Successful treatment of suicidal verapamil poisoning with calcium gluconate

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A 33 year old man ingested approximately 3000 mg of verapamil in attempted suicide. Verapamil and norverapamil concentrations 4-5 h after ingestion were 1250 and 1350 ng/ml. The patient had a heart rate of 79 beats/min, a systolic blood pressure of 60 mm Hg and atrioventricular dissociation. Metaraminol had no significant effect on blood pressure or heart rate. During infusion of 10 ml 10% calcium gluconate, systolic blood pressure rose to 80 mm Hg and both QRS and P waves changed polarity. The clinical condition improved and sinus rhythm was established 5 h later. Calcium can be recommended as the first line of treatment in verapamil intoxication.

The use of verapamil is increasing; the number of patients at risk from deliberate or accidental poisoning is likely to increase. There are few published reports describing verapamil intoxication and experience with the treatment of such patients, especially the use of calcium gluconate, should be of interest.

Case report

A 33 year old man had a two year history of atrial fibrillation. He complained of palpitation and was referred for cardiological evaluation. There was no known history of coronary heart disease, his blood pressure was normal, and he had no other cardiac complaints. Echocardiography showed normal valve motion, a normal left ventricle, no shunts, but an enlarged right ventricle. Cardiac catheterization was scheduled. His palpitation was treated with verapamil (Isoptin, Knoll).

On the 28 May at 5 a.m. the patient, in a fit of acute depression, ingested approximately seventy-five 40 mg tablets verapamil. He was admitted to hospital 2-3 h thereafter and was initially treated with gastric lavage. On admission he had a systolic blood pressure of 80 mm Hg which subsequently fell to 60 mm Hg. The heart rate was 79 beats/min, and the ECG showed atrioventricular dissociation (Fig. 1). The patient was first given an injection of 5 mg metaraminol i.m. (Aramine MSD) without significant effect on blood pressure or heart rate. Calcium gluconate (10 ml of a 10% solution) was thereafter given during a 10 min period. During the injection, blood pressure rose from 60 to 80 mm Hg and the QRS complexes became narrower and changed polarity (Fig. 2). The P waves also changed polarity. Atrioventricular dissociation persisted for 5 h before reversal to sinus rhythm. The patient’s clinical condition was good and did not necessitate any further treatment with calcium. Verapamil and norverapamil concentrations were assayed with a high pressure liquid chromatographic method. Plasma verapamil concentrations were 1206-6 ng/ml after 4-5 h and 510-5 ng/ml after 11 h. The concentrations of the cardioactive metabolite norverapamil were 1255-9 ng/ml in the first sample, declining to 837-8 ng/ml in the second (Fig. 3). The patient’s further clinical course was uneventful and he was referred to the Department of Psychiatry for anti-depressive treatment.

Discussion

One case of fatal verapamil poisoning has been reported in the literature. A 42 year old woman...
with diabetes, obesity, heart and liver disease died 3 h after taking an overdose. The plasma verapamil concentration (analysed with gas chromatography) taken postmortem was 590 ng/ml. Spiegelhalder and associates\[^\text{1}\] reported a verapamil concentra-


Suicidal verapamil poisoning

Atrial rate: 60
Ventricular rate: 80
QRS: 0.09 s

09:25 a.m.
Prior to calcium infusion

Atrial rate: 58
Ventricular rate: 73
QRS: 0.06 s

09:35 a.m.
Following infusion of calcium

Figure 2 ECG changes before and following calcium infusion recorded with a monitoring lead (V5, at a paper speed of 50 mm/s).

Figure 3 Verapamil and norverapamil concentrations 4.5 and 11 h after ingestion of approximately 3000 mg verapamil analysed with high pressure liquid chromatography. --- = Norverapamil; ... = verapamil.

Da Silva and associates\(^6\) described the case of a 14 year old girl who ingested 2400 mg verapamil. She was confused, and hypotensive with respiration of Kussmaul type and third degree AV block with a heart rate of 40 and a metabolic acidosis. She was treated with atropine without effect and calcium gluconate solution after which heart rate rose to 55 beats/min.

Perkins\(^7\) reported a case similar to ours. A 19 year old woman with mitral valve prolapse and ventricular extra-systoles ingested 3000 mg of verapamil. Treatment with calcium gluconate resulted in ECG changes and clinical effects which were similar to those reported in our case. The plasma verapamil concentration was 4000 ng/ml 5 h after ingestion.

We also measured norverapamil, which has a significant hemodynamic effects in the anesthetized dog\(^8\). Norverapamil concentrations in the same range as verapamil concentrations in patients on oral therapy\(^9,10\). We found that the mean predose verapamil and norverapamil concentrations were 108 and 174 mg/ml, respectively, while
1 h post-dose concentrations were 424 and 273 ng/ml in patients on maintenance treatment with 160 mg t.i.d.[8]. Our patients had verapamil and norverapamil concentrations far exceeding therapeutic levels. The first blood sample was taken after 4.5 h and with the rapid elimination half-time of verapamil, concentrations must have been extremely high following ingestion, probably in the range between 2000 and 4000 ng/ml.

Verapamil exerts potent depressant effects on both the sinus and atrioventricular node[9]. Calcium infusion reverts the electrophysiological effects of verapamil in the experimental animal[12]. Our patient had AV dissociation with an accelerated junctional rhythm. Following calcium infusion both the P wave polarity and the QRS width and polarity changed, reflecting partial reversal of the depressant action on the conduction system.

Our case is the third case reported where treatment with calcium gluconate has been successful. We gave only a single injection of calcium, but Perkins[7] gave repeated injections and also infused calcium with no adverse effects. One case with calcium treatment for nifedipine poisoning has been published[12]. Primary therapy with beta-agonists has been recommended for verapamil overdose, but can be potentially dangerous in patients with arrhythmias. Marked hypotension is a common feature in verapamil poisoning and is caused by the relaxant effect on vascular smooth muscle.

The favorable experience with intravenous calcium suggests that calcium should be the first line of treatment.

References