

Severe suicidal digoxin and propranolol toxicity with insulin overdose

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Abstract

We present a case of a 32-year-old male doctor, with type I diabetes mellitus on daily insulin therapy, who allegedly consumed large doses of digoxin and propranolol along with simultaneous administration of large dose of insulin with suicidal intent. Initial investigations revealed serum digoxin levels of 7.5 ng/ml, serum insulin 500 μ IU/ml, and serum C-peptide 0.43 ng/ml. He was managed with charcoal-based hemoperfusion for digoxin overdose along with injection glucagon for propranolol overdose. His blood sugar levels were maintained with continuous infusion of 20% dextrose till the patient was allowed to take oral diet. Significant clinical improvement was noticed with this therapy which was evident by progressively declining serum digoxin levels, normalization of pulse rate, and adequate blood glucose levels. Finally, with a good hemodynamic profile and a serum digoxin level well within normal limits, he was discharged following consultation with a psychiatrist.

Keywords: Digoxin toxicity, hemoperfusion, propranolol

Access this article online

Website: www.ijccm.org

DOI: 10.4103/0972-5229.128709

Quick Response Code:



Introduction

Digoxin, a cardiac glycoside and propranolol, a nonselective beta-adrenergic antagonist are widely used for cardiovascular disorders. We present a case of suicidal ingestion of large quantities of digoxin along with propranolol and simultaneous administration of a large dose of insulin, which was effectively managed by using charcoal hemoperfusion and glucagon infusion.

Case Report

A 32-year-old male doctor, known case of type I diabetes mellitus for last 4 years, on glargine insulin 30 units once daily and regular insulin 15 units thrice daily, presented to our casualty with an alleged history of ingestion of 100 tablets of 0.25 mg digoxin (total dose 25 mg) and 50 tablets of 40 mg propranolol (total dose 2 g) along with subcutaneous injection of 1,600 units of regular insulin about 2 h prior

to presentation. He was conscious with the following vital parameters: Heart rate 74/min, blood pressure 106/70 mmHg, respiratory rate 26/min, random blood sugar level 58 mg/dl, and was maintaining normal oxygen saturation on room air. Systemic examination was unremarkable. His initial electrocardiograph showed normal sinus rhythm. Arterial blood gas analysis revealed: pH 7.391, $p\text{CO}_2$ 32.8 mmHg, $p\text{O}_2$ 102.4 mmHg, HCO_3 19.5 mEq/l, Na 136 mEq/l, and K 3.73 mEq/l. He complained of nausea and had one episode of vomiting in the casualty. Gastric lavage was immediately done with 100 g activated charcoal and he was given 50 ml of intravenous (IV) 25% dextrose injection along with other relevant supportive management. Routine laboratory investigations were sent for along with serum digoxin levels, serum insulin, and C-peptide levels and urine toxicology screen. He was shifted to the intensive care unit (ICU) for further medical management.

In the ICU, the patient had bradycardia (maximum heart rate of 58/min and a minimum heart rate of 39/min). Injection atropine 0.6 mg IV was administered on two occasions. In view of recurrent hypoglycemia, IV bolus of 50 ml of 25% dextrose, followed by infusion

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of 20% dextrose at the rate of 100 ml/h was started. Initial investigations revealed serum digoxin levels of 7.5 ng/ml (normal range 0.7-2 ng/ml), serum insulin 500 µIU/ml, and serum C-peptide 0.43 ng/ml (normal range 0.48-3.3 ng/ml). Blood counts, liver, and renal function tests along with serum electrolytes and serial blood gas analysis were normal. Electrocardiograph showed sinus bradycardia.

Immediate cardiology opinion was taken because of high serum digoxin levels and propranolol toxicity. To manage propranolol overdose, injection glucagon 5 mg slow IV bolus followed by an infusion at 5 mg/h was started. As digoxin specific antibody fragments (Fab) were unavailable, we tried to find other alternative approaches. As per the opinion of the nephrologist hemoperfusion with charcoal-based cartridge (Gambro Adsorba 300C and 150C) with a blood flow of 150 ml/h was done for 15 h after a written informed consent from the attendants. Close observation and regular monitoring of serum electrolytes with digoxin levels were done during this entire period.

