

**WHEN SHOULD PATIENTS TAKE THEIR BLOOD PRESSURE TABLETS?**

**KEY RECOMMENDATIONS**

- At night... in suitable patients
- But better to take them every day in the day then occasionally at night...
- So advice should be:

**“The most important thing is to remember to take them every day. If you can take them at bedtime, they probably work better.”<sup>1</sup>**

**HOW DO WE KNOW THAT?**

From the gloriously name “Hygia Chronotherapy Trial” which randomised just shy of 20,000 hypertensive patients to take **all** their antihypertensive medication(s) at night or upon waking<sup>2</sup>. The patients were followed for up to 6 years with at least a yearly 48h ABPM.

**REALLY? AND WHAT WAS THE IMPACT?**

Significant! I won't lie, I've just cut and pasted the summary from the Red Whale pearl on the subject<sup>1</sup>:

*The bedtime dosing group had almost half as many cardiovascular events as the morning dosing group (HR 0.55, CI 0.5–0.61) [...].*

*Those taking their pills in the evening had:*

- *Better BP control.*
- *Lower BP when sleeping but still good control in the daytime.*
- *Fewer of them were ‘non-dippers’: BP should naturally fall at night, and those whose BP doesn't do this are called ‘non-dippers’. Non-dippers have higher CV risk than dippers. At randomisation, 50% of each arm were non-dippers. During treatment, that fell to 37.5% in the bedtime dosing arm but stayed at 50% in the morning dosing arm.*

Do note that hazard ratio reduction in the night time pill-takers is approximately 50% (0.55) but the paper does not allow for the calculation of absolute risk reduction –and that hazard ratios are about “relative rates not relative risks.”<sup>3</sup> Still, this is an impressive and significant finding and I would encourage suggesting night-time pill taking in suitable patients.

**AND WHAT'S A SUITABLE PATIENT?**

Perhaps it's better to think about who might be an unsuitable patient. NICE's Medicines Evidence Commentary on the topic helps us with this<sup>4</sup>. The commentary highlights that: “patient centred adverse events were poorly reported” making hard to truly assess the impact of night-time pill taking on “sleep disturbance due to nocturia, falls and dizzy episodes due to postural hypotension”; it advises caution in:

- older people
- in those at risk of falls

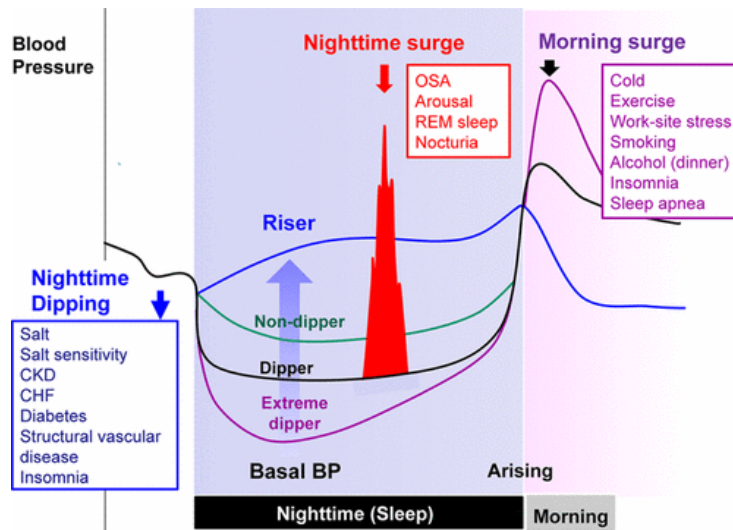
- in those in whom such a change may reduce concordance with medication (for example [...] diuretics)

Remember though that thiazide-like diuretics at lower doses have good antihypertensive effect with limited diuresis so might actually not cause much nocturia. However, it might be advisable to avoid night-time medication in patient with recognised postural hypotension and/or a significant dip in average nocturnal BPs on ABPM.

### FAB, I’M IN. BUT WHAT’S THIS ABOUT DIPPERS AND NON-DIPPERS?

Due to a variety of physiological factors, people’s night-time (well sleep-time) blood pressure is typical 10%-20% lower than their day-time (wake-time) blood pressure, a change known as the nocturnal dip. Individuals’ whose nocturnal dip is <10% as non-dippers, which is bad news because these patient have an increased risk of CVD and CKD<sup>5</sup>. A few unfortunate individuals known as “riser” even have a nocturnal elevation in blood pressure!

Graphically it looks like this:



Source: ref 5.

Giving antihypertensive medication at night-time helps “create” a beneficial night-time dip but should probably be avoided in “extreme dippers”.

### REFERENCES

1. Red Whale. When should I take my blood pressure pills? (2019). Available at: [https://www.gp-update.co.uk/SM4/Mutable/Uploads/pdf\\_file/PEARL-on-Evening-dosing-of-BP-meds\\_1.pdf](https://www.gp-update.co.uk/SM4/Mutable/Uploads/pdf_file/PEARL-on-Evening-dosing-of-BP-meds_1.pdf). (Accessed: 5th February 2020)
2. Hermida, R. C. *et al.* Bedtime hypertension treatment improves cardiovascular risk reduction: the Hygia Chronotherapy Trial. *Eur. Heart J.* (2019). doi:10.1093/eurheartj/ehz754
3. Sutradhar, R. & Austin, P. C. Relative rates not relative risks: addressing a widespread misinterpretation of hazard ratios. *Ann. Epidemiol.* **28**, 54–57 (2018).
4. National Institute for Health and Care Excellence. Medicines evidence commentary: Antihypertensive drug treatment: does bedtime administration improve cardiovascular risk reduction? (2020). Available at: <http://arms.evidence.nhs.uk/resources/hub/1066527/attachment>. (Accessed: 21st February 2020)
5. Kario, K. Nocturnal Hypertension. *Hypertension* **71**, 997–1009 (2018).