As Different As Night From Day: Does Dosing Antihypertensives At Night Decrease Cardiovascular Risk in Patients with Type 2 Diabetes?

Nicole Mendenhall
PharmD Candidate 2018
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Objectives

- **Understand** the risk factors associated with type 2 diabetes
- Be able to **explain** how hypertension in combination with type 2 diabetes increases cardiovascular risk
- **Distinguish** between dippers vs. non-dippers in regards to blood pressure
- **Delineate** between:
  - Ambulatory blood pressure monitoring
  - Clinical blood pressure monitoring
- **Interpret** the data from the following studies to make the best clinical decisions for patients in this population
On my ambulatory care rotation I saw a lot of patients with both diabetes and hypertension many of whom were struggling to manage both disease states.

The University of Utah ambulatory care pharmacists are trying to target patients with both disease states, who are currently uncontrolled in both areas and will be focusing on helping these patients to better manage their health.

We never discussed a specific time of day as possibly being better than another for patients on antihypertensives in either our cardiovascular or diabetes therapeutics modules.
BACKGROUND
Prevalence of Hypertension in Type 2 Diabetes

“As of 2015, 33.3 million americans are living with diabetes. Approximately 31.5 million americans have Type 2 diabetes.”

“Diabetes remains the 7th leading cause of death. In 2015, 252,806 deaths listed diabetes as the underlying or contributing cause of death.”

“Hypertension is present in more than 50% of patients with diabetes.”

See References 1-5
Cardiovascular Disease (CVD) in Type 2 Diabetes

Cardiovascular Disease in Diabetes:

- Atherosclerotic Cardiovascular Disease: ASCVD includes:
  - Acute coronary syndromes (ACS)
  - Myocardial infarction (MI)
  - Stable or unstable angina
  - Coronary or arterial revascularization
  - Stroke
  - Transient ischemic attack
  - Peripheral arterial disease (PAD)

“ASCVD... is the leading cause of morbidity and mortality in patients with diabetes.”

Coexisting conditions can cause Increased Risk:

- Hypertension
- Dyslipidemia
- Diabetes itself confers an independent risk

See References 6-7.
Dippers vs. Non-Dippers:

<table>
<thead>
<tr>
<th>Class</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reverse Dipper</td>
<td>&lt; 0% decrease in BP, rather BP is increased</td>
</tr>
<tr>
<td>Non-dipper</td>
<td>0% - 9.9% decrease in BP</td>
</tr>
<tr>
<td>Dipper</td>
<td>&gt; 10% decrease in BP</td>
</tr>
</tbody>
</table>

See Reference 10.
**BRIEF HYPERTENSION OVERVIEW**

- **Normotensive (Dipper)**
- **Normotensive + Non-Dipper**
- **High BP + Non-dipper**

See References 11-12.
Ambulatory Blood Pressure Monitoring (ABPM):

- Involves checking BP at regular intervals for a 24 hour period
  - Every 20 minutes during the day
  - Every 30 minutes at night
- Indications for ABPM:
  - Suspected nocturnal HTN
  - HTN despite treatment
  - High risk for CVD
  - White coat HTN

Clinic BP Monitoring:

- Involves checking BP at the physician's office with either a conventional or automated BP cuff
- Generally it is recommended that clinic BP readings be taken when:
  - Patients are sitting
  - Have had a period of time to rest
  - Have no prior smoking or caffeine intake
  - Have an appropriately sized cuff for arm or leg

See References 13-14.
Ambulatory Blood Pressure Monitoring (ABPM):

- Elevated APMB:
  - Awake: BP > 135/85 mm Hg
  - Asleep: BP > 120/70 mm Hg
- Benefits:
  - Rather than getting a snapshot of BP, there is a continuous picture of what a patient’s BP looks like over the course of 24 hours

Clinic BP Monitoring:

- Elevated Clinic BP:
  - Awake: BP ≥ 140/90 mm Hg
  - Asleep: not done
- Benefits:
  - Easy to take
  - Can be done in a variety of settings
  - Quick

See References 13-14.
JNC-8 Guidelines for Hypertension -2014:

- BP Goal for Patients with Diabetes:
  - <140/90 mmHg
- Time of Day Dosing:
  - JNC-8 does not recommend a specific time of day to take blood pressure medications
  - There are no recommendations regarding time of day dosing for BP lowering agents

ADA Standards for Medical Care in Diabetes-2017:

- BP Goal for Patients with Diabetes:
  - <140/90 mmHg
- Time of Day Dosing:
  - The ADA guidelines suggest that there may be an association between bedtime dosing of antihypertensives and decreased ASCVD risk.
  - Clinicians can “Consider administering one or more antihypertensive medications at bedtime.”