By the end of day 1 of ICU stay, patient showed significant improvement and serum digoxin levels showed a decreasing trend [Figure 1]. On day 2, his heart rate varied between 58-66/min. Dextrose (20%) infusion was continued at a rate of 100 ml/h for 30 h and then reduced to a rate of 80 ml/h for the next 20 h. His random blood sugar levels hovered around 200 mg/dl. On day 3 he was started on oral diet and his maintenance Dextrose infusion was tapered down

and finally stopped (total dose of IV glucose 1,115 g) [Figure 2].

Glucagon infusion was given at a rate of 5 mg/h for the 19 h and then tapered to 2 mg/h which was continued for next 21 h targeting a heart rate above 50/min and adequate perfusion (total dose of IV glucagon 142 mg) [Figure 3].

On day 4, with a good hemodynamic profile and a serum digoxin level of 1.4 ng/ml, he was shifted to the step down unit. He continued to remain asymptomatic there and was discharged on the 6th day after consultation with a psychiatrist.

Discussion

Suicide risk appears to be increased in medical practitioners (relative risk varying between 1.1 and 3.4 in male and 2.5 and 5.7 among female doctors).^[1]

In our case it was a male postgraduate doctor with suicidal intent, who allegedly consumed large doses of digoxin and propranolol and simultaneously also self-administered a large dose of insulin.

Oral digoxin is readily absorbed through the gastrointestinal tract with peak serum concentrations achieved at 30-90 min. It has high oral bioavailability, volume of distribution of 5.1-7.4 l/kg and a narrow therapeutic index (0.7-2.0 ng/ml). Management of digoxin overdose includes gastric lavage, atropine,

