LETTERS TO THE EDITOR

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Knowledge is the best medicine

Sir – The Department of Health, in association with the Irish Pharmaceutical Healthcare Association (IPHA) have recently launched a health promotion campaign entitled Knowledge is the best Medicine. Their aim is to help Irish patients to become responsible consumers of prescription medicines. They have produced a booklet that is informative and easy to read. It encourages patients to ask about their prescribed medicines, and any side effects that they might experience, as well as wisely advising them that they may not receive a prescription at every visit to their doctor.

Non-compliance with prescribed medicines remains a problem in general medicine, and particularly so in the field of psychiatry.2 This campaign is therefore to be welcomed by psychiatrists. The importance of doctor-patient communication in ensuring optimal compliance is not a new concept however, and has been well documented previously.3 In order to ensure that we can reply to the questions patients will now ask, having been encouraged by this campaign, we will need to keep abreast of current developments in psychopharmacology and pharmacokinetics. Many routinely used antidepressants and antipsychotics are metabolised by cytochrome p450 enzymes in the liver. Inhibition of these enzymes by concomitant use of other psychotropics or prescribed medicines can lead to elevated serum levels of medication that can cause toxicity. Many of these interactions are now documented, furthermore it is now possible to predict cytochrome-mediated adverse drug reactions using in vitro techniques, thus many potentially adverse interactions may now be avoided.4 If we arm ourselves with such current 'knowledge' we will be more likely to prescribe safely to this new population of informed responsible consumers!

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Late-onset liver abnormalities associated with long-term lofepramine treatment

Sir - Lofepramine is an effective antidepressant with fewer side-effects than standard tricyclic antidepressants.¹ By the end of 1987, however, the Committee on Safety of Medicines had received 57 reports of liver function abnormalities associated with lofepramine.² All cases reported abnormal liver function tests during the first eight weeks of treatment which resolved on discontinuation of lofepramine. A recent

report further suggests that most liver function abnormalities on lofepramine are transient and will normalise within the first 12 weeks of treatment.³ Long-term effects of lofepramine on liver function are unknown. We report two cases of asymptomatic late-onset liver abnormalities in patients with recurrent depressives disorders on long-term lofepramine treatment.

Case 1: A 55 year old woman on lofepramine 210mg daily for nine months was discovered to have a raised gamma glutamyl transferase (GGT) of 62iu/l (normal range < 25 for females, < 35 for males). She was asymptomatic, had no other blood abnormalities and consumed minimal alcohol. Plasma levels of desipramine, the active metabolite of lofepramine, were subtherapeutic at 26g/l (normal range $50\mu g/l-150\mu g/l$). Lofepramine was reduced to 70mg/day and the GTT normalised, suggesting a dose-related effect. An alternative antidepressant was commenced and she remained well with no further biochemical abnormalities.

Case 2: A 65 year old man on lofepramine 210mg daily for three years was found on routine blood testing to have a raised GGT (88iu/l) which continued to rise and peaked at 152iu/l over a four week period. No other blood abnormalities were present. He did not drink alcohol and was on no other medications. Investigative blood tests were negative. Plasma levels of desipramine were subtherapeutic at 30µg/l. Discontinuation of lofepramine resulted in normalisation of GGT over six weeks and continued so on instigation and maintenance with another antidepressant.

Discussion: Desipramine is the principal metabolite of lofepramine and has been associated with hepatotoxicity.4 Lack et al,5 however, have described a case in which a patient developed liver function abnormalities on lofepramine. These abnormalities settled on the patients' withdrawal, recurred on re-exposure, but were absent when desipramine was substituted. This suggests that hepatotoxicity may be caused by lofepramine itself, rather than it's metabolite desipramine. Contrary to previous reports of lofepramine-associated liver function abnormalities,3 these two patients had liver abnormalities that were neither early nor transient and only manifested after many months of treatment. Both experienced normalisation of liver function on reduction or withdrawal of lofepramine. These cases illustrate the importance of periodic monitoring of liver function in all patients on lofepramine.

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