

DIAGNOSTIC TESTS

Home sleep studies

Although I recommend that patients having difficulties with CPAP should see a sleep physician, only a small proportion of them do. Sleep physicians often fine-tune treatment of sleep apnoea in more difficult cases including complex sleep apnoea. Their global assessment adds significant value to the general management of these patients, particularly in finding the cause and diagnosing and managing other comorbidities. The sleep physician's broad training, not only in sleep disorders but in general medicine and the psychiatric aspects of sleep, provides an important oversight. All patients with sleep apnoea adversely affecting their driving or with a potentially dangerous occupation should be seen by a sleep physician. To do otherwise could have legal ramifications.

Other requirements

Other secondary elements are also needed, for example dietitians and dentists for mandibular splints.

Patients may also need a support person to assist them with treatment.

Conclusion

Home sleep studies are a viable alternative to laboratory sleep studies and are here to stay. I predict they will eventually be the main screening tool for sleep apnoea in the community complementing the important role of the sleep laboratory polysomnogram. For home sleep studies to be effective, several elements are required, including a patient who can use the equipment. Patients with more complicated sleep apnoea, multiple comorbidities and serious other sleep disorders should see a sleep physician. <

Professor Allen does reporting of home sleep studies for Healthy Sleep Solutions, but has no financial interest in the company.



SELF-TEST QUESTIONS

True or false?

11. The devices for home sleep studies have not been validated against sleep laboratory polysomnograms.
12. Opioids can cause central sleep apnoea.

Answers on page 71

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Medicinal mishap

Dabigatran – a new safe drug to replace an old poison?

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Case

An 89-year-old woman was admitted to hospital with melaena. She had a history of atrial fibrillation, type 2 diabetes complicated by hypertension, ischaemic heart disease and nephropathy (creatinine clearance of 29 mL/min, using the Cockcroft-Gault equation).

The patient was taking several drugs for her conditions. These included warfarin which she had taken for 12 years, without any adverse events. Three weeks before admission she was switched to dabigatran, 110 mg twice a day, for prevention of stroke in association with atrial fibrillation.

On admission, her serum creatinine was elevated (172 micromol/L with an estimated creatinine

clearance of 18 mL/min) and her haemoglobin was 61 g/L. Despite warfarin therapy ceasing three weeks earlier, the INR was 2.5 and the activated partial thromboplastin time (aPTT) was 84 seconds (normal range 25–35 seconds).

There is no specific antidote for dabigatran. She was given fresh frozen plasma, vitamin K and six units of packed red cells.¹ Upper gastrointestinal endoscopy found no pathology and the bleeding settled spontaneously.

The patient required prolonged rehabilitation after the haemorrhage. She was not discharged home until two months later.

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Comment

Dabigatran, a direct thrombin inhibitor, is approved in Australia for stroke prevention in patients with non-valvular atrial fibrillation and at least one other risk factor for stroke. Since 2009, the Therapeutic Goods Administration has received 297 reports of adverse drug events associated with dabigatran² and the European Medicines Agency recently reported 256 fatal bleeding events worldwide.³ The US Food and Drug Administration is reviewing postmarketing reports of major bleeds.⁴ Other organisations have released formal recommendations for the use of dabigatran.⁵

Compared to warfarin, the risk of major bleeding in a large clinical trial of dabigatran for stroke prevention in atrial fibrillation was equivalent (at 150 mg twice daily) or less (at 110 mg twice daily).⁶ Important exclusion criteria in this trial included 'a condition that increased the risk of haemorrhage', active liver disease and a creatinine clearance less than 30 mL/min. A *post hoc* analysis of this trial suggested the risk of bleeding with dabigatran may be greater in patients over 75 years of age.⁷

Currently, no assay of dabigatran's effect on coagulation is available and monitoring is not recommended. Interpretation of the INR is problematic with dabigatran, as results are variable and not predictable. An aPTT more than twice the reference range is suggestive of over-anticoagulation.⁸ Of interest, when enoxaparin was first marketed no

monitoring was deemed necessary, however, factor Xa monitoring is now increasingly used.⁹

Dabigatran possesses clinically important pharmacokinetic properties.^{10,11} It is predominantly renally cleared with a half-life of 12–14 hours in patients with normal renal function. The half-life is extended as renal function declines. Current recommendations suggest withholding therapy when creatinine clearance is less than 30 mL/min. Although not relevant to this case, dabigatran is a P-glycoprotein substrate and therefore has the potential to interact with P-glycoprotein inhibitors such as amiodarone and verapamil.

Conclusion

This case highlights the dangers of switching patients stabilised on treatment to newer therapies, especially if there are few data on safety and effectiveness in a particular group of patients. The risk of a drug in 'real world' use is often underestimated in clinical trials, as they are often designed to demonstrate efficacy rather than test safety. The trials generally study a highly selected patient group – with a long list of exclusions designed to mitigate risk – and the patients are intensively followed in a manner not typically feasible in routine practice. The true risk of a drug is generally unclear until there is considerable postmarketing experience.

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FURTHER READING

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