The incidence of positive swabs showed a linear increase with the number of swabs taken; being 58% in the 31 patients from whom one swab was taken and increasing to 89% in the 45 patients from whom six or more swabs were taken. Of the 82 patients from whom more than two swabs were taken, 68 were positive for *C albicans* and four for other species of candida; negative results were interspersed among positive ones irrespective of treatment. The incidence of oral candida was unaffected by admission to the hospice (69% of patients) or by the wearing of dentures (77% of patients).

The table shows that there was a significant correlation between white lesions of the mouth and candida ($p<0{\cdot}01$; 95% confidence interval $+0{\cdot}08$ to $+0{\cdot}42$). No correlation was shown between candida and any other mouth symptom. No significant improvement occurred in the symptoms or signs of the 43 patients who received oral nystatin. A total of 510 swabs were taken; 226 grew *C albicans*, 62 grew other species of candida, and 222 did not grow any candida. Statistical analysis of these results against symptoms and drugs was invalid as these were not strictly independent swabs.

Comment

The observed prevalence of candida in 56% of all swabs correlates with results of previous studies,[4] but a high proportion (23%) of positive swabs were taken in the presence of white curd like lesions. Staphylococcal white lesions of the mouth occurred in two patients.[5] Swabs from patients receiving oral morphine mixture showed a slightly lower prevalence of candida, which may have been an effect of preservative in the mixture on the mouth flora.

These results do not confirm that oral candida is associated with symptoms or signs in the mouth, although oral candidiasis is common among the terminally ill. Prophylactic antifungal treatment has not been beneficial in previous studies,[2] and oral candida and symptoms were unaffected by nystatin in this study. Candidal infection may be the result rather than the cause of mouth problems, indicating that general mouth hygiene is more important than antifungal treatment.

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1 Arendorf TM, Walker DM. Oral candidal populations in health and disease. *Br Dent J* 1979;**147**:267-72.
2 Barrett AP. Evaluation of nystatin in prevention and elimination of oropharyngeal candida in immunosuppressed patients. *Oral Surg* 1984;**58**:148-51.
3 Donnelly JP, Starke LD, Galton DA, *et al.* Oral ketoconazole and amphotericin B for the prevention of yeast colonisation in patients with acute leukaemia. *J Hosp Infect* 1984;**5**:83-91.
4 Shipman B. Clinical evaluation of oral candida in cancer chemotherapy patients. *J Prosthet Dent* 1979;**41**:63-7.
5 Tydesley WR, Rotter E, Sells RA. Bacterial thrush like lesions in the mouth in renal transplant patients. *Lancet* 1977;i:485-6.

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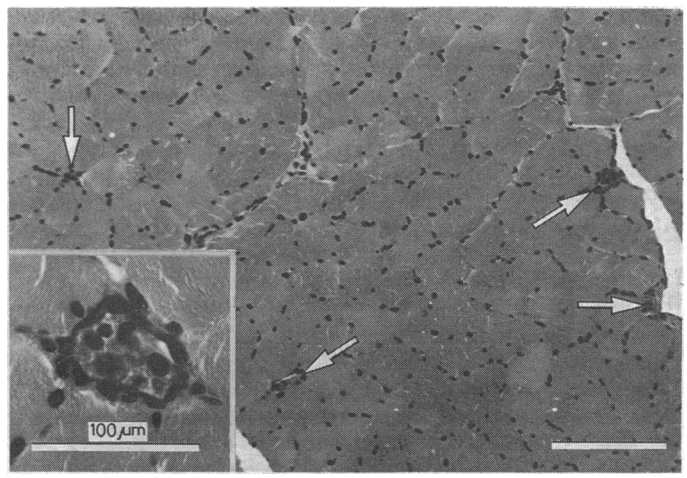
Myopathy after short term administration of procainamide

Myopathy as a direct result of short term intravenous or oral treatment with procainamide has not been previously recorded. We report such a case of severe generalised myopathy confirmed by electromyography and histological examination.

