

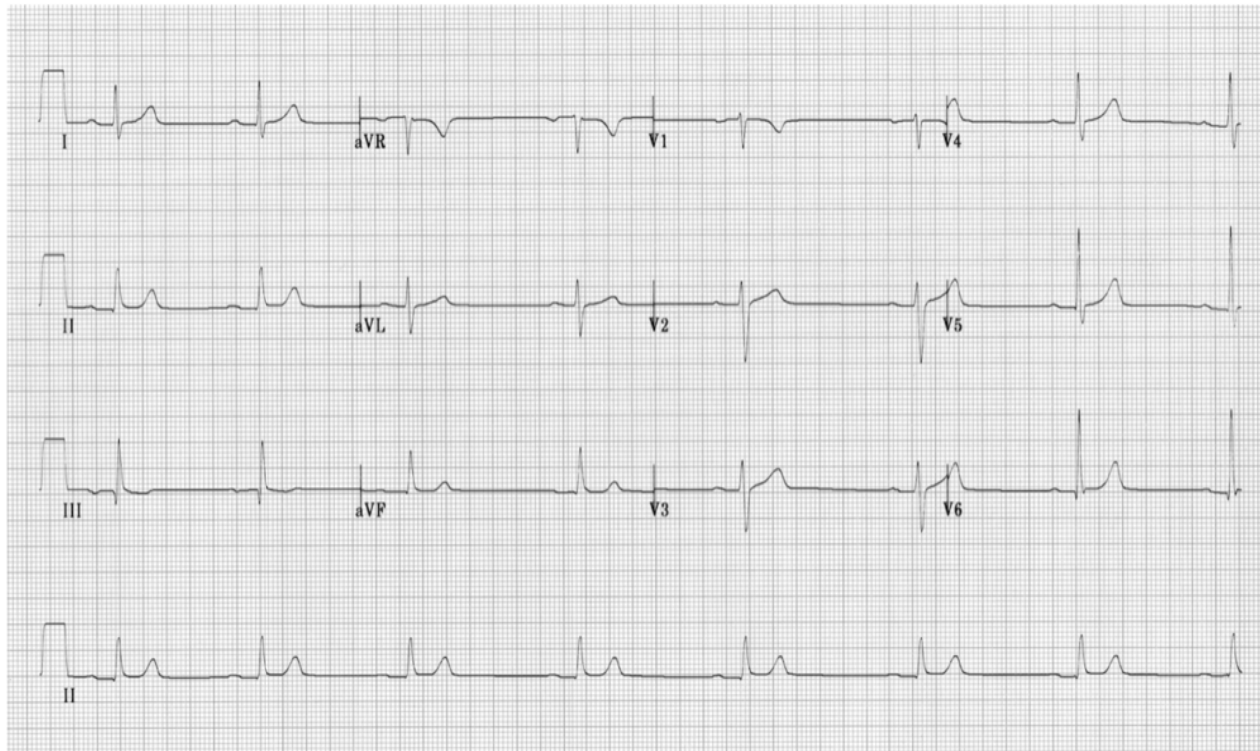
Toxicology Clinics-Bench to Bedside Toxic ECG

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A 57-year-old female was brought to the emergency room with H/o found drowsy in her room by family. There was an empty pill bottle at the scene, but it was left at the patient's home. She refuses to reveal what medications she takes, and the family is unsure whether she had as well. Her Vitals: HR 45b/min, BP 85/50mmHg, SpO2 99% on RA, Temp 98 F

An ECG is done immediately and is shown below:



How would you interpret this?

Prolonged PR interval and bradycardia with a first-degree AV block.

What additional “vital signs” could be helpful in an overdose patient who is bradycardic and hypotensive?

Capillary blood glucose! Both calcium channel blockers and beta-blockers can cause similar clinical presentations. However, calcium channel blockers will cause hyperglycemia, while beta-blockers will cause hypoglycemia.

Why hyperglycemia in calcium channel blockers?

