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It is a pleasure to have contributed, albeit inadvertently, to Professor Cheng's continuing medical education.

Editor
Postgraduate Medical Journal

Ketanserin overdose: a case report

Sir,
Ketanserin (3-{2-[4-(4-fluorobenzoyl)-1-piperidinyl]-ethyl}-2,4-[1H,3H]-quinazolinedione) is a serotonin antagonist available in Great Britain on a named patient basis for the treatment of Raynaud's disease, peripheral vascular disease and hypertension. The recommended daily dose is 20–40 mg twice daily. Known side effects include sedation, dizziness, headache, dry mouth and nausea¹ as well as prolongation of the QTc time and ventricular arrhythmias.^{2,3} There are no published data on its effects in overdose in man. We report a case of self-poisoning with ketanserin and discuss its clinical manifestations.

A 16 year old schoolgirl with a history of Raynaud's disease presented 90 minutes after taking 160 20 mg tablets of ketanserin. She was somnolent and uncooperative but easily rousable and fully orientated. Her blood pressure was 100/60 mmHg, pulse 60/min and regular, temperature and respiration were normal. She was flushed and well perfused; hands, feet and ears, usually cold and cyanosed, were pink and warm. Her fingers were slightly swollen, there was conjunctival injection and the pupils were constricted but briskly reactive. No other abnormalities were found on physical examination. Potassium was low at 3.3 mmol/l, sodium, urea, creatinine and full blood count were normal. The electrocardiogram showed a prolongation of the QTc time to 0.53 ms. Gastric lavage was performed within 2 hours of ingestion. Treatment was supportive with elevation of legs and intravenous normal saline. Nausea, headaches or blurred vision were not observed or reported. Her blood pressure remained low at 90/50 mmHg during the first 12 hours. There was a relative bradycardia of 70/min and she felt faint on rising. By the next morning, 18 hours after admission, her blood pressure was 120/80 mmHg with normal postural response and a heart rate of 90/min. She remained well after discontinuation of intravenous fluids. Twenty-four hours after ingestion of the tablets she was still flushed, but her hands and feet were cool as usual.

Ketanserin levels were 2873 ng/ml 3 hours and 151 ng/ml 18 hours after ingestion. Ketanserinol concentration was 1155 ng/ml at 3 hours and 1117 ng/ml at 18 hours. Liver functions and repeat urea, electrolytes and creatinine were normal.

Ketanserin is well absorbed, achieving peak levels 30–120 min after oral administration but bioavailability is poor (50%) because of extensive first pass hepatic metabolism.⁴ The mean terminal half life following single oral doses is 10–18 hours but increases to 29 hours after

multiple doses because of reoxidation of its metabolite ketanserinol to ketanserin.¹ Steady state plasma levels during chronic oral treatment with 40 mg twice daily are 100–140 ng/ml.⁵ The patient reported here took 3200 mg (59 mg/kg) ketanserin. Her levels fell from 2873 ng/ml at 2 hours to 151 ng/ml 18 hours after ingestion. This decline is much faster than expected from the elimination half-life. It is notable that the level of ketanserinol remained high. A failure of the reoxidation mechanism in the presence of very high ketanserin levels would explain the observed rapid clearance of ketanserin.

In conclusion, on the basis of this experience, ketanserin appears to be relatively safe in overdose in humans. The main problems were hypotension and relative bradycardia. We did not observe ventricular arrhythmias but the prolonged QTc time clearly put her at risk of developing torsades de pointe. Hypothermia might also be predicted, unless ambient temperatures are warm. However, more serious effects are clearly possible in elderly or hypertensive patients, and more experience is required to exclude significant toxicity.

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Hepatitis B virus (HBV) and human immunodeficiency virus (HIV) infection in Spanish leprosy patients

Sir,
In 1967, Blumberg first reported an association between leprosy and the so-called Australian antigen. Moreover, he later reported that the prevalence of chronic HBV infection differed between lepromatous and tuberculoid forms of leprosy.¹ Some authors have confirmed a high prevalence of chronic HBV infection in leprosy patients,^{2,3} while others have denied such an association.⁴ Likewise, more recently, a possible link between leprosy and HIV infection has also been reported, namely, a high prevalence of HIV infection among leprosy patients⁵ as well as a worse course of leprosy when HIV infection is associated.⁶ Since most of these studies have been per-

formed in areas where the endemicity of the reported infections is very high, we have conducted a study to evaluate the prevalence of HBV and HIV infection in leprosy patients in our country, which has a relatively low endemicity of HBV, HIV and leprosy.