Case report

A 51 year old Nigerian man presented with acute inferior myocardial infarction. Ventricular tachycardia and ventricular fibrillation developed, and over the first six hours he required direct current conversion 24 times despite bolus doses and an infusion of lignocaine (total dose 930 mg over five hours). Throughout this period he was mechanically ventilated. Because of recurrent ventricular fibrillation procainamide was started, with an intravenous bolus of 250 mg followed by an infusion of 3 mg/min. Sinus rhythm was established, and he was extubated. Attempts to reduce the rate of infusion of procainamide resulted in ventricular tachycardia. Oral procainamide (Durules 1·5 g twice daily) was started and the infusion stopped 24 hours later. Total serum creatine kinase activity was raised at 9849 units. Isoenzyme fractions confirmed this to be of skeletal muscle origin.

Four days after admission he complained of weakness of the arms and legs and developed involuntary dystonic arm movements, ataxia, and paradoxical chest movements. Respiration deteriorated, necessitating reventilation; oral procainamide was stopped and an infusion restarted. The skeletal muscle isoenzyme activity remained >9000 units. Normal blood gas tensions were easily achieved during mechanical ventilation (oxygen tension 16·8 kPa (126 mm Hg), carbon dioxide tension 5·3 kPa (40 mm Hg) on 50% oxygen). An electrocardiogram showed prolongation of the QRS interval (initially 0·08 s, extending to 0·12 s), and the blood procainamide concentration was 48 mg/l (normal 4-10 mg/l). The procainamide infusion was stopped and lignocaine substituted at 2 mg/min (blood concentration 3 mg/l). The neurological signs gradually improved, and he was extubated. Creatine kinase activity rapidly returned to normal.



Transverse section of vastus lateralis muscle showing myophagic fibres. Inset: Detail of myophagic fibre. (Haematoxylin and eosin.)

Electromyography showed a sensory polyneuropathy and myopathy. Biopsy of the right vastus lateralis muscle showed acute myopathic features ranging from hyaline eosinophilic sarcoplasm to myophagia. There was no evidence of vasculitis or primary inflammatory myopathy (figure). Myocardial biopsy specimens were normal.

He gradually recovered and was discharged taking tocainide 600 mg twice daily. Six weeks later he continued to complain of breathlessness but had no evidence of heart failure. Results of tests of respiratory muscle function were below the lower limit of normal but two weeks later were normal, subsequent left vastus lateralis biopsy showed only minimal abnormality associated with an advanced stage of degeneration of muscle fibres.

Comment

Several criteria for reporting adverse drug reactions have been recommended, including timing, associated conditions, and rechallenge or "dechallenge."[1] According to these criteria, our patient's myopathy was probably an adverse reaction to procainamide. The onset of the neurological abnormalities was temporally related to the high procainamide concentrations and to other recognised toxic manifestations of procainamide, such as prolongation of QRS interval and cerebellar ataxia.[2] Clearly, rechallenge could not be performed. The patient improved rapidly, however, when procainamide was stopped and did not relapse when tocainide or lignocaine was introduced.

The dosage of procainamide administered was within that recommended by the manufacturers. The high serum concentration achieved was probably due to several factors, including renal impairment (after the hypotensive period associated with multiple cardiac arrests) and heart failure.

Toxicity is common when procainamide concentrations are above 16 mg/l[3] and includes headaches, insomnia, dizziness, ataxia, and hallucinations. Myopathy and myositis have been reported after long term, but not short term, ingestion of procainamide.[4] In this case biopsy showed changes of acute or subacute infarction of the muscle with no evidence of the changes similar to those of collagen disease that are often a complication of procainamide.

Multiple defibrillations may cause muscle damage, but this is only localised.[5] We believe, therefore, that this myopathy was due to a direct toxic action of procainamide. The drug's manufacturers and the Committee on Safety of Medicines have not received any similar reports.

