

Cholestyramine, A Cost-Effective Yet Efficacious Anti-Dote in Digoxin Toxicity

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Abstract— Digoxin is a cardiac glycoside obtained from *digitalis lanata*, is a positive inotropic and negative chronotropic agent. Digoxin works by blocking Na-K ATPase pump resulting in raised intracellular sodium which in turn raise intracellular calcium in the myocytes resulting in increase in inotropic effect [1, 2]. Digoxin causes several adverse effects in overdose leading to both bradyarrhythmias and tachyarrhythmias. The approved antidote, digoxin-specific antibody fragments (DIGIFAB), is costly yet effective option for managing digoxin toxicity [3] we describe the cases in which levels of digoxin fell to acceptable therapeutic levels with the use of Cholestyramine.

Keywords— Digoxin; toxicity; cholestyramine.

I. INTRODUCTION

Digoxin is a cardiac glycoside obtained from *digitalis lanata*, is a positive inotropic and negative chronotropic agent. Digoxin works by blocking Na-K ATPase pump resulting in raised intracellular sodium which in turn raise intracellular calcium in the myocytes resulting in increase in inotropic effect [1, 2]. It is used in managing congestive cardiac failure with atrial fibrillation and control ventricular rate in atrial fibrillation. Digoxin causes several adverse effects in overdose leading to both bradyarrhythmias and tachyarrhythmias. The approved antidote, digoxin-specific antibody fragments (DIGIFAB), is costly yet effective option for managing digoxin toxicity [3] but availability in our setup is limited.

II. DISCUSSION

Manifestations of digoxin toxicity are variable and can be sub-grouped into cardiac and non-cardiac effects. Non-cardiac presentations include nausea, vomiting, lethargy, decreased level of consciousness, headaches and clumsiness. Cardiac related effects are bradycardias including any form of heart blocks and tachyarrhythmia [4]. Digoxin has a narrow therapeutic index resulting in toxicity with minor changes in dosing, renal impairment and electrolyte abnormalities [5]. Establishing the cause of digoxin toxicity is essential as it is affected by many factors including dose of digoxin, drug-drug interactions, electrolyte imbalances (low potassium, low magnesium and high calcium) [4] and worsening renal function. Toxicity should also be quantified by sending levels of digoxin and matching it with specific laboratory cut-offs.

Over the last many years digoxin related specific antibody fragments (DIGIFAB) has been the standard of care in digoxin toxicity but its availability due to its cost in our setup is

compromised. Cholestyramine was used initially in management of digoxin toxicity when it was an integral component of heart failure regimen back in 1970s. But its use was not validated by further studies and introduction of DIGIFAB in early 2000s.

In a case report published in 1988 bile acid-binding drug cholestyramine 4 grams was given to a patient every 6 hourly with digoxin toxicity and serum digoxin levels checked subsequently showed brisk decline. Patient's symptoms also alleviated after the treatment which pointed towards the fact that bile acid-binding medicines like colestipol and cholestyramine affects the enterohepatic circulation of digoxin resulting in its removal from the body. These drugs potentially constitute important measures in managing digoxin toxicity in the scenario where DIGIFAB is not available [6]. In a study done in 1971 in rats and guinea pigs showed, cholestyramine bonded significant amounts of Digoxin in vitro and subsequently resulted in accelerated excretion of digoxin via fecal route [7].

We are describing three case studies of patients that presented to us to with manifestations of digoxin toxicity, subsequently were found to have raised digoxin levels. We did not use DIGIFAB as it is not available in our clinical setting. Charcoal was not used as patients presented late during the course of their toxicity. This agent is particularly important in a scenario when patient has taken a recent over dose of Digoxin[4].

Cholestyramine was used as it is easily available in our setup and also is considerably cheaper than DIGIFAB.

III. CASE REPORTS

Case#1

69 female with history of hypertension, ischemic cardiomyopathy (Ejection fraction of 20%), peripheral

vascular disease, chronic kidney disease presented with history of chest discomfort and nausea for 2 days. She was on Aspirin 75 mg, Digoxin 0.125mg and Lasix 40 mg once a day. Examination revealed Heart rate of 72/min and blood pressure of 110/72 with basal fine crepitations. 12 lead ECG showed sinus bradycardia with left anterior fascicular block. Laboratory workup showed deranged renal function with creatinine of 2.2 mg/dl, potassium of 5.1 mmol/L and digoxin levels of 2.29 ng/ml (lab value above 2 ng/ml signifying toxicity). Troponins were mildly raised being 0.231 ng/ml and 0.375 ng/ml respectively. Echocardiogram showed ejection fraction of 20% with almost global hypokinesia. Patient was started on cholestyramine 4 grams every 6 hourly for 2 days and Patient's symptoms of nausea and chest discomfort also started to settle. Digoxin levels were followed which reduced to 0.79 ng/ml and Patient was discharged home.

