Hypertension: a “sprint” to the finish

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Sunnybrook Health Sciences Centre

Disclosures

- I have no current or past relationships with commercial entities
- I have received a speaker’s fee from the Ontario Pharmacists Association for this learning activity

Learning Objectives

Following this presentation, you should be able to:
- Explain the assessment of hypertension
- Describe the pharmacologic and non-pharmacological treatment options
- Outline the role of the pharmacist in hypertension
What is Hypertension?

BP = CO x TPR
CO = HR x Stroke Volume (SV)

TPR = Total Peripheral Resistance
SV = Stroke Volume

What Causes Hypertension?

- Primary hypertension
  - 90% of patients
  - No specific cause

- Secondary hypertension
  - 10% of patients
  - Identifiable and possibly reversible cause

Pathophysiology

Stiffening of arteries
Increased flow velocity

Increase in SBP and DBP

ASSESSMENT & DIAGNOSIS
Diagnosis of Hypertension

AOBP: Automated Office blood pressure
ABPM: Ambulatory blood pressure measurement

What’s preferred?
- Automated office blood pressures (AOBP) are the preferred method for measurement in a physician office.

In Office Assessment
- Measurements should be taken with provider outside of exam room to prevent white coat effect
- Multiple readings taken
- Mean value calculated

How Do They Compare?
- Non-Automatic office BP readings
- Automated office BP readings
- Home BP readings
- Ambulatory BP readings
Choosing a Monitor

Choose the right cuff size
Width: 40% of arm circumference
Length: 80-100% of arm circumference

Recommended by Hypertension Canada

Measuring Blood Pressure

Rest for 5 minutes prior to measurement***

- Place 3 cm above the elbow crease
- Arm at heart level
- No talking, feet uncrossed
- Arm should be bare or with thin clothing

Measuring Blood Pressure

- Take 3 measurements (home BPM):
  - Disregard the first and average the final two
- Wait at least 1 minute between readings to avoid venous congestion
- Measure both arms at least once and then use consistently higher arm

Pharmacist Recommendations

- Encourage and measure blood pressure at appropriate intervals
- Devices validated by Hypertension Canada
- Help patients take quality measurements
- Make recommendations to optimize therapy based on blood pressure readings and patient specific factors
Trivia Break

Which animal has the highest blood pressure?

- Tiger
- Polar bear
- Giraffe
- Dog

GOALS OF THERAPY
Why is High Blood Pressure Bad?

*Increase in systolic BP by 10mmHg associated with:*

- 14% increase in all-cause mortality
- 12% increase in cardiovascular mortality
- 12% increase in stroke
- 8% increase in cardiovascular events


Should We Treat?

- 35-40% reduction in stroke incidence
- 20-25% reduction in myocardial infarction
- 50% reduction in heart failure
- 10% reduction in total mortality

2016 Canadian Hypertension Education Program Recommendations

When to Start Therapy

<table>
<thead>
<tr>
<th>Population</th>
<th>SBP</th>
<th>DBP</th>
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<tr>
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<td>≥ 130</td>
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<td>Moderate to high risk</td>
<td>≥ 140</td>
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</tr>
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<td></td>
<td></td>
</tr>
<tr>
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2016 Canadian Hypertension Education Program Recommendations
Goals of Therapy

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<tr>
<td><strong>SPRINT Population (HIGH RISK)</strong></td>
<td>≤ 120</td>
<td>n/a</td>
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<td>Low risk</td>
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Low risk – High Risk with target organ damage or CV risk factors

2016 Canadian Hypertension Education Program Recommendations

SPRINT Trial

- **Primary Outcome**: first occurrence MI, stroke, heart failure, or death from cardiovascular causes

- **Increased cardiovascular risk**: (aka: SPRINT pop'n)
  - 1 or more of the following
    - Cardiovascular disease other than stroke
    - Chronic kidney disease
      - non-diabetic nephropathy, proteinuria < 1 g/d,
      - estimated glomerular filtration rate 20-59 mL/min/1.73m²
    - Framingham risk score ≥ 15 %
    - Age ≥ 75 years

