

Vitamin D deficiency is common in frail institutionalised older people in northern Sydney

Philip N Sambrook,* Ian D Cameron,[†]
Robert G Cumming,[‡] Stephen R Lord,[§]
Jennifer M Schwarz,[¶] Angelika Trube,^{**}
Lynette M March^{††}

*Professor of Rheumatology, †Associate Professor, Rehabilitation Studies Unit, ‡Associate Professor, Department of Public Health and Community Medicine, ¶FREE Study Coordinator, Institute of Bone and Joint Research, **Senior Technical Officer, Department of Veterinary Sciences, University of Sydney, Sydney, NSW

<sambrook@med.usyd.edu.au>; §Associate Professor, Prince of Wales Medical Research Institute, Sydney, NSW; ††Associate Professor, Public Health Unit, and Department of Rheumatology, Royal North Shore Hospital, Sydney, NSW.

TO THE EDITOR: Although treatment with vitamin D has been shown to reduce hip fracture risk in elderly institutionalised people,¹ there has been a perception that vitamin D deficiency is generally uncommon in countries with high sunlight exposure such as Australia.

We studied the prevalence of vitamin D deficiency in older people in residential aged-care facilities (hostels and nursing homes) in the northern Sydney area as part of the FREE study (Fracture Risk Epidemiology in the Elderly), a prospective study of fracture incidence in more than 2000 participants. Here, we report baseline serum 25(OH) vitamin D concentrations in the first 386 participants, determined in partially purified lipid extracts using a competitive protein binding assay.²

The sample comprised 252 women and 134 men (mean \pm SE age, 86.7 \pm 0.6 v 81.2 \pm 0.7 years, respectively; $P < 0.001$). The mean serum 25(OH)D level was 17 nmol/L (SD, 12) and median serum 25(OH)D level was 15 nmol/L (interquartile range, 9 to 22). Vitamin D deficiency (defined as a serum 25(OH)D concentration < 28 nmol/L) was present in 86% of women and 68% of men. There was no significant difference in serum vitamin D

levels between women in nursing homes versus women in hostels, nor between men in nursing homes versus those in hostels. Although serum vitamin D levels were low throughout the year, a small rise was observed in summer ($P < 0.01$). Length of stay in the residential facility was not a predictor of serum vitamin D level. Mean parathyroid hormone levels were 93 pg/mL (normal range, 12–72 pg/mL) and rose when vitamin D levels dropped below 21 nmol/L, indicating secondary hyperparathyroidism.

A number of previous studies have suggested a high prevalence of vitamin D deficiency in older institutionalised Australians in southern States,^{2–4} but we are unaware of any published studies in Sydney (latitude 33°S). However, as the prevalence of vitamin D deficiency in older people living in the community in Geelong is low,⁵ our study suggests that factors like confinement indoors is more important than latitude.

Given the relationship between vitamin D status and fracture, with more than 72 500 nursing home residents and 60 200 hostel residents in Australia in 1997, our findings indicate that vitamin D deficiency represents a significant public health problem in elderly institutionalised Australians regardless of geographical location. Importantly, this problem could be solved relatively simply by measures such as a short period of daily sunlight exposure or giving moderate doses of vitamin D annually to nursing home and hostel residents.

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Perhexiline toxicity related to citalopram use

Karin Nyfort-Hansen

Clinical Pharmacist, Pharmacy Department, Repatriation General Hospital, Daw Park, SA 5041
karin.nyfort-hansen@rgh.sa.gov.au

TO THE EDITOR: Selective serotonin reuptake inhibitors (SSRIs) are commonly prescribed for patients with cardiovascular disease, including those taking perhexiline for severe ischaemic heart disease. Elevated serum perhexiline concentrations have been observed during therapy with the SSRIs fluoxetine and paroxetine, which are known to be strong inhibitors of cytochrome P450 2D6, the enzyme system responsible for the hepatic metabolism of perhexiline.¹ The Adverse Drug Reactions Advisory Committee has received five reports of a possible interaction between perhexiline and SSRIs, but none of these involved the SSRIs citalopram or fluvoxamine, which are generally considered to be weak inhibitors of cytochrome P450 2D6. I describe here a case of perhexiline toxicity that occurred within 10 days of starting citalopram therapy.

An 82-year-old man was admitted to hospital for drainage of a femoral abscess. His medical history included bilateral hip replacements, ischaemic heart disease, hypertension, renal artery stenosis, renal calculi, gout, gastroesophageal reflux disease and prostate cancer. His medications included (daily) aspirin 100 mg, isosorbide mononitrate 120 mg, pravastatin 40 mg, allopurinol 300 mg, celecoxib 200 mg, lorazepam 2 mg, nitrazepam 10 mg; (twice daily) perhexiline 100 mg; and paracetamol and tramadol as needed.

On Day 51 after admission the patient underwent first-stage revision of an infected hip implant under general anaesthesia, and on Day 60 citalopram was commenced (10 mg daily for four days, then 20 mg daily). On Day 70, the patient complained of diarrhoea, nausea and dizziness. Citalopram was discontinued but the nausea was slow to settle. After a perhexiline assay on Day 75 revealed a high serum concentration (see Box), the perhexiline dose was reduced to 100 mg daily and the patient's nausea settled.

