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DRUG POINTS

Calculate the QT interval in patients taking drugs for dementia

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A 76 year old woman was referred acutely after two syncopal episodes. She had a history of depression and Alzheimer's disease. No cardiac problems were reported. On admission her blood pressure was 160/112 mm Hg but she had a sinus bradycardia (42 beats/min) and the cardiac monitor showed paroxysmal ventricular tachycardia (torsade de pointes). The resting electrocardiogram showed gross prolongation of the QT segment (corrected QT interval 590-777 ms). She was treated with intravenous magnesium, an infusion of isoprenaline, and then temporary cardiac pacing (100 beats/min) with complete suppression of the dysrhythmia. Initial biochemistry (serum potassium, magnesium, and calcium) gave normal results, and the 12 hour troponin T (0.06 µg/l) was borderline. Her drug history included donepezil 10 mg (for two years), omeprazole 20 mg, escitalopram 10 mg, and propranolol 80 mg (started five days before admission for an essential tremor and anxiety symptoms). Donepezil, escitalopram, and propranolol were discontinued, and the QT interval normalised (corrected QT interval 436 ms). Depressive symptoms were treated with mirtazapine, and the patient required nursing home care. Subsequent review of the notes showed that a normal electrocardiogram had been obtained 18 months previously during investigation of palpitations.

About 3% of prescriptions in the United Kingdom represent non-cardiac drugs with proarrhythmic

potential.¹ The drugs associated with prolonged QT interval include antiarrhythmics, antihistamines, antimicrobials, tricyclic antidepressants, and selective serotonin re-uptake inhibitors.² QT prolongation with acetylcholinesterase inhibitors for dementia (rivastigmine) has been reported.³ Adverse effects reported for donepezil include bradycardia (uncommon) and heart block (rare). The data sheet for donepezil refers to "potential for synergistic activity with ... betablocking agents which have an effect on cardiac conduction." Escitalopram is very rarely associated with prolongation of the QT interval. It inhibits CYP 2D6, the enzyme responsible for the metabolism of donepezil, and escitalopram metabolism is inhibited by omeprazole.

Doctors need to be aware of potential drug interactions with donepezil. Calculating the corrected QT interval may be a life saving arithmetical exercise when elderly patients are treated for dementia.

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