Hypertension in Clinical Practice
Case Study

Dr. Tarek El Zawawy
Professor of Cardiology, Alex. University
CardioAlex Conference 2010

Case Study

- Mr. SB is a 40 year old male, smoker, active, with no significant past medical history & on no medication, with confirmed elevation in BP on repeated visits.

- Symptoms:
  - Headache
  - Visual disturbances.

- Family History:
  - Father With 20 years of Hypertension & IHD
  - Hypertensive Brother at the age of 51.

- Past History:
  - Treatment for mental depression for 3 years
Case Study (Cont.)

- **Physical Examination:**
  - Height: 178 cm
  - Weight: **96 kg**
  - BP: **150/90**
  - Heart rate: 76
  - Chest: Clear to P&A
  - Heart: Regular rhythm, 0 gallops or murmurs audible
  - Abdomen: soft, 0 bruits or organomegaly

- **ECG:** voltage criteria for LVH

- **Chest X-Ray:** Normal heart size, 0 Lung Pathology

- **Urine analysis:** Normal

Case Study (Cont.)

- **Laboratory Findings:**
  - Na 140,
  - K 3.9,
  - Cl 102,
  - **FBS 115,**
  - **OGTT 160**
  - BUN 15,
  - Creatinine 1.1,
  - **Cholesterol 270 (LDL 210, HDL 45),**
  - **Triglycerides 250,**
  - Hct 42
Q1: What is the initial diagnosis of Mrs. SB?

- Grade I Hypertension, Obese, IGT & Dyslipidemia
- Grade II Hypertension, Obese & Diabetic
- Grade I Hypertension, Obese & Dyslipidemia
- Grade II Hypertension, Obese, Diabetic & Dyslipidemia

### JNC VII Classification

<table>
<thead>
<tr>
<th>Category</th>
<th>SBP (mm Hg)</th>
<th>DBP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt; 120</td>
<td>&lt; 80</td>
</tr>
<tr>
<td>Pre – hypertension</td>
<td>120-139</td>
<td>80-90</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>140 – 159</td>
<td>90 – 99</td>
</tr>
<tr>
<td>Stage 2</td>
<td>160 and above</td>
<td>100 and above</td>
</tr>
</tbody>
</table>
Risk Stratification according to ESC/ESH

Q2: How do you classify this patient according to ESC-ESH risk stratification?

- Low added risk
- Moderate added risk
- High added risk
- Very high added risk
**Q3: According to Guidelines, This patient should be treated by ...**

- Pharmacological treatment only
- Lifestyle modification only
- Pharmacological treatment & Lifestyle modification
- Just Stop Smoking
Initiation of antihypertensive treatment (ESC 2007)

<table>
<thead>
<tr>
<th>Blood pressure (mmHg)</th>
<th>Normal SBP 120–129 or DBP 80–84</th>
<th>High normal SBP 130–139 or DBP 85–89</th>
<th>Grade 1 HT SBP 140–159 or DBP 90–99</th>
<th>Grade 2 HT SBP 160–179 or DBP 100–109</th>
<th>Grade 3 HT SBP ≥180 or DBP ≥110</th>
</tr>
</thead>
<tbody>
<tr>
<td>No other factors</td>
<td>No BP intervention</td>
<td>No BP intervention</td>
<td>Lifestyle changes for several months then drug treatment if BP uncontrolled</td>
<td>Lifestyle changes for several weeks then drug treatment if BP uncontrolled</td>
<td>Lifestyle changes + Immediate drug treatment</td>
</tr>
<tr>
<td>1–2 risk factors</td>
<td>Lifestyle changes</td>
<td>Lifestyle changes</td>
<td>Lifestyle changes for several weeks then drug treatment if BP uncontrolled</td>
<td>Lifestyle changes for several weeks then drug treatment if BP uncontrolled</td>
<td>Lifestyle changes + Immediate drug treatment</td>
</tr>
<tr>
<td>≥3 risk factors, MS or OD</td>
<td>Lifestyle changes and consider drug treatment</td>
<td>Lifestyle changes + Drug treatment</td>
<td>Lifestyle changes + Drug treatment</td>
<td>Lifestyle changes + Drug treatment</td>
<td>Lifestyle changes + Immediate drug treatment</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Lifestyle changes + Drug treatment</td>
<td>Lifestyle changes + Drug treatment</td>
<td>Lifestyle changes + Drug treatment</td>
<td>Lifestyle changes + Drug treatment</td>
<td>Lifestyle changes + Immediate drug treatment</td>
</tr>
<tr>
<td>Established CV or renal disease</td>
<td>Lifestyle changes + Immediate drug treatment</td>
<td>Lifestyle changes + Immediate drug treatment</td>
<td>Lifestyle changes + Immediate drug treatment</td>
<td>Lifestyle changes + Immediate drug treatment</td>
<td>Lifestyle changes + Immediate drug treatment</td>
</tr>
</tbody>
</table>

