Hypertension and Hyperlipidemia

- 1)A 68 yo man with hypertension is seen in follow up. His BP in clinic is 150/96 P 80 . BP's last year were all 130/80 or less. He gets multiple home readings which are all over 150 systolic and 90 diastolic. PMH: Hypertension, Depression, prediabetes, bilateral collar bone fractures (6 weeks ago) Medications: Lisinopril 20 mg, chlorthalidone 25 mg
- What is the most likely cause for his worsening HTN?

A) Renal artery stenosis
B) Hyperaldosteronism
C) Pheochromocytoma
D) Medication use
E) Cushing syndrome

Common Causes of Secondary Hypertension

- Sleep Apnea
- NSAID use (most important in patients on ACEI/ARBS/Diuretics)
- Medications- OCP, Venlafaxine, licorice
- Recreational drugs- amphetamines, cocaine
- ETOH

Pearls on When to Think of Rare Causes of Secondary HTN

- Fibromuscular dysplasia- 90% in women, some have carotid disease
- Renal artery stenosis (atherosclerosis)- flash pulmonary edema, sudden worsening of renal function with treatment, worsening htn in patient with known atherosclerosis
- Pheochromocytoma- headache/sweating/tachycardia/orthostatic hypotension/hypertension during procedures/surgery/after receiving meds

2) A 60 yo woman presents for follow-up of hypertension. She has been taking medication (Lisinopril) for the past 3 months. Her most recent outside blood pressure readings are 156/94, 150/96, 158/92. PMH: Type 2 DM, GERD, depression. Meds: Lisinopril 20mg qd, Rabeprazole 20mg qd, Sertraline 50 mg qd, Glyburide 10 mg qd.

What do you recommend?

A) No changes in therapy

B) Increase Lisinopril to 20 mg BID

C) Add Metoprolol XL100 mg

D) Add Amlodipine (Norvasc) 5mg qd

E) Add Clonidine .1mg BID

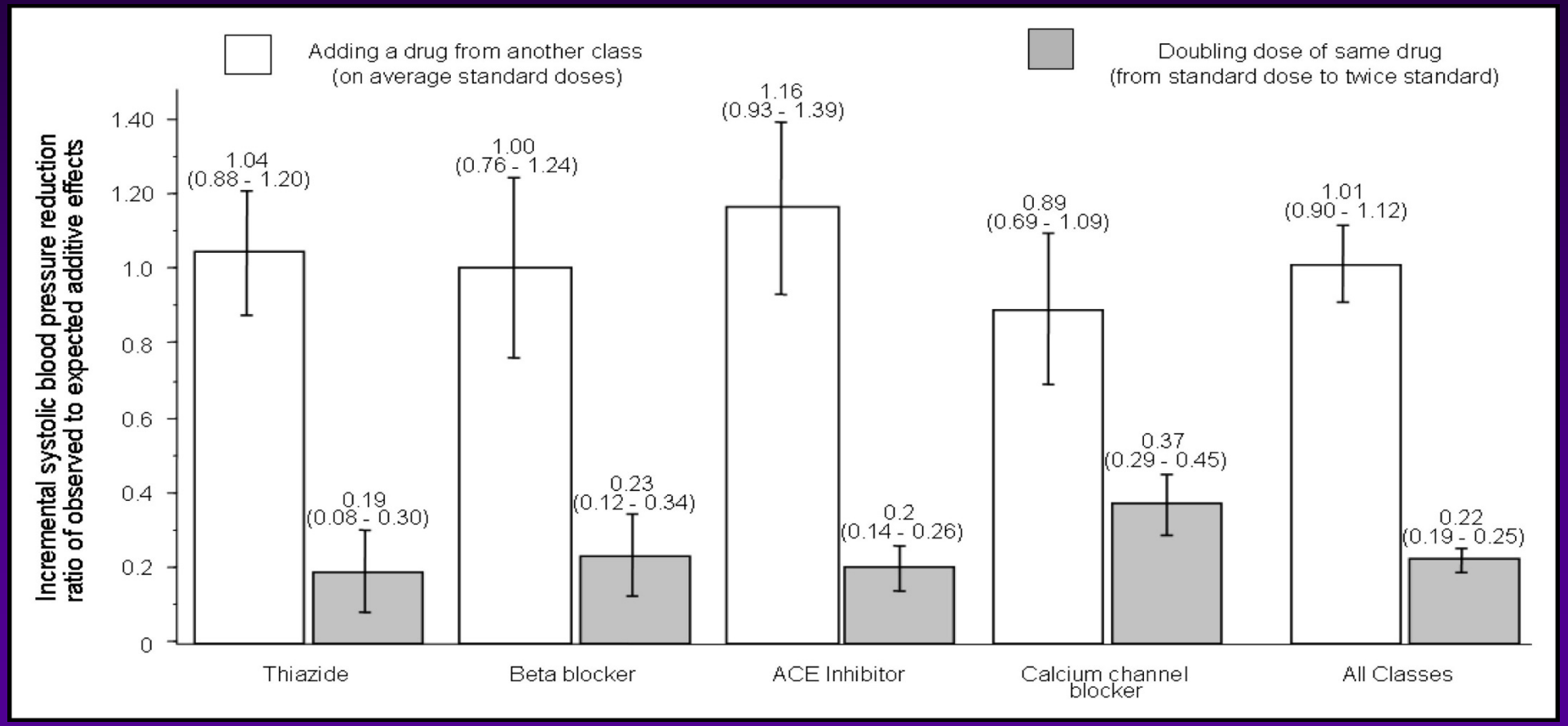
Double the dose or add a second agent?

