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Case Report

Case report on the interaction between furosemide and digoxin that caused digoxin toxicity

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Abstract

Toxicity from digitalis is a typical clinical issue. In this case, the interaction of digoxin and furosemide is becoming more widely recognised as a major cause of digitalis toxicity. We present an abnormal ECG that demonstrates digoxin-induced cardiotoxicity. We report a case of a Digoxin toxicity in a 79-year-old male patient admitted with complains of nausea, increase frequency of micturition, decrease appetite, increase nocturia, shortness of breathing. The patient is taking furosemide and digoxin as past medication for Heart block and Chronic kidney disease treatment. In patient, Serum digoxin level is high due to hypokalemia because of digoxin and furosemide drug interaction. The Electrocardiogram interpretation shows sinus bradycardia, ST segment depression, and T wave inversion which mainly due to digoxin toxicity. So for the management digoxin is omitted from the current treatment. The patient needs to be constantly monitored since digitalis poisoning is deadly. A digoxin-binding antibody is the only treatment for digoxin overdose that can reverse its effects by its antidote but it's not available. So, the most successful course of treatment is symptomatic or efficient methods of extracorporeal drug removal.

Keywords: Digoxin toxicity, furosemide, hypokalemia, cardiotoxicity, complete heart block, ST segment depression.

INTRODUCTION

Digoxin, a cardiac glycoside, is commonly treat patients with conditions such as heart failure with reduced ejection fraction and atrial fibrillation. [1-3] Digoxin increases intracellular calcium, resulting in increased contractility. [1, 2] A therapeutic concentration of digoxin is reported as 0.8-2.0 ng/mL. [4, 5] Because of its narrow therapeutic index, patients on digoxin are at risk for toxicity, which can manifest with nausea, vomiting, visual changes, altered mental status, hyperkalemia, and cardiovascular collapse. [1-5] Symptoms of digoxin-induced cardiotoxicity are difficult to be identified and may become fatal too. [6]

In individuals with digoxin toxicity, digoxin-specific antibody fragments offer a treatment alternative; however, the indications for these antibody fragments are unclear. Ingestions of 10 mg or more in adults, 4 mg or more in children, or ingestions that result in a steady-state concentration of 10 ng/mL, or in chronic ingestions, digoxin concentrations exceeding 6 ng/mL in adults or 4 ng/mL in children, are among the indications for the use of digoxin-specific antibody fragments, according to the package insert (FDA). Others report a serum digoxin concentration of >12 ng/mL or >15 ng/mL at any time as treatment indications. [7, 8] In this article, we discuss a case of digoxin intoxication in a clinical pharmacist prospect.

CASE REPORT

A 79 Years old male patient was admitted to intensive care unit with presented complaints of nausea and vomiting from last 6 to 7 days, increase frequency of micturition, decrease appetite, increase nocturia 4 times at night, Shortness of breathing since last night and increase over last week, hiccup(++). Medical history of him revealed that he was a known type-2 diabetic patient since last 15 years, with ongoing oral hypoglycemic therapy. Moreover he was suffering with coronary artery disease with triple vessel disease. Before 9 years he underwent surgical procedure of coronary artery bypass grafting (CABG). Patient was also known case of chronic renal failure and on conservative therapy. His past medical history is TAB. Lanoxin (Digoxin) - 0.25mg OD, TAB. Glycomet SR (Metformin) – 500mg BD, TAB. Lasix (Furosemide) – 40mg. In on patient examination, He was found to have bradycardia (40 beats per minute) and he was having persisting hiccup (++). His vitals were- bloodpressure-124/59mmHg, temperature-normal, respiratory rate-15/min, SPO2-96%. In the systemic examination, the cardio-vascular system examination, the heart sounds S1 and S2 were normal. The patient was conscious and oriented during the central nervous system examination. The respiratory system examination shows a positive bilateral air entry was perceived on examining the respiratory system. On GIT examination, his abdomen was soft. In ECG we found, the electrocardiogram changes caused by digoxin show a down-sloping ST-segment depression, also known as a "reverse check" sign which shows in figure 1. Due to digoxin toxicity, deepened Q wave and complete heart block is shown in figure 2. The other lab investigations, 2D ECHO and ECG interpretations shown in Table-1 and Table- 2.

