DIGOXIN PRESCRIPTION IN CONTEMPORARY HEART FAILURE

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Conflict of Interest: Nil
CLINICAL CASE

- 58yr old gentleman, lifelong smoker

- Anterior STEMI and PPCI to LAD 2010 (other coronaries unobstructed)

- Severe LVSD

- NYHA III

- Stabilises on medical Rx
  - Bisoprolol 10mg od
  - Ramipril 5mg bd
  - Eplerenone 37.5mg od
  - Frusemide 40mg od
  - Atorvastatin 80mg od
  - Aspirin 75mg od
  - Clopidogrel 75mg od
ECG
CRT-D implanted 2011 with good response

HF decompensation 2013
- Peripheral oedema, ascites, NYHA III
- HR 65 SR, BP 96/50 mmHg
- eGFR 53 ml/min/1.73m²
- K⁺ 5.2 mmol/L

Responds well to iv diuretics

Discharge medications
- Bisoprolol 10mg
- Ramipril 3.75mg bd
- Eplerenone 25mg od
- Frusemide 80mg od

7.3.2.7. Digoxin: Recommendation

Class IIa

1. Digoxin can be beneficial in patients with HFrEF, unless contraindicated, to decrease hospitalizations for HF. (Level of Evidence: B)

Audience poll: Would you add in digoxin?
DIG TRIAL

- 6800 patients SR, HF, EF <45%
- Recruited 1991-1993
- 94% on ACEi
- BB / MRA use unknown
- Median digoxin dose 250 mcg/d
- Mean digoxin level 0.86 ng/ml
- No effect on all cause mortality
- Reduction in HF hospitalisation

The Digitalis Investigation Group, *NEJM* 1997
POST-HOC ANALYSES

• Reduced all cause and HF death at 1 yr \(^1\)

• Reduced all cause mortality in patients with digoxin levels 0.5-0.8 ng/mL \(^2\)

• Reduced HF death at 2 yrs in patients with cardiomegally, but no difference in EF<25% or NYHA III-IV patients \(^3\)

\(^1\)Ahmed A, *Am J Cardiol* 2009  
\(^2\)Rathore SS, *JAMA* 2003  
\(^3\)Gheorghiade M, *Eur J Heart Fail* 2013
SIGNAL OF HARM?

- Small increase in non-HF cardiac death in digoxin arm of DIG trial
  - but no difference in ventricular arrhythmia or cardiac arrest

- Increased all cause mortality with serum digoxin $>1.2$ ng/ml

- Increased all cause mortality in women

- Increased mortality and HF hospitalisation in patients taking digoxin in Val-HeFT study

[4] Butler J, Congest Heart Fail 2010
DIGOXIN USE IN ADVANCED HF

- Retrospective database review
- 455 patients referred for transplant
- 35% had AF
- 50% taking digoxin
  - Median dose 130 mcg/d
  - Median digoxin level 0.75 ng/ml
- 91% BB, 93% ACE / ARB, 46% MRA, 71% ICD / CRT
- Worse outcome in digoxin group, particularly if in SR
- No difference in outcome according to gender

HR 2.28
P<0.001

Georgiopoulou V, Circ Heart Fail 2009
Prospective, observational study
2900 patients, new HF, no prior digoxin
Stratified by new digoxin prescription
23% had AF
50% BB, 55% ACE / ARB, 3% MRA
47% ICD / CRT
Higher mortality in digoxin group
No difference in HF hospitalisation
No difference in outcomes in men v women and BB v no-BB
**MEDICARE REGISTRY**

- 921 patients with new digoxin prescription on discharge following HF admission
- Propensity matched control group
- 30% BB, 69% ACE / ARB
- MRA / Device use unknown
- Digoxin therapy associated with:
  - Reduced 30 d and 1 yr all cause readmission
  - 28% RRR 1 yr HF readmission
  - 17% RRR 1 yr all cause mortality

SUMMARY

• Digoxin therapy for heart failure is recommended by international guidelines

• The DIG trial was conducted with large doses of digoxin and in an era before modern pharmacology and devices were widely applied

• Optimal dosing and the benefit of adding digoxin to modern heart failure therapies is unclear

• There may be a signal of harm

• A large randomised trial addressing these issues may be warranted