**What is the Goal of BP in this patient?**
## AHA Perspective/Hypertension Management and BP Goals Summary of Main Recommendations

<table>
<thead>
<tr>
<th>Area of concern</th>
<th>BP Target (mm Hg)</th>
<th>Lifestyle † modification</th>
<th>Specific Drug Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>General CAD prevention</td>
<td>&lt;140/90</td>
<td>Yes</td>
<td>Any effective antihypertensive drug or combination‡</td>
</tr>
<tr>
<td>High CAD risk*</td>
<td>&lt;130/80</td>
<td>Yes</td>
<td>ACEI or ARB or CCB or thiazide or combination</td>
</tr>
<tr>
<td>Stable angina</td>
<td>&lt;130/80</td>
<td>Yes</td>
<td>B-blocker and ACEI or ARB</td>
</tr>
<tr>
<td>UA/NSTEMI</td>
<td>&lt;130/80</td>
<td>Yes</td>
<td>B-blocker and ACEI or ARB §</td>
</tr>
<tr>
<td>STEMI</td>
<td>&lt;130/80</td>
<td>Yes</td>
<td>B-blocker and ACEI or ARB §</td>
</tr>
<tr>
<td>LVD</td>
<td>&lt;120/80</td>
<td>Yes</td>
<td>ACEI or ARB and B-blocker and aldosterone antagonist and thiazide or loop diuretic and hydral/nitrate (blacks)</td>
</tr>
</tbody>
</table>

* diabetes, CKD, CAD or equivalent  
† weight loss if appropriate, healthy diet, exercise, smoking cessation and alcohol moderation  
‡ evidence supports ACEI or ARB, CCB, or thiazide as first-line  
§ if anterior MI is present, if HTN persists, if LVD or HF is present, if diabetic

adapted from Rosendorff C, et al. *Circulation* 2007;115:published online

---

**Box 8  Position statement: Goals of treatment**

- In hypertensive patients, the primary goal of treatment is to achieve maximum reduction in the long-term total risk of cardiovascular disease.  
- This requires treatment of the raised BP per se as well as of all associated reversible risk factors.  
- BP should be reduced to at least below 140/90 mmHg (systolic/diastolic), and to lower values, if tolerated, in all hypertensive patients.  
- Target BP should be at least <130/80 mmHg in diabetics and in high or very high risk patients, such as those with associated clinical conditions (stroke, myocardial infarction, renal dysfunction, proteinuria).  
- Despite use of combination treatment, reducing systolic BP to <140 mmHg may be difficult and more so if the target is a reduction to <130 mmHg. Additional difficulties should be expected in elderly and diabetic patients, and, in general, in patients with cardiovascular damage.  
- In order to more easily achieve goal BP, antihypertensive treatment should be initiated before significant cardiovascular damage develops.
### Lifestyle Modifications

- Weight reduction
- Restriction of sodium intake
- Reduction in dietary fat and cholesterol
- Avoidance of tobacco
- Restriction of alcohol consumption
- Use of biofeedback, relaxation techniques
- Regular physical exercise

### Lifestyle Modification

<table>
<thead>
<tr>
<th>Modification</th>
<th>Approximate SBP reduction (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight reduction</td>
<td>5–20 mmHg/10 kg weight loss</td>
</tr>
<tr>
<td>Adopt DASH eating plan</td>
<td>8–14 mmHg</td>
</tr>
<tr>
<td>Dietary sodium reduction</td>
<td>2–8 mmHg</td>
</tr>
<tr>
<td>Physical activity</td>
<td>4–9 mmHg</td>
</tr>
<tr>
<td>Moderation of alcohol consumption</td>
<td>2–4 mmHg</td>
</tr>
</tbody>
</table>
Q4: With regards to pharmacological treatment, the ideal anti hypertensive is...