Seventy leprosy patients (52 male; mean age 59.8 years, range 37–86 years; 52 lepromatous, 14 tuberculoid, 5 borderline) were randomly selected from the Centres of Treatment and Control of Leprosy of Jaen and Trillo, Spain. None of the patients had any other risk factor for HBV or HIV infection. Sera from all patients were tested for HIV antibodies (ELISA) and HBV markers (HBsAg, anti-HBs and anti-HBc – Ausria, Ausab, Corab; Abbot Labs, North Chicago, Ill, USA). Positivity for HIV antibodies or HBsAg was not found in any case. However, 32 patients (45.7%) had serological evidence of past HBV infection (positivity of anti-HBc with or without anti-HBs). When patients with evidence of past HBV infection were compared with those without it, no differences were found regarding sex, site of origin (rural or urban) nor clinical type of leprosy. However, cases with past HBV infection tended to be older than patients with negative markers (63.1 ± 7.0 vs 57.1 ± 10.9 years, $P < 0.01$, Student's *t*-test); and a history of institutionalization in leprosy centres for more than a year was more frequent among HBV-marker-positive patients (68.7% vs 28.9%, $P < 0.001$, Chi-square test). Furthermore, the time since the initial diagnosis of leprosy was longer in subjects with serological evidence of past HBV infection than in patients without it (35.6 ± 13.0 vs 21.6 ± 12.1 years, $P < 0.001$, Student's *t*-test). These three factors, namely age, institutionalization and time of evolution of leprosy, were independently correlated with HBV-marker-positivity in a multivariate analysis (stepwise logistic regression).

In spite of lacking a control group, these results suggest that there is a high prevalence of markers of past HBV infection in leprosy patients (45.7%), since the same figure in the Spanish general population is 18.2%.⁷ Similar results have been observed in Greece.⁸ This high prevalence may be due to leprosy itself, since it is well known that a history of skin disease is a risk factor for HBV infection.⁹ Besides, other associated factors, such as institutionalization, may be present. Interestingly, a similar high frequency of past HBV infection has been reported in Spanish mentally retarded institutionalized patients.¹⁰ Increasing prevalence of past HBV infection with age has been reported before.¹¹ However, leprosy patients seem to have normal immunological response to HBV since no case of chronic HBV infection was found in our study despite the high frequency of past infection. Moreover, in our experience, there is no relationship between leprosy and HIV infection other than the common and unfortunate comparison of AIDS as 'leprosy of the twentieth century'.

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Benign hepatic tumours of unusual size in two Samoan siblings

Sir,

Most benign hepatic tumours are less than 10 cm in diameter and rarely give rise to symptomatic abdominal masses.^{1–3} Two cases of large benign hepatic tumours in adult Samoan siblings are described. The first case was a hepatic cavernous haemangioma while the second one was a liver cell adenoma.

Case 1 – A 43 year old Samoan woman was admitted to the Western Samoa National Hospital, with a mass in the right upper quadrant of the abdomen for a year. She had previously had 10 deliveries and one miscarriage. Macroscopically the resection specimen was a solid dark brown tumour measuring $15 \times 13 \times 5$ cm adjacent to the left hepatic lobe. The tumour was demarcated from the surrounding liver parenchyma but was not encapsulated. Microscopically it was of 'cavernous haemangioma' of the liver. There was no sign of recurrence 2 years later.

Case 2 – A 35 year old Samoan woman was hospitalized one year after her sister (Case 1) with right upper quadrant pain and nausea. She was multiparous with 5 deliveries. She had a history of long-acting progesterone injections for the purpose of birth control, irregularly for a few years. Examination showed a mass in the right upper quadrant of the abdomen. Explorative laparotomy revealed a tumour in the right lobe of the liver, and