Neuropsychiatric complications related to use of prazosin in patients with renal failure

Although postural hypotension and syncope are well known side effects of prazosin, neuropsychiatric complications have rarely been recorded. We report on three neuropsychiatric patients who recovered completely after the drug was withdrawn.

Case reports

Case 1—A 63 year old housewife who had been receiving continuous ambulatory peritoneal dialysis for one year for diabetic renal failure was admitted because of impaired drainage of peritoneal dialysate. She also had hypertension, diabetes, retinopathy, peripheral neuropathy, and autonomic neuropathy. Her blood pressure was not well controlled despite treatment with metoprolol, and prazosin was started and increased to 2 mg three times daily. Over the next four weeks she became confused and suffered from visual hallucinations and paranoid ideas. No significant biochemical changes occurred, however, and her autonomic dysfunction did not change. An electroencephalogram showed intermittent diffuse slow wave abnormality, which was consistent with metabolic encephalopathy. Prazosin was stopped, and she recovered over eight weeks.

Case 2—A 70 year old woman with a 15 year history of diabetes mellitus stabilised by glibenclamide was admitted after three weeks of intermittent drowsiness, confusion, and uninhibited behaviour such as undressing. She also had longstanding hypertension, treated initially with metyldopa, but prazosin 5 mg three times daily had been started six weeks previously for better control. Over the past year she had developed diabetc renal failure, with urea concentration 19-6 (normal 3-8) mmol/l (117-6-18 mg/100 ml) and creatinine concentration 280 (50-120) mmol/1 (3-17-5-71-36 mg/100 ml). She was afebrile and had no focal neurological deficit. There was no evidence of hypercalcaemia, hypokalaemia, or hypomagnesaemia, and no abnormal fluid composition and results of other biochemical investigations were normal. Over the next few days her mental state fluctuated, and an electroencephalogram was performed, which showed diffusely abnormal trace with no focal features. We suspected that this might be related to prazosin, which was stopped over the next three days; her mental state improved dramatically. Two months after discharge her mental state and behaviour were normal, and a repeat electroencephalogram showed great improvement.

Case 3—A 40 year old man with a 20 year history of insulin dependent diabetes and hypertension was admitted because of sudden left hemiparesis. Computed tomography of his head showed a lacunar infarct in the right internal capsule. While in hospital he had two grand mal seizures, controlled with phenytoin.

Prazosin 2 mg three times daily was also started because his blood pressure was not well controlled with metyldopa alone. His hemiparesis improved gradually and he returned home. He was readmitted two weeks later, however, because of psychotic behaviour. He was paranoid, with signs of organic psychosis, strong delusions of grandeur, and hallucinations. There was no biochemical evidence of hypoglycaemia or phentoyin toxicity, and an electroencephalogram showed intermittent slow waves over the right hemisphere, compatible with the vascular lesion. His renal function was mildly impaired, but it remained stable throughout his psychosis. Prazosin was stopped and the hypertension controlled with metoprolol. The psychosis was settled with a short course of chlorpromazine and trilafontine. Eight months after discharge and withdrawal of the major tranquiliser paroxadana had not recurred.

Comment

We think that the increased abnormalities in the central nervous system in our three patients were due to prazosin, because their chronic renal failure might have affected the clearance of prazosin.

The results of pharmacokinetic studies in chronic renal failure are not yet consistent,1 2 though the 50% increase in the free fraction of prazosin observed in patients with chronic renal failure1 might explain the apparent association of central nervous system toxicity with renal failure. Animal studies also support the observation that prazosin could be responsible for the abnormal symptoms of the central nervous system.3 5

We advise the cautious use of prazosin in patients with renal failure. The Committee on Safety of Medicines and the drug manufacturer have told us about one notification of paranoya and five of hallucination since 1974.