross Hospital, London, and the pharmaceutical company marketing astemizole showed results consistent with astemizole overdose. Despite the lignocaine infusion further episodes of ventricular tachyarrhythmia occurred. An amiodarone infusion was therefore substituted with a loading dose of 300 mg followed by an infusion rate of 300 mg over one hour. This also failed to prevent episodes of ventricular tachyarrhythmia.

A 12 lead electrocardiogram recorded on admission to the intensive therapy unit and before the administration of antiarrhythmic agents showed a prolonged Q-T interval (figure). Q-T interval corrected for heart rate (Q-T_c) was 0·65 s (normal 0·36-0·42 s). Recorded strips of ventricular tachyarrhythmia showed the changing morphology of ventricular complex characteristic of torsade de pointes (figure). An isoprenaline infusion was begun at an initial dose of 1 μg/min, which shortened the Q-T_c interval to 0·58 s. Seventeen episodes of ventricular tachycardia occurred before the use of isoprenaline, 11 of which did not revert spontaneously or respond to a blow over the sternum and thus required DC cardioversion. One further episode occurred during the isoprenaline infusion. This was controlled by increasing the infusion rate.

Over the next five days the isoprenaline infusion was gradually reduced, the dose being governed by the Q-T_c interval. There were no further episodes of torsade de pointes. Serial electrocardiograms showed the Q-T_c interval to have reduced to 0·41 s before the patient left hospital. She was discharged home with advice not to take astemizole in the future. Follow up in the outpatient department confirmed that she was well with a normal Q-T_c interval.

Comment

Torsade de pointes is a recognised complication of treatment with antiarrhythmic agents, whose mode of action includes prolongation of the Q-T interval. Such drugs include membrane stabilisers (for example, lignocaine, flecainide); sotalol,[2] a β blocker with additional group III antiarrhythmic properties; and amiodarone. There are no reports, however, of torsade de pointes occurring after the use of either anti-H_1 or anti-H_2 antihistamines.

Astemizole is currently used in doses of up to 100 mg/day for mastocytosis. The events after the overdose in this patient (with 200 mg) question the safety of treatment with high dose astemizole.

I thank Dr P L Golding for permission to report this case.

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Exposure to quinalbarbitone sodium in pharmaceutical workers

Few studies have been reported of exposure to and absorption of drugs among operatives in the pharmaceutical industry. All too often the measures taken to prevent contamination of the product are believed to protect the worker also. In workers manufacturing oral contraceptive pills, however, gynaecomastia and menstrual disorders due to the absorption of ethinyloestradiol have been recorded,[1] as has adrenocortical suppression in workers making synthetic glucocorticosteroids.[2] We report finding a group of workers manufacturing quinalbarbitone sodium who were exposed to the drug and had absorbed measurable amounts, a hazard that would have been overlooked in the absence of biological testing.

Methods and results

A small pharmaceutical company manufactured quinalbarbitone sodium capsules using semiautomatic encapsulating machines. Filling the machine hoppers with quinalbarbitone sodium powder and inserting empty capsules into moulds were performed by hand. A female process worker developed a rash on