Titrate single drug vs combo?

- Meta-analysis of 11,000 patients from 42 trials comparing single dose with up titration vs switch to combo therapy

Am J Med 2009;122:290-300

Adding a second agent is about 5-fold more effective



Am J Med 2009;122:290-300

Based on RCTs of HTN, at least 75% of patients will require combination therapy to achieve BP targets

Am J Hypertens 2010;4:42-50

Combination Therapy

- Low doses of thiazide can be very effective in combination with ACE inhibitors (12.5 mg of thiazide)
- Thiazide ACE combination can be further enhanced by moderate dietary salt restriction
- ACE/Amlodipine combination may have CV benefits slightly better than ACE/diuretic in high risk diabetic paients

- 3) A 57 yo woman presents with elevated BP's (160/92, 166/96, 170/98,164/92) on four outside BP readings over 2 months. Review of recent clinic visits show BP's of 160/90, 158/94 and 166/96. She is otherwise healthy with no chronic medical problems. BMP: Na 140 K 4.2 Cl 100 Bun 14 Cr .8. What treatment would have the best chance of reaching target BP's?
- A) Amlodipine 5 mg
- B) Losartan 100 mg
- C) Losartan 100 mg /Chlorthalidone 12.5 mg
- D) Losartan 100 mg/ Hydrochlorothiazide 25 mg

Efficacy of Low-Dose Chlorthalidone and Hydrochlorothiazide

- Randomized, double-blind, multicenter, controlled trial in India.
- Fifty-four patients were randomized 1:1:1 to receive HCTZ-controlled release (CR) 12.5 mg daily, HCTZ 12.5 mg daily, or chlorthalidone 6.25 mg daily.
- Chlorthalidone and HCTZ-CR both reduced the mean 24-hour ambulatory systolic BP at 12 weeks by a mean of 11.1 and 10.3 mm Hg, respectively (P <0.001 and P =0.002, respectively). HCTZ was associated with a mean systolic pressure decrease of 6 mm Hg that was not significant compared to baseline.
- J Am Coll Cardiol; 2016;67 (February): 379-389.

