

# CASE REPORT

## PAROXETINE AND DIGITALIS

In this age of multiple medications, particularly in the elderly, there is an increasing likelihood of drug interactions. This recent case study from the *Lancet* is a case in point.

A 68-year-old woman, with no history of major psychiatric illness, presented to a neuropsychiatry department in February 2005 in Japan with a major depressive disorder, with moderate sadness, inner tension, difficulty in concentrating, severe sleep impairment and appetite loss. She also had atrial fibrillation (AF), which had been treated with 0.25 mg digoxin daily and 1 mg warfarin daily for 2 years. Blood tests were essentially normal.

She was admitted to the psychiatric ward and on the 3rd day she was started on paroxetine 20 mg/d for depression. By day 5 she had developed nausea, dizziness and vomiting. By day 7 she developed delirium with visual hallucinations and disorientation. On day 10 she was unable to walk and on day 11 her doctors suspected digitalis intoxication. Her serum digoxin was 5.2 ng/ml (normal 0.5 - 2.0 ng/ml) and her ECG showed many ventricular premature contractions and complete A-V block. There were no electrolyte disturbances. All medications were discontinued from day 12. She had bradycardia as a rebound effect of digoxin discontinuation from day 13 to day 15 and her AF recurred.

A few days later she was again started on digoxin and warfarin. The delirium with disorientation started to recover and was gone completely by day 28. However, she remained moderately depressed. She became bedridden during these events and developed aspiration pneumonia because she

had difficulty swallowing. She was started on antibiotics, but her physical condition did not change. She was moved to a medical ward in May 2005, but died of her pneumonia in June 2005.

The authors point out that negative affective states such as depression are associated with premature mortality and an increased risk of coronary heart disease, type 2 diabetes and disability. Patients who have chronic medical illness and comorbid depression generally respond well to antidepressants. Interestingly, more anxious patients are at greater risk of developing AF than the normal population, which means that there is always the danger that digoxin will be prescribed concomitantly with antidepressants. Before she was started on paroxetine, this patient had no signs of digitalis intoxication, suggesting that it was the co-prescription of paroxetine that caused this. There are several laboratory studies that show that paroxetine decreases CYP2D6 activity, resulting in drug interactions. One study showed potent inhibition of P-glycoprotein with paroxetine. The high concentrations of digoxin when this patient was on paroxetine may well have resulted from P-glycoprotein inhibition in the kidney.

The signs of nausea, vomiting and dizziness are not only signs of digoxin toxicity, but of some side-effects of paroxetine. The authors suggest that in a patient who is on digoxin and an antidepressant, digoxin levels must be measured regularly to monitor for toxicity.

Yasui-Furukori N, Kaneko S. *Lancet* 2006; **367**: 788.

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## SINGLE SUTURE

### CORTISOL AND PHOBIAS

People who experience social phobia or spider phobia respond well to cortisol treatment. Phobias trigger the release of cortisol in the brain, which probably helps by impairing memory retrieval during the attack. A double-blind placebo-controlled study of phobic people carried out in Switzerland showed that oral cortisol given an hour before being exposed to a fear stimulus resulted in the experience of less anxiety. The group examined 40 subjects with social phobia and 20 subjects with spider phobia. In the social phobia study subjects were injected with cortisol 1 hour before encountering a social stressor. In the spider study, subjects took oral cortisol 1 hour before being shown a photograph of a spider. The loss of fear lasted for 2 days after the cortisol was given. Control subjects who reported the least anxiety released the most cortisol, which supports a feedback mechanism.

Soravia Leila M, et al. *Proc Natl Acad Sciences* 2006; **103**: 5585-5590.