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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

Dry your eyes (*JAMA.* 2001; **286**: 2114-19)

Dry eye, which can be an adverse reaction to drugs, is responsible for considerable discomfort, and increases the risk of eye infections.

A recent cohort study of 25,665 postmenopausal women draws attention to the dry eye syndrome associated with hormone replacement therapy (HRT). HRT was associated with a risk ratio of 1.69 (95% confidence interval (CI) 1.49-1.91) with oestrogen use and 1.29 (95% CI 1.13-1.48) for oestrogen plus progesterone/progestin, compared with women who did not use HRT. Every three-year period of use of HRT carried a 15% increase in the risk of dry eye syndrome.

Dry eye has been associated with other medication including anti-hypertensives, proton pump inhibitors, H_2-antagonists, anticholinergics, isotretinoin, and antidepressants.

We have received 11 reports of dry eye or blepharitis, including cases related to ACE inhibitors, beta-blockers, minoxidil, and statins.

We welcome reports of dry eye suspected to be due to new medications, denoted by the black triangle, and to drugs not presently recognized as causing it.

Excipients (*British Journal of General Practice*. 2001;51:570)

The active drug is not the only cause of adverse drug reactions. Occasionally the excipients, 'inert' substances used as lubricants, bulking agents and colourings, in the medicine may be the culprit. An example is a recent reported case of a 53-year-old man who was taking erythromycin and had a persistent productive cough. The patient stated he had a previous history of aspirin allergy and was advised that there was no known cross sensitivity between erythromycin and aspirin. After two days, the patient was suffering from tingling and swelling in the feet and fingers, similar to that he had experienced with aspirin.

On investigation of the patient information leaflet, it was found that the erythromycin capsules contained the colouring agent E110 (Sunset Yellow FCF). E110 is a synthetic 'coal tar' azo-dye used as a colourant in food, which can cause allergic reactions including rash, gastric upset, vomiting, 'nettle rash' and swelling of the skin. Individuals with asthma or aspirin allergy are more at risk.

We have received 8 reports of reactions to excipients. As reactions to excipients are unusual, we would welcome any reports of this nature, particularly if the reaction is serious.

Sildenafil: hard to swallow - (*American Journal of Gastroenterology.2001*: **96**: 2516-2518)

A 61-year old man developed oesophageal ulceration after taking a single 50mg dose of sildenafil (Viagra®) without water. He felt the tablet had become lodged in his oesophagus and within a few hours reported retrosternal burning pain and painful swallowing. He was admitted to hospital with progressive pain on swallowing and dysphagia, and endoscopy revealed multiple irregular erosions in the upper oesophagus and multiple ulcers in the lower and middle oesophagus.

A saturated solution of sildenafil (50mg in 10mls) was found to be acidic (pH=4.4, *cf* fasting stomach acid pH of 1.9–2.6). The authors suggest it would be wise to advise patients to take sildenafil tablets with an adequate amount of water (200ml of plain water is recommended by the manufacturer) an hour before sexual activity.

We have received five reports related to the upper gastrointestinal tract in men taking sildenafil: belching followed by vomiting, dyspepsia and bloated stomach, heartburn, and reflux oesophaghitis. We would welcome any similar reports of unpleasant gastrointestinal adverse effects.

NSAIDs: failing the heart (*European Journal of Clinical Pharmacology*. 2001; **57**: 71)

An ecological study of the entire Swedish population has recently shown an association between outpatient use of NSAIDs and admissions to hospital with heart failure. NSAIDs can promote fluid retention, worsen heart failure in susceptible patients, and impair the effect of diuretics. One in six first hospital admissions with heart failure may be due to NSAID use. (*Ann Intern Med* 2000; **160**: 777)

The study looked at all discharges with a primary diagnosis of heart failure (17,093) and five years-national sales data from the national government-owned pharmacy corporation of both prescription and over the counter sales. NSAID use was associated with an adjusted relative risk of 1.08 (95% confidence interval 1.04-1.12) This increased risk remained after adjustment for gender, age, socio-economic status, cardiovascular mortality, and the use of other drugs.

We have received a report of one case of worsening heart failure in a 77-year old woman who had been taking diclofenac 75mg for 8 days. We welcome any reports of similar reactions.

Influenza vaccine, INteRaction?

We have received three reports of raised INR in patients anti-coagulated with warfarin, who had received influenza vaccine in the preceding month. The target INR in their conditions was 2.5, but reached 4.1, 4.2 and 6 in the three cases. No bleeding occurred in any of the patients.

Whether influenza vaccine interacts with warfarin has been controversial. A number of studies have failed to show that influenza vaccine has an effect on anticoagulation with warfarin. However, a small number of individual cases with raised INRs have occurred (in one case life threatening). Although the balance of evidence shows that influenza vaccine can be safely used with warfarin, it would be wise to be alert for rare cases of any unpredictable bleeding or raised INR following vaccination.

We would welcome any serious suspected adverse drug reactions to influenza vaccine or to warfarin. Any reports of suspected drug interactions would be welcome.

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
alemtuzumab	▼ Mabcampath®	chronic lymphocytic leukaemia
apomorphine	▼ Uprima®	sublingual tablet for erectile dysfunction
budesonide and formoterol	▼ Symbicort®	treatment of asthma
imatinib	▼ Glivec®	chronic myeloid leukaemia
latanoprost and timolol	▼ Xalacom®	reduction of intraocular pressure in open angle glaucoma
levocetirizine	▼ Xyzal®	seasonal and perennial allergic rhