The Prudent Prescriber

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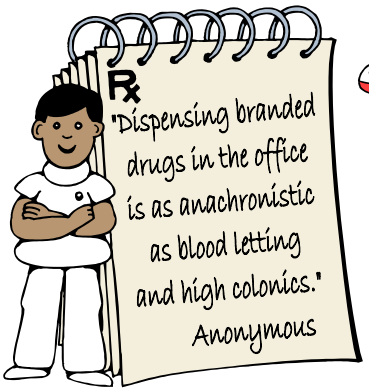


April 2013

Management of Hypertension: The World is changing

Pharm Reps ≠ Rational Prescribing
(PR) (RP)

Beta Blockers Fading!

Cochrane 2012 update of the 2007 review of the role of beta-blockade as first line therapy for hypertension.

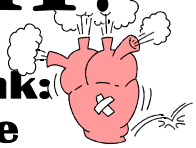
- RCTs of at least one year duration, which assessed the effects of beta-blockers (BB) compared to placebo or other drugs, as first line therapy for hypertension, on morbidity and mortality in adults.
- 13 RCTs:
  - 4 trials (23,613 patients) BB vs. placebo or no treatment
  - 5 trials (18,241 patients) BB vs. diuretics
  - 4 trials (44,825 patients) BB vs. CCB
  - 3 trials (10,828 patients) BB vs. RAS inhibitors
  - Three quarters of the 40,245 patients on BB were taking atenolol.

Results:

1. Total mortality was not significantly different between BB and placebo.
2. Total mortality was higher with BB than with CCB.
3. Total CV disease was lower with BB than with placebo (RR 0.88). This was primarily related to a significant decrease in stroke (RR 0.80), as there was no significant difference in CHD between placebo and BB.
4. The effect of BB on CVD was significantly worse than that of CCB (RR 1.18), but was not different from that of diuretics or RAS inhibitors.
5. There was an increase in stroke with BB compared to CCBs (RR 1.24) and RAS inhibitors (RR 1.30).
6. Participants on BB were more likely to discontinue treatment due to adverse events than those on RAS inhibitors (RR 1.41), but there was no significant difference compared with diuretics or CCBs.

Antibiotics do NOT help acute bronchitis

CHF?



Think:
- **Ace**
- **Aldactone**
- **B-blocker**
- **Dig**
- **Diuretic**

Avoid these expensive "me-too" drugs:

- Intermezzo
- Vimovo
- Livalo
- Pristiq
- Viibyrd
- Edarbi
- Nesina

ß-blockers in post-MI save lives

Treat diabetics BP to 130/80

Pill splitters save BIG

NOW AVAILABLE ON THE GENERIC MARQUEE

- Plavix→clopidogrel
- Avapro→irbesartan
- Tricor→fenofibrate micronized
- Arthrotec→diclofenac/misoprostol
- Diovan HCT→valsartan/HCTZ
- Atacand HCT→candesartan/HCTZ
- Maxalt→rizatriptan

Cochrane Take Home

- BB are not recommended as first line treatment for hypertension compared to placebo due to their modest effect on stroke and no significant reduction in mortality or coronary heart disease.
- These RCTs suggest that first line BBs for elevated BP were not as good at decreasing mortality and morbidity as other classes of drugs: diuretics, CCBs, and RAS inhibitors

Prescriber's Letter Take on BB

- BB should be 4th line for uncomplicated hypertension…. after a diuretic, ACE or ARB and a CCB.

NICE (National Institute for Health and Clinical Excellence) Guidelines on BB

- BB should be placed as 5th line treatment – behind diuretics, ACE/ARB, CCB and Alpha Blockers for uncomplicated hypertension.
- "BB are the least cost-effective treatment."

Beta Blocker Niche

- Continue to give BB indefinitely for heart failure; bisoprolol, metoprolol ER and carvedilol are most studied.
- Give a BB for at least 2-3 years after a MI. Metoprolol and carvedilol are well tolerated and available as generics.

Whither atenolol?

- Atenolol has a particularly bad reputation…because most hypertension trials evaluating cardiovascular risk used atenolol.
- It is not clear whether this is a class effect or indeed whether atenolol is worse than other beta blockers.
- One concern with atenolol is that it's approved for once daily dosing, but its effects don't always last all day.
- Don't start atenolol if patients need a beta blocker for hypertension.
- For patients with poor blood pressure control already on atenolol, consider giving it twice-daily or switching to another antihypertensive.

Predicting JNC 8 …it's promised this spring.

"It's tough to make predictions, especially about the future."

Yogi Berra

Condition	mmHg
Essential HTN	<140/90
DM	130-134/80
CKD	<140/90, <130/80 if proteinuria
Elderly	<140 if <age 79; <150 if age 80

- Either a thiazide-type diuretic, CCB, ACE/ARB will be recommended as initial drug therapy for most patients.
- Chlorthalidone should be highlighted as the evidence based thiazide-type diuretic of choice.
- After initial dose adjustment, combining drugs from different classes is 5 times more effective in lowering BP than doubling the dose of one drug.
- If BP is more than 20/10 above goal start with two drugs. Data indicate quicker to goal, but beware postural hypotension.

Evidence for Chlorthalidone

- Retrospective analysis of the MRFIT study showed that the CLD regimen reduced mortality more than the HCTZ regimen. (Hazard Ratio 0.79)
- SHEP and ALLHAT studies have demonstrated better reductions in CV morbidity with CLD than HCTZ.
- Chlorthalidone has a longer half-life, 45-60 hrs vs. 8-15 hrs for HCTZ
- Chlorthalidone has a longer duration of action 48-72 hrs vs.16-24 hrs for HCTZ
- Chlorthalidone has greater BP lowering efficacy, particularly at night. Mean SBP reduction for HCTZ 50mg -6.4mmHg vs. CLD 25mg -13.4mmHg.

The nuts and bolts of chlorthalidone

- Available as 25, 50 and 100mg unscored tablets.
- Recommended starting dose in hypertension is 12 .5mg per day with maximal dose of 50mg a day, but diminishing effect beyond 25mg per day.
- Have to split CLD to get lowest dose.
- Multiple studies have shown statistical, but no clinical differences in side effects (hypokalemia, hyperglycemia) between HCTZ and CLD.

An elderly male with early cataracts split 30 of the 25mg size tablets with a cheap pill splitter with reasonable division of 27 of 30 pills

- There are no ACE/chlorthalidone combos in US.
- Edarbyclor (azilsartan medoxomil/chlorthalidone) available as 40/12.5 and 40/25; is the only ARB/CLD combo.
- Chlorthalidone ($11--$22/mo) pricier than HCTZ ($4/mo).

Abbreviations: BB= Beta Blocker; CCB= Calcium Channel Blocker; RAS Inhibitors= Renin-Angiotensin System inhibitors (ACE/ ARB); CLD= chlorthalidone; HCTZ= hydrochlorothiazide

You may access previous issues at http://www.rmhp.org/providers/prudent-prescriber.

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