

INAPPROPRIATE USE OF DIGOXIN IN MEDICAL PRACTICEDebasish Das¹, Ambika Prasad Mohanty²**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: Digoxin, the old golden molecule is one of the commonly prescribed drugs prescribed by general medical practitioners when a patient presents with dyspnea. In spite of being arrhythmogenic and having narrow therapeutic window, physicians do not even hesitate to use even where it could be catastrophic. Most are unaware of the classical indications where as others use it in myth that it is life saving and miraculous although numerous studies clearly delineates that it does not improve cardiac mortality although delay hospitalization. Our study was a miniature one to improve the cautiousness before digoxin use in medical practice and delineate its irrational use among patients with cardiovascular disease. We studied 4562 patients who were consulted in AIIMS Cardiology and Medicine OPD between October 2014 to June 2015 having digoxin among their therapeutic armamentarium and delineated their irrational use even in toxic conditions. Rational use was only evident in 2007 (44%) cases where as it was advocated wrongly in 2555 (56%) of cases, most sufferers being rheumatic heart disease (51.27%) population, hypertensive heart disease (17.88%), coronary artery disease (5.44%), COPD (12.88%) and CKD (0.9%) patients being in decreasing order. In RHD scenario mitral stenosis patients suffered most (56%) followed by aortic stenosis patients (25%) compared to regurgitant lesions which are better tolerated.

KEYWORDS: Digoxin, Irrational, Lanoxin, Evident, CHF, RHD, Mitral stenosis, Dyspnea.

INTRODUCTION: Although medical care is on rise with time, most of the people access general physicians in locality and later avail the specialist care due to inaccessibility, unawareness and constraints. It is a common notion among many that digoxin heals dyspnea quickly although its half-life is 36 hrs. It is a common practice among physicians to write lanoxin (Digoxin) and lasix (Furosemide) if any one comes with dyspnea and physician thinks it to be cardiac dyspnea. Classical indications of its use include chronic atrial fibrillation, congestive heart failure & isolated right ventricular failure not responsive to conventional antifailure regimen. In spite of being previously delineated as a miraculous molecule because of its unique inotropic-bradycardic action in CHF and improving LV filling in atrial fibrillation, it is not recently recommended in acute heart failure. Digoxin inhibits sympathetic nerve discharge before its hemodynamic effects, vagomimetic, inotropic at low doses and even natriuretic, thus being remaining helpful in chronic heart failure. Sick cardiac patient's underlying hypoxemia, acidosis, dyselectronemia, multiple antifailure regimen drug interaction exacerbates digoxin toxicity; that is why it is usually not recommended in acute heart failure. Increased sensitivity of digoxin in rheumatic carditis, viral myocarditis, and thyrocardiacs restricts its use in them where as in periphery hospitals those are not diagnosed even due to lack of infrastructure and poor history taking and examination. In lean elderly females it is notorious to show its toxicity. Being a renally excreted drug it is just

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administered even without a kidney function test. Digoxin increases mortality when used in high dose as evidenced in DIG trial,¹ that is why it is recommended to use in its lowest effective dose always. WPW syndrome, HOCM, AV block stands out as clear-cut contraindications where as people administer it without doing an ECG even or thorough auscultation. GI irritation although observed not uncommonly people do not withdraw it even a patient complains off. Appearance of signs of digoxin toxicity or multiple ectopics in ECG, physicians do not recommend an ECG in follow up, rather advise them to continue it as proton pump inhibitors for treatment of GERD.

We carefully evaluated and dictated the wrong patients with digoxin, stopped the drug; otherwise many unseen cardiac deaths may be due to a wrong digoxin prescription by a local physician.

METHODS: We evaluated 4562 patients presenting to the Cardiology and Medicine OPD having lanoxin in their prescription by the local physician. We evaluated all the cases with all routine blood chemistry including renal function test, ECG, ECHO, angiography, Troponin T assay, spirometry and chest X ray PA view and other necessary allied investigations and established the diagnosis in undiagnosed cases. Cross referral to other departments were also done to establish a proper diagnosis when the patient was thought to be non-cardiac. We discouraged the irrational use of lanoxin tablet in those people where it was unethical. We advised regular follow up with RFT and ECG to all patients even when the use was justified. Digoxin is not life-saving but life taking, this is the message we have given to the patient when it was unjustified. At the end of the study all the data were presented in percentage, graphs as presented below. The rational use of the drug included:

- Chronic atrial fibrillation (AF).
- Chronic heart failure & isolated right ventricular failure not responsive to conventional antifailure regimen (ACEI, β blocker & diuretics) with depressed EF.