- **Exclusion criteria**: Diabetes mellitus or prior stroke

SPRINT: SBPs Achieved

Average no. of medications:
- Intensive care: 2.8
- Standard care: 1.8


Hypertension: a “sprint” to the finish

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**Primary Outcome**

- Hazard ratio with intensive treatment, 0.75 (95% CI 0.64–0.89)

**Adverse Events**

- Intensive treatment group showed increased:
  - Hypotension
  - Syncope
  - Electrolyte abnormalities
    - Hyponatremia
    - Hypokalemia
  - Acute kidney injury

**SPRINT Trial Take Home Points**

- High risk patients without diabetes or history of stroke treated to SBP ≤ 120 had decreased death and cardiovascular disease

- Significantly more adverse effects

- More work has to be done in high risk group

**When to Start Therapy**

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*2016 Canadian Hypertension Education Program Recommendations*
What about the Elderly?
2017 Guideline Update

- Age and frailty removed from guidelines
- Rationale: elderly hypertensives benefit from blood pressure reduction regardless of frailty

Dosing Strategies

1. Start one agent → titrate to maximum → add second drug

2. Start one agent → add second before achieving max dose of first

3. Start with two agents

How Do They Compare?

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Population</th>
<th>Goal BP, mm Hg</th>
<th>Initial Drug Treatment Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014 Hypertension guideline</td>
<td>General ≥60 y</td>
<td>&lt;150/90</td>
<td>Nonblack: thiazide-type diuretic, ACEI, ARB, or CCB</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>CKD</td>
<td>&lt;140/90</td>
<td>ACEI or ARB</td>
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| CIEP 2013 | General ≥60 y | <140/90 | Thiazide, β-blocker (age <60y), ACEI (nonblack), or ARB |
| | General <60 y | <150/90 | |
| | Diabetes | <130/80 | ACEI or ARB with additional CV risk ACEI, ARB, thiazide, or DHPCCS without additional CV risk |
| | CKD | <140/90 | ACEI or ARB |

Another Set of Guidelines?

PHARMACOLOGICAL MANAGEMENT

Hypertension: a “sprint” to the finish

The Journal of Clinical Hypertension Vol 16 | No 1 | January 2014
**Health Behaviour Management**

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduce foods with added sodium</td>
<td>→ 2000 mg/day</td>
</tr>
<tr>
<td>Weight loss</td>
<td>BMI &lt;25 kg/m²</td>
</tr>
<tr>
<td>Alcohol restriction</td>
<td>≤ 2 drinks/day</td>
</tr>
<tr>
<td>Physical activity</td>
<td>30-60 minutes 4-7 days/week</td>
</tr>
<tr>
<td>Dietary patterns</td>
<td>DASH diet</td>
</tr>
<tr>
<td>Smoking cessation</td>
<td>Smoke-free environment</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>Men &lt; 302 cm Women &lt; 88 cm</td>
</tr>
<tr>
<td>Potassium supplementation</td>
<td>NEW RECOMMENDATION</td>
</tr>
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**Benefit of BP Lowering in the Low Risk**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number-needed-to-treat to prevent a CV event/death</th>
</tr>
</thead>
<tbody>
<tr>
<td>No risk factors (except age / male)</td>
<td>140-159 / 90-99</td>
</tr>
<tr>
<td>≥ 1 risk factor</td>
<td>≥ 160 / ≥ 100</td>
</tr>
<tr>
<td>Cardiovascular disease or TOD</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>9</td>
</tr>
</tbody>
</table>

**The “old” Treatment Algorithm**

- Initial therapy
- Lifestyle modification
- Dual Combination
  - Thiazide diuretic
  - ACEI
  - ARB
  - Long-acting CCB
- CONSIDER
  - Nonadherence
  - Secondary HTN
  - Interfering drugs or lifestyle
  - White coat effect
- Triple or Quadruple Therapy
- Beta-blocker

