

A case of Digoxin toxicity due to renal insufficiency and drug-drug interaction

Kotadia RB¹, Kubavat AR²

¹ 2nd Year Resident
² Associate Professor
 Department of Pharmacology, PDU
 Govt. Medical College, Rajkot.

ABSTRACT

Background: Digoxin is a cardiac glycoside indicated for the control of resting ventricular rate in patients with chronic atrial fibrillation in adults. The drug has a narrow therapeutic range (0.5 – 2 ng/ml) that leads to toxicity. However, we report a case of serious digoxin toxicity.

Methods: A K/C/O AF with CVA, 57 year old male patient presented with c/o vomiting, chest pain, ghabaraman, dizziness and generalized-weakness. The patient was also having renal calculi with on and off hydro-nephrosis. He was prescribed with Digoxin (0.125 mg) 5 day in a weak along with Tab Atorvastatin 40 mg, Tab Aspirin 150 mg and Tab Clopidogrel 75 mg OD since 1 year. The physician observed ECG changes indicating Bradycardia and A-V block as a suspected ADR of Digoxin and was confirmed by Laboratory investigation and causality assessment, immediately Digoxin was stopped. The symptoms improved significantly after withdrawal of the drug and Injection Atropine 0.5 mg intravenously stat.

Discussion: The most frequent causes of toxicity are renal insufficiency and overdosing. Digoxin is primarily excreted by the kidneys; therefore, patients with impaired renal function require smaller than usual maintenance doses of digoxin. Atorvastatin can lead to increase Digoxin plasma concentration by 22% requiring reduction in dosage.

Conclusion: Dosage of Digoxin should be decided only obtaining results of Renal and Liver function test and checking drug-drug interaction with drugs prescribed simultaneously. TDM should be done regularly & periodically in patients with Digoxin Therapy.

Keywords: Digoxin, Renal insufficiency, Drug-drug interaction.

Corresponding Author

Ravi Kotadia,
 2nd year Resident,
 PDU Govt. Medical College Rajkot.
 Drravikotadia44@gmail.com

Copyright: © the author(s) and publisher. JPDS is an official publication of Society of Pharmacovigilance, India.



This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial

INTRODUCTION

Digoxin is a cardiac glycoside. It is extracted from the leaves of the plant Digitalis lanata. Digoxin at therapeutic concentrations mildly inhibit the cardiac Na⁺/K⁺ ATPase, causing an increase in intracellular calcium, intracellular sodium and extracellular potassium. In the heart, this leads to an increase in myocardium's strength of contraction and excitability, as well as to a decrease in conduction and depolarization velocity in the atrio-ventricular node. Approved indications to digoxin are mild to moderate heart failure in adults, increasing myocardial contractility in pediatric patients with heart failure and control of resting ventricular rate in patients with chronic atrial fibrillation in adults.

Signs and symptoms of digoxin toxicity include anorexia, nausea, vomiting, visual changes and cardiac arrhythmias; atrial tachycardia with block; AV dissociation; accelerated junctional (nodal) rhythm; unifocal or multifocal premature contractions (especially bigeminy or trigeminy); ventricular tachycardia and ventricular fibrillation. Toxicity is usually associated with digoxin levels greater than 2 ng/ml although symptoms may also occur at lower levels. Low

body weight, advanced age or impaired renal function, hypokalemia, hypercalcemia or hypomagnesemia may predispose to digoxin toxicity.

Awareness of drug interactions is relevant not only to achieve appropriate maintenance therapy but also to avoid adverse events, especially with drugs having low therapeutic index. Here, physician report a case of Digoxin Toxicity due to renal insufficiency and a drug-drug interaction.

CASE REPORT

STUDY DESIGN

A 57 years old male patient was admitted in general medicine ward with complaints of vomiting, chest pain, ghabaraman, dizziness and generalized-weakness since 3 days. The patient was a known case of chronic atrial fibrillation since 1 year and known case of Cardio Vascular Attack since 12 years. He was a known smoker since 20 years. He was prescribed with Digoxin (0.125 mg) 5 day in a weak

along with Tab Atorvastatin 40 mg, Tab Aspirin 150 mg and Tab Clopidogrel 75 mg all drugs once in a day since 1 year.

On general examination, patient was conscious and oriented to time, place and person. He was afebrile, PR was 68 beats per minute, BP was 90/80 mm of Hg and Respiratory rate was 20 cycles per minute. On systemic examination CVS shows S1S2 present, CNS shows no abnormalities, pupils were reactive to light. Ultrasound abdomen & pelvis showed mild Hydro nephrosis with dilated ureter up to 4 mm calculus noted at left vesico-uretric junction and ECG shows sinus bradycardia, A-V block and Reverse check sign.