Inappropriate use includes:

- Rheumatic heart disease (MS, MR, AS, AR) without AF or LV systolic dysfunction or CHF.
- Hypertensive heart disease with acute LVF.
- Acute coronary syndrome with acute decompensate heart failure (ADHF).
- CAD with ADHF.
- HFpEF (Heart failure with preserved EF).
- COPD with acute exacerbation.
- CKD.
- Thyroid disorders.
- Dyselectronemia.
- WPW syndrome.
- HCM.
- AV block.
- Sinus bradycardia.
- Myocarditis.
- Acute rheumatic fever.

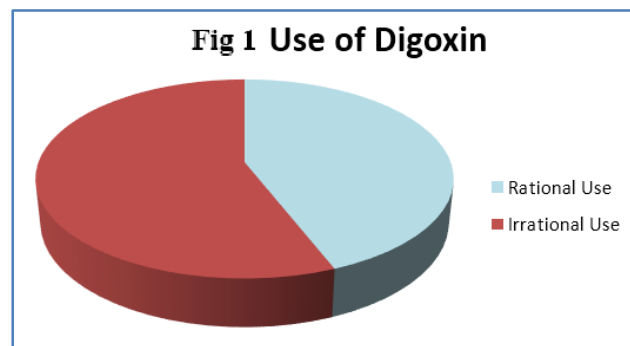
ORIGINAL ARTICLE

- Elderly (>70 years) frail females.
- ECG showing digoxin toxicity.
- ECG with multiple ectopics.
- Very high dose (>0.25 mg/day).
- Used along with Verapamil, β blocker or amiodarone without dose modification.
- Loading dose practice.

RESULTS:

Digoxin	No. of Cases	Percentage (%)
Rational Use	2007	44
Irrational Use	2555	56

Table No 1

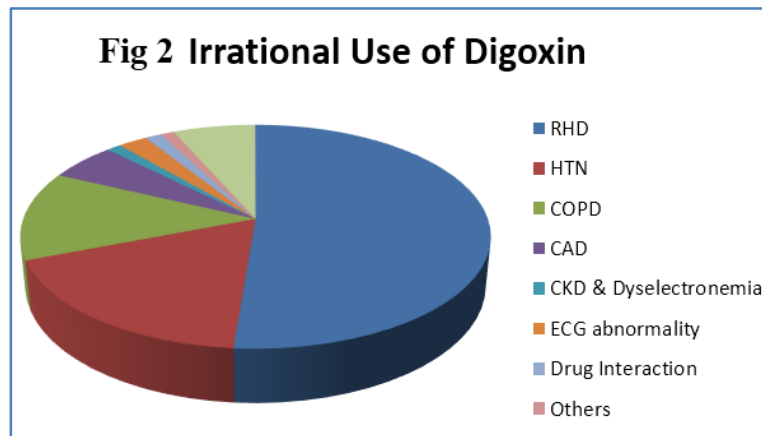


Irrational Use in Cases	No	Percentage (%)
RHD	1310	51.27
Hypertensive Heart disease	457	17.88
HFpEF	170	6.6
COPD	329	12.88
CAD	139	5.44
CKD	23	0.9
Thyroid disorders	3	0.11
Dyselectronemia	7	0.27
WPW syndrome	0	0
HCM	1	0.03
AV block	2	0.06
Sinus bradycardia	28	1.09
Myocarditis	2	0.078
Acute rheumatic fever	8	0.313
Elderly(>70 years) frail females	12	0.47

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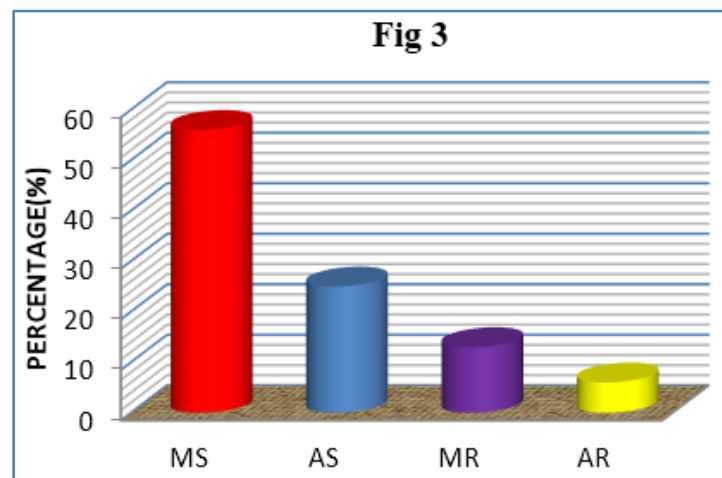
ECG showing digoxin toxicity, ectopics	20	0.8
Very high dose(>0.125 mg/day>70 years)	10	0.4
Used along with Verapamil, β blocker or amiodarone without dose modification	34	1.33
Loading dose practice	0	0

Table No 2



RHD	No of Cases (%)
Predominant MS	734(56%)
Predominant AS	328(25%)
Predominant MR	170(13%)
Predominant AR	78(6%)