- With Effective BP control regardless of other attributes
- With Effective BP control with evidence of CV protection
- With Effective BP control, Evidence of CV protection & with high safety profile
- Any Antihypertensive class

JNC VII: Algorithm for Treatment of Hypertension

1. Lifestyle modifications
   - Not at goal blood pressure (BP)*

2. Hypertension without compelling indications
   - Stage 1: Thiazide-type diuretics for most. May consider ACE inhibitor, ARB, β-blocker, CCB, or combination

3. Hypertension with compelling indications
   - Stage 2: Two-drug combination for most (usually including thiazide-type diuretic)
   - Drug(s) for the compelling indications
     - Other antihypertensive drugs (diuretics, ACE inhibitor, ARB, β-blocker, CCB) as needed

4. If not at goal, optimise dosages or add additional drugs until goal BP is achieved.
   - Consider consultation with hypertension specialist

*BP goal <140/90 mmHg or <130/80 mmHg for those with diabetes or chronic kidney disease

Chobanian et al. JAMA 2003;289:2560–72
What about BB or Diuretics?

Reappraisal of European guidelines on hypertension management: a European Society of Hypertension Task Force document

There is no doubt that β-blockers as well as diuretics (especially when combined together) have adverse metabolic effects and facilitate new-onset diabetes [157,158] in predisposed patients such as those with the metabolic syndrome or impaired glucose tolerance [55,159,160].


Deleterious effects of Angiotensin II

SNS = Sympathetic nervous system

Ang II

↑PAI-1/ thrombosis
Platelet aggregation
Superoxide production
Vascular smooth muscle growth
↑Collagen

Remodeling

↑Aldosterone
↑Vasopressin
↑Endothelin

Abnormal vasoconstriction
Activate SNS

Angiotensin II Plays a Central Role in Organ Damage

Q5: RAAS Blockade is the future of Hypertension Management. Do we use ACEi or ARBs?

- **ACEi**

- **ARBs**
The sites of action of ACE inhibition and AT₁-receptor blockade in the renin-angiotensin system

<table>
<thead>
<tr>
<th><strong>Step of RAAS Blockade</strong></th>
<th><strong>ARBs</strong></th>
<th><strong>ACEi</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Receptor Level</td>
<td>Preserve AT₁II beneficial effect</td>
<td>Deprive the body from AT₁II beneficial effect</td>
</tr>
<tr>
<td>Bradykinin Metabolism</td>
<td>Don't Interfere</td>
<td>Prevent</td>
</tr>
<tr>
<td></td>
<td>No Dry Cough</td>
<td>Dry Cough</td>
</tr>
<tr>
<td>Non ACE Pathway Activation</td>
<td>Non Activated</td>
<td>Activated</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BP uncontrolled over time</td>
</tr>
</tbody>
</table>
Rates of Persistence With Therapy Differs Between Drug Classes

Persistence with antihypertensive medication at 24 months in 24,718 patients included in the Saskatchewan database

Persistence defined as prescription refill within 21 days of the target month

Lindholm J Hum Hypertens 2002;16:S3–S8

Effects of Different Antihypertensive Agents on Incidence of Diabetes

Network meta-analysis assessing the effects of different antihypertensive agents on incidence of diabetes in 48 randomised groups from 22 clinical trials* (n=143,153)

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Odds Ratio of Incident Diabetes</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARB</td>
<td>0.57 (0.46–0.72)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>0.67 (0.56–0.80)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CCB</td>
<td>0.75 (0.62–0.90)</td>
<td>0.002</td>
</tr>
<tr>
<td>Placebo</td>
<td>0.77 (0.63–0.94)</td>
<td>0.009</td>
</tr>
<tr>
<td>β-blocker</td>
<td>0.90 (0.75–1.09)</td>
<td>0.30</td>
</tr>
<tr>
<td>Diuretic</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*17 trials enrolled patients with hypertension, three enrolled high-risk patients and one enrolled patients with heart failure (HF)

ARB=angiotensin receptor blocker; ACE=angiotensin-converting enzyme; CCB=calcium channel blocker

Q6: Are Drugs in the Same class Possessing the similar clinical benefits?

