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Junior staff

SIR,—I read Professor C Wastell's letter with admiration for his purpose and sadness at the stereotyped reality he rightly denotes.[1] Recently, in the course of a clinic, after I had politely introduced myself a patient strongly objected that I was not the doctor he was there to see. He indicated the small piece of paper given to him at the clinic reception, which clearly specified "Dr Reg."

This anonymity exemplifies the lack of commitment to non-consultant doctors that is evident through all grades. As a way of working it not only devalues "junior doctors" but, worse, fails best to serve patients, who are often left confused about whom they have been sent to see and deceived at not being seen by a "senior doctor." There should be a list of doctors working in each department on display for patients to see, and the doors of consulting rooms should be clearly labelled with each doctor's name and seniority. The junior-senior divide needs to be carefully scrutinised. After all, whose side are we on?

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1 Wastell C. Junior staff. *BMJ* 1991;**302**:1278. (25 May.)

SIR,—I heartily agree with Professor C Wastell's condemnation of the term "junior doctor."[1] Many years ago, at the height of the senior registrar bulge, an elderly medical senior registrar at Westminster Hospital told me that he hoped to achieve fame by being the first junior doctor to have a prostatectomy.

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1 Wastell C. Junior staff. *BMJ* 1991;**302**:1278. (25 May.)

Drug Points

Torsades de pointes complicating treatment with terfenadine

Drs T J MACCONNELL and A J STANNERS (Bristol Royal Infirmary, Bristol BS2 8HW) write: A previously healthy 45 year old woman with recurrent urticaria and no relevant family history was admitted to hospital after three syncopal episodes at home. The first, three days before admission, had been dismissed as a faint. On the day of admission she had two further collapses, her husband having performed cardiac massage on the second occasion.

On her arrival in hospital a monitored episode of ventricular tachycardia was observed. Her terfenadine was stopped and a lignocaine infusion started. Later on the day of admission she had a further episode of ventricular tachycardia. Review of the electrocardiogram taken on admission, before she received lignocaine, showed a prolonged QT interval of 600 ms with a QTc of 0·56 s (normal 0·35-0·43 s). Torsades de pointes was diagnosed; the lignocaine was discontinued as it may lengthen a QT interval.

For six weeks before her admission the patient's only drug had been terfenadine. The initial dose was 60 mg twice a day, doubling after two weeks and increasing to 120 mg three times a day two weeks before admission. There was no history of alcohol abuse and a clinical examination was unremarkable. Measurement of serum electrolytes showed her concentrations of potassium to be 4·1 mmol, corrected calcium 2·26 mmol, and magnesium 0·7 mmol. Urea concentration and results of liver function tests were also normal. The initial plasma terfenadine concentration, measured by high performance liquid chromatography 12 hours after the last dose, was 471 ng/ml of metabolite 1 only. Interestingly, she had taken 360 mg of terfenadine daily eight years previously without ill effect. After the lignocaine was stopped she had two further episodes of torsades de pointes associated with syncope. A temporary ventricular pacing wire was inserted and the rate set at 90 beats/min, and there were no further arrhythmias. After 24 hours the QT interval had returned to normal (400 ms), with a QTc of 0·41 s. A 24 hour tape showed only three premature ventricular contractions, so the pacing wire was removed. An echocardiogram was normal.

Terfenadine is a specific histamine (H_1) receptor antagonist. It is used by dermatologists and general practitioners at doses up to 360 mg a day, although the maximum dose recommended by the data sheet is 120 mg a day. Prolongation of the QT interval has previously been observed in adults taking 120-240 mg of terfenadine a day. Ventricular arrhythmias have also been noted but only in terfenadine overdose or when combined with hepatic enzyme inhibitors such as ketoconazole (H C Masheter, Merrell Dow, personal communication). A previous case report postulated ventricular arrhythmia as a cause of convulsion in a 21 year old woman who had self poisoned on terfenadine.[2] She was initially noted to have a prolonged QT interval.

Astemizole, which is also a long acting H_1 antihistamine, has also been reported as causing torsade de pointes when taken in overdose.[3,4] As there are histamine receptors in the heart, H_1 antihistamine agents may have a direct cardiotoxic effect at higher doses.

Analysis of terfenadine concentrations in our patient showed higher concentrations of metabolites than might be expected at a dose of 360 mg daily. The absence of unmetabolised terfenadine, concomitant drug treatment, and normal results of a liver function test would suggest, however, that her excretion of terfenadine was within the normal range.