Initially the patient was admitted in emergency department and was administered with oral cardiac glycoside Digoxin 0.125 mg once a day for 5 days/week, oral antiplatelet drugs Aspirin 300 mg + Clopidogrel 300 mg once a day (f/b 150mg), oral hypolipidemic drug Atorvastatin 80 mg HS (f/b 40mg), antianginal drug Sorbitrate 5 mg sublingually once a day and parenteral antibiotics (Piptaz 2.25 gm iv twice a day), anti-ulcerative (Pantop 40 mg & Zoffer 4mg twice a day).

Then patient was sifted in general medicine ward. Laboratory investigation showed Serum Digoxin: 5.05 ng/ml, Creatinine: 7.1 mg/dl, Urea: 148 mg/dl, Electrolyte K+: 2.8 mmol/L an Electrolyte Na+: 125 mmol/L.

Based on above findings physician suspected it as Adverse Drug Reaction (sinus bradycardia, A-V block). The patient was diagnosed with Digoxin Toxicity. In order to confirm the relationship between the effect and drug, dechallenge test was done and the drug was withdrawn from the regimen and as antidote Injection Atropine 0.5 mg was given intravenously stat.

After 4 days of dechallenge (because half-life of digoxin is around 36 to 48 hours) the ECG was repeated again to check the improvement which showed no abnormality. On the same day the following findings were observed: PR 82 bpm, BP 108/70 mm of Hg. Laboratory investigation were Creatinine: 6.1 mg/dl, Urea: 144 mg/dl, Electrolyte K+: 3.7 mmol/L, Electrolyte Na+: 130 mmol/L.

The symptoms improved significantly after withdrawal of the drug.

ADR ANALYSIS

To evaluate the relationship between the drug and reaction, we have performed causality assessment.

The suspected ADR was **“probable”** (as per Naranjo’s and WHO causality assessment scale) and **“level - 4 severity”** as per Modified Hartwig and Siegle scale. The ADR was **“probably preventable”** by using Modified Schumock and Thornton scale.

DISCUSSION

Digoxin has been used extensively in patients with atrial fibrillation and heart failure. Digoxin is cleared from the body predominantly by the kidneys, with insignificant contribution from hepatic metabolism in subjects with good renal function. Hence, it is not uncommon to find high levels of plasma digoxin in patients with renal insufficiency.

The most frequent causes of toxicity are renal insufficiency and overdosing. Digoxin is primarily excreted by the kidneys; therefore, patients with impaired renal function require smaller than usual maintenance doses of digoxin.

Digoxin toxicity is related to serum concentration. As digoxin serum levels increase above 1.2 ng/mL, there is a potential for increase in adverse reactions. Furthermore, lower potassium levels increases the risk for adverse reactions.

Atorvastatin can lead to increase Digoxin plasma concentration by 22% requiring reduction in dosage. Because of considerable variability of pharmacodynamic interactions, the dosage of digoxin should be individualized when patients receive these medications concurrently and measure serum digoxin concentrations before initiating concomitant drugs.

In this case the patient have a history of renal calculi with hydro nephrosis and concomitant medication history of drug Atorvastatin. So, the plasma concentration of Serum Digoxin level is high (5.05 ng/ml).

CONCLUSION

Dosage of Digoxin should be decided only obtaining results of Renal and Liver function test and checking drug-drug interaction with drugs prescribed simultaneously. TDM should be done regularly & periodically in patients with Digoxin Therapy.

REFERENCES

1. Brunton LL, Dandan RH, Knollmann BC. **Goodman & Gilman's The Pharmacological Basis of Therapeutics**. 13th Edition. USA: McGraw Hill; 2018. P.527-572.
2. Fdagov. Fdagov. Available at : https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/020405s0131bl.pdf (Accessed 7/10/2019)
3. WHO-UMC causality assessment- Uppsala Monitoring Centre. Available at : https://www.who.int/medicines/areas/quality_safety/safety_efficacy/WHOcausalit_y_assessment.pdf (Accessed 7/10/2019)
4. Naranjo CA, Busto U, Sellars EM, Sandor P, Ruiz I, Roberts EA and Janecek E. Method for estimating the Probability of Adverse Drug Reactions. Clin Pharmacol Ther. 1981; 30:239-45.
5. Hartwig SC, Siegel J and Schneider PJ. Preventability and Severity Assessment in Reporting Adverse Drug reactions. American Journal of Hospital Pharmacy.1992;49:2229-31
6. Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. Hosp Pharm. 1992; 27:538.