re:ACTION April 2002 No.24

An occasional bulletin from the West Midlands Centre for Adverse Drug Reaction Reporting

Please let us know if you would like to receive this bulletin by email:
help@csmwm.org

RECENT REPORTS

Contrasting views: metformin and radiography *(Clin. Radiol.*1999; **54**:29)

Lactic acidosis is a rare but serious adverse effect of metformin, with a reported mortality of 50%. Cases are usually associated with uncontrolled cardiac failure, recent myocardial infarction, hepatic or renal failure, severe infection, trauma, or ketoacidosis. All of these are contra-indications to taking metformin.

The Royal College of Radiologists and the manufacturers of metformin also advise that metformin should not be used in the 48 hours before or after intravenous contrast media. However, a systematic review of the literature concluded that the risk of lactic acidosis with iodinated contrast media in patients correctly prescribed metformin (i.e. those with normal renal function) was negligible. Lactic acidosis associated with metformin has an incidence of 0.03 per 1000 patient years, only 10% of which may be related to the use of contrast media. The risk benefit of stopping metformin has been questioned, given the rarity of the reaction. (*Clinical Radiology* 1998;**53**:310)

We would be interested in any reports of lactic acidosis (or other serious adverse effects) associated with either metformin or contrast media alone or in combination.

Ingrowing toenails with indinavir and ritonavir (*Ann. Pharmacother.* 2001; **35**: 881)

A recent case report describes 5 HIV-positive patients who suffered recurrent ingrowing toenails while taking combination antiretroviral therapy including indinavir and ritonavir. Three of the patients had to have nails removed. Indinavir may increase activity of retinoic acid in the body, and ritonavir increases the bioavailability of indinavir, resulting in greater indinavir concentrations.

Antiretrovirals are often licensed with limited pre-marketing data and we welcome reports of reactions to drugs used to treat HIV infection. Doctors, pharmacists and specialist HIV nurses can also report suspected reactions to drugs used to treat HIV infection via the HIV adverse drug reaction reporting scheme.

Bladdered: Urinary retention with fentanyl (*Pediatrics* 2001;**108**;1012)

Two children developed hydronephrosis and large distended bladders, after 2-4 days treatment with continuous fentanyl infusion at a dose of 3 micrograms/kg/hr. Neither child had anatomical reasons for retention, and both recovered after catheterisation. The authors suggest that preterm infants receiving fentanyl should have an indwelling urinary catheter or be closely observed for the development of bladder distension.

We have received one report of reduced urine output, associated with weight gain and oedema, in a 45 year-old man, following the use of fentanyl patches.

Reports of adverse reactions in children are especially welcome, as existing data on the use of medicines in children are limited.

"Do I not bleed"?: warfarin and Cox IIs

(*ADRAC Bulletin*: 2002; **21**: 3)

In *re:Action 21* we described a case report of an interaction between warfarin and celecoxib. The Australian Therapeutic Goods Administration has recently highlighted 8 reports of an interaction between rofecoxib and warfarin. Measured INR was 3.8–11.8 one and six weeks after starting rofecoxib in patients whose INR had previously been stable on warfarin. The mechanism for this suspected interaction is unknown at present.

At CSM West Midlands, we have had a total of 189 reports of reactions to rofecoxib since it was licensed. One case reported a rise in INR to 7.9 in a patient on rofecoxib and warfarin. A further three cases of gastrointestinal bleeding have been reported in patients taking both rofecoxib and warfarin, although INRs were not supplied.

We welcome any reports of suspected reactions to or interactions with celecoxib or rofecoxib

Suicide with beta-blockers: A real risk?

(*Brit. J. Clin. Pharm.* 2001; **52**: 313-318)

β-adrenoceptor antagonists have been suggested to induce depression, but do they increase the risk of suicide? A large cohort study of 58 529 patients taking β-adrenoceptor antagonists, calcium channel antagonists or ACE inhibitors compared suicide rates in the cohort to suicide rates in the general population in Denmark.

The suicide risk was increased in β-adrenoceptor antagonist users (n=31 462): 53 observed suicides *vs* 32.4 expected; standardised mortality ratio of 1.6 (95% confidence interval: 1.2-2.1). No significant risk was associated with calcium channel blockers or ACE inhibitors.

It was also found that the association with suicide was restricted to those cohorts taking medium and high lipid solubility β-adrenoceptor antagonists. Low lipid soluble or hydrophilic β-adrenoceptor antagonists had no association with suicide. Theoretically, hydrophilic β-adrenoceptor antagonists should not cross the blood brain barrier and therefore may have less effect on the central nervous system.

We welcome reports of serious or unusual suspected psychiatric reactions to medicines.

REPORTING TO CSM West Midlands

We welcome Yellow Card reports on all suspected adverse reactions to new (▼) drugs including vaccines and unlicensed herbal remedies and *all suspected reactions to all drugs used in children*, and on all serious or unusual reactions to well-established drugs. You do not have to be certain that a drug caused a reaction in order to report.

You can **download a copy of the redesigned yellow card in Adobe PDF format** from our website (http://csmwm.org).

Please send reports to: CSM West Midlands, Freepost SW2991, BIRMINGHAM, B18 7BR.
No stamp is needed. If you would like a supply of pre-addressed and reply-paid yellow cards, please contact the above address.

SOME ADDITIONS TO THE LIST OF INTENSIVELY MONITORED DRUGS

Approved name	Trade name	Indication
bexarotene	▼ Targretin ®	skin manifestations of advanced cutaneous T cell lymphoma
tacrolimus	▼ Protopic ®	moderate to severe dermatitis
tenofovir	▼ Viread ®	HIV patients experiencing virological failure

The entire list of about 220 intensively monitored drugs can be obtained from the centre or on our website: http://csmwm.org. Please report **all** adverse reactions you suspect are due to intensively monitored drugs. Please send any comments to: Dr R E Ferner at CSM West Midlands, or email: r.e.ferner@bham.ac.uk