A combination of 2 first line drugs may be considered as initial therapy if the blood pressure is ≥130 mmHg systolic or ≥80 mmHg diastolic above target.
The New 2017 Algorithm

**Monotherapy**
- Thiazide / thiazide-like diuretics
- Beta blockers (< 60 yrs)
- ACE inhibitor
- ARB
- Calcium channel blockers

**Combination**
1) ACE inhibitor + CCB
2) ARB + CCB
3) ACEI / ARB + diuretic

Add on if not to target
Suggested combinations:
Diuretic OR CCB with ACEI, ARB or BB

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**Diuretics**

- Examples:
  - Hydrochlorothiazide
  - Indapamide
  - Chlorthalidone

- Great option for African Canadians

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**New for 2017**

- Preference towards long acting thiazide-like diuretics
  - Chlorthalidone
  - Indapamide

- Thiazide vs thiazide-like?

---

**What’s wrong with Hydrochlorothiazide?**

- Meta-analysis of 21 studies

- As compared to hydrochlorothiazide, thiazide-like diuretics resulted in:
  - 12 % additional risk reduction in cardiovascular events
  - 21 % additional risk reduction in heart failure

- Similar adverse effects
Safety Considerations for Thiazide Diuretics

- Ventricular arrhythmias
  - Hypokalemia
  - Hypomagnesemia
- Digoxin toxicity
- Hyponatremia
- Volume depletion
- Prerenal azotemia


Hypertension: a “sprint” to the finish
Trivia Break

KDur tablets are commonly used to replace potassium in hypokalemia

One banana is equivalent to how many mmol of potassium?

- 5 mmol
- 8 mmol
- 16 mmol
- 20 mmol

Why Not Beta Blockers?

Meta-analysis of ≥16,000 patients ≥60 years

- 7 trials used diuretics as first line therapy
- 2 trials used beta blockers as first line therapy
- 1 trial used either beta blockers (67%) or diuretics (33%) as first line therapy


Blood Pressure Response

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Patients</th>
<th>First Drug</th>
<th>Response Rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kumar et al. 1981</td>
<td>44</td>
<td>Thiazide</td>
<td>79</td>
</tr>
<tr>
<td>European Working Party on High Blood Pressure in the Elderly: 1985</td>
<td>416</td>
<td>Hydrochlorothiazide and HCTZ</td>
<td>65</td>
</tr>
<tr>
<td>Systolic Hypertension in the Elderly Program Pilot: 1985</td>
<td>443</td>
<td>Chlorothiazide</td>
<td>88</td>
</tr>
<tr>
<td>Systolic Hypertension in the Elderly Program: 1991</td>
<td>2385</td>
<td>Chlorothiazide</td>
<td>68</td>
</tr>
<tr>
<td>Swedish Trial in Old Patients: 1991</td>
<td>246</td>
<td>Hydrochlorothiazide and amiodore sodium</td>
<td>90</td>
</tr>
<tr>
<td>Medical Research Council Working Party: 1992</td>
<td>1081</td>
<td>Hydrochlorothiazide and amiodore sodium</td>
<td>62</td>
</tr>
<tr>
<td>β-Blockers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coop et al. 1986</td>
<td>419</td>
<td>Atenolol</td>
<td>33</td>
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<tr>
<td>Swedish Trial in Old Patients: 1991</td>
<td>219</td>
<td>Metoprolol</td>
<td>22</td>
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<tr>
<td>Swedish Trial in Old Patients: 1991</td>
<td>160</td>
<td>Atenolol</td>
<td>32</td>
</tr>
<tr>
<td>Swedish Trial in Old Patients: 1991</td>
<td>120</td>
<td>Pindolol</td>
<td>26</td>
</tr>
<tr>
<td>Medical Research Council Working Party: 1992</td>
<td>1122</td>
<td>Atenolol</td>
<td>48</td>
</tr>
</tbody>
</table>

Do Beta Blockers Reduce Risk?


