the fingers, painful limitation of the hips, and bony swelling of the right knee. Radiographs of the joints showed widespread degenerative changes with no evidence of erosions. His latex test result was negative. Close questioning disclosed that he had been taking two Elestol tablets three times a day for at least 15 years for his hands. It also transpired that in 1972 he underwent an open prostatectomy without steroid cover. Ophthalmological examination was performed by Mr B Cobb and showed no retinopathy or loss of central visual acuity.

Comment

This man was ingesting 240 mg of chloroquine phosphate, 4.5 mg of prednisone, and 1.2 g of aspirin daily. He presented with chloroquine pigmentation of the skin, a well-known complication.³ He was most fortunate not to have suffered ocular damage and not to have had adrenal suppression problems at the time of his operation. Neither his general practitioner nor the surgeon seemed to be aware of the problems with this preparation.

Until recently Elestol was listed in the *Monthly Index of Medical Specialities (MIMS)* under the heading "Anti-inflammatory agents." Since the regrouping of headings in *MIMS* Elestol has been listed under "Corticosteroids and related drugs," and now the note "Ophthalmological examination necessary during prolonged admin" has been added. Nevertheless, the indications for the drug remain "rheumatoid arthritis, osteoarthritis, muscular rheumatism." There is also a note under the entry advising referral to the notes at the beginning of the section, and included in this note, underlined, is the advice to refer to individual product literature. There is, however, no entry for Elestol in the *Data Sheet Compendium*,⁴ the reason given being that the drug is not being "actively marketed."⁵

We feel that this agent is a particularly dangerous combination and that there is a strong case for its discontinuance.

¹ Popert, A J, *Rheumatology and Rehabilitation*, 1976, **15**, 235.

² Arden, G B, and Kolb, H, *British Medical Journal*, 1966, **1**, 270.

³ Rook, A, Wilkinson, D S, and Ebling, F J G, *Textbook of Dermatology*, 2nd edn. Oxford, Blackwell Scientific, 1972.

⁴ Association of British Pharmaceutical Industries, *Data Sheet Compendium*. London, 1976.

⁵ Allen, H B, personal communication.

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Lewisham Hospital, London SE13 6LH

A K CLARKE, MRCP, senior registrar in rheumatology and rehabilitation (present address: Royal National Hospital for Rheumatic Diseases, Upper Borough Walls, Bath)

R LL MEYRICK, FRCP, clinical assistant, skin unit

Severe cerebral confusion produced by prajmalium bitartrate

Patients usually tolerate prajmalium bitartrate (Neo-gilurhythm) well, and side effects, which include nausea, gastrointestinal disturbances, dizziness, bradycardia, and intraventricular disturbances, are not widespread. We describe here a patient who suffered cerebral confusion after taking prajmalium bitartrate. Such an effect has not been described before.

Case report

A 67-year-old White man had suffered from diabetes mellitus for 10 years, but he was well controlled on oral treatment. Eight years earlier he had suffered from a proved myocardial infarction. He had had no other illnesses and there was no personal or family history of drug allergy or cerebral disease. He was well until he was admitted to a different hospital with palpitations, and the electrocardiograph showed a supraventricular tachycardia at 150 beats/min.

He was given oral prajmalium bitartrate 100 mg daily in divided doses. Within 24 hours he developed signs of confusion, unrest, disorientation in time and place, and did not respond to simple commands or requests. The prajmalium bitartrate was discontinued and his arrhythmia controlled with quinidine sulphate. Within a few hours the signs of confusion disappeared completely and there was no residual neurological deficit.

He was readmitted four months later with a resistant ventricular tachycardia that responded only to direct-current electric shock, which was administered after intravenous lignocaine and procaineamide had failed to convert him. He subsequently responded well to ajmaline (Gilurhythm), given intravenously to control the residual ventricular ectopics, and was then given oral prajmalium bitartrate 100 mg in divided doses as maintenance treatment. Within 36 hours he again developed signs of confusion and disorientation in time and place. The drug was discontinued and ajmaline substituted intravenously. The confusion promptly disappeared but the ventricular arrhythmia recurred. Despite intensive treatment, during which the patient remained unconfused, the arrhythmia could not be suppressed, and he died some days later.

Comment

Confusional states have not been previously noted on oral prajmalium bitartrate treatment.¹ Our patient developed this condition on two separate occasions, during which time he received no other drug common to both periods or known to produce disorientation. Furthermore, his cerebral state improved immediately after discontinuing the drug, and it seems reasonable to accept that prajmalium bitartrate was the direct cause of the confusion. Routine blood tests including measurement of serum electrolytes, blood sugar, and blood gases were normal on both occasions. Despite the similarity in structure between prajmalium bitartrate and ajmaline, the latter did not produce cerebral changes when given intravenously, whereas prajmalium bitartrate was associated with these symptoms when given in an acceptable dose by mouth. This contrasts with the results of Weidner and Philipson,² who did not find any difference in the toxicity of the two drugs.