Inappropriate Digoxin Use Across Rhd



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DISCUSSION: Our study delineated inappropriate use of digoxin in 56% of cases when absence of AF and preserved LV systolic function were considered the major criteria besides others. Although LVSD and chronic AF are the only two FDA approved indications for use of digoxin,² it is not the drug of choice for either of these two conditions. The role of digoxin in asymptomatic LVSD patients on optimum dosage of ACE inhibitors, beta-blockers, and spironolactone and those with preserved LV systolic function has not yet been established. In a study conducted by Bitekar et al³ inappropriate use of digoxin in elderly community was 38.7% where incorrect diagnosis of HF was commonest cause besides paroxysmal AF and undetermined indications. Ahmed et al found that digoxin misuse in hospitalized HF patient was 37%.⁴ Even British researchers followed 484 heart failure patients for three years and found that the mortality among those taking digoxin was 38.9% as compared to only 21.3% among controls. The researchers conclude that the use of digoxin in heart failure patients is associated with an adverse prognosis and suggest that beta-blockers and spironolactone may be a better choice for ameliorating the symptoms of heart failure.⁵ Researchers at the Health Care Department in Maryland found that in the period 1985 through 1991 over 200,000 of 3.3 million digitalis users, in 73% of all cases the reason for prescribing the digitalis in the first place was unclear or weak. In our clinical scenario physicians administer digoxin even in COPD and unevaluated dyspneic patients with pedal edema. It is detrimental to administer digoxin in HFrEF which accounted 6.6% of cases. It is mistake of the physicians when patients land up in acute pulmonary edema secondary to hypertension and they administer digoxin (17.88% in our study), in severe hypoxemic condition of acute pulmonary edema digoxin turns out to be toxic. But it is the commonest concept in physicians that RHD patients are treated with lanoxin and lasix, they even prescribe it in RHD patients without AF and LV systolic dysfunction inspite of its narrow therapeutic index and toxicity. Dyspnea means digoxin and diuretic to many physicians although classical indications are quite limited in evidence based practice. Injured myocardium in CAD triggers array of arrhythmias including malignant bidirectional VT if administered digoxin. Although in acute coronary syndrome AF well responds to β blockers, even cardiologists administer it without a trial of β blockers, digoxin in setting of ischemic myocardium increase mortality. Our hospitals in periphery are not equipped with an ECG machine even, it is difficult for physicians to diagnose acute coronary syndrome but atleast they should not give digoxin, undiagnosed CAD accounted 5.44% cases in our study. Although digoxin is a well validated therapy in AF, it is hazardous in paroxysmal AF which can be treated with other antiarrhythmics like β blockers with less toxicity.⁶ CKD patients develop digoxin toxicity, at least serum creatinine and serum potassium should be done before administering digoxin, 17 of 23 CKD patients in our study presented with either severe bradycardia or arrhythmia in ECG. Thyrocardiacs in our study presented with their symptom deterioration after they were administered digoxin by their local physicians. Myocarditis patients presented with bizarre ECG pattern after they were treated with digoxin. Rheumatic carditis usually presents with preserved LV systolic function, it is acute MR that makes the patient dyspneic, 8 acute rheumatic carditis cases were treated with digoxin even without an ACEI. There is increased sensitivity to digoxin in rheumatic carditis, if at all it would be used its dose should be reduced to half in presence of compelling indications. The American Geriatrics Society (AGS) updated the Beers Criteria last year which identify high risk medications (HRMs) in older adults >70 years.⁷ The criteria reviewed

ORIGINAL ARTICLE

covered 2 types of statements: (1) medications or medication classes that should generally be avoided in persons 65 years or older because they are either ineffective or they pose unnecessarily high risk for older persons and alternative is available and (2) medications that should not be used in older persons known to have specific medical conditions. Digoxin (Lanoxin®) is one of the most highly utilized High Risk Medications (HRMs) in our senior care medicare population that fulfills Beers criteria. Concerns with digoxin (Lanoxin) daily doses >0.125mg in elderly >65 years include reduced renal clearance which can increase toxicity and in heart failure, higher doses are associated with no additional benefit and may increase toxicity. In DIG study it was found Digoxin is particularly dangerous for patients over the age of 60 years. With high dose and elderly patients it was used in 22 cases that were to get its untoward action. Ectopics are the mother of arrhythmia runs; people do not withdraw digoxin when they find ectopics in ECG, abnormal ECG was evident in 50 cases, today's ectopics with digoxin would be tomorrow's PSVT or VT. It is advisable not to start and continue digoxin without an ECG. Dose modification is needed when digoxin is used with other medications like Verapamil, β blockers and amiodarone but this mistake was evident in 34 cases. Danish and American researchers concluded that digoxin treatment increases the risk of invasive breast cancer among postmenopausal women and that this risk increases with increasing duration of treatment, so it should be avoided in elderly females.⁸