- YES
- NO

Pharmacological differences

Selectivity on AT1 Receptor

Valsartan is 30,000 times more selective for AT1 receptors than AT2
Clinical impact

Superior blood pressure control

Proven efficacy in Endothelial dysfunction

Evidence of Superior cardiovascular protection

Evidence of Superior Renal protection

VALSARTAN 160 Significantly Reduces SBP by 20 mm Hg to Get Patients to Goal

Results from a 8-week study in 767 patients# with stage 2 systolic hypertension (VALOR study)

<table>
<thead>
<tr>
<th>Drug</th>
<th>SBP change</th>
<th>DBP change</th>
</tr>
</thead>
<tbody>
<tr>
<td>VALSARTAN 160 mg</td>
<td>-20.7*</td>
<td>-6.6</td>
</tr>
</tbody>
</table>

DBP: baseline to 8 weeks (mm Hg)

-20.7*: p<0.05 vs. baseline; †p<0.05 vs. VALSARTAN 160 mg monotherapy; ‡p<0.05 vs. DIOVAN 160 mg; Response= SBP <140 mmHg or decrease in SBP ≥20 mmHg after 8 weeks of treatment

VALSARTAN Provides Effective BP Reductions Irrespective of Time of Administration

Results from a 3-month study in 148 non-dipper patients with mild-to-moderate essential hypertension#

VALSARTAN 160 mg o.d.

Morning administration

Evening administration

<table>
<thead>
<tr>
<th>Time after dose administration (hours)</th>
<th>Mean change in SBP (mm Hg)</th>
<th>Mean change in DBP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>-13.1*</td>
<td>-10.3*</td>
</tr>
<tr>
<td>3</td>
<td>-8.5*</td>
<td>-14.7*</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

p=NS between time of administration

#with <10% decline in nocturnal relative to diurnal BP and SBP/DBP ≥140/90 and ≤179/109; *p<0.001 vs. baseline

Hermida et al. J Hypertens 2005;23(10):1913-1922

Tareg® 160 Reduce BP Beyond 24 Hours

Results from a 8-week study in 256 patients with mild-to-moderate hypertension#

#sitting DBP between 95 and 115 mm Hg at baseline, *intervals 2-24, n=21 (15 treated with valsartan 80 mg, 6 with 160 mg) intervals 26-48, n=10 (9 treated with valsartan 80 mg, 1 with 160 mg), hour 25-48 without dose

**VALSARTAN Reduces The Risk of Diabetes in Patients with High CV Risk on Monotherapy**

Results from a 4.1-year study† in 7,080 patients with HTN‡ and high risk of cardiac events (VALUE study, post-hoc analysis)

![Graph showing reduced risk of diabetes with valsartan compared to amlodipine]

**Valsartan® Reduces the Risk of New-onset Diabetes Better than Losartan**

Results from a retrospective cohort study# in 14,588 patients with HTN, initiating Valsartan or losartan monotherapy for 7 years

![Graph showing lower risk of diabetes with valsartan compared to losartan]

---

†Follow-up period: 4-6 (mean 4.2) years; †Patients with BP<140/90 still receiving monotherapy at the end of the 6 months up-titration; *Valsartan vs. amlodipine, p=0.012, NOD=new-onset diabetes

Julius et al. Hypertension 2006;48:385-391

#Using a US healthcare claims database; *Unadjusted risk, valsartan vs. losartan (95% CI: 0.63-0.95); new-onset diabetes identified as ≥2 outpatient diagnoses (≥7 days apart), ≥1 inpatient diagnosis, or ≥1 prescriptions for antidiabetic medication

Valsartan: Extensively Studied Across the Cardiovascular Continuum

Summary

- Central to the success of any antihypertensive regimen
  - Efficacy
  - 24-hour BP control
  - Compliance & persistence

- Factors favouring good compliance and persistence include
  - Once-daily dosing
  - Tolerability

- Valsartan 160 provide rapid blood pressure reduction & better control throughout 24 hours.

- Valsartan is the most studied ARB with evidences across the whole CV continuum

*Not all patients in these studies received valsartan
†Independent, investigator-initiated study
