effect shown in highly selected subgroups of patients cannot, however, be extrapolated to other groups of patients, although other studies, including those with a wider, less selected population,[9 12] indicate that even low-risk patients may profit from long-term beta-adrenoceptor blockade.

There has been much debate about analysis, presentation, and interpretation of beta-blocker post-infarction trials.[28-30] We have presented our data so that end-point differences based on both the "intention-to-treat" and "in-trial" differences can be calculated, but we have chosen to analyse the results according to intention to treat. We hope that our results will make a small contribution to an important debate.

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SHORT REPORTS

Sinus arrest during treatment with amiodarone

Amiodarone (Cordarone X) is widely used for treating resistant cardiac tachyarrhythmias and is generally assumed to have few limiting side effects.[1] We report two cases of sinus arrest, with depressed automaticity of escape foci, that required pacing after administration of amiodarone.

Case reports

Case 1—A 61-year-old man with a remote anteroseptal myocardial infarction presented with recurrent sustained ventricular tachycardia. A week before admission a permanent ventricular pacemaker had been inserted for transitory complete heart block. Electrocardiography showed right bundle-branch block, left posterior hemiblock, and evidence of an old anteroseptal infarction. When not paced his rhythm was sinus with first-degree atrioventricular block. Comprehensive intracardiac electrophysiological study disclosed a corrected sinus node recovery time of 220 ms (normal <525 ms), A-H interval 120 ms (normal 60-140 ms), and H-V interval 85 ms (normal 30-55 ms). Two morphologically distinct types of ventricular tachycardia could be induced. Quinidine, procainamide, propranolol, digoxin, disopyramide, mexiletine, and several combinations of these failed to suppress the tachycardia. Amiodarone 600 mg daily was started. Six weeks later ventricular extrastimulation induced poorly tolerated ventricular tachycardia. In the meantime no spontaneous ventricular tachycardia had occurred and ambulatory electrocardiography showed complete suppression of ventricular ectopic activity. At that time no sinus node activity was present and the patient was pacemaker-dependent without an escape focus. Apart from amiodarone the only known cardioactive agents that he was taking were metoprolol and digoxin, both in conventional dosage and for several months before these studies. Electrolyte concentrations were normal. The patient was discharged taking these agents as no non-pharmacological treatment was indicated.

Case 2—A 67-year-old man with a history of myocardial infarctions in 1968 and 1977 presented with recurrent drug-resistant ventricular tachycardia that required numerous cardioversions. He was in congestive cardiac failure and had severe peripheral vascular disease and mild chronic renal failure. Electrocardiography showed normal sinus rhythm with an intraventricular conduction defect and evidence of old anteroseptal and inferior infarctions. Electrophysiological study showed a corrected sinus node recovery time of 270 ms, A-H interval 125 ms, and H-V interval 80 ms. Sustained ventricular tachycardia (160/min) was induced by ventricular extrastimulation. Serial drug testing with many agents failed to suppress his arrhythmia. Treatment was initiated with amiodarone 1 g daily. Ventricular ectopy was suppressed, and nine days later repeat ventricular stimulation disclosed inducible ventricular tachycardia (125/min). Amiodarone was continued, and two days

later the patient was in slow junctional rhythm (35 beats/min), hypotensive, and poorly perfused. He responded promptly to ventricular pacing. At the time his other treatment included digoxin, frusemide, and isosorbide dinitrate. There was no electrolyte abnormality. No rise in enzyme activity occurred, and his serum digoxin concentration was 2·2 mg/l. Amiodarone was withdrawn and intermittent sinus node activity returned next day; within two days periods of normal sinus rhythm were noted. Spontaneous ventricular tachycardia requiring cardioversion recurred, however, so an atrioventricular sequential pacer was inserted and amiodarone reinstituted. As no other treatment was suitable for this patient he was discharged with this regimen.

Comment

Sinus bradycardia and sinoatrial block have been described as side effects of amiodarone,[2 3] but to our knowledge sinus arrest has not been reported and no such case has been notified either to Sanofi Inc, the US agent for the manufacturers of the drug, or to the Food and Drug Administration. Both patients had normal sinus node automaticity as shown by corrected sinus node recovery times within the normal range, this being considered the best available test of sinus node automaticity and possibly of overall node function.[4]

Amiodarone depressed automaticity by inhibiting phase 4 depolarisation in the sinus node of rabbits in vitro,[5] and these observations suggest that such a mechanism may account for this potentially lethal complication in susceptible patients.