Combination of ARB + Diuretic

- Azilsartan + chlorthalidone SBP -35.1
- Azilsartan + hydrochlorothiazide -29.5

- P<.001

- Am J Med 2012 ;25:1229

4) A 58 yo woman is seen for treatment of hypertension. She has not ever had good control of her hypertension since treatment was started 2 years ago. She has been taking her medications faithfully. Meds: Felodipine (Plendil), Atenolol , Clonidine, and Losartan (Cozaar). On exam her BP is 200/106 P-55.Labs- BUN 30, Cr 2.0, Na 137, K 4.0. ECG- LVH

What would you recommend?

A) Increase felodipine from 10mg a day to 10mg BID

B) Increase losartan from 50mg BID to 100mg BID

C) Add hydrochlorathiazide 12.5 mg qd

D) Add hydrochlorathiazide 25 mg qd

E) Add furosemide 40 mg BID

- A 55 yo woman presents with persistent hypertension. She has been taking clorthalidone, lisinopril, amlodipine and metoprolol. BP today is 158/96. Outside readings are similar (160/96, 154/94, 166/98).
- Labs: Na 134 K 4.2 Bun 12 Cr 1.0
- What do you recommend?

A) Replace clorthalidone with furosemide
B) Add Diltiazem
C) Add Clonidine
D) Add Spironolactone
E) Switch amlodipine to minoxidil

Primary Hyperaldosteronism

- Most common cause of secondary hypertension in Hypertension clinics (up 25%)
- Estimated to be present in 5-10% of patients with hypertension
- Surprisingly, >50% of patients DO NOT have hypokalemia- Classic board presentation would be patient with hypertension, hypokalemia and alkalosis
- Work up- Plasma renin activity and aldosterone concentration, CT scan in patients with positive results*

Adding Spironolactone for Refractory Hypertension

- Average blood pressure reduction of 17-20/4-9 mmHg, with the largest reductions seen in patients with SBP >150 mmHg at baseline (1,2).
- In a study of 175 patients with refractory hypertension on a mean of 4 blood pressure medications, addition of spironolactone resulted in a lowering of blood pressure by an average of 16/9 mmHg, with about half of the patients on the medication achieving a goal blood pressure of < 140/90 mmHg (3).
- 1) Cochrane DB Syst Rev 2010 Aug 4;8:CD008169
- 2) J Hum Hypertens 2015;29:159-166
- 3) Hypertension 2010;55:147-152

Aldosterone, Hypertension and Antihypertensive Therapy

- Community based cohort with (477) and without HTN (1073), plasma aldosterone levels were measured
- In those with hypertension, number of antihypertensive drugs were recorded
- Subjects with HTN had higher aldosterone leves (6.4) than those who did not have HTN (4.1)
- The more antihypertensive drugs that patients were on, the higher the aldosterone level (0 drugs=4.8, 1=6.4, 2=7.1, 3=7.9, p=.002)

- Mayo Clinic Proc 2018; 93(8): 980-990.

- 6)A 64yo woman presents for follow up. She has a PMH of osteopenia (T -2.3 at her hip) and GERD. She has had 3 outside BP readings of 160/90, 158/88, and 164/92 . Today in clinic her BP is 158/86. Her BP a year ago was 154/88. Meds: Omeprazole and Vitamin D.
- Which would be the best treatment recommendation?
- A) Monitor BP, no therapy
- B) Chlorthalidone
- C) Lisinopril
- D) Metoprolol
- E) Diltiazem

Benefit of Thiazide Diuretics for Calcium

- Meta-analysis of 5 trials with 756 patients enrolled
- Serum calcium levels higher in thiazide treated patients (Difference +.33, 95%CI .16-.50)
- Urinary calcium lower in thiazide treated patients (- .35, 95% CI -.52- -.17)

- Drug Des Devel Ther. 2018 Nov 14;12:3929-3935.