Etiologies?

- ↑ systemic vascular resistance
- ↑ arterial stiffness
- ↑ vascular hypertrophy
- ↓ exercise tolerance
- Predominantly systolic hypertension

Safety Considerations

- May exacerbate fatigue
- May cause confusion or depression
- More prone to arrhythmias (AV block)

Practical Considerations

- Dosing frequency: once versus twice daily
- Available strengths and splitting tablets
- Short versus long acting formulations
ACE Inhibitors and ARBs

ONTARGET study
- 25,620 vascular disease or high risk diabetic patients
- To determine the effectiveness of telmisartan 80mg daily versus ramipril 10mg daily
- To determine if the combination of the 2 drugs was more effective than ramipril alone in reducing the composite endpoint of death from CV causes, MI, stroke or hospitalization of heart failure

Changes in Blood Pressure

<table>
<thead>
<tr>
<th></th>
<th>Ramipril</th>
<th>Telmisartan</th>
<th>Combination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic</td>
<td>-6.0</td>
<td>-6.9</td>
<td>-8.4</td>
</tr>
<tr>
<td>Diastolic</td>
<td>-4.6</td>
<td>-5.2</td>
<td>-6.0</td>
</tr>
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ONTARGET

NEJM 2008; 358:1547-59
Ontarget

Time to Primary Outcome

- Cumulative Hazard Rates
- Years of Follow-up

<table>
<thead>
<tr>
<th>Year</th>
<th>Ramipril</th>
<th>Tel. &amp; Ram.</th>
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<tr>
<td>Yr 1</td>
<td>8576</td>
<td>8502</td>
</tr>
<tr>
<td>Yr 2</td>
<td>8214</td>
<td>8134</td>
</tr>
<tr>
<td>Yr 3</td>
<td>7832</td>
<td>7740</td>
</tr>
<tr>
<td>Yr 4</td>
<td>7473</td>
<td>7377</td>
</tr>
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Safety Considerations
- Renal insufficiency
- Use of NSAIDs
- Hyperkalemia

Calcium Channel Blockers

ASCOT-BPLA
- Randomized controlled trial of 19,257 patients
- Hypertension + age 40-79yrs ≥ 3 other cardiac risk factors
- Amlodipine 5-10mg (+Perindopril 4-8mg) OR
- Atenolol 50-100mg (+Bendroflumethiazide 1.25–2.5 mg)

ASCOT-BPLA
- Hypertension: a "sprint" to the finish

Lancet 2005; 366: 895–906

Lancet 2005; 366: 895–906
ASCOT-BPLA

Hypertension: a “sprint” to the finish

Safety Considerations

- Careful titration
- Peripheral edema
- Arrhythmias - AV blocking effects
- Careful combining with beta blockers

Follow-Up

**Diagnosis of hypertension**

- Non Pharmacological treatment
- ± Pharmacological treatment

Are BP readings below target during 2 consecutive visits?

- Yes
- No

Follow-up at 3-6 month intervals

- Symptoms, Severe hypertension, Intolerance to anti-hypertensive treatment or Target Organ Damage
  - Yes
  - No

More frequent visits

Visits every 1 to 2 mos

2012 Canadian Hypertension Education Program Recommendations
### Therapy for Compelling Indications

#### Hypertension: a “sprint” to the finish

### Overview of Compelling Indications

#### Diabetes
- No Albuminuria / CKD:
  - ACE inhibitors
  - ARBs
  - Dihydropyridine CCBs
  - Thiazide diuretics
- Microalbuminuria, renal disease, CV disease:
  - ACE inhibitors or ARBs

