Beta-blockers: Now what?

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Beta-blockers: What’s known

• 30 Years
• 30 Careers
• Physician clarity regarding indications/benefits/risk?
• 30 Beers
Objectives

• Define common indications for beta-blockade
• Clarify current recommendations for use of beta-blockers as antihypertensives
• Review beta-blocker use in CHF
• Examine controversy concerning perioperative beta-blockade
Beta-Blocker Uses

- Hypertension
- Arrhythmias
- Angina/Coronary artery disease
- Acute coronary syndromes
- Congestive Heart Failure
- Postmyocardial infarction
- Perioperative
Beta-Blocker Uses

- Hypertension
- Congestive Heart Failure
- Perioperative prevention of cardiac events
HYPERTENSION
Beta-blocker as a first-line antihypertensive?

• Many physicians still think so
  – What class of drugs have proven to reduce the risk of stroke in hypertensive patients?
  – What class of anithypertensives have been proven to reduce mortality?

• Answer: Beta blockers

• But is it true?
Beta-blocker as a first-line antihypertensive?

• Multiple studies fail to demonstrate reduction in mortality or stroke over other antihypertensive agents
• Better choices for monotherapy: diuretics, calcium channel blockers, RAAS blockers
Meta-analyses: Beta-blockers and Hypertension
Beta-blockers vs. others

- Beta-blockers showed no mortality benefit as single antihypertensive agents
- Primary prevention of MI equal to diuretics, calcium channel blockers, and renin-angiotensin-aldosterone antagonists
- STROKE: 20-30% higher incidence

Bangalore S. *JACC*; 50; 7; 2007; 563-72.
CONGESTIVE HEART FAILURE
Congestive Heart Failure

- Randomized controlled clinical trials show 35% reduction in total mortality with certain agents (carvedilol, metoprolol, bisoprolol)
- Recommended for all patients with reduced LVEF and symptoms of HF
- Hospitalizations for heart failure: 25-45% mortality at one year
Beta-blockers and CHF

QuickTime™ and a decompressor are needed to see this picture.

Bangalore S. JACC; 50; 7; 2007; 563
Withdraw beta-blockers in patients hospitalized with CHF?

- OPTIMIZE-HF: multicenter, prospective collection of 5791 patients
- Subgroup 2373 who were eligible for beta blockers
- 79 withdrawn from beta-blockers; 1350 continued

- Mortality at 60-90 days:
  - Twice the mortality rate in patients whose beta-blockers were withdrawn (HR 2.34, CI 1.20-4.55)
PERIOPERATIVE USE
A Tale of Two Studies

DECREASE and POISE
DECREASE STUDY

173 Patients with + DSE
High risk vascular su

- 59 Patients
  Bisoprolol
  - 2 Patients
    Died of cardiac ca
  - 0 Patients
    Nonfatal MI

- 53 Patients
  No beta blocker
  - 9 Patients
    Died of cardiac ca
  - 9 Patients
    Nonfatal MI

Overall combined endpoint 3.4% in bisoprolol and 34% in control group

Poldermans, NEJM, 1999
DECREASE - Observations

• Perioperative beta blockers can save lives in patients at high risk for perioperative ischemia/myocardial infarction

• Criticisms:
  – All of these patients had an indication for beta-blockade prior to surgery
  – Small study (only 112 patients randomized)
POISE

8351 Patients
High Risk: CAD, PVD, S
Major vascular surg

4174 Patients
Metoprolol XL
100mg 2-4 hours be
200mg/day for 30

Combined en
CV Death, No Nonfatal Cardi
5.8%

Total Morta
3.1%

Stroke
1%
Nonfatal str
0.6%

4177 Patients
Placebo

Combined en
CV Death, No Nonfatal Cardi
6.9%

Total Morta
2.3%

Stroke
.5%
Nonfatal str
0.3%

Devereaux, PJ. Lancet; 371: 1839-47.
Stroke

- 15% of patients enrolled in POISE had prior atherothrombotic stroke
- Patients in metoprolol arm had decrease in afib
- 60 strokes in metoprolol subgroup
  - 49 ischemic
  - 3 hemorrhagic
  - 8 uncertain
POISE or Poison?

• Here’s how it all went down:
  Metoprolol extended-release
    -100mg 2-4 hours before surgery
    -100mg 6 hours after surgery
    -200mg 12 hours later and every day for 30 days
    -15mg IV every 6 hours if NPO

Metroprololol held if heart rate <45 or blood pressure <100; then restarted at 100mg every day
## Metroprolol XL Dosing

<table>
<thead>
<tr>
<th>Titrated</th>
<th>POISE</th>
<th>Primary Care Clinic</th>
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</thead>
<tbody>
<tr>
<td>No - started immediately prior to surgery</td>
<td>200mg QD x 1 day; then 200 qd for 30 days</td>
<td>Yes</td>
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<tr>
<td>Maximum starting dose</td>
<td>25-100mg QD for one week; Increase weekly up to 400mg</td>
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POISE: Observations

- High starting dose of oral metoprolol may have contributed to stroke rate
- IV dose may have contributed to stroke
- Hemodynamic parameters for holding subsequent doses may have been too low
- If using perioperative beta-blockers, TITRATE
Beta-blockers: Dos and Don’ts

DON’T

– Use as first line therapy for hypertension
– Withdraw beta-blockers perioperatively
– “POISE-on” the patient

DO

– Titrate to hemodynamics
– Continue beta-blockers perioperatively
– Weigh risk vs. benefit
# Evidence for Beta-Blocker Use

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Weak to none</th>
<th>Some Evidence</th>
<th>Strong Evidence</th>
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<tbody>
<tr>
<td>Hypertension</td>
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<tr>
<td>Heart failure</td>
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<td>Acute coronary syndrome</td>
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<tr>
<td>Post MI</td>
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<td>Stable angina without MI</td>
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<td>Perioperative</td>
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<td>HOCM</td>
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Bangalore S. JACC; 50; 7; 2007; 563-7
FUTURE

• Large, randomized, controlled perioperative study titrating beta-blocker dose to heart rate and blood pressure
• Published data describing adverse events in patients receiving perioperative beta blockers who have postoperative anemia
• Studies on nonselective beta blockers (carvedilol)
• Revised recommendations of perioperative beta blocker use