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# Unexpected bradycardia after a first dose of doxazosin

James Edward Pigot <sup>1</sup>, Matthew Chak Hin Szeto <sup>2</sup>

<sup>1</sup>General Medicine, Maidstone and Tunbridge Wells NHS Trust, Maidstone, UK

<sup>2</sup>Acute Medicine and Rheumatology, Maidstone and Tunbridge Wells NHS Trust, Maidstone, UK

## Correspondence to

Dr James Edward Pigot, Respiratory, Maidstone and Tunbridge Wells NHS Trust, Maidstone ME16 9Q, UK; james.pigot@nhs.net

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An 89-year-old man with a medical history of hypertension, prostate cancer and postural hypotension presented to the emergency department with worsening headache and fatigue. His general practitioner had recently stopped his daily 10 mg of amlodipine due to symptoms of postural hypotension. On initial assessment, his heart rate was 67 beats per minute, blood pressure 219/104 mm Hg, respiratory rate 16 breaths per minute and oxygen saturations 98% on room air. He did not have any chest pain, signs of heart failure, acute kidney injury or new confusion. An ECG showed first-degree atrioventricular block.

The patient was given 4 mg of modified-release doxazosin for his hypertension. There was no documentation in the emergency department notes about why this had been chosen as the first-line intervention.

Two hours later, he complained to nursing staff that he was about to pass out. Repeat observations showed a blood pressure of 60/30 mm Hg and a heart rate of 46 beats per minute. A second ECG showed a narrow complex escape rhythm (figure 1).

He received 1.5 L of 0.9% sodium chloride solution and 800 µg of atropine to good effect symptomatically. His heart rate and blood pressure improved to 80 beats per minute and 160/90 mm Hg, respectively.

Due to receiving modified-release doxazosin, which has a peak concentration level in the blood 8 hours after being taken as opposed to 2 hours for standard-release doxazosin, he was admitted for observation overnight.

Overnight, he received a further 500 µg of atropine with 500 mL of 0.9% sodium chloride solution after dropping his blood pressure to 65/40 mm Hg with a heart rate of 48 beats per minute.

He was discharged home the following day once he was asymptomatic (figure 2).

The medication doxazosin belongs to the class of medications known as alpha-adrenergic blockers. This group of medications lowers blood pressure by causing vasodilatation of vascular smooth muscle. This is usually accompanied by a reflex tachycardia as the heart compensates to maintain cardiac output.

Alpha-blockers are well documented to exhibit the first-dose phenomenon, whereby there is a sudden and severe fall in blood pressure, especially during postural change.<sup>1</sup>

It is for this reason that alpha-blockers are contraindicated in patients with known postural hypotension.

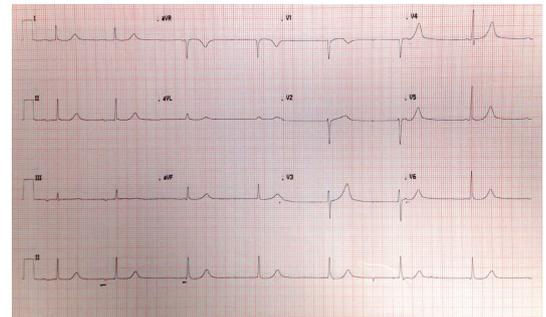


Figure 1 ECG showing narrow complex escape rhythm.

Although X's marked hypotension could be explained, his accompanying bradycardia was unusual.

A literature review showed that alpha-blockers are more commonly associated with a reflex tachycardia in response to hypotension, and it is very unusual for an accompanying bradycardia.<sup>2,3</sup>

One possible explanation for the above finding in this patient could be attributed to the Bezold-Jarisch reflex.<sup>4</sup>

During periods of significant hypotension, this can lead to the ventricles being drastically under filled. This in turn can lead to stimulation of the cardiac vagal afferent fibres of the parasympathetic nervous system and inhibition of the sympathetic nervous system, resulting in further vasodilatation, hypotension and a paradoxical bradycardia, instead of a compensatory tachycardia, which further compounds the symptoms.<sup>4</sup>

This response could be further exaggerated in patients with autonomic failure as manifested through postural hypotension.<sup>5</sup>

The key learning points from this episode were:

1. Recognise the first-dose phenomenon of alpha-blockers and in the need for caution when prescribing for elderly patients.

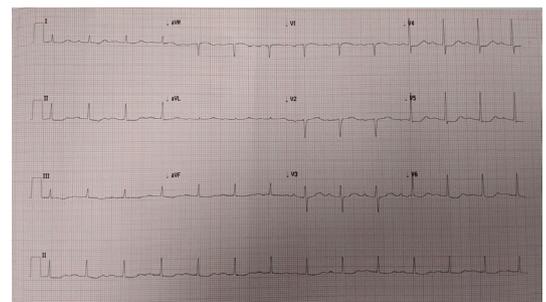


Figure 2 ECG taken once the patient was asymptomatic the following morning.



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2. Apply National Institute for Health and Care Excellence (NICE) guidance to measure standing as well as seated blood pressure in patients over 80 years old. If postural hypotension is detected, to treat based on standing blood pressure.
3. Ensuring that an adequate period of observation is conducted in those who experience an adverse drug reaction due to modified-release tablets.
4. Explain the Bezold-Jarisch reflex and its potentially life-threatening implication.

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### ORCID iDs

James Edward Pigot <http://orcid.org/0000-0001-6207-488X>

Matthew Chak Hin Szeto <http://orcid.org/0000-0002-8881-5196>

### REFERENCES

- 1 Elliott HL, McLean K, Sumner DJ, *et al*. Immediate cardiovascular responses to oral prazosin--effects of concurrent beta-blockers. *Clin Pharmacol Ther* 1981;29:303–9.
- 2 Stoschitzky K, Stoschitzky G, Wonisch M, *et al*. Differential effects of urapidil and doxazosin on heart rate. *Eur J Clin Pharmacol* 2007;63:259–62.
- 3 Frick MH, Halttunen P, Himanen P, *et al*. A long-term double-blind comparison of doxazosin and atenolol in patients with mild to moderate essential hypertension. *Br J Clin Pharmacol* 1986;21 Suppl 1:55S–62.
- 4 Campagna JA, Carter C. Clinical relevance of the Bezold-Jarisch reflex. *Anesthesiology* 2003;98:1250–60.
- 5 Smit AA, Halliwill JR, Low PA, *et al*. Pathophysiological basis of orthostatic hypotension in autonomic failure. *J Physiol* 1999;519 Pt 1:1–10.