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Alveolitis after treatment with amiodarone

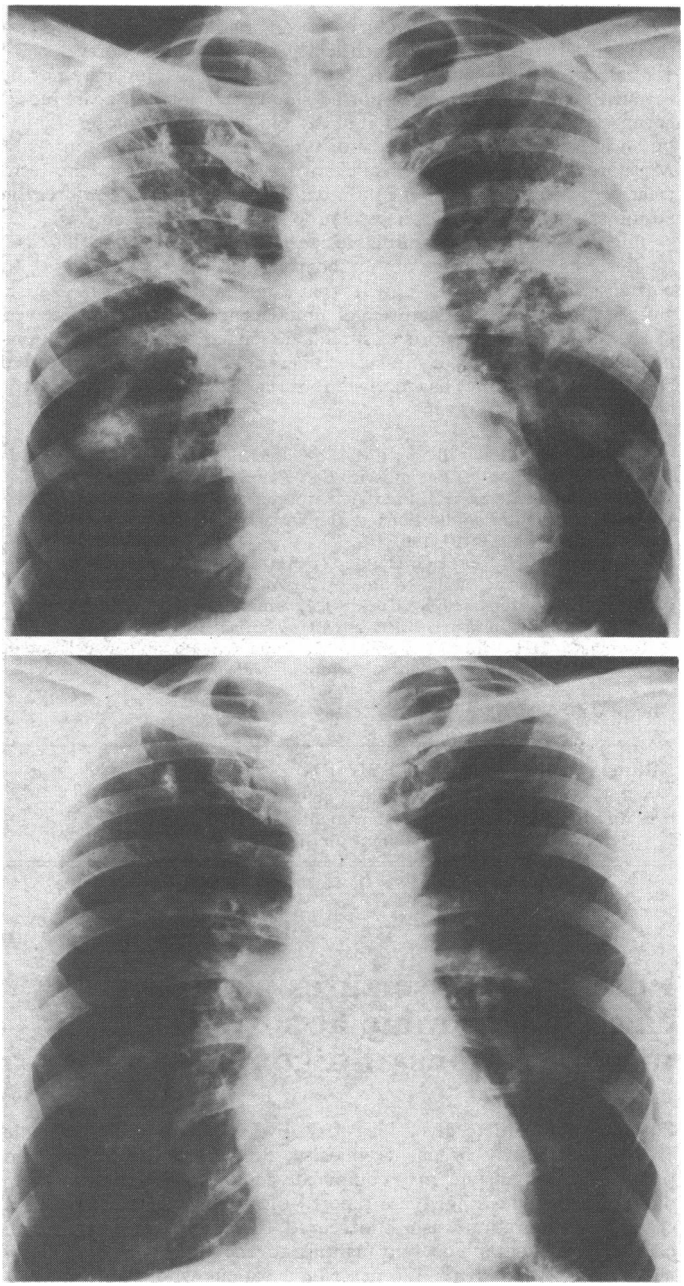
Amiodarone has been widely used in Europe and the United States for its antiarrhythmic and antianginal properties. It has recently become available in Britain. We report a case of severe pulmonary reaction in a patient given this drug.

Case report

A 69-year-old man presented in November 1980 with a six-month history of palpitations at rest. He denied exertional dyspnoea but had a chronic productive cough related to cigarette smoking and a mild seronegative arthritis controlled by indomethacin. Clinical examination showed no other abnormality and chest radiographs were clear apart from an old small calcified focus at the right apex. A 24-hour electrocardiogram suggested sick-sinus syndrome and treatment was started with amiodarone (Cordarone X) 100 mg twice daily for one week, increasing to 200 mg twice daily. He rapidly became asymptomatic. Six weeks later he developed exertional dyspnoea, which gradually increased over the next two months and prompted referral to a respiratory physician. Four days before he had discontinued amiodarone himself, believing it to be responsible. He was dyspnoeic on minimal exertion, and examination showed widespread bilateral late inspiratory crepitations but no evidence of finger clubbing.

There was extensive bilateral fluffy opacification in the chest *x*-ray film (fig: top). Pressure of oxygen was 7·7 kPa (57·9 mm Hg) breathing air. Lung volumes showed a mild restrictive pattern with a total lung capacity of 5·6 l (76% predicted), and carbon monoxide transfer factor was reduced to 2·3 mmol/min/kPa (6·7 ml/min/mm Hg; 28% predicted). Erythrocyte sedimentation rate was 60 mm in first hour, liver function values and immunoglobulin concentrations normal, and antinuclear factor not detectable. The patient was too ill for lung biopsy. His known cardiac disease plus the mild negative inotropic action of amiodarone suggested pulmonary oedema. Diuretics, however, failed to produce an improvement. Two weeks after stopping amiodarone he was less dyspnoeic but the chest radiograph and transfer factor were unchanged. He began prednisolone 60 mg daily with rapid improvement in exercise tolerance and progressive clearing of his lung fields (fig: bottom). Serial estimations of transfer factor showed a rise to 3·8 mmol/min/kPa (11·3 ml/min/mm Hg; 38% predicted) after six days and to 3·9 mmol/min/kPa (11·6 ml/min/mm Hg; 48% predicted) after 24 days.

He remained well and continued to take indomethacin and a reducing dose of prednisolone. His palpitations did not recur.



Radiographs of chest showing (top) bilateral fluffy opacification and (bottom) improvement after prednisolone 60 mg daily.