See References 6, 9.
Current guidelines suggestions are either not defined or unclear:

- With the current discrepancies between the two guidelines, what time of day should we be recommending that patients take their antihypertensive medications?
Questions?
Study 1: Sleep-Time Blood Pressure as a Therapeutic Target for Cardiovascular Risk Reduction in Type 2 Diabetes

Overview

Study Design: follow up study to MAPEC (Ambulatory blood pressure monitoring for prediction of cardiovascular events).

Study Location: single center in Spain

Study Length: median follow up time of 5.4 years (0.5-8.4 years)

Primary Outcome: total cardiovascular morbidity and mortality

Secondary Outcome: major cardiovascular events

Participants: N = 607

Inclusion Criteria:
- Primary hypertension or untreated normotension
- Type 2 diabetes
- 18 years of age or older
- Had referral to a hospital for ABPM
- Participants of the MAPEC study

Exclusion Criteria:
- Pregnancy
- History of alcohol/drug abuse
- Night/shift work employment
- Diagnosis of AIDS
- Type 1 diabetes
- Secondary hypertension
- Pre-existing CVD disorders
- Intolerance to ABPM
- Inability to communicate and comply with all study requirements

Study Groups

607 Study Participants

159 Normotensive Patients

448 Hypertensive Patients

Patient with hypertension were treated for hypertension

Agents used:
- **ARBs**: Valsartan, Telmisartan, and Olmesartan
- **CCBs**: Amlodipine, and nifedipine
- **Additional Agents**: A hydrochlorothiazide, or a nondihydropyridine CCB

**Methods**

**Important Method Points:**
- **48 Hr ABPM & Wrist Actigraphy:**
  - Inclusion and at each follow-up visit, roughly every 6-12 months
  - Every 3 months if a therapy change occurred
  - Patients were required to wear a wrist monitor to establish sleep/wake pattern

- **Clinic BP Measurements:**
  - Six BP measurements were obtained by the same investigator
  - After patient had rested in a seated position for > 10 minutes

- **Therapy Changes:**
  - Patients with uncontrolled ABPM after three months of therapy were allowed to add another BP lowering agent
  - Change had to be consistent with current guidelines

**Measured Outcomes**

**Primary Outcome:** Total CVD Morbidity and Mortality
- Death from all causes
- Cardiovascular events:
  - Myocardial Infarction
  - Angina pectoris
  - Coronary revascularization
- Cerebrovascular events:
  - Stroke
  - Transient ischemic attack
- Heart failure
- Acute arterial occlusion

**Secondary Outcome:**
- Major CVD Events
  - CVD deaths
  - Myocardial infarction
  - Stroke of any type

Statistical Analysis

Intention to treat analysis: all study participants were included in the analysis

Corrections made to ABPM:
- Systolic: > 250 mmHg, or < 70 mmHg were not included
- Diastolic: >150 mmHg, or < 40 mmHg were not included

Ambulatory Blood Pressure Means: average of all valid readings obtained during daytime or nighttime based on wrist actigraphy

T-Test: compared parametric data of demographics and clinical characteristics

X² Test: compared non-parametric data of demographics and clinical characteristics

**Statistical Analysis**

**Cox Proportional Hazards Model:** (95% CI) estimated hazard ratios with events associated with treatment, adjusted for confounding variables.

**Cox Regression Analysis:** used to determine the predictive values of blood pressure reduction on cardiovascular outcomes

**Akaike Information Criteria (AIC):** comparison of prognostic values of blood pressure and clinic blood pressure using models derived by AIC.