Table 1 Laboratory examination data of the patient on the day of admission

Parameter	Observed Value	Reference Value
Haemoglobin	7.4 g/Dl	13-17 g/dL
Total RBC	2.57 mill/cmm	4.5-6.5 mill/cmm
Total WBC	8580 /cmm	4000-10000 /cmm
Platelet Count	201000 /cmm	140000-410000 /cmm
Serum bicarbonate	29.1 mmol/L	22-30 mmol/L
Serum creatinine	5.25 mg/dl	0.4-1.2 mg/dl
Serum potassium	5.83 mEq/L	3.6-5.0 mEq/L
Troponin-1	0.04 ng/ml	0.0-0.02 ng/ml
Creatinine phosphate MB fraction	11.2 U/L	0-24 U/L
Albumin	(+) 50 mg/dl	TRACE : 15mg/dl (+) : 50mg/dl (++) : 100mg/dl (+++) : 300mg/dl (++++) : 1000mg/dl
Sugar	(+) 50 mg/dl	TRACE : 30mg/dl (+) : 50mg/dl (++) : 100mg/dl (+++) : 300mg/dl (++++) : 1000mg/dl
Digoxin Level	3.48 ng/ml	0.5-2.0 ng/ml

Table 2 Cardiac specific investigational test of the patient

Cardiac specific investigation test	Interpretation
2D ECHO	LV size is dilated with LVEF is 20%. Severe hypokinesia in apico lateral LA is also dilated
ECG	Sinus bradycardia Deepened Q wave (lead III) Atrioventricular dissociation Complete heart block (lead II) Anteroseptal myocardial infraction ST-T abnormality (lead I &V6) T wave abnormality (lead V5 &V6)

He is well diagnosed with Digoxin toxicity, complete heart block, ischemic heart disease, severe left ventricular dysfunction, chronic kidney disease, and diabetes mellitus. On admission patient's heart rate was 40/min, so patient was treated with inj. Atropine. Patient had arrived with complaints of loss of appetite, nausea and bradycardia were suggestive of digoxin toxicity hence tab. Digoxin was omitted from treatment. He was symptomatically treated and improved well and his digoxin level was reduced. Calcium gluconate injection (10 mL of 10% solution) given immediately to this patient. Maintenance treatment continued with inj. Zostum (Cefoperazone + Salbactum) 1.5gm BD, inj. Pantop (Pantoprazole) 40mg BD, inj. Emeset (Ondansetron) 4cc SOS, tab. Domstal (Domperidone) 10mg TDS, tab. Orcibest (Orciprenaline) 10mg TDS, tab. Veltum (Tamsulosin) 0.4mg OD, tab. Atorva (Atorvastatin) 40mg OD, tab. Febuget (Febuxostat) 40mg OD, tab. Sporlac DS (Lactic acid bacillus tablet) 1 tab QDS, tab. Torsid (Torasemide) 20mg BD, tab. Clavix (Clopidogrel) 75mg OD, tab. Glimison (Glimepiride) 1mg BD, tab. Vibact (Probiotic) 1 tab BD, tab. Prometil-md

(Prochlorperazine) 5mg TDS, tab. Ecovog (Voglibose) 0.3mg BD, tab. Deri retard (Deriphyllin) 150mg BD, tab. Mucomix (Acetylcysteine) 600mg BD. From 3rd day to 7th day patient was hemodynamically stable with no bed sore, improved clinically and all reports were normal including digoxin level (1.8ng/ml), serum potassium, serum creatinine and heart rate. Heart rate was gradually raised 70/min.