RHD people suffer most when digoxin use inappropriateness is taken into accounts. Physicians think mitral stenosis treatment includes lanoxin and lasix although classical indication includes MS with AF and right heart failure. Digoxin misuse was commonest in mitral stenosis patients (56% of RHD population) followed by Aortic stenosis without AF or LV systolic dysfunction (25%). Stenotic lesions become more symptomatic as compared to regurgitant lesion, that is why digoxin misuse was more common in MS and AS (81%) as compared to MR and AR(19%). Lanoxin and lasix are so commonly misused drugs in RHD that people bring them from local hospitals even without prescriptions.

Recent cardiovascular guidelines are far from recommending lanoxin in management of RHD, CAD, ADHF and CHF except in presence of AF and LV systolic dysfunction when the conventional therapy fails. AF is also not an absolute indication because it is definitely contraindicated in vagal AF as it tends to promote the arrhythmia and may block the action of conventional antiarrhythmic treatment. Digoxin may truly be the medicine from hell if certainly be used by people with lone AF.⁹ If a medicine is needed for control of heart rate, then calcium channel blockers such as verapamil or diltiazem or beta-blockers like atenolol or metoprolol would be better choices – except for vagal afibbers who should not take beta-blockers. Qureshi et al found that Digoxin use in atrial fibrillation is associated with increased risk of mortality in a meta-analysis of more than 200,000 patients.¹⁰ Although inotropic-bradycardic action of lanoxin is uniquely beneficial in HF; its use should be rational and recommended to bring out its beneficial effects. Building thousand temples brings credit but destroying one becomes catastrophe. Killing even one cardiac patient by digoxin misuse cannot be tolerated in today's practice, that is why physicians should use it in presence of chronic AF and chronic HF with LV systolic dysfunction after trial of conventional therapy and also being well versed with its contraindications. Never forget to do an ECG and Kidney function test before administering digoxin.

ORIGINAL ARTICLE

CONCLUSION: In summary, inappropriate prescription of digoxin is a common and serious global healthcare problem leading to increased risk for adverse outcomes. In this study, we showed that 56% of patients presenting to the outpatient cardiology OPD in AIIMS were receiving digoxin with inappropriate indications. Due to its narrow therapeutic index and toxicity, digoxin should be used more carefully according to the current evidence and guidelines. An educational program to reduce inappropriate use of digoxin in patients is urgently needed.

REFERENCES:

1. The Digitalis Investigation Group. The effect of digoxin on mortality and morbidity in patients with heart failure. *N Engl J Med.* 1997; 336: 525–533.
2. Packer M, Cohn J, Abraham W, et al. The consensus recommendation for the management of chronic heart failure. *Am J Cardiol.* 1999; 83: 1A–38A.
3. Bitekar M, Duman D et.al. Inappropriate use of digoxin in elderly patients presenting to an outpatient cardiology clinic of a tertiary hospital in Turkey; *Türk Kardiyol Dern Ars - Arch Turk Soc Cardiol* 2011; 39(5): 365-370 doi: 10.5543/tkda.2011.01530.
4. Ahmed A, Allman R et al. Inappropriate Use of Digoxin in Older Hospitalized Heart Failure Patients. *Journal of Gerontology: Medical sciences* copyright 2002 by The Gerontological Society of America 2002, Vol. 57A, No. 2, M138–M143 M138.
5. Lindsay, SJ, et al. Digoxin and mortality in chronic heart failure. *The Lancet*, Vol. 354, September 18, 1999, p. 1003.
6. Paul M, Wilbert S et al. Prevalence of Inappropriate Use of Digoxin in 136 Patients on Digoxin and Prevalence of Use of Warfarin or Aspirin in 89 Patients With Persistent or Paroxysmal Atrial Fibrillation: *American Journal of Therapeutics*: November/December 2009 - Volume 16 - Issue 6 - p41-43.
7. Fick. D., Cooper, J., et al. Updating the Beers Criteria for Potentially Inappropriate Medication Use in Older Patients. *Arch Intern Med.* 2003; 163: 2716-2724.
8. Ahern, TP, et al. Digoxin treatment is associated with an increased incidence of breast cancer: a population-based case-control study. *Breast cancer Research*, Vol. 10, No. 6, December 2008.
9. Larsen H. Digoxin: The Medicine from Hell? *The AFIB Report* May 2009 p1-6.
10. Qureshi W, Alirhayim Z, Ahmed A. Digoxin Use in Atrial Fibrillation Is Associated with Increased Risk of Mortality: A Systematic Review and Meta-Analysis of More than 200,000 Patients. *JACC* March 17, 2015, Volume 65, Issue 10, p 289-96.

ORIGINAL ARTICLE

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