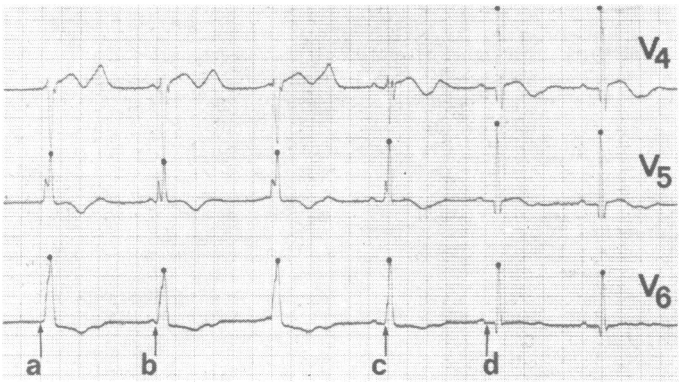
Serious verapamil poisoning: treatment with intravenous calcium gluconate

Verapamil is an antiarrhythmic and antianginal drug which selectively inhibits membrane transport and release of calcium from the endoplasmic reticulum, depressing the sinus node and atrioventricular conduction as well as producing a negative inotropic effect on the myocardium. Here I describe a patient who suffered the adverse haemodynamic and electrocardiographic effects consequent upon self-poisoning with 3·2 g of verapamil and was successfully resuscitated by intravenous administration of calcium gluconate.

Case Report

A 19-year-old woman with a four-year history of ventricular extrasystoles associated with a prolapsing mitral valve swallowed eighty 40-mg tablets of verapamil after a domestic argument. On admission and after gastric lavage she had a bradycardia of 55 and was hypotensive (blood pressure 80/60 mm Hg). The ECG showed a nodal bradycardia with abnormal intraventricular conduction and prominent U waves. Five hours after the tablets had been swallowed her hands and feet became cold and cyanosed and her systolic blood pressure fell to 60 mm Hg. In view of the history of arrhythmia, β-adrenergic agonists such as orciprenaline normally recommended for the treatment of verapamil poisoning were considered to be contraindicated. The patient was given a slow intravenous injection of calcium gluconate (10 ml of 10% calcium gluconate) over five minutes with continuous electrocardiographic monitoring (figure). Initially the ECG showed periods of either nodal bradycardia with an intraventricular conduction defect or alternate sinus and nodal beats, but within 10 minutes sinus rhythm was restored. Blood pressure rose slowly to 90/60 mm Hg and the signs of diminished peripheral perfusion receded.



Simultaneous electrocardiographic recording of leads V4, V5, and V6 during a calcium gluconate infusion: (*a*) nodal beat with wide QRS and prominent U wave; (*b*) return of atrial activity; (*c*) normal P wave and P-R interval with wide QRS complex; (*d*) return to normal electrocardiogram.

Sinus bradycardia persisted for eight hours and then reverted to a nodal bradycardia with an intraventricular conduction defect but without a fall in blood pressure. This arrhythmia responded temporarily to 10 ml of 10% of calcium gluconate given intravenously but required a continuing infusion of calcium gluconate (5 mmol/hour) to maintain sinus rhythm. Apart from an infrequent ventricular extrasystole the patient maintained sinus rhythm for 12 hours, at which point the calcium infusion was discontinued. Blood pressure was maintained at 100/60 mm Hg, although sinus bradycardia persisted for 36 hours after admission. The patient's further recovery was uneventful. The blood verapamil concentration was 4 μg/ml five hours after ingestion, compared with therapeutic concentrations of about 30 ng/g plasma.

Comment

The only published reports[1 2] which describe the successful resuscitation of a patient after self-poisoning with verapamil do not give blood concentrations of the drug, nor was verapamil the sole agent responsible for the poisoning, having been ingested as Isoptin S dragees (verapamil 40 mg and pentobarbitone 20 mg); the synergistic cardiac depressant effect mediated by pentobarbitone, therefore, cannot be separately assessed. The maximum effect on atrioventricular conduction produced by oral verapamil in therapeutic doses occurs five hours after ingestion[3]; this would correlate well with the onset of hypotension and bradyarrhythmia seen in this patient.

