High-dose intravenous glucagon in severe tricyclic poisoning

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Summary

A case of dothiepin poisoning complicated by cardiogenic shock is described. Hypotension was resistant to conventional inotropes but responded rapidly to high-dose intravenous glucagon. Glucagon should be considered as a useful therapeutic positive inotrope and a potentially anti-arrhythmic agent in severe tricyclic antidepressant overdose.

Keywords: tricyclic antidepressants; dothiepin; poisoning; cardiogenic shock; glucagon; inotropic support

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Tricyclic antidepressants are widely prescribed for depressive disorders, insomnia and chronic pain conditions. Unfortunately, these agents are also commonly taken in overdose, causing life-threatening arrhythmias, hypotension and seizures. In a significant proportion of cases, hypotension is profound and resistant to conventional therapeutic strategies. Glucagon is a rarely used positive inotrope, and we report its successful use in the treatment of severe cardiogenic shock secondary to dothiepin excess.

Case report

A 36-year-old woman was brought to casualty unconscious. A drug overdose was suspected and the ambulance crew reported that coproxamol, ibuprofen, antidepressants and alcohol had been present in the house. On examination she had spontaneous respiration, a tachycardia of 120 beats/min, blood pressure of 60/30 mmHg, dilated pupils, bilateral brisk reflexes, extensor plantar responses and a Glasgow Coma Scale of 7. Shortly after transfer to the intensive care unit (ICU), a respiratory arrest necessitated intubation and ventilation. Full blood count and renal function were normal, potassium 3.2 mmol/l, INR 1.5 and pH 7.29. Electrocardiogram showed a broad complex tachycardia with QRS width of 0.16–0.2 s, rate 100 beats/min. Colloid and crystalline solutions were given, with an initial brief rise in blood pressure. Charcoal and lactulose were administered via a nasogastric tube and an acetyl-cysteine infusion was commenced. Grand mal seizures were controlled with diazepam and etomidate. Adrenaline, nor-adrenaline, ephedrine, dobutamine and aminophylline were used in an attempt to correct persisting systolic hypotension of 50–60 mmHg. Two hours after ICU admission, a systolic pressure of 70 mmHg was achieved using infusions of 2 mg/h adrenaline, and 3 µg/kg/min dobutamine. On the advice of Guy's Poisons Unit, a 10-mg bolus of intravenous glucagon was given. This was followed by an immediate sustained rise in systolic pressure to over 90 mmHg which persisted for 3 hours (figure) following which she again became profoundly hypotensive. Two further 1-mg boluses of intravenous glucagon were administered with no effect. A further bolus of 10 mg stimulated a rapid increase in blood pressure which was then maintained overnight with infusions of 5 µg/kg/min dobutamine, 2 mg/h adrenaline, and 2.5 µg/kg/min dopamine. One hour after the second 10-mg dose of glucagon she reverted to sinus rhythm. The following day she was awake and responding to commands. Ventilation and inotropic support were weaned off over the next 24 hours. Initially higher mental functions were impaired with short-term memory loss, intermittent confusion and visual hallucinations but by day 5 she had made a full recovery and was transferred to psychiatric care. Admission serum toxicology showed dothiepin: 2.58 mg/l, desmethyldothiepin: 0.51 mg/l, paracetamol: 135 mg/l, diazepam: 0.33 mg/l, nordiazepam: 0.12 mg/l,

Figure Blood pressure response to inotropic support

propoxyphene: not detected, confirming that a substantial overdose of a tricyclic antidepressant had been ingested.

Discussion

Tricyclic antidepressants are still commonly prescribed, despite the advent of newer and safer alternatives. Dothiepin in particular has been associated with high intrinsic toxicity in excess.¹ Tricyclic poisoning is complicated by profound hypotension, dysrhythmias, and seizures, and has a high mortality rate. Circulatory shock may be refractory to inotropic support.² Such hypotension is brought about by inhibition of noradrenaline uptake at central presynaptic sites, blockade of peripheral postsynaptic adrenergic receptors and reduced myocardial catecholamine levels. Glucagon has dose-dependent positive inotropic and chronotropic qualities.³ It increases myocardial intracellular calcium concentration by stimulating adenylyl cyclase, thus enhancing myocardial contractility. This action is thought to occur at nonadrenergic receptors. Thus it is an established treatment for toxicity due to excessive beta-blockade and has been used in calcium channel blocker overdose.⁴ Additional antiarrhythmogenic properties may be due to

Clinical features of tricyclic antidepressant overdose

- dilated pupils
- respiratory depression
- coma
- hypotension due to arrhythmias, reduced cardiac output, and peripheral vasodilatation
- seizures

direct membrane effects. Glucagon has rarely been used in the treatment of severe tricyclic poisoning⁵ but theoretically it is a valuable vasoactive agent as its actions are independent of the adrenoreceptors which are affected in tricyclic excess. In our patient, refractory hypotension secondary to proven dothiepin toxicity persisted despite the use of several standard inotropes. The adjunct of high-dose glucagon appeared to make an important contribution to cardiovascular stabilisation during the resuscitation period. We therefore suggest that the use of glucagon at these dosages should be further evaluated in this situation and more frequently considered for use in cases of severe hypotension and arrhythmias secondary to tricyclic antidepressant toxicity.

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4 Doyon S, Roberts J. The use of glucagon in a calcium channel blocker overdose. *Ann Emerg Med* 1993;**22**:1229–33.

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