DISCUSSION

Digoxin has a narrow therapeutic range, and its serum levels fluctuate as a result of changes in age, body weight, renal function, hepatic impairment, and concurrent drug administrations. Digoxin toxicity may be caused by an impaired volume of distribution of digoxin due to decreased renal function (digoxin is primarily excreted by the kidneys) or congestive cardiac failure. [9] Digoxin and furosemide interaction occur in this case based on the patient's previous medication history. Because furosemide causes hypokalemia, digoxin binds more strongly to the Na^+/K^+ ATPase pump, exerting an inhibitory effect. Which lead to increase sodium and calcium concentration inside the cell and increase potassium concentration outside the cell due to this hyperkalemia is caused by digoxin toxicity. However, the patient's potassium level (5.83mEq/L) is increase. [10] Calcium gluconate is used to treat hyperkalemia by stabilising cardiac cell membranes. Any patient presenting with hyperkalemia and alterations in their EKG, which point to a hyperkalemic emergency, should be given calcium right away. Increased cardiac myocyte threshold potential caused by elevated potassium levels causes the destabilisation of cardiac membranes. Supplemental calcium lowers the threshold needed to reestablish the transmembrane voltage gradient in this case patient treated with calcium gluconate injection. Despite the fact that calcium shields myocytes from potassium, it does not treat hyperkalemia, a condition that is typically treated with other medications like insulin, dextrose or sodium bicarbonate, which moves potassium into cells, and sodium polystyrene sulphate, which increases potassium excretion through stools. However, dialysis, especially in individuals with renal failure, is the most effective method of potassium excretion. [11, 12] In the case of acute poisoning, the patient may be asymptomatic for 1-2 hours before symptoms such as nausea, vomiting, diarrhoea, and abdominal pain appear. Regardless of the hemodynamic situation, lethargy, confusion, and weakness follow. Chronic toxicity causes less specific initial symptoms such as anorexia, nausea, vomiting, diarrhoea, abdominal pain, weight loss, delirium, confusion, drowsiness, headache, hallucinations, visual disturbance (chromatopsia, particularly xanthopsia), instability, syncope or fainting due to low cardiac output associated with an altered heart rate. [6] Digoxin-induced electrocardiogram changes show a down-sloping ST-segment depression, also known as a "reverse check" sign. With abnormal Q waves and T wave inversions, the ST segments may appear "scooped." Digoxin consumption results in a shorter QT interval, a longer PR interval, and T wave inversion or flattening. [13] Digoxin can help patients with systolic heart failure, also known as heart failure with reduced ejection fraction (HFrEF), who have an ejection fraction less than 40%. In our case patient's LVEF is 20%. [14] Digoxin serum levels should range between 0.8 and 2 ng/mL. It is critical to draw blood at least 6 to 8 hours after the last dose when measuring digoxin serum levels. The toxicity increases as serum drug levels exceed 2.0 ng/mL. The prescriber should check levels after any recent medication change. In direct proportion to the patient's glomerular filtration rate, the kidneys excrete approximately 70% of digoxin. To assess renal function, the doctor must order regular electrocardiograms and blood tests, and electrolytes must be closely monitored. [15, 16]