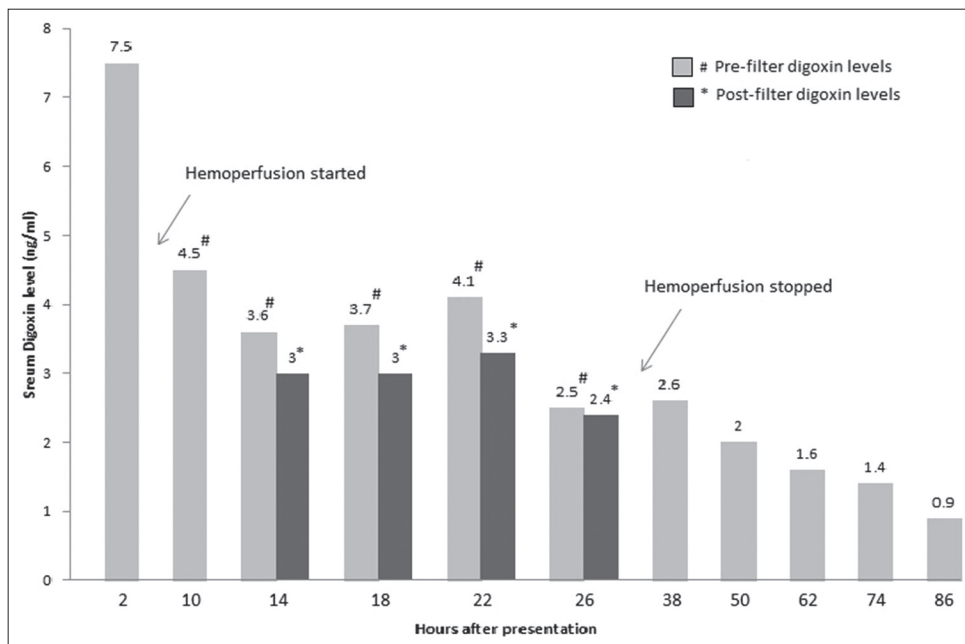


Figure 1: Serum digoxin levels

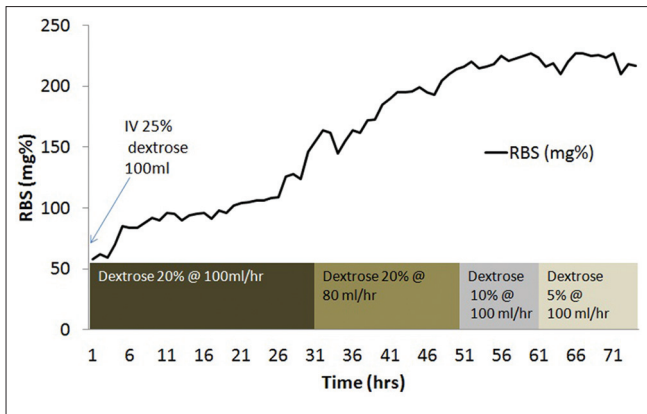


Figure 2: Dextrose infusion and random blood sugar levels

or cardiac pacing for symptomatic bradycardia and lignocaine or phenytoin for ventricular arrhythmias. Digoxin-specific antibody fragments (Fab) are considered first-line therapy, but it is not widely available in India.

Hemodialysis is not effective in digoxin overdose due to its large volume of distribution.^[2] However, digoxin can be effectively removed by hemoperfusion with charcoal or resin filters.^[3] We successfully used charcoal hemoperfusion for specific treatment of digoxin overdose in this patient, as evident by the rapid decline in serum digoxin levels.

Propranolol is a nonselective beta-adrenergic blocker, well-absorbed after oral administration with bioavailability of 30%. It has high lipid solubility and high protein binding (90%) with $t_{1/2}$ of 3-5 h. Treatment of overdose is primarily supportive. Glucagon exerts positive inotropic and chronotropic effects on the myocardium by stimulating adenylyl cyclase and providing cyclic adenosine monophosphate (cAMP) necessary for myocardial cell performance in the face of beta-adrenergic receptor blockade.^[4] Our patient responded well to this therapy evident by the increase in pulse rate after bolus dose and steady maintenance on continuous infusion.

Hyperinsulinemic euglycemia has been used for the management of cardiac drug-induced shock especially beta-blockers and calcium channel blockers.^[5] The mechanism of insulin's beneficial effect is not fully understood. We postulate that the coadministration of massive dose of insulin in this case may have turned out to be protective for our patient against propranolol toxicity.

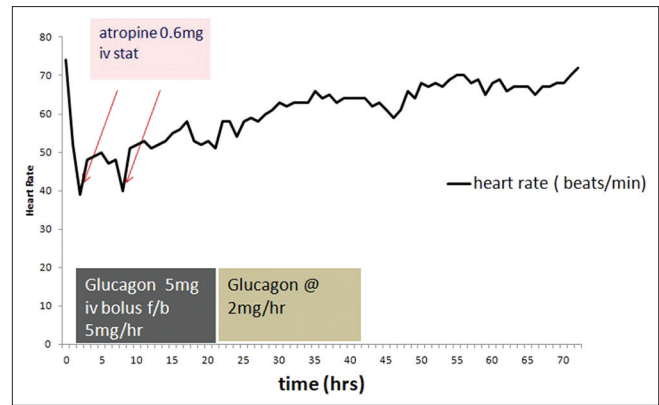


Figure 3: Heart rate

Exogenous hyperinsulinemia due to surreptitious use of insulin is diagnosed as hypoglycemia with elevated insulin (at least 3 μ IU/ml) with low C-peptide levels (less than 0.6 ng/ml).^[6] Our patient showed persistent low plasma glucose levels with very high serum insulin levels and low C-peptide levels confirming exogenous hyperinsulinemia (Whipple's triad).

The total amount of IV glucose administered to our patient was 1,115 g given over a period of 68 h. Literature reports the average requirement of glucose to be between 160 and 1,100 g till full recovery, while the duration of treatment to vary from 12 to 62 h.^[6]

Thus, this case of multiple drug overdose was managed successfully using specific pharmacologic therapy, hemoperfusion along with basic supportive measures.

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How to cite this article: Garg A, Panda S, Dalvi P, Mehra S, Ray S, Singh VK. Severe suicidal digoxin and propranolol toxicity with insulin overdose. *Indian J Crit Care Med* 2014;18:173-5.

Source of Support: Nil, **Conflict of Interest:** None declared.