Medical Safety and Global Health

Extended Abstract

Global Toxicology 2020: Cholestyramine, A Cost-Effective Yet Efficacious Anti-Dote in Digoxin Toxicity-Mahreen Muzammil, Aga Khan University, Pakistan

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.

I. Introduction: Digoxin is a heart glycoside acquired from digitalis lanata, is a positive inotropic and negative chronotropic operator. Digoxin works by blocking Na-K ATPase siphon bringing about brought intracellular sodium which up in turn raise intracellular calcium in the myocytes bringing about increment in inotropic impact [1, 2]. It is utilized in overseeing congestive heart disappointment with atrial fibrillation and control ventricular rate in atrial fibrillation. Digoxin makes a few antagonistic impacts in overdose driving both bradyarrhythmias and tachyarrhythmias. The affirmed cure, digoxin-explicit counter acting agent pieces (DIGIFAB), is exorbitant yet compelling alternative for overseeing digoxin poisonousness [3] however accessibility in our arrangement is restricted.

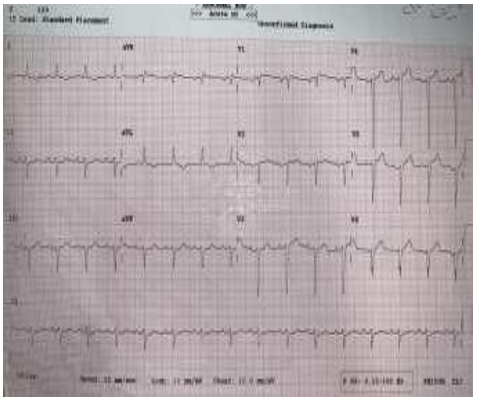
II. Conversation: Manifestations of digoxin poisonousness are variable and can be sub-assembled into heart and non-cardiovascular impacts. Non-heart introductions incorporate queasiness, spewing, dormancy, diminished degree of cognizance, migraines and ungainliness. Cardiovascular related impacts are bradycardias including any type of heart squares and tachyarrhythmia [4]. Digoxin has a thin restorative list bringing about harmfulness with minor changes in dosing, renal disability and electrolyte irregularities [5]. Building up the reason for digoxin harmfulness is basic as it is influenced by numerous components including portion of digoxin, sedate medication collaborations, electrolyte lopsided characteristics (low potassium, low magnesium and high calcium) [4] and intensifying renal capacity. Harmfulness ought to likewise be evaluated by sending levels of digoxin and coordinating it with explicit research center shorts. In the course of the last numerous years digoxin related explicit counter acting agent sections (DIGIFAB) has been the standard of care in digoxin harmfulness yet its

accessibility because of its expense in our arrangement is undermined. Cholestyramine was utilized at first in the board of digoxin harmfulness when it was a fundamental segment of cardiovascular breakdown routine back in 1970s. In any case, its utilization was not approved by further investigations and presentation of DIGIFAB in mid 2000s. For a situation report distributed in 1988 bile corrosive restricting medication cholestyramine 4 grams was given to a patient each 6 hourly with digoxin harmfulness and serum digoxin levels checked consequently demonstrated energetic decrease. Patient's side effects additionally mitigated after the treatment which pointed towards the way that bile corrosive restricting meds like colestipol and cholestyramine influences the enterohepatic dissemination of digoxin bringing about its expulsion from the body. These medications conceivably establish significant measures in overseeing digoxin poisonousness in the situation where DIGIFAB isn't accessible [6]. In an investigation done in 1971 in rodents and guinea pigs appeared, cholestyramine reinforced critical measures of Digoxin in vitro and therefore brought about quickened discharge of digoxin by means of fecal course [7]. We are portraying three contextual investigations of patients that introduced to us to with indications of digoxin poisonousness, in this way were found to have raised digoxin levels. We didn't utilize DIGIFAB as it isn't accessible in our clinical setting. Charcoal was not utilized as patients introduced late over the span of their poisonousness. This specialist is especially significant in a situation when patient has taken an ongoing over portion of Digoxin[4]. Cholestyramine was utilized as it is effectively accessible in our arrangement and furthermore is significantly less expensive than DIGIFAB.