**P-Value Corrective Changes:** Differences between groups for baseline demographics and characteristics were significant if $P < 0.002$, this was done to correct for multiple testing

Baseline Demographics

Table 1 | Baseline characteristics of investigated patients with type 2 diabetes

<table>
<thead>
<tr>
<th>Variable</th>
<th>No event</th>
<th>Event</th>
<th>$P$ between groups</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients, $n$</td>
<td>500</td>
<td>107</td>
<td></td>
</tr>
<tr>
<td>Anemia, %</td>
<td>12.2</td>
<td>32.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Albuminuria, %</td>
<td>21.4</td>
<td>45.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chronic kidney disease, %</td>
<td>35.6</td>
<td>67.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age, years</td>
<td>58.6 ± 12.4</td>
<td>65.1 ± 10.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clinic SBP, mm Hg$^b$</td>
<td>153 ± 22</td>
<td>168 ± 29</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clinic DBP, mm Hg$^b$</td>
<td>84 ± 12</td>
<td>86 ± 16</td>
<td>0.20</td>
</tr>
</tbody>
</table>

Due to correction factors, a $P$ Value < 0.002 is considered significant.

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<th>Variable</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Asleep SBP mean, mm Hg</td>
<td>121 ± 18</td>
<td>144 ± 21</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>48 h SBP mean, mm Hg</td>
<td>128 ± 16</td>
<td>143 ± 18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sleep-time relative SBP decline, %</td>
<td>7.7 ± 7.6</td>
<td>−1.0 ± 8.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Asleep DBP mean, mm Hg</td>
<td>67 ± 10</td>
<td>73 ± 12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>48 h DBP mean, mm Hg</td>
<td>74 ± 10</td>
<td>75 ± 12</td>
<td>0.09</td>
</tr>
<tr>
<td>Sleep-time relative DBP decline, %</td>
<td>13.0 ± 8.3</td>
<td>5.0 ± 8.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nondipper, %</td>
<td>59.8</td>
<td>94.4</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Events during follow up:

- Total Events Documented: 107
- Major Events Documented: 35
- Total Deaths: 18
- CVD Related Deaths: 10

CVD Risk was associated with:

- Older age
  - HR: 1.04 (1.02-1.06) P < 0.001
- Male sex
  - HR: 1.79 (1.17-2.73) P < 0.01
- Anemia
  - HR: 2.26 (1.49-3.42) P < 0.001
- CKD
  - HR: 2.02 (1.35-3.02) P < 0.001

### Results

Adjustments were applied for: Age, Sex, CKD, and Anemia

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Total CVD events</th>
<th>Major CVD events</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adjusted HR</td>
<td>Further adjustment by clinic BP</td>
</tr>
<tr>
<td>Clinic</td>
<td>1.44 (1.19–1.74)*</td>
<td>—</td>
</tr>
<tr>
<td>Awake mean</td>
<td>1.38 (1.17–1.63)*</td>
<td>1.22 (0.99–1.50)</td>
</tr>
<tr>
<td>Asleep mean</td>
<td>1.71 (1.45–2.01)*</td>
<td>1.74 (1.40–2.17)*</td>
</tr>
<tr>
<td>48 h mean</td>
<td>1.51 (1.28–1.77)*</td>
<td>1.41 (1.14–1.75)**</td>
</tr>
<tr>
<td>Sleep-time relative decline</td>
<td>0.58 (0.49–0.69)*</td>
<td>0.62 (0.52–0.74)*</td>
</tr>
</tbody>
</table>

*p < 0.001  
**p < 0.01  
***p < 0.05
Patients with elevated sleep BP had a significantly higher hazard ratio than those with normal asleep BP, independent of awake BP.
In patients with type 2 diabetes, CVD risk is associated with elevated asleep BP mean, independent of the level of clinic BP measurements.
**Strengths and Weaknesses**

<table>
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<tr>
<td>Large sample size based on the fact that 48 hour ABPM was required</td>
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<td>Different BP medications were used during the study - mimics real world</td>
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<tr>
<td>Multiple measures of ambulatory BP, rather than just a single measure at baseline</td>
<td>Small sample size</td>
</tr>
<tr>
<td>Wrist actigraphy to determine sleep/wake activities</td>
<td>Different BP medications were used during the study - no ability to draw conclusions from a certain class of BP lowering agents</td>
</tr>
<tr>
<td></td>
<td>Do not use ABPM in clinical setting very often, unsure of how feasible that would be for patients or healthcare professionals</td>
</tr>
</tbody>
</table>
Author’s Conclusions

- Sleep time blood pressure is the most significant independent prognostic marker of cardiovascular events in patients with type 2 diabetes.