Calcium channel blocker overdoses can result in:

- hypoinsulinemia, as insulin release, is dependent on calcium influx into islet beta-cells through L-type calcium channels
- calcium channel blocker-induced insulin resistance
- calcium channel blockers also impair the cardiac myocyte adaptive response of shifting from using free fatty acids, their favored “resting state” energy substrate, to carbohydrates, due to:

- o impaired uptake of glucose and free fatty acids by cardiac myocytes
- o inhibition of calcium-dependent mitochondrial activity required for glucose catabolism

What other findings are common ECG findings in CCB toxicity?

Bradycardia and first-degree AV block are often seen in the first stages of CCB toxicity. The ECG changes can progress to second and third-degree AV blocks. Junctional bradycardia is also a possibility.

How does CCB toxicity affect cardiac physiology?

It blocks calcium channels! Antagonism of calcium channels in the SA and AV nodes leads to slower heart rate and conduction blocks.

With this ECG and high glucose level in this clinical picture, what would be your management strategy?

In this case, we have a high suspicion for acute poisoning, likely an overdose of a CCB. While getting blood work and checking for other ingestions would be part of the workup, we already have enough clinical pictures and ECG information to begin interventions. The patient was still able to speak to you at the initial presentation; however, she has a high likelihood of clinical deterioration.

- ABC's. Intervene on any life threats. The patient may be obtunded and require an airway.
- Consider decontamination. Remember, there are standard and extended-release formulations.
- Hemodynamics. Start fluids, consider vasopressors if needed. Atropine for symptomatic bradycardia. Calcium for temporary hemodynamic support.
- HIET

What is HIET?

High-dose insulin euglycemic Therapy has become an intervention used more often and earlier in severe calcium channel blocker toxicity.

How do HIET works?

HIET may allow the heart to overcome the '**metabolic starvation**' that results from calcium channel blocker toxicity (and other poisonings, such as beta-blockers), which compounds the direct cardiotoxic effects.

HIET may be best used adjunctively with other measures such as catecholamines for two reasons:

- insulin-mediated inotropy is not catecholamine-mediated and is not affected by β blockers, so additive effects are likely
- although insulin appears to improve myocardial contractility, it has no chronotropic impact and may cause vasodilation

What is HIET protocol?

Commence therapy with

- Glucose 25 g (50 mL of 50% solution) IV bolus, unless marked hyperglycaemia (blood glucose > 22 mmol/L) is present
- Short-acting insulin 1 IU/kg bolus to maximally saturate insulin receptors

Continue therapy with

- Short-acting insulin infusion starting at 0.5 IU/kg/h and titrated every 30 min to a maximum of 5 IU/kg/h*
- Dextrose 25 g/h IV infusion titrated to maintain euglycaemia (blood glucose), 5.5-14 mmol/L; central venous access may be required to allow use of concentrated solutions (eg. 50% dextrose and limit excess volume administration

Monitor

- Glucose – every 20 min for first hour, then every 1h
- Potassium – replace only if < 2.5 mmol/L and there is of source of potassium loss

Therapeutic end points:

- Improvement in myocardial ejection fraction ($> 50\%$); in increased BP (systolic BP > 90 mm Hg in adults)
- Adequate heart rate (> 60 beats/min)
- Resolution of acidaemia; euglycaemia; adequate urine output (1-2 mL/kg/h)
- Reversal of cardiac conduction abnormalities (QRS interval < 120 ms)
- Improved mentation

Therapy is weaned after the withdrawal of other vasopressors, as cardiotoxicity resolves. Dextrose may be required after cessation of insulin.

IV = intravenous. BP = blood pressure. *The maximum safe and effective rate of infusion is

unknown but may be even higher than 5 IU/kg/h. In animal studies, insulin infusions as high as 10 IU/kg/h have been safely used.¹¹

What are the adverse effects of HIET?

Adverse events are predictable, uncommon, and easily managed. It includes

- hypoglycemia
- hypokalaemia
- hypomagnesemia
- hypophosphatemia

Further reading

1. Greene SL, Gawarammana I, Wood DM, Jones AL, Dargan PI. Relative safety of hyperinsulinaemia/euglycaemia therapy in the management of calcium channel blocker overdose: a prospective observational study. *Intensive Care Med.* 2007 Nov;33(11):2019-24. doi: 10.1007/s00134-007-0768-y. Epub 2007 Jul 11. PMID: 17622512.

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