III. CASE REPORTS

Case#1

69 female with history of hypertension, ischemic cardiomyopathy (Ejection part of 20%), fringe vascular infection, ceaseless kidney malady gave history of chest inconvenience and sickness for 2 days. She was on Aspirin 75 mg, Digoxin 0.125mg and Lasix 40 mg once per day. Assessment uncovered Heart pace of 72/min and pulse of 110/72 with basal fine crepitations. 12 lead ECG demonstrated sinus bradycardia with left front fascicular square. Research center workup indicated unhinged renal capacity with creatinine of 2.2 mg/dl, potassium of 5.1 mmol/L and digoxin levels of 2.29 ng/ml (lab esteem over 2 ng/ml meaning harmfulness). Troponins were somewhat raised being 0.231 ng/ml and 0.375 ng/ml separately. Echocardiogram indicated launch division of 20% with practically worldwide hypokinesia. Persistent was begun on cholestyramine 4 grams each 6 hourly for 2 days and Patient's indications of queasiness and chest inconvenience likewise began to settle. Digoxin levels were followed which decreased to 0.79 ng/ml and Patient was released home.



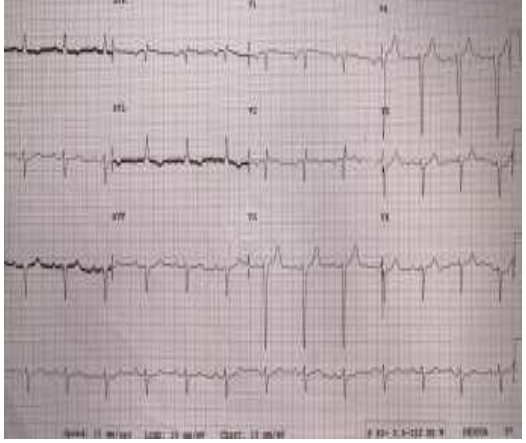


Fig. 1(a) Pre-treatment EKG showing slow heart rate

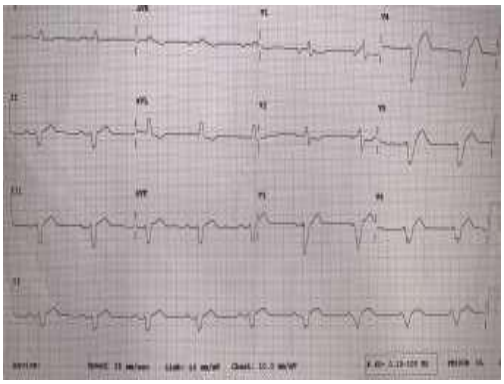
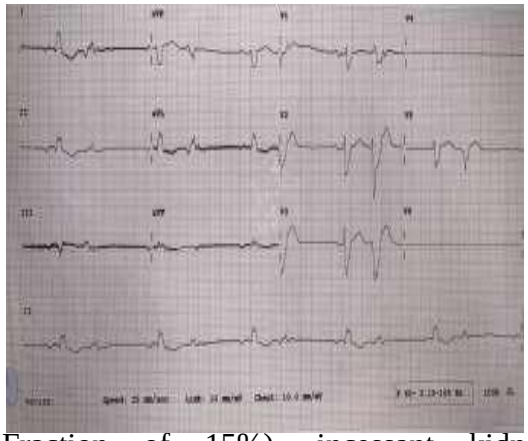


Fig. 1(b) Post Treatment E Fig

Case#2

65 male with history of hypertension

n, ischemiccardiomyopathy (Ejection



Fraction of 15%), incessant kidney infection s/p ICD position for essential counteraction gave history of languor and exacerbating dyspnea for 3 days. He was on Ascard 75 mg, Lasix 80 mg, spironolactone 25 mg and Digoxin 0.125 mg once per day. Assessment uncovered HR of 60/min and Blood weight of 104/61, changed mental status as laziness yet no central neurological shortage. 12 lead ECG indicated bradycardia with left hub deviation, left front fascicular square and ventricular bigeminy. Research facility workup indicated raised creatinine of 5.1 mg/dl, potassium of 5.5 mmol/L and Digoxin levels of 3.89 ng/ml at first.

Troponins were somewhat raised 0.153 ng/ml and 0.181 ng/ml separately. Echocardiogram demonstrated discharge division of 15% with extreme mitral spewing forth. Tolerant got cholestyramine 4 grams each 6 hourly for 1 day and Digoxin levels were followed which diminished to 1.66 ng/ml following 2 days and in the long run to 1.11 ng/ml at the fourth day of affirmation. Bradycardia improved and languor additionally got settled. Renal capacity with creatinine improved to 1.6 mg/dl and patient was released home.