Troponins were mildly raised 0.153 ng/ml and 0.181 ng/ml respectively. Echocardiogram showed ejection fraction of 15% with severe mitral regurgitation. Patient received cholestyramine 4 grams every 6 hourly for 1 day and Digoxin levels were followed which reduced to 1.66 ng/ml after 2 days and eventually to 1.11 ng/ml at the 4th day of admission. Bradycardia improved and drowsiness also got resolved. Renal function with creatinine improved to 1.6 mg/dl and patient was discharged home.

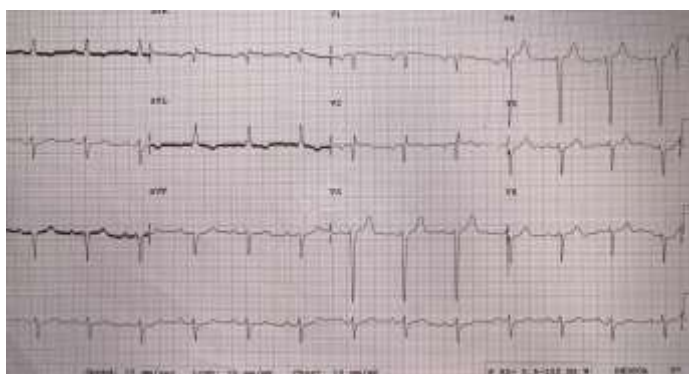


Fig. 1(a) Pre-treatment EKG showing slow heart rate.

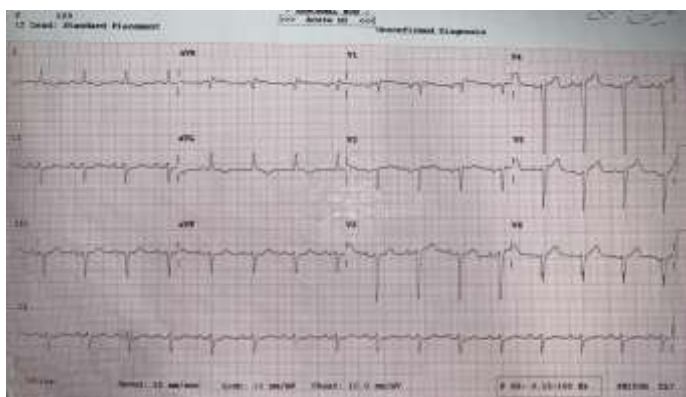


Fig. 1(b) Post Treatment EKG

Case#2

65 male with history of hypertension, ischemic cardiomyopathy (Ejection Fraction of 15%), chronic kidney disease s/p ICD placement for primary prevention presented with history of drowsiness and worsening dyspnea for 3 days. He was on Ascard 75 mg, Lasix 80 mg, spironolactone 25 mg and Digoxin 0.125 mg once a day. Examination revealed HR of 60/min and Blood pressure of 104/61, altered mental status in the form of drowsiness but no focal neurological deficit. 12 lead ECG showed bradycardia with left axis deviation, left anterior fascicular block and ventricular bigeminy. Laboratory workup showed raised creatinine of 5.1 mg/dl, potassium of 5.5 mmol/L and Digoxin levels of 3.89 ng/ml initially.

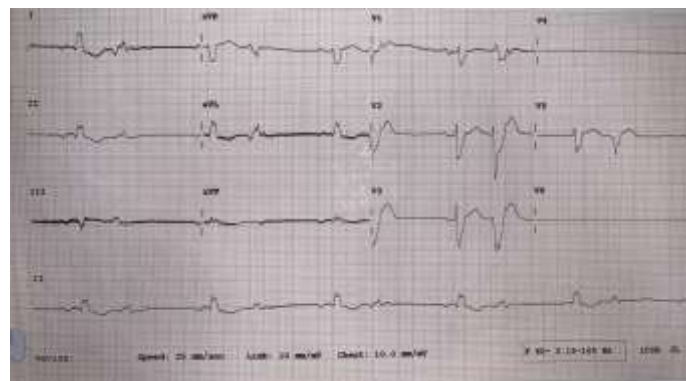


Fig. 2(a) Pre-treatment EKG signifying Ventricular Bigemny.