#### Non diabetic CKD with proteinuria
- ACE inhibitors, ARBs
- Diuretics

#### Acute Coronary Syndrome / Coronary Artery Disease:
- Beta blockers
- ACE inhibitors, ARBs

#### Congestive Heart Failure:
- Beta blockers
- ACE Inhibitors
- Spironolactone, eplerenone

#### Atrial Fibrillation:
- Beta blockers
- Non-dihydropyridine calcium channel blockers

#### Stroke:
- ACE inhibitors
- Thiazide diuretics

### Key Points

- Patients may be taking these medications despite normal blood pressures
- Would accept much lower blood pressures as long as asymptomatic

### COMBINATION THERAPY
The New 2017 Algorithm

Monotherapy

-or-

Combination

- Thiazide or thiazide-like diuretic
- Beta blockers (< 60 yrs)
- ACE inhibitor
- ARB
- Calcium channel blockers

Add on if not to target
Suggested combinations:
Diuretic OR CCB with
ACEI, ARB or BB

- Increased blood pressure control
- Increased adherence
- Decreased adverse effects

Suggested combinations:
Diuretic OR CCB with
ACEI, ARB or BB

Combination Therapy: the GOOD…

Medications at admission
- ASA and Clopidogrel
- Telmisartan 40mg daily
- Metoprolol 12.5mg BID
- Atorvastatin 40mg daily

Medications at discharge
- ASA and Clopidogrel
- Twynsta 40/5 daily
- Metoprolol 25mg BID
- Atorvastatin 40 daily

STITCH Trial

- 45 family practice sites in Ontario

- Intervention:
  - Combination therapy
  - Guideline based therapy (CHEP)

- Combination arm 20% more likely to reach target

Combination Therapy: the BAD…

HR: ~150
Metoprolol 100mg TID
Diltiazem CD 240mg daily
Digoxin 0.125mg daily
HR: 30-40
BP: 90/65
Combination Therapy: the UGLY!

- ACEI or ARB therapy plus Aliskiren 300mg daily or placebo in type 2 diabetics and renal impairment and/or CV disease

ALTITUDE Study

- Stopped early
- No apparent benefits
- Increased incidence of adverse effects:
  - Renal complications and hyperkalemia
  - Hypotension

Primary Outcome:

- Time to:
  - CV death
  - Cardiac arrest
  - MI, CVA
  - CHF hospitalization
  - ESRD, 2x SrCr

AND FINALLY…
Fall Risk in Elderly Again Linked to Antihypertension Therapy, but Early After Starting Drugs

- 90,000 Medicare patients, average age 81 years
- First 15 days of therapy initiation or change: ↑36% fall risk
- 16–90 days: no change

Limitations:
- Cause of falls: dizziness versus hypotension
- Dose administration: morning or night?

Orthostatic Hypotension

- **Definition**: decrease in blood pressure > 20/10 mmHg when changing from sitting to standing
- ~300-800ml of blood pools in extremities

- Most pronounced after resting
- Increased incidence with age

- **Symptoms**: Dizziness and lightheadedness

and finally… it’s not just about the antihypertensives

- It’s about vascular protection!
- Consider statin therapy
- Consider ASA therapy in hypertensives ≥ 50 years
- Smoking cessation

2015 Canadian Hypertension Education Program Recommendations
Pharmacist Recommendations

Empower patients to self monitor

Educate patients about their disease verbally and in writing

Use an interdisciplinary approach including pharmacists!

Pharmacist Recommendations

Monitor blood pressure q4-8 weeks until at target × 2 consecutive readings then q3-6 months

Recommend dose increases or additional medication if required

Educate patients that doses and medications may increase

Pharmacist Recommendations

Follow up with patients started on therapy regardless of indication

Use refill visits to assess adherence, adverse effects and response

For late refills - assess barriers that could be preventing adherence

References

• Hypertension Canada’s 2017 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults

• AHA 2011 Expert Consensus Document on Hypertension in the Elderly
  – Journal of the American College of Cardiology. 2011;57;2037-2114

• 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults- JNC 8
  – Journal of the American Medical Association
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