WHAT IS THE ROLE OF DIGITALIS IN THE TREATMENT OF HEART FAILURE IN SINUS RHYTHM?
WHAT IS THE ROLE OF DIGITALIS IN THE TREATMENT OF HEART FAILURE IN SINUS RHYTHM?

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Definition:

Heart failure is the inability of the heart to maintain an output adequate to meet the metabolic demands of the body.
Many etiologies of CHF

- Coronary artery disease
- Hypertension
- Valvular heart disease
- Congenital heart disease
- Toxins
- Peripartum cardiomyopathy
- Many others

McMurray, Pfeffer. JACC 2004;44:2398-405
Pinski. JAMA 2003;289:754-6
NYHA Classification

- **Class I**
  - Asymptomatic

- **Class II**
  - Symptoms with moderate exertion

- **Class III**
  - Symptoms with minimal exertion

- **Class IV**
  - Symptoms at rest
Drugs for CCF

- Vasodilators – ACE Inhibitors
- Diuretics
- Beta blockers
- Digoxin
- Other Cardiac Inotropes – Dobutamine, Milrinone
Heart Failure

**Normal**

- Asymptomatic LV dysfunction
  - EF <40%

**Symptomatic CHF**

**NYHA II**

- Diuretics mild
- Neurohormonal inhibitors
- Digoxin?

**Symptomatic CHF**

**NYHA - III**

- Loop Diuretics

**Symptomatic CHF**

**NYHA - IV**

- Inotropes
- Specialized therapy
- Transplant

**Secondary prevention**

- Modification of physical activity

ACEI
# PHARMACOLOGIC THERAPY

<table>
<thead>
<tr>
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<th>Improved symptoms</th>
<th>Decreased mortality</th>
<th>Prevention of CHF</th>
<th>Neurohumoral Control</th>
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<tbody>
<tr>
<td><strong>DIURETICS</strong></td>
<td>yes</td>
<td>?</td>
<td>?</td>
<td>NO</td>
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<tr>
<td><strong>DIGOXIN</strong></td>
<td>yes</td>
<td>=</td>
<td>minimal</td>
<td>yes</td>
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<td><strong>INOTROPES</strong></td>
<td>yes</td>
<td>mort.</td>
<td>?</td>
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<td>Vasodil.(Nitrates)</td>
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<td>yes</td>
<td>?</td>
<td>no</td>
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<tr>
<td><strong>ACEI</strong></td>
<td>yes</td>
<td>YES</td>
<td>yes</td>
<td>YES</td>
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<tr>
<td>Other neurohormonal</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>control drugs</td>
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<td>+ / -</td>
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</table>
Digoxin

- Used in heart failure for more than 200 years
- Improves symptoms for patients on diuretic and ACE inhibitor
- No overall impact on survival
Cardiac glycosides: **Digoxin**:

- Inhibition of Na/K ATPase pump increase intracellular sodium concentration – eventually increase cytosolic calcium.
- It restores the vagal tone and abolishes the sympathetic over activity.
DIGOXIN

Na-K ATPase

Na\(^+\) K\(^+\)

Na-Ca Exchange

Na\(^+\) Ca\(^{++}\)

Myofilaments

K\(^+\) Na\(^+\)

Ca\(^{++}\)

CONTRACTILITY
DIGOXIN
HEMODYNAMIC EFFECTS

- Cardiac output
- LV ejection fraction
- LVEDP
- Exercise tolerance
- Natriuresis
- Neurohormonal activation
Debate

MacKenzie and Lewis have taught generations of British medical students that digitalis was of little value unless the patient was in atrial fibrillation.
Evidence

Positive intropic effect of Digoxin has been documented both in failing & non-failing human heart by –

• *Braunwald & Colleagues* -
  • by measuring the left ventricular peak diastolic pressure

• *Sonnenblick et al 1966* -
  • Myocardial force velocity

• *Weissler et al 1966* -
  • Measurement of systolic time interval
When to use Digoxin in sinus rhythm?

Indications:
- ischaemic
- primary myocardial disease
- symptoms and signs cannot be controlled with a diuretic alone
- persisting cardiomegaly and gallop rhythm
The Digitalis Investigation Group

Mortality Due to Worsening Heart Failure (%)

- Placebo
- Digoxin

Total Mortality

- Placebo
- Digoxin

n=6800 patients, EF <45%, normal sinus rhythm

*NEJM.* 1997;336:525.
Thank You