It would seem reasonable to consider alternative antiarrhythmic agents for use in patients who develop a confusional state when receiving prajmalium bitartrate.

¹ Weidner, A, personal communication.

² Weidner, A, and Philipson, G V, *Arzneimittel-Forschung*, 1971, **21**, 685.

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Municipal Government Medical Centre, Tel-Aviv, Israel

J B LESSING, MD, physician

I J COPPERMAN, MRCP, physician

Peripheral and autonomic neuropathy after treatment with perhexiline maleate

Perhexiline maleate is a useful drug in the prophylaxis of angina pectoris.¹ Nevertheless, its potential value may be limited by the occasional development of side effects, including peripheral neuropathy^{2 3} and myopathy.⁴ We describe the details of three patients who developed peripheral and autonomic neuropathy after treatment with this drug.

Case reports

Case 1—A 56-year-old man underwent aortocoronary saphenous vein graft to the right coronary artery in 1971 for relief of angina pectoris. Six months after operation his symptoms recurred due to occlusion of the graft. He gained no benefit from propranolol but his symptoms were partially relieved by perhexiline. In June 1976, having taken his drug for 10 months (200-400 mg/day), he presented with symptoms of numbness and pain in both legs, paraesthesiae in both hands, and postural dizziness. Examination confirmed sensory loss in "glove-and-stocking" distribution with weakness of all muscle groups in the legs. Systolic blood pressure was 100 mm Hg lying and 70 mm Hg erect. Motor nerve conduction velocity (MCV) was delayed in both arms and legs and the Valsalva ratio (VR)⁵ reduced (table). The drug was withdrawn and over the next two weeks his symptoms improved, with relief of pain and paraesthesiae and resolution of postural dizziness. There was associated improvement in postural hypotension and in MCV in the arms, but MCV in the legs and VR remained abnormal three weeks after stopping treatment. Withdrawal of perhexiline was associated with return of severe anginal symptoms at rest, again unrelieved by propranolol, so

Individual values for two patients for erect and supine blood pressure, terminal latency (TL) and motor nerve conduction velocity (MCV) of ulnar and peroneal nerves, and Valsalva ratio (VR)⁵ at presentation and after withdrawal of perhexiline

Variable	Normal ranges	Patient 1				Patient 2				
		14 June 1976	21 June 1976	28 June 1976	5 July 1976	21 June 1976	5 July 1976	19 July 1976	13 September 1976	14 February 1977
Blood pressure (mm Hg):										
Supine		110/60	120/80	110/70	110/70	110/70	105/70	110/60	110/70	115/75
Erect		70	90/70	100/60	100/70	90/70	85/60	90/60	105/70	110/70
Ulnar nerve:										
TL (ms)	2.1-3.4	4.8	4.0	3.8	3.9	6.1	5.8	4.5	3.9	4.0
MCV (m/s)	46.5-72.6	42.5	44.4	50.8	49.1	46.6	44.8	45.5	54.9	52.4
Peroneal nerve:										
TL (ms)	3.7-6.1	9.1	8.2	8.4	8.1	12.4	10.5	9.6	6.5	5.8
MCV (m/s)	42.1-63.5	30.3	35.2	34.0	34.1	31.6	36.3	38.4	40.2	44.3
Valsalva ratio	>1.50	1.10	1.04	1.09	1.09	1.28	1.35	1.62	1.84	1.80

coronary angiography was carried out. He subsequently died after a further attempt at surgical revascularisation.

Case 2—A 60-year-old man presented in 1968 with symptoms of angina pectoris that progressed despite treatment with propranolol. In 1973 after coronary angiography he underwent triple aortocoronary saphenous vein grafts, but there was no real improvement in his symptoms, and he remained severely incapacitated. In July 1975 he started treatment with perhexiline (200 mg increased to 400 mg/day) with some relief of angina. He returned in June 1976 with a two-month history of weakness and paraesthesiae in both legs and numbness in both feet, and distressing symptoms of postural dizziness. Examination showed sensory blunting below the knee with weakness of all muscle groups in the legs. Systolic blood pressure was 110 mm Hg lying and 90 mm Hg erect. MCV in both arms and legs was delayed and VR reduced (table). Four weeks after withdrawal of perhexiline, his postural hypotension had resolved and VR had become normal. The symptoms of neuropathy had also improved, although three months after discontinuing the drug he still had paraesthesiae in both feet with reduced MCV in the peroneal nerve. He remained incapacitated by angina.