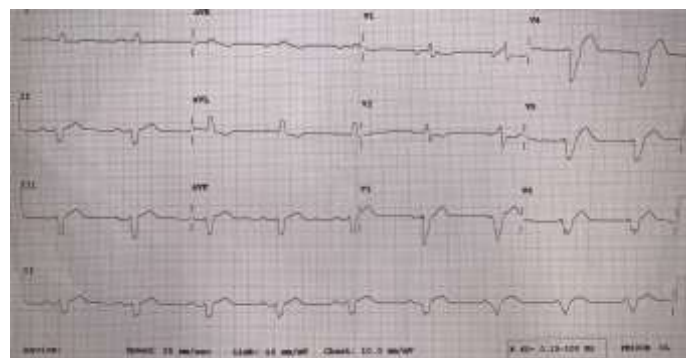


Fig. 2(b) Post Treatment EKG

Case #3

76-year-old male with hypertension, ischemic cardiomyopathy (Ejection Fraction 25-30%) admitted with history of generalized weakness and drowsiness for 2 days. He was on Ascard 75 mg, Spiromide 20 mg and Digoxin 0.25 once a day. Examination revealed HR of 54/min Blood pressure of 109/54, patient was drowsy but arousable and chest examination showed no crepitations. 12 lead ECG showed bradycardia with complete AV dissociation (complete heart block) and junctional escape rhythm. Laboratory workup showed deranged creatinine of 2.1 mg/dl potassium of 4.8 mmol/L and Digoxin levels of 3.65 ng/ml. Troponins were normal (0.06 ng/ml and 0.06 ng/ml respectively). Echocardiogram showed ejection fraction of 30% and Grade II diastolic dysfunction. Patient received 4 grams of cholestyramine every 6 hourly for 3 days and Digoxin levels were monitored. Levels reduced to 3.14 ng/ml and then to 1.98 ng/ml and subsequently to 1.36ng/ml on the 3rd day of admission. Patient received Electrophysiology review and was advised to undergo CRT-P (cardiac resynchronization therapy and pacemaker) which patient denied to have it because of

financial constraints. His renal function improved to 0.9 mg/dl and electrolytes also remained within normal ranges.

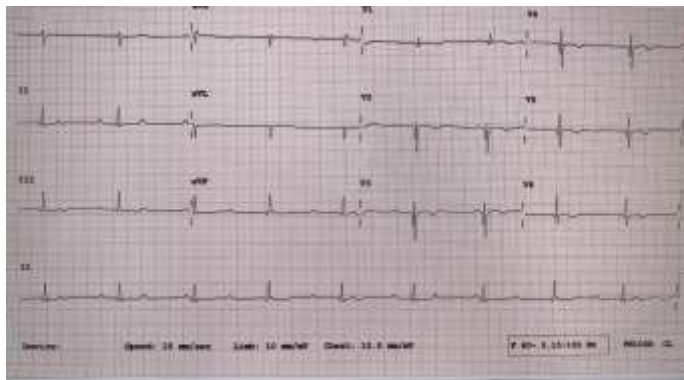


Fig. 3(a) Pre-treatment EKG signifying complete heart block

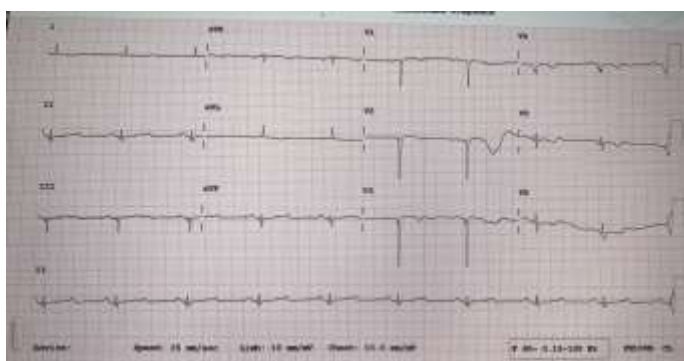


Fig. 3(b) Post treatment EKG

IV. CONCLUSION

This case study signifies that cholestyramine is a potential fruitful option as antidote in digoxin Toxicity in a low-income country which is very cost-effective in our setup as availability of DIGIFAB in our setup is limited because of its cost. But a more research is warranted in this area to validate cholestyramine as antidote in Digoxin Toxicity.

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