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%) conceded with history of summed up shortcoming and tiredness for 2 days. He was on Ascard 75 mg, Spiromide 20 mg and Digoxin 0.25 once per day. Assessment uncovered HR of 54/min Blood weight of 109/54, persistent was sleepy however arousable and chest assessment demonstrated no crepitations. 12 lead ECG indicated bradycardia with complete AV separation (complete heart square) and junctional get away from cadence. Research facility workup indicated disturbed creatinine of

2.1 mg/dl potassium of 4.8 mmol/L and Digoxin levels of 3.65 ng/ml. Troponins were ordinary (0.06 ng/ml and 0.06 ng/ml separately). Echocardiogram demonstrated launch division of 30% and Grade II diastolic brokenness. Tolerant got 4 grams of cholestyramine each 6 hourly for 3 days and Digoxin levels were checked. Levels decreased to 3.14 ng/ml and afterward to 1.98 ng/ml and therefore to 1.36ng/ml on the third day of affirmation. Persistent got Electrophysiology survey and was encouraged to experience CRT-P (cardiovascular resynchronization treatment and pacemaker) which patient denied to have it as a result of monetary limitations. His renal capacity improved to 0.9 mg/dl and electrolytes additionally stayed inside ordinary reaches.

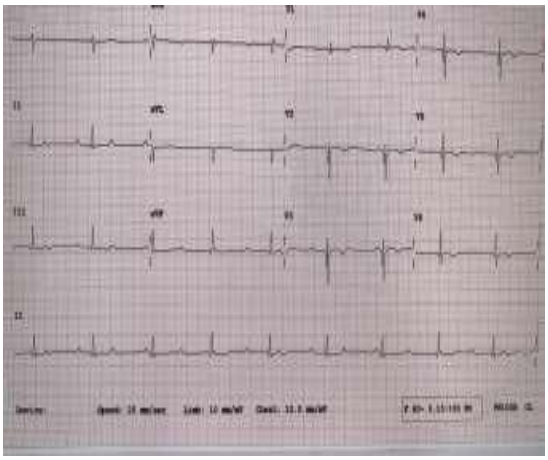


Fig. 3(a) Pre-treatment EKG signifying complete heart block

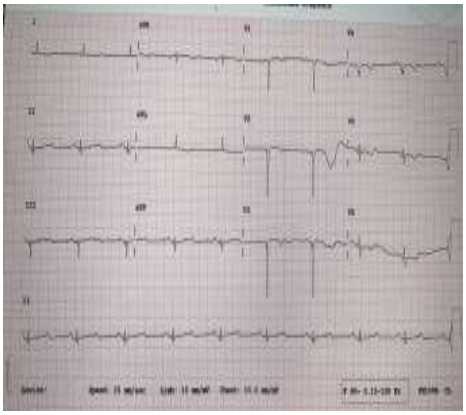


Fig. 3(b)Post treatment EKG

IV. CONCLUSION

This contextual analysis implies that cholestyramine is a likely productive alternative as remedy in digoxin Toxicity in a low-pay nation which is very practical in our arrangement as accessibility of DIGIFAB in our arrangement is restricted in view of its expense. In any case, a more examination is justified here to approve cholestyramine as antitoxin in Digoxin Toxicity.

Reference

[1] Eichhorn, E.J. and M. Gheorghiade, Digoxin. Prog Cardiovasc Dis, 2002. 44(4): p. 251-66.

[2] Li-Saw-Hee, F.L. and G.Y. Lip, Digoxin revisited. Qjm, 1998. 91(4): p. 259-64.

[3] Chan, B.S. and N.A. Buckley, Digoxin-specific antibody fragments in the treatment of digoxin toxicity. Clin Toxicol (Phila), 2014. 52(8): p. 824-36.

[4] Lip, G.Y., M.J. Metcalfe, and F.G. Dunn, Diagnosis and treatment of digoxin toxicity. Postgraduate medical journal, 1993. 69(811): p. 337- 339.

[5] Bauman, J.L., R.J. Didomenico, and W.L. Galanter, Mechanisms, manifestations, and management of digoxin toxicity in the modern era. Am J Cardiovasc Drugs, 2006. 6(2): p. 77-86.

[6] Henderson, R.P. and C.P. Solomon, Use of cholestyramine in the treatment of digoxin intoxication. Archives of Internal Medicine, 1988. 148(3): p. 745-746.

[7] Caldwell, J.H. and N.J. Greenberger, Interruption of the

enterohepatic circulation of digitoxin by cholestyramine. I. Protection against lethal digitoxin intoxication. J Clin Invest, 1971. 50(12): p. 26
[8] 26-37.

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