Unlike β-blocking drugs verapamil does not alter myocardial responsiveness to β-adrenergic agonists. The manufacturer's recommended treatment of acute atrioventricular block or asystole precipitated by intravenous verapamil is an intravenous or intracardiac injection of orciprenaline or adrenaline followed by 10-20 ml of a 10% calcium gluconate solution. In this case it is believed that return of normal cardiac function may be attributed to calcium gluconate alone. The use of β-adrenergic agonists may constitute a definite risk to a patient with previous episodes of arrhythmia or myocardial ischaemia.

Verapamil is being increasingly used in managing angina and certain arrhythmias, and the number of patients at risk from deliberate or accidental poisoning is likely to increase. An increasing incidence of poisoning has also been seen with other antiarrhythmic agents such as disopyramide[4] and beta-blockers.[5] Knowledge of the physiological effects of these drugs and their potential antidotes, together with facilities for continuous electrocardiographic monitoring in an intensive care unit, should enable many patients to survive serious myocardial depression.

I thank Dr E B Mullock of Abbott Laboratories who performed the plasma verapamil assay, Miss S Tempest of the Poisons Information Centre at the Leeds General Infirmary, and Professor G P McNicol and Dr M R Lee for their help with the manuscript.

[1] Montiero, M L A, *et al*, *Archives of Brazilian Cardiology*, 1977, **30**, suppl No. 2, p 401.
[2] Beitzke, A, *et al*, *Pädiatrie und Pädologie*, 1976, **11**, 570.
[3] Singh, B N, *Drugs*, 1978, **15**, 178.
[4] Hayler, H, *et al*, *Lancet*, 1978, **1**, 968.
[5] *British Medical Journal*, 1978, **1**, 1010.

(*Accepted 1 August 1978*)

University of Leeds Department of Medicine, Leeds General Infirmary, Leeds LS1 3EX
C M PERKINS, MRCP, teaching fellow in medicine

Cerebrovascular accident after a "skipjack" reaction in a patient taking isoniazid

Patients on anti-tuberculous chemotherapy have had reactions after eating "skipjack," a sea fish commonly consumed in Sri Lanka.[1 2] The reactions—usually manifesting as headache, palpitations, erythema, redness of the eyes, itching, diarrhoea, and wheezing—are thought to be due to histamine absorbed in large quantities from the fish. Isoniazid, being a potent inhibitor of histaminase, interferes with the degradation of histamine, causing it to accumulate in the tissues. We report on a patient who, in addition to those transient symptoms, had a cerebrovascular accident after a skipjack meal.

Case report

A 50-year-old Indian labourer was admitted to hospital with pulmonary tuberculosis. He was treated with streptomycin 750 mg intramuscularly each morning and Unithiben (thiacetazone 37·5 mg and isoniazid 75 mg) four tablets every night. Two weeks after starting treatment the hospital lunch inadvertently included skipjack in a curry, which our patient and another ate against the advice of other patients who had experienced symptoms previously. Within 15 minutes both patients had reactions. Our patient developed flushing of the body, sweating, and giddiness. He went to bed. On waking about two hours later his left arm was paralysed and there was some stiffness of the left leg and numbness of the left half of the body. He had marked spastic weakness of the left arm, minimal weakness of the face, and mild weakness of hip flexion on the same side. The tendon jerks on the left were exaggerated and the plantar response was extensor. The cardiovascular system and the abdomen were clinically normal. The blood pressure about six hours after the onset of symptoms was 120/80 mm Hg.

The results of the following laboratory investigations were normal: white cell count and differential count, blood Wassermann reaction, blood sugar, serum Na^+ and K^+, serum cholesterol, and urine analysis. The ESR was 40 mm in one hour. An ECG and radiographs of the skull were normal.