Thiazide Diuretic Usage and Risk of Fracture

- Eleven eligible cohort studies involving 2,193,160 participants were included for analysis
- Thiazide diuretic users, as compared with non-users, had a significant 14% reduction in the risk of all fractures (relative risk [RR], 0.86; 95% confidence interval [CI], 0.80-0.93; p = 0.009) and an 18% reduction in the risk of hip fracture (RR, 0.82; 95%CI, 0.80-0.93; p = 0.009)
- Osteoporos Int. 2018 Jul;29(7):1515-1524.

- A 48 yo man with hypertension presents for annual follow up. His last lipids were checked 5 years ago (TC 190, LDL 125, HDL 45, Tri-100). Meds: Nifedipine and chlorthalidone. Exam: BP 140/60 P 80 chest – clear
- Cardiac- nl S1S2 no M. Ext- 2+ edema
- Lab- TC 255 LDL 170 HDL 40 Tri 160
- What is appropriate next step?

A) Start pravastatin
B) Start atorvastatin
C) Start ezetimide
D) Check CMP,Ua and TSH
E) Check BMP, Testosterone

Secondary Hyperlipidemia

Increased LDL

- Hypothyroidism
- Nephrotic Syndrome
- Cholestatic liver disease

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- A 61 yo woman with hyperlipidemia,

Type 2 DM, and a family history of early MI had coronary artery stenting. She is taking 40 mg of pravastatin and metformin. Labs: A1c 6.5%,

- TC 210, HDL 45, LDL 119, TG 183

Most appropriate treatment?

A) Pravastatin 80 mg
B) Atorvastatin 80 mg
C) Atorvastatin 80 mg + Niacin 1000mg
D) Niacin 1000mg

- 65 yo man presents for primary care visit. He has no symptoms. PMH:hypertension, GERD. nonsmoker
- PE: BP 120/70 P 66
- Labs: HBA1C 5.2, Bun 10 Cr 1.1 TC 190 LDL 135 HDL 42
- What do you recommend?

A) Diet and exercise , recheck cholesterol
B) Fenofibrate
C) Pravastatin 40 mg
D) Atorvastatin 80 mg
E) No intervention

Using AHA Cardiac Risk Calculator

- Risk of MI/Stroke 14.1% over next 10 years
- Recommendation: Low to Moderate intensity statin (Pravastatin 40mg/Atorvastatin 20 mg)
- In general, if 65 with 1 or more risk factors, will have > 7.5% risk over 10 years

USPSTF Has Weighed In

- The USPSTF recommends initiating use of low- to moderate-dose statins in adults aged 40 to 75 years without a history of CVD who have 1 or more CVD risk factors (dyslipidemia, diabetes, hypertension, or smoking) and a calculated 10-year CVD event risk of 10% or greater (B recommendation).

- JAMA. 2016 Nov 15;316(19):1997-2007.

While undergoing evaluation following a hysterectomy, a 50 yo is noted to have TC 245, HDL 56, TG 645. She has an A1c of 5.6%. PMH: Migraine, hypertension.Her exam is normal and her medications include propranolol, hydrochlorothiazide, and oral estrogen.

What do you recommend now?

A. No change in therapy.
B. Add niacin.
C. Add gemfibrozil.
D. Stop propranolol and oral estrogen.

Audience Response
next slide

Elevated Triglycerides

- Moderate elevation (300-800)- non fasting state, medications (estrogen, b blockers, PI, Isotretinoin, clozapine,olanzapine), Hypothyroidism, insulin resistance
- Severe Elevation (>885)- Familial hypertriglyceridemia, medications (PI, Clozapine/olanzapine)

Ezetimibe

- 2nd line lowering
- Inhibits cholesterol absorption at brush border
- Lowers LDL by 15–25%
- Approved for use alone or with statin or fenofibrate
- Increased risk of statin induced myopathy
- Avoid use with gemfibrozil

Bile Acid Sequestrants (Resins)

- Cholestyramine, colestipol
- May increase TG
- Slightly ↑ HDL
- Lower LDL by 10–25%
- Adjuvant in combination with statins, rarely used now
- Side effects: Nausea, vomiting, bloating