Case 3—A 61-year-old man with insulin-dependent diabetes mellitus of 30 years' duration was diagnosed as having autonomic neuropathy in 1975 because of clinical features (impotence, dizziness on standing, and intermittent nocturnal diarrhoea) and test results showing abnormal autonomic function (VR 1.10, blood-pressure response of 10 mm Hg to sustained hand-grip, and postural fall in systolic blood pressure of 50 mm Hg). He was started on fludrocortisone 0.1 mg daily, and after six months his blood pressure was satisfactory at 130/80 mm Hg lying and 105/70 mm Hg standing, with no symptoms of postural hypotension. During the next year he developed severe angina with no relief from increasing doses of oxprenolol, so in May 1976 this drug was stopped and he was started on perhexiline (400 mg/day). After a few weeks the patient noticed paraesthesiae in both feet and hands and recurrence of his symptoms of postural hypotension. He stopped perhexiline, and when seen two weeks later the paraesthesiae had completely resolved and he no longer felt dizzy, blood-pressure readings being 110/70 mm Hg lying and 90/60 mm Hg standing.

Comment

Three patients developed clinical features of peripheral and autonomic neuropathy on perhexiline maleate. In two cases the features

developed after prolonged treatment, and the diagnosis was confirmed by abnormal results of motor nerve conduction velocity and autonomic function tests. In the third case deterioration of known autonomic neuropathy secondary to diabetes mellitus occurred after a short period on the drug. In all three cases there was symptomatic improvement within a few weeks of discontinuing treatment, suggesting a direct association with the drug. Improvement in motor nerve conduction velocity and autonomic function test results lagged behind the symptomatic improvement in these patients, but in patient 2 results of these tests were almost normal three months after discontinuing the drug.

Lhermitte *et al*³ have postulated that peripheral neuropathy may represent individual susceptibility perhaps secondary to some latent inborn metabolic disorder. Further information on the incidence of test results showing impairment of motor nerve conduction velocity and autonomic function in patients taking perhexiline without symptoms or signs of neuropathy is needed before accepting this theory. The development of symptomatic autonomic neuropathy, particularly postural hypotension, is obviously an undesirable side effect in any patient with angina pectoris.

¹ Burns-Cox, C J, *et al*, *British Medical Journal*, 1971, **4**, 586.

² Boussier, M G, *et al*, *Nouvelle Presse Médicale*, 1976, **5**, 652.

³ Lhermitte, F, *et al*, *British Medical Journal*, 1976, **1**, 1256.

⁴ Tomlinson, I W, and Rosenthal, F D, *British Medical Journal*, 1977, **1**, 1319.

⁵ Levin, A B, *American Journal of Cardiology*, 1966, **18**, 90.

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The Royal Infirmary, Edinburgh EH3 9YW

D M FRASER, MRCP, senior registrar

I W CAMPBELL, MRCP, senior registrar

H C MILLER, MRCP, consultant cardiologist

SHORT REPORTS

Leukapheresis for papilloedema in chronic granulocytic leukaemia

Although retinal vein distension, fundal haemorrhages, and blurring of the optic disc margins are well-recognised features of chronic granulocytic leukaemia (CGL), true papilloedema is relatively rare.¹ We report a case where bilateral papilloedema was present at diagnosis and improved after repeated leukapheresis on a continuous flow cell separator.

Case history

A 33-year-old woman was admitted to hospital with a 12-month history of anorexia, weight loss, and fatigue. She admitted to recent deterioration in vision. She was pale and thin with splenomegaly to below the umbilicus. Both optic fundi showed venous distension, haemorrhages, and papilloedema consistent with leukaemic retinitis. The findings of full neurological exami-

nation were otherwise normal. Peripheral blood findings were as follows: Hb 7.4 g/dl; platelets $470 \times 10^9/l$; total WBC $260 \times 10^9/l$ (neutrophils 44%, metamyelocytes 9%, myelocytes 18%, promyelocytes 18%, eosinophils 2%, basophils 1%, lymphocytes 2%, blast cells 6%, nucleated RBCs 4/100 WBC). Leucocyte alkaline phosphatase score 5 (normal 20-120). Bone marrow examination yielded initially a dry tap, but a later aspirate showed gross myeloid hyperplasia, and an increase in eosinophils and megakaryocytes, consistent with a diagnosis of CGL. The Philadelphia chromosome was present. Trephe bone marrow biopsy showed no features of myelofibrosis. Immunoglobulin concentrations were normal and no paraprotein band was detected. Whole blood viscosity, measured at 37°C in an Ostwald viscometer,² was approximately twice normal (ratio patient's blood/water = 7.7; ratio control blood matched for haematocrit value/water = 4.2). An EMI brain scan showed no abnormality—in particular, no dilatation of the ventricular system to suggest raised intracranial pressure. Fluorescein angiography confirmed swelling of the optic nerve head.

CGL was diagnosed and, because of the very high WBC count, primary treatment was by leukapheresis, initially daily and later twice weekly, on a continuous flow cell separator. A total of 3.22×10^{12} leucocytes, of which 1.86×10^{12} were immature myeloid cells, were removed over a period of 26 days. By day 21, after eight such treatments, there was considerable improvement in the eye signs, with disappearance of most of the haemorrhages and