Previous perhexiline concentrations on a dose of 100 mg twice daily had ranged from 0.29 to 0.34 mg/L over a two-year period. Tests of renal and hepatic function were normal throughout the patient's hospital stay. While in hospital, the patient was given

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Serum concentrations (mg/L) of perhexiline and perhexiline metabolite

	Day 48	Day 75	Day 95
Perhexiline (therapeutic range, 0.15–0.60 mg/L)	0.37	0.82	0.27
Perhexiline metabolite	3.53	0.37	2.22
Ratio of perhexiline to perhexiline metabolite	0.10	2.22	0.12

celecoxib (a cytochrome P450 2D6 inhibitor) at a constant dose between Days 1 and 95, and meropenem (not a documented cytochrome P450 2D6 inhibitor) between Days 51 and 95. These patterns of administration suggest that neither of these drugs had a significant effect on perhexiline concentration. On the other hand, the laboratory evidence of a marked inhibition of perhexiline metabolism during treatment with citalopram suggests that caution is required when prescribing citalopram (or any other SSRI) for a patient taking perhexiline.²

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Cholestasis associated with the use of pravastatin sodium

Robert G Batey,* Michelle Harvey†

*Director, †Gastroenterology Pharmacist, Gastroenterology Department, John Hunter Hospital, Locked Bag 1, Hunter Region Mail Centre, NSW 2310. rbatey@hunter.health.nsw.gov.au

TO THE EDITOR: Hydroxymethylglutaryl coenzyme-A (HMG Co-A) reductase inhibitors (or statins) are widely prescribed, and any class-specific side effect has the potential to affect many thousands of patients. The statin drugs are well recognised as a cause of mild and usually transient hepatitis.¹⁻³ Cholestatic liver injury has been reported with simvastatin⁴

and atorvastatin,⁵ but pravastatin has only been implicated as a cause in one report.⁶

We report a 64-year-old woman who was twice treated with pravastatin sodium and who, on both occasions, demonstrated cholestasis, which, at its peak, was associated with minimal hepatocellular injury.

Our patient presented to the liver clinic of the John Hunter Hospital in 2001 for investigation of abnormal liver function test results. She was taking diltiazem, aspirin, irbesartan plus hydrochlorothiazide, and pravastatin as therapy for hypertension and hyperlipidaemia. She consumed less than 10 g alcohol per week. Liver function tests showed a predominant elevation of alkaline phosphatase and γ -glutamyltransferase, with a minimal rise in alanine and aspartate aminotransferases, a picture consistent with cholestasis rather than hepatocellular disease (see Box). She had started taking pravastatin in the three months preceding her referral, and commented that when she was taking the drug in the previous year she had also had abnormal liver test results. Her liver function test results in 1998 were normal.

Two ultrasound examinations of the liver, performed after five months of taking pravastatin in the first period and two months after beginning her second period of therapy, showed normal liver size and echogenicity, and no sign of obstructive liver disease. Tissue antibodies, viral studies for hepatitis viruses, α_1 -antitrypsin and iron studies were all either normal or negative. Renal function was normal throughout. She had no biochemical evidence of impaired hepatocellular function, and for this reason liver biopsy and endoscopic retrograde cholangiopancreatography were not undertaken.

In view of the association the patient made between previously ceasing therapy with the drug (because she felt unwell) and improving liver function, therapy (which was recommenced by the cardiologist for hyperlipidaemia) was again suspended and within two months liver test results improved markedly.

We believe that in the absence of other markers of liver disease and with improve-

ment of liver function on both occasions that therapy with pravastatin was suspended, it is likely that this patient has twice developed a cholestatic response to pravastatin.

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Paracetamol recall: a natural experiment influencing analgesic poisoning

David Gunnell

Senior Lecturer in Public Health Medicine and Epidemiology, Department of Social Medicine, Canyng Hall, Whiteladies Road, Bristol BS8 2PR, UK d.j.gunnell@bristol.ac.uk

TO THE EDITOR: A potentially important, if somewhat crude, means of suicide prevention involves restricting the availability of commonly used methods. In 1967, for example, restrictions on barbiturate prescribing in Australia led to declines in its use for suicide and in overall suicides.¹ A crucial concern with this approach is that distressed individuals might use alternative, more lethal, methods. In Britain, there is just such a concern in relation to recent legislation restricting the availability of paracetamol.¹

Analysis of the natural experiment investigated by Balit and colleagues² does not, however, provide useful insights into the impact of paracetamol sales restrictions. Their most consistent finding was that, despite restricted availability for the period studied, paracetamol accounted for about

Patient's liver function test results during and after two periods of pravastatin therapy

Test	Normal range	Initial period					Second period*			
		Pravastatin			No pravastatin		Pravastatin		No pravastatin	
		Month 0	Month 4	Month 5	Month 6	Month 10	Month 0	Month 1	Month 2	Month 3
Bilirubin (μ mol/L)	< 20	7	13	5	7	10	11	11	7	9
Alkaline phosphatase (U/L)	< 115	230	362	220	213	242	291	347	186	171
γ -Glutamyltransferase (U/L)	< 25	259	625	353	231	195	297	463	167	126
Alanine aminotransferase (U/L)	< 40	26	85	31	25	28	25	49	16	18

*Commenced seven months after initial episode. Patient's results were normal two years before the initial period.