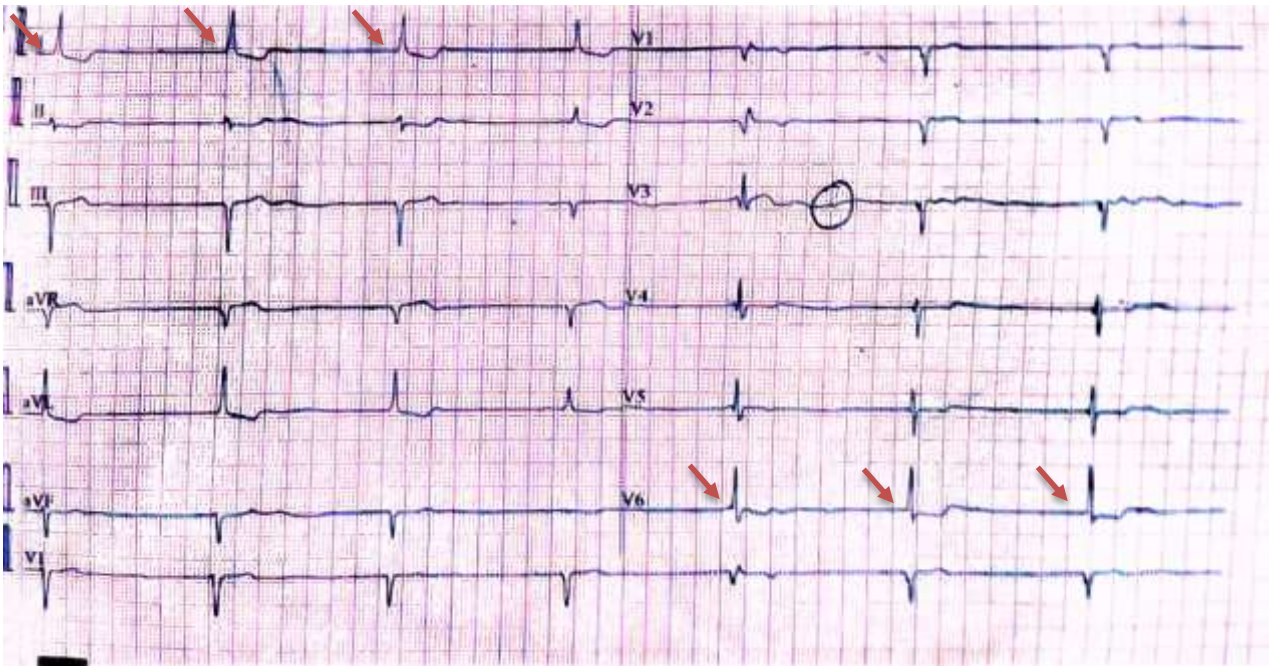

Figure 1: ST SEGMENT DEPRESSION AND T WAVE INVERSION (LEAD I & V6) IN ECG

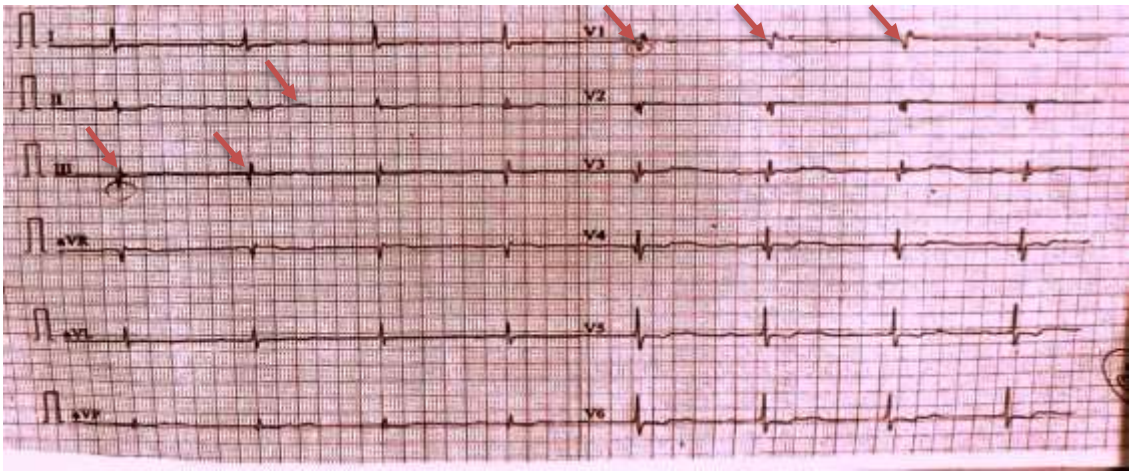

Figure 2: DEEPENED Q WAVE (LEAD III & V1) AND COMPLETE HEART BLOCK (LEAD II) IN ECG

CONCLUSION

Since digitalis poisoning is dangerous, the patient must be continuously watched over until the risks are assessed, the treatment is given, and until it is determined that the risk of death is improbable. This case describes the risk of serious interaction between digoxin and furosemide, which can be life-threatening and dangerous. The only medication that can reverse the effects of digoxin poisoning is a digoxin-binding antibody which is not available. Due to the lack of specific antidotes (antidigitalis antibodies) and effective ways to remove the medication extracorporeally, symptomatic treatment, which includes resolving electrolyte imbalances and controlling heart rate, continues to be the most successful.

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LIST OF ABBREVIATION

ECG	Electrocardiogram
LVEF	Left ventricular ejection fraction
BD	Twice a day
TDS	Three times daily

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests.

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