1 Jones JG. Criteria for general reports of suspected adverse drug reactions. *Clinical Pharmacy* 1982;**1**:554-5.
2 Schwartz AB, Klasner SC, Yee S, Turchyn M. Cerebellar ataxia due to procainamide toxicity. *Arch Intern Med* 1984;**144**:2260-1.

3 Koch-Weser J, Klein SW. Procainamide dosage schedules, plasma concentrations, and clinical effects. *JAMA* 1971;**215**:1454-60.
4 Fontiverus ES, Cumming WJK, Hudson P. Procainamide induced myocitis. *J Neurol Sci* 1980;**45**:143-7.
5 Smith GT, Beeuwkes R, Tomkiewicz ZM, Tadarki A, Lown B. Pathological changes in skin and skeletal muscle following alternating current and capacitor discharge. *Am J Pathol* 1965;**47**:1-17.

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Twenty four hour ambulatory electrocardiography in patients with chronic atrial fibrillation

Ambulatory electrocardiography is widely used to detect paroxysmal cardiac arrhythmias.[1] Asymptomatic arrhythmias may be detected, but their clinical importance cannot be assessed without comparative findings in healthy people.[1,2] Little attention has been paid to ambulatory electrocardiography in patients with established atrial fibrillation, in whom unexplained symptoms may prompt a search for a superimposed arrhythmia.

Patients, methods, and results

Seventy patients with chronic atrial fibrillation were investigated using 24 hour ambulatory electrocardiography (Oxford Medilog or Reynolds Tracker recorder, Reynolds Pathfinder 2 analyser). None had symptoms suggesting additional arrhythmias. In all patients the atrial fibrillation was "controlled" in that a change in treatment was not considered to be necessary. Satisfactory recordings were obtained in 66 patients (24 men and 42 women aged 38-94 (mean 63) years). Forty four patients had mitral valve disease (12 had undergone valve replacement), and the remainder had various cardiac conditions. Suppressant drugs comprised digoxin (62·5-750 μg/day) in 59 cases, β blocking drugs in eight, and verapamil in one. Most patients took additional drugs such as diuretics and anticoagulants. Heart rate was recorded in the clinic and blood taken for assay of serum digoxin concentration.

The figure shows the frequency distribution of fastest and slowest heart rates, longest pauses, and ventricular arrhythmias. The fastest heart rate occurred during the daytime in all patients and the slowest at night in 63 of 66. The difference between fastest and slowest rates in individual patients ranged from 35 to 141 beats/min (mean 86). Heart rate measured in the clinic correlated poorly with fastest heart rate ($r=0·51$) and slowest heart rate ($r=0·37$). Only 16 of 27 patients with ambulatory heart rates above 140 beats/min had heart rates in the clinic above 90 beats/min, and in seven of 23 with rates in the clinic above 90 beats/min ambulatory rates did not exceed 140 beats/min. Daytime pauses of more than 2·0 seconds occurred in 16 of the 66 patients. No patient had daytime pauses longer than 2·8 seconds.

In the 59 patients taking digoxin there was no significant relation between serum digoxin concentration and fastest heart rate, slowest heart rate, duration of pauses, or frequency of ventricular arrhythmias. Five patients with serum digoxin concentrations above 2·0 μg/l but without clinically suspected digitalis toxicity could not be identified on the basis of bradycardia, pauses, or ventricular arrhythmias. No patient reported symptoms related to the documented changes in heart rate and arrhythmias.

Comment

Our results show the extremes of heart rate, duration of pauses, and frequency of ventricular arrhythmias detected by ambulatory electrocardiography in patients with clinically controlled atrial fibrillation. Recordings from symptomatic patients should be considered in the light of these findings before they are used as the basis for introducing or changing treatment.