Nicotinic Acid

- Blocks LDL synthesis
- ↓ LDL by 5–25%
- ↑ HDL by 15–35%
  ↓ TG by 20–50%
- Flushing, hyperuricemia, hepatotoxicity
- ? effect on mortality
- No benefit when added to statin

Fibrates

- Gemfibrozil
  - ↓ TG by 50%
  - ↑ HDL by 15%
  - ↓ LDL
- Fenofibrate best combination with a statin (less drug interactions)
  - ↓ VLDL
  - Reduce TG by 50%

- A 68 yo man presents for follow up after recent MI. He has had 4 prior MI's over the past 12 years. He has had a 3 vessel CABG, and 2 stents placed. He quit smoking after his 1st MI 12 years ago. BP ranges from 110-130/ 55-65.

Medications: Losartan 100 mg , ASA 81 mg, Atorvastatin 80 mg , ezetimibe 10. Labs: TC 150 HDL 36 LDL 78 Trigly 200. What is the best treatment to reduce his risk of reinfarction?

A) Add chlorthalidone
B) Add Niacin
C) Add Evolocumab
D) Add Bempedoic acid
E) Add Fenofibrate

PCSK9 inhibitors

- Indicated for Homozygous or heterozygous familial hypercholesterolemia
- Statin intolerant patients at high cardiovascular risk
- Very high risk patients with CVD unable to achieve LDL <70 with maximal statin/ezetimibe

- A 66 yo woman is discharged from the hospital after an MI. Her discharge medications include atorvastatin 40 mg, lisinopril 20 mg, ASA 81 mg and clopidogrel 75mg. At her follow up appt she mentions that she has muscle pain and stiffness in both legs and her back. Labs: TSH 2.0 Vitamin D 40 . She stops the atorvastatin for 2 weeks with resolution of her symptoms
- What do you recommend?
- A) Restart atorvastatin
- B) Start Rosuvastatin twice a week
- C) Start Ezitimibe
- D) Start a PCSK9 inhibitor

Nocebo Effect and SAMS

- 60 patients with a hx of SAMS were entered into the trial
- The patients received four bottles containing atorvastatin at a dose of 20 mg, four bottles containing placebo, and four empty bottles; each bottle was to be used for a 1-month period according to a random sequence.
- The mean symptom intensity was 8.0 during no-tablet months (95% CI, 4.7 to 11.3),15.4 during placebo months (95% CI, 12.1 to18.7; P<0.001 for the comparison with no-tablet months), and 16.3 during statin months (95%CI, 13.0 to 19.6; P<0.001 for the comparison with no-tablet months and P=0.39 for the comparison with placebo months) .
- N Engl J Med 2020; 383;22

SAMS- How Good is Rechallenge?

- Retrospective study of 118 patients referred to a lipid clinic as being statin intolerant (muscle symptoms on 2 or more statins)
- Patients were either rechallenged with the same statin, a different statin or non statin therapy
- Tolerability 71% same statin, 53% statin switch and 57% non statin therapy
- Can J Card 2017;33:666-673

Approach to Management of Myalgias on Statins

- Check CK ,TSH, Vitamin D
- Review for drug interactions- especially ca channel bl
- Stop statin, when symptoms disappear restart statin at lower dose (up to 70% success with same statin rechallenge*) or change statin (30-40% success*)
- Can switch to intermittent potent statin
- Ezetimibe or PCSK9 inhibitor in appropriate patients

Answers

1) D- medication use
2) D- add amlodipine
3) C- Losartan/chlortalidone
4) E- Add Furosemide
5) D- Add spironolactone
6) B- chlorthalidone
7) D- chack CMP,Ua,TSH
8) B- Atorvastatin
9) C- Pravastatin
10) D- stop propranolol and oral estrogen
11) C- Add Evolocumab
12) A- restart atorvastatin