Seminarian’s Conclusions

- Based on the study results ABPM appears to be a better risk estimator of cardiovascular outcomes than clinic blood pressure
- The study also shows that cardiovascular risk is independent of
  - Clinic blood pressure
  - Awake blood pressure
- Those at risk for an event were more likely to be:
  - Male
  - Age > 65 years
  - Had CKD or anemia at baseline
  - Non-dippers at baseline
  - Have elevated sleep SBP

However, this study is based off of models predicted by AIC and we typically do not treat patients based off models.
Questions?
Study 2: Influence of Time of Day Blood Pressure-Lowering Treatment on Cardiovascular Risk in Hypertensive Patients with Type 2 Diabetes
Study Design: prospective, randomized, open-label, blinded-endpoint study (PROBE)

Study Location: single center in Spain

Study Length: median follow up time: 5.4 years (0.5-8.4 years)

Primary Outcome: total cardiovascular morbidity and mortality

Secondary Outcome: major cardiovascular events
Randomized: N = 448

Inclusion Criteria:
- Primary hypertension
- Type 2 diabetes
- 18 years of age or older
- Had referral to a hospital for ABPM

Exclusion Criteria:
- Pregnancy
- History of alcohol/drug abuse
- Night/shift work employment
- Diagnosis of AIDS
- Type 1 diabetes
- Secondary hypertension
- Pre-existing CVD disorders
- Intolerance to ABPM
- Inability to communicate and comply with all study requirements
Study population was randomized into two treatment groups:

- **Group 1:** Ingesting >1 antihypertensive medications at night: 216
- **Group 2:** Ingesting antihypertensive medications in the morning: 232

**Blood Pressure Lowering Agents that could be used in Each Group:**

**ARBs:** Valsartan, Telmisartan, and Olmesartan

**CCBs:** Amlodipine, and nifedipine

**Additional Agents:** A hydrochlorothiazide, or a nondihydropyridine CCBs
Methods

Important Method Points:

● **48 Hr ABPM & Wrist Actigraphy:**
  ○ Inclusion
  ○ At each follow-up visit, roughly every 6-12 months
  ○ Every 3 months if a therapy change occurred
  ○ Patients were required to wear a wrist monitor to establish sleep/wake pattern

● **Clinic BP Measurements:**
  ○ Six BP measurements were obtained by the same investigator
  ○ After patient had rested in a seated position for > 10 minutes

● **Therapy Changes:**
  ○ Patients with uncontrolled ABPM after three months of therapy were allowed to add another BP lowering agent
  ○ Change had to be consistent with current guidelines

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**Measured Outcomes**

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  - Angina pectoris
  - Coronary revascularization
- Cerebrovascular events:
  - Stroke
  - Transient ischemic attack
- Heart failure
- Acute arterial occlusion

**Secondary Outcome:**
Major CVD Events
- CVD deaths
- Myocardial infarction
- Stroke of any type
Statistical Analysis

**Intention to treat analysis:** all randomized patients are included in the analysis

**Corrections made to ABPM:**
- Systolic: > 250 mmHg, or < 70 mmHg were not included
- Diastolic: > 150 mmHg, or < 40 mmHg were not included

**T-Test:** compared parametric data of demographics and clinical characteristics

**X² Test:** compared non-parametric data of demographics and clinical characteristics

**Cox Proportional Hazards Model:** estimated hazard ratios with events associated with treatment, adjusted for confounding variables

**Kaplan Meier Product-Limit Method:** generate survival curves

## Baseline Demographics

<table>
<thead>
<tr>
<th>Demographic characteristics</th>
<th>Awakening</th>
<th>Bedtime</th>
<th>$P$ between groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>$n$</td>
<td>232</td>
<td>216</td>
<td>0.345</td>
</tr>
<tr>
<td>Sex (% men)</td>
<td>59.1</td>
<td>54.6</td>
<td>0.688</td>
</tr>
<tr>
<td>Previous CVD events (%)</td>
<td>8.2</td>
<td>9.3</td>
<td>0.779</td>
</tr>
<tr>
<td>Duration of known diabetes (years)</td>
<td>8.9 ± 8.4</td>
<td>8.7 ± 8.0</td>
<td>0.674</td>
</tr>
<tr>
<td>Duration of known hypertension (years)</td>
<td>7.4 ± 8.2</td>
<td>7.6 ± 8.7</td>
<td>0.804</td>
</tr>
</tbody>
</table>

