Taking blood pressure-lowering medications at night

**Clinical Question:** Will taking one or more antihypertensive drugs at night improve cardiovascular disease (CVD) outcomes and reduce drug side-effects?

**Evidence:**

MAPEC¹, a 5.6 year trial of 2156 hypertensive patients (52% female, mean age 56, 20% diabetes, 13% smoker)

- Randomized to antihypertensives taken upon awakening versus 1 or more medications taken at bedtime (with 47% taking all antihypertensives at bedtime)
- Blood pressure (BP) results: No difference at start. After
  - Daytime: Awakening 125/75 versus bedtime 125/76
  - Nighttime: Awakening 116/65 versus bedtime 111/63
- Outcomes: Statistically significant reduction in
  - Mortality: Awakening 2.6% vs bedtime 1.1%, Number Needed to Treat (NNT) 67
  - Total CVD events: Awakening 17.3% vs bedtime 6.3%, NNT 9
- Limitations: Poorly described randomization and allocation of patients, lack of blinding, no reporting of adverse events, no correction for multiple analysis, and CVD event rates inexplicably higher than expected (very unusual in clinical trials).
- Diabetic² and chronic kidney disease³ patients had similar benefits.

**Context:**

- Observational studies⁴-⁶ have demonstrated that nighttime ambulatory BP is a better predictor of CVD events than either in-office BP or daytime BP.
- Other RCTs⁷-⁹ have demonstrated a greater reduction in nighttime BP with bedtime administration of most antihypertensive classes.
- JNC 7 (US hypertension guidelines)¹⁰ states that hypertension is >135/85 awake and >120/75 asleep for ambulatory BP.
- We could not identify any other large trials specifically addressing CVD for antihypertensives taken at bedtime.
  - However, ramipril was given at bedtime in the HOPE trial. The daytime office BP changed little (3/2mmHg) so the benefits (3.8% reduction in CVD events...
in 5 years) were assumed due to a unique property of Ramipril.\textsuperscript{11} However, the night-time BP was 17/8 mmHg better.\textsuperscript{12}

**Bottom-line:** Taking one or more BP meds before bed may potentially help reduce cardiovascular risk but due to limitations of the evidence, strong recommendations are difficult.

Authors: Ricky Turgeon, G. Michael Allan MD CCFP

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