Cardiac arrest following chlormethiazole infusion in chronic alcoholics

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Summary
Two chronic alcoholics who had cardiac arrests (one fatal) while receiving chlormethiazole by infusion are reported. Although a causal relationship has not been indisputably established, caution is advised when administering this drug to chronic alcoholics during withdrawal.

Introduction
Chlormethiazole is a sedative and hypnotic with marked anti-convulsant properties. It is widely used in the treatment of states characterized by convulsions and agitation, including delirium tremens. Although rarely causing side effects, the drug has been shown to depress the respiratory centre (Lechat, 1966) and toxic interactions with alcohol have been found in animals (Vapaatalo and Karppanen, 1969). Sudden deaths ascribed to chlormethiazole therapy have been attributed to respiratory depression, and alcohol abuse seems to be a predisposing factor (Pentikainen, Valtonen and Miettinen, 1976). Two cases are reported where cardiac arrest, without evidence of preceding respiratory depression, followed chlormethiazole infusion in the treatment of delirium tremens.

Case 1
A 65-year-old Caucasian with a long history of alcohol abuse was admitted following a haematemesis. He had been drinking heavily for one month until 24 hr before admission. Concurrent therapy was atenolol for hypertension. He was confused and disorientated. Blood pressure (BP) was 160/110 mmHg. Electrocardiography showed sinus tachycardia and left ventricular hypertrophy but no ischaemic features. Chest X-ray was normal. Hb and haematocrit were normal but platelets were $55 \times 10^9/\text{l}$; blood film showed target cells. Electrolytes and urea were normal, serum bilirubin 35 $\mu$d/l, aspartate transaminase (AST) 64 u./l, $\gamma$-glutamyl transpeptidase 58 u./l, lactic dehydrogenase 800 u./l and creatinine kinase 880 u./l. Endoscopy was technically unsatisfactory and cimetidine by infusion was commenced.

Initial restlessness progressed to delirium tremens after 24 hr. He was given parenteral diazepam, chlorpromazine and chlormethiazole and, after 2 hr, satisfactory control of symptoms was achieved by chlormethiazole 0.8% infusion alone. Sixteen hr later he developed ventricular tachycardia. He was resuscitated and recovered uneventfully. Investigations excluded myocardial infarction. Total dose of chlormethiazole was 11.2 g.

Case 2
A 54-year-old Asian was assaulted after leaving a bar. X-ray showed severe facial bone fractures. He was conscious although drowsy, disorientated and amnesic. Pulse was normal and BP 190/110 mmHg. Serum sodium was 132 mmol/l, other electrolytes and urea normal, albumin 32 g/l, AST 206 u./l and alanine transaminase 56 u./l. Treatment was with i.v. fluids and prophylactic antibiotics.

After 12 hr, his restlessness required increasingly frequent parenteral diazepam and chlorpromazine with little effect. Whisky proved more successful. Before facio-maxillary surgery he was given oral chlormethiazole and, postoperatively, this was infused intermittently, controlling his symptoms. Three days after surgery, he developed cardiac asystole following a one-hr infusion of 100 ml 0.8% chlormethiazole, its only administration in the previous 24 hr. Resuscitation was unsuccessful. The only other drug treatment was 10 mg of diazepam in divided doses in the 6 hr before death. At post-mortem, the findings were an insignificant pulmonary
Cases of fatal cardiac arrest have been reported following abrupt withdrawal of alcohol from chronic alcoholics. The incidence of accidental death is highest in patients receiving sedatives that are associated with withdrawal symptoms, and in patients with known alcoholism who have a history of alcohol withdrawal. In such patients, potassium concentrations before admission are often normal or slightly reduced. However, after withdrawal, when the concentrations decline, cardiac arrhythmias are likely to occur. In some cases, the arrhythmias are so severe that the patient dies. In the case reported here, compliance with atenolol given for hypertension may have been incomplete but there is no evidence of sudden discontinuation nor resultant coronary insufficiency.

### Case Reports

#### Case 1

Cohen et al. (1979) have recently reported that cardiac arrhythmias may follow bolus i.v. injections of cimetidine. Case 1 was given cimetidine by this route but by slow infusion and this had been discontinued for more than 2 hr before the cardiac arrest. The second patient had suffered severe injuries but clinically was recovering satisfactorily. The post-mortem findings did not suggest that his injuries contributed to his death. Both cases show a clear temporal relationship between chlorothiazide infusion and the development of serious cardiac arrhythmias. Although a causal relationship has not been established, these findings suggest that this therapy should be administered with caution to alcoholics during acute withdrawal.

### Acknowledgments

We wish to thank Dr W. D. Alexander and Mr K. F. Moos for permission to report these cases.

### References


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Postgrad Med J 1980 56: 742-743
doi: 10.1136/pgmj.56.660.742

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