Our report confirms that terfenadine used at doses of 360 mg a day can cause prolongation of the QT interval. The QT interval returns to normal once the drug has been stopped. The prolonged QT interval may result in torsades de pointes causing syncope. To the best of our knowledge this is the first reported case of torsades de pointes induced by an enhanced therapeutic dose of terfenadine in isolation. We recommend that the data sheet dose should not be exceeded without careful consideration, especially as there is no good evidence of increased efficacy of higher doses.[5] Overdrive ventricular pacing proved effective in treating torsades de pointes induced by terfenadine.

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4 Simons FER, Kesselman MS, Giddins NG, Pelech AN, Simons KJ. Astemizole induced torsade de pointes. *Lancet* 1988;ii:624.
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Torsades de pointes complicating treatment with terodiline

Drs ANDREW A MCLEOD, SIMON THOROGOOD, and SUSAN BARNETT (Cardiac Department, Poole General Hospital, Dorset BH15 2JB) write: Terodiline hydrochloride has recently been introduced to treat urinary incontinence and is most effective in detrusor muscle instability.[1] We report a case of serious ventricular arrhythmias due to treatment with terodiline.

An 83 year old woman was admitted to hospital complaining of up to two years' dizziness and occasional loss of consciousness. She gave a history of a vulval operation and subsequent urinary incontinence, which had been treated with an indwelling catheter and terodiline for two years. Drug treatment on admission to hospital was terodiline 37·5 mg daily, digoxin 0·125 mg daily, frusemide 20 mg daily, ispaghula husk two sachets daily, and lactulose 10 ml twice daily. No abnormal clinical signs were found apart from a bigeminal pulse. An electrocardiogram showed a prolonged QT interval of approximately 0·7 s with a ventricular rate of 63 beats/minute (QTc interval 0·72 s). First degree atrioventricular block was present (PR interval 0·24 s). A 24 hour electrocardiogram showed multiple episodes of ventricular tachycardia of torsades de pointes morphology. Serum magnesium concentration was 0·73 mmol/l (normal range 0·7-1·1), calcium 2·19 mmol/l (2·25-2·62), and albumin 41 g/l (35-48). Her digoxin concentration was 0·4 nmol/l (therapeutic range 0·9-1·8) and her potassium concentration 4·1 mmol/l (normal 3·5-5·0). All drug treatment was stopped, and she was given 5 g magnesium as magnesium sulphate by intravenous infusion. Two days later her QT interval was 0·5 s with a heart rate of 54 beats/minute (QTc interval 0·47 s). Oral atenolol 50 mg daily was started. After 10 days in hospital she had had no further attacks and was discharged. The QT interval was 0·54 s with a heart rate of 48 beats/minute (QTc interval 0·48 s).

A week later she complained of recurrent dizziness. She had restarted terodiline 37·5 mg daily. Her other treatment consisted of bisacodyl, lactulose, and atenolol. She was admitted for further investigation. The PR interval was 0·26 s and the QT interval 0·7 s with a heart rate of 49 beats/minute (QTc interval 0·63 s). Serum calcium, magnesium, and potassium concentrations were normal. The atenolol was stopped. A dual chamber pacemaker was implanted and left in fully automatic (DDD) mode. No further attacks of loss of consciousness or torsades de pointes occurred. After seeing a review indicating terodiline's similarity to prenylamine,[2] a drug known to cause torsades de pointes,[3] we changed her antispasmodic treatment to flavoxate. Two weeks later the QT interval was 0·38 s after spontaneous beats and 0·40 s after paced beats (QTc interval 0·46 s). Her bradycardia had also resolved.

The onset of symptoms in our patient was closely related to the start of treatment with terodiline, and the electrocardiographic abnormalities resolved when terodiline was stopped. Kabi Pharmacia has data on three episodes of torsades de pointes that occurred during clinical studies with terodiline.

The datasheet for terodiline indicates the need to reduce doses in the elderly. The mean elimination half life more than doubles in the elderly from 60 to 130 hours.[2] This implies that steady state levels may not be reached until a month after the start of treatment. Side effects may therefore not be immediately apparent. Terodiline is effective in urinary incontinence because of its dual action as an anticholinergic agent and calcium antagonist. Bradycardia should alert clinicians to the predominance of its calcium antagonist effect.

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