Nocturnal pauses of up to 4·0 seconds and daytime pauses of up to 2·8 seconds may not require cardiac pacing unless they coincide with symptoms. Pauses, nocturnal bradycardia, and ventricular arrhythmias were common in patients who had no clinical or biochemical evidence of digoxin toxicity, and they should not be used to determine digoxin dosage. Intuitive selection of the dose of digoxin, however, often fails to achieve desired serum digoxin concentrations.[3] Resting heart rate is an unreliable indicator of both digoxin concentration and control of heart rate during exercise.[4,5] Heart rate during exercise is a major determinant of symptoms such as breathlessness, but the best method of assessing control of heart rate on exercise is uncertain. Standardised exercise tests allow comparison of the heart rate responses to certain levels of exercise but take no account of the different exercise requirements of people during daily activities. Ambulatory electrocardiography can assess variation in heart rate during daily life, but the optimal extremes of heart rate may differ between patients. Nevertheless, this technique may be useful for comparing the control of heart rate by different drugs in individual patients with atrial fibrillation.

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1 Petch M. Lessons from ambulatory electrocardiography. *Br Med J* 1985;**291**:617-9.
2 Bjerregaard P. *Continuous ambulatory electrocardiography in healthy adult subjects over a 24-hour period*. Copenhagen: Mohn Aps; 1983.
3 Dodds SM, Nicholson PW, Rodgers EM, Mawer GE, Kenyon WI. Digoxin prescribing: an evaluation of clinical judgement. *Br Med J* 1978;ii:668-9.
4 Chamberlain DA, White RJ, Howard MR, Smith TW. Plasma digoxin concentrations in patients with atrial fibrillation. *Br Med J* 1970;iii:429-32.
5 Redfors A. Digoxin dosage and ventricular rate at rest and exercise in patients with atrial fibrillation. *Acta Med Scand* 1971;**190**:321-33.

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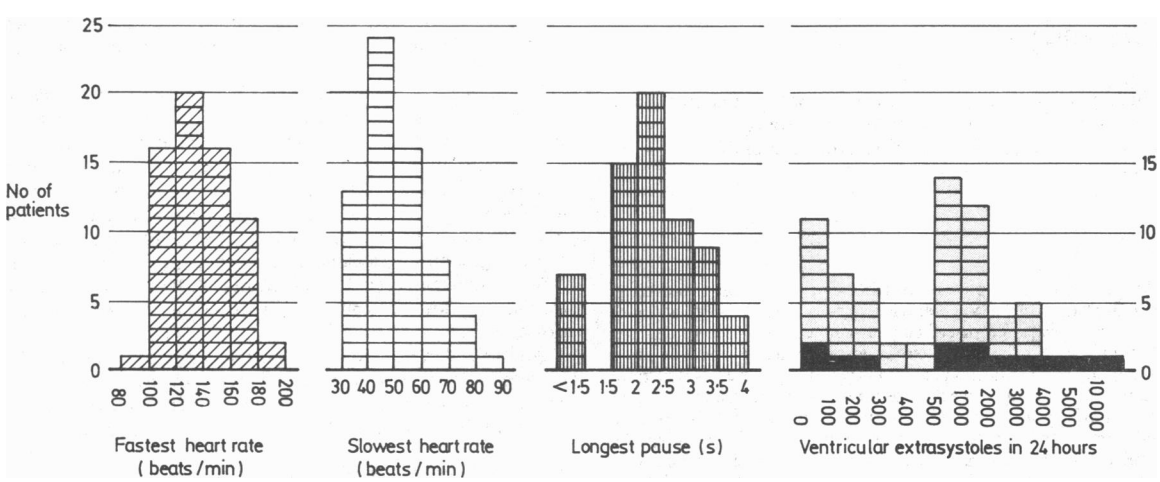

Heart rates, longest pauses, and ventricular arrhythmias during 24 hour electrocardiography in 66 patients with chronic atrial fibrillation. (Solid areas in graph of ventricular arrhythmias indicate patients with tachycardia.)