Taking blood pressure–lowering medications at night

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Clinical question
Will taking 1 or more antihypertensive drugs at night improve cardiovascular disease (CVD) outcomes and reduce drug side effects?

Evidence
In MAPEC, a 5.6-year trial (N=2156 hypertensive patients; 52% female, mean age 56, 20% had diabetes, 13% smoked), patients were randomized to take antihypertensive medications upon awakening or to take 1 or more medications at bedtime (47% took all antihypertensives at bedtime).

- Blood pressure (BP) results:
  - Daytime BP for both groups was approximately 125/75 mm Hg.
  - Nighttime BP was 5/2 mm Hg lower for the bedtime medication group than the morning medication group (111/63 mm Hg vs 116/65 mm Hg).

- Outcomes: Statistically significant reduction in
  - mortality (morning 2.6% vs bedtime 1.1%; number needed to treat = 67) and
  - total CVD events (morning 17.3% vs bedtime 6.3%; number needed to treat = 9).

- Limitations: Poorly described randomization and allocation of patients, lack of blinding, no reporting of adverse events, no correction for multiple analysis, CVD event rates inexplicably higher than expected (very unusual in clinical trials), and outcome research from 1 group only.

- Patients with diabetes2 or chronic kidney disease3 had similar benefits.

Context

- Observational studies4,5 have demonstrated that nighttime ambulatory BP is a better predictor of CVD events than either in-office BP or daytime BP.

- A Cochrane systematic review of 21 RCTs of various BP medications showed that taking BP drugs in the evening (vs morning) resulted in greater 24-hour BP reduction (1 to 2 mm Hg) in most antihypertensive classes.6

- We did not identify any other large trials specifically addressing CVD for BP medications taken at bedtime.

- However, ramipril was given at bedtime in the HOPE trial. The daytime office BP changed little (3/2 mm Hg), so the benefits (3.8% reduction in CVD events in 5 years) were assumed to be due to a unique property of ramipril.8 But nighttime BP was 17/8 mm Hg better.9

Bottom line
Taking 1 or more BP medications at bedtime might help reduce CVD risk, but owing to limitations of the evidence, it is difficult to make strong recommendations.

Implementation

Ambulatory or 24-hour BP monitoring is being encouraged more by guidelines and societies.10,11 Among the benefits of ambulatory BP monitoring is the ability to examine nighttime BP and the normal nocturnal dip in BP.11 When using ambulatory BP, the Joint National Committee 7 (who created the US hypertension guidelines)12 states that hypertension includes nighttime or sleeping BP above 120/75 mm Hg (as well as daytime BP above 135/85 mm Hg). Canadian guidelines13 state that clinicians should consider the magnitude of the nocturnal BP dip when prescribing, as patients “dipping” less than 10% at night are at increased CVD risk. Ambulatory BP can provide useful information in the management of hypertension.

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The opinions expressed in this Tools for Practice article are those of the authors and do not necessarily mirror the perspective and policy of the Alberta College of Family Physicians.

References