### Ambulatory blood pressure

<table>
<thead>
<tr>
<th></th>
<th>Awakening</th>
<th>Bedtime</th>
<th>$P$ between groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asleep SBP mean (mmHg)</td>
<td>128.5 ± 21.7</td>
<td>129.2 ± 20.2</td>
<td>0.702</td>
</tr>
<tr>
<td>Sleep time relative SBP decline (%)</td>
<td>5.2 ± 8.3</td>
<td>5.0 ± 8.7</td>
<td>0.346</td>
</tr>
<tr>
<td>Asleep DBP mean (mmHg)</td>
<td>68.3 ± 11.4</td>
<td>69.3 ± 10.9</td>
<td>0.432</td>
</tr>
<tr>
<td>Sleep time relative DBP decline (%)</td>
<td>10.7 ± 8.7</td>
<td>10.1 ± 8.9</td>
<td>0.558</td>
</tr>
<tr>
<td>Nondipper (%)</td>
<td>72.4</td>
<td>70.0</td>
<td>0.558</td>
</tr>
</tbody>
</table>
Outcomes: Primary & Secondary

* Number of patients that experienced the event listed in parenthesis ()..

<table>
<thead>
<tr>
<th></th>
<th>Awakening</th>
<th>Bedtime</th>
<th>P between groups</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n</strong></td>
<td>232</td>
<td>216</td>
<td></td>
</tr>
<tr>
<td><strong>Primary end points</strong>*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>54.24 (68)</td>
<td>19.80 (23)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Major events</td>
<td>17.55 (22)</td>
<td>5.16 (6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Secondary end points</strong>*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total death</td>
<td>6.38 (8)</td>
<td>2.58 (3)</td>
<td>0.097</td>
</tr>
<tr>
<td>Cardiovascular death</td>
<td>4.79 (6)</td>
<td>0.86 (1)</td>
<td>0.038</td>
</tr>
<tr>
<td>Other cause</td>
<td>1.60 (2)</td>
<td>1.72 (2)</td>
<td>0.968</td>
</tr>
<tr>
<td>Cardiovascular events</td>
<td>15.95 (20)</td>
<td>6.89 (8)</td>
<td>0.008</td>
</tr>
<tr>
<td>Cerebrovascular events</td>
<td>6.38 (8)</td>
<td>0.86 (1)</td>
<td>0.010</td>
</tr>
<tr>
<td>Heart failure</td>
<td>13.56 (17)</td>
<td>6.02 (7)</td>
<td>0.020</td>
</tr>
<tr>
<td>Other events</td>
<td>11.96 (15)</td>
<td>3.44 (4)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Outcomes

Hazard Ratios for Primary & Secondary Outcomes:

HR: 0.33 (0.21 - 0.54)  P < 0.001
HR: 0.25 (0.10 - 0.61)  P = 0.003
### Outcomes: Ambulatory BP Monitoring

Results Reported as means ± S.D.

<table>
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<tbody>
<tr>
<td>n</td>
<td>232</td>
<td>216</td>
<td></td>
</tr>
<tr>
<td>Awake SBP mean (mmHg)</td>
<td>127.1 ± 17.8</td>
<td>126.8 ± 14.6</td>
<td>0.861</td>
</tr>
<tr>
<td>Asleep SBP mean (mmHg)</td>
<td>122.4 ± 21.8</td>
<td>115.0 ± 17.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>48-h SBP mean (mmHg)</td>
<td>125.5 ± 18.3</td>
<td>122.8 ± 15.0</td>
<td>0.097</td>
</tr>
<tr>
<td>Sleep time relative SBP decline (%)</td>
<td>3.7 ± 10.3</td>
<td>9.4 ± 7.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Awake DBP mean (mmHg)</td>
<td>70.5 ± 10.8</td>
<td>71.0 ± 10.7</td>
<td>0.621</td>
</tr>
<tr>
<td>Asleep DBP mean (mmHg)</td>
<td>63.7 ± 11.3</td>
<td>60.2 ± 10.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>48-h DBP mean (mmHg)</td>
<td>68.2 ± 10.4</td>
<td>67.4 ± 10.1</td>
<td>0.406</td>
</tr>
<tr>
<td>Sleep time relative DBP decline (%)</td>
<td>9.3 ± 11.4</td>
<td>14.9 ± 9.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nondipper (%)</td>
<td>76.3</td>
<td>49.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Controlled ambulatory blood pressure (%)</td>
<td>50.9</td>
<td>62.5</td>
<td>0.013</td>
</tr>
<tr>
<td>Controlled awake blood pressure (%)</td>
<td>75.4</td>
<td>72.2</td>
<td>0.439</td>
</tr>
<tr>
<td>Controlled asleep blood pressure (%)</td>
<td>54.7</td>
<td>70.8</td>
<td>&lt;0.001</td>
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Outcomes

Kaplan Meier Survival Curve:
## Strengths and Limitations

<table>
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<tr>
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<th><strong>Weaknesses</strong></th>
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</thead>
<tbody>
<tr>
<td>Large sample size based on the fact that patients had to do ABPM throughout the trial</td>
<td>Single center study done in Spain</td>
</tr>
<tr>
<td>PROBE study design developed to conduct long term morbidity and mortality trials</td>
<td>Small sample size</td>
</tr>
<tr>
<td>Multiple measurements of ABPM throughout the study, rather than one at baseline</td>
<td>Different blood pressure medications were used during the study - no ability to draw conclusions from a certain class of blood pressure lowering agents</td>
</tr>
<tr>
<td>Wrist actigraphy monitoring for determining sleep/wake times</td>
<td>Open label</td>
</tr>
<tr>
<td>Different blood pressure medications were used during the study - mimics real life</td>
<td>Do not commonly use ABPM in practice, unsure of how applicable or feasible this study may be</td>
</tr>
</tbody>
</table>
In hypertensive patients with type 2 diabetes, we recommend ingesting blood pressure lowering medications at night.

Ingesting blood pressure lowering agents at night:
- Improves overall blood pressure control
- Decreases the prevalence of non-dipping
- Significantly reduces cardiovascular disease risk

Treatment at bedtime is the most cost-effective, simple strategy of successfully achieving the therapeutic goals of adequate asleep blood pressure reduction and preserving or reestablishing the normal 24 h blood pressure dipping pattern.
Seminarian’s Conclusions

- Improving circadian BP levels, rather than just day-time BP levels decreases the risk of CVD in patients with type 2 diabetes
- The percentage of non-dippers decreased in the group where blood pressure medications were ingested at night rather than in the morning
- No conclusions can be made about the cost effectiveness of this study as that was not evaluated anywhere yet mentioned in the authors conclusions
- The best practice would be to evaluate whether or not patients are willing to take BP meds at night and the keep a consistent schedule.
Questions?
Overall Conclusions
Final Conclusion

• It is not wrong to encourage patients to take their BP medications at night
  ○ Based on the data from the study, there is no harm associated with ingestion BP agents at night

• ABPM may not be the most feasible way to evaluate BP in all hypertensive patients
  ○ One third of americans have high blood pressure, evaluating each one, even on an annual basis with ABPM seems unrealistic
  ○ ABPM while commonly used in studies to evaluate effectiveness, is not commonly used in the outpatient setting
    ■ Clinic BP measurements can be made virtually anywhere
    ■ Blood Pressure cuffs are available to buy in most retail stores for at home monitoring
    ■ Clinic BP measurements are easy to take and results come back in a timely manner
  ○ Current guidelines on both hypertension and diabetes have no recommendations involving Ambulatory Blood Pressure Monitoring
Pharmacist’s role

● Encourage adherence:
  ○ While dosing these agents at night may have additional benefit, if the patient is not compliant with taking their medication in the first place then it won’t matter when we have asked them to ingest it.

● If it is easier for the patient to take their blood pressure medication at night, encourage it:
  ○ Based on the data there appears to be no harm in taking BP medications at night vs taking them in the morning, do what works best for the patient

● Roll for Ambulatory Care Pharmacists:
  ○ If ABPM begins to play more of a roll in the evaluation and treatment of hypertension, I think that Ambulatory Care pharmacists will play a significant role in monitoring patients with hypertension
  ○ They would have the necessary resources to assess ABPM and make changes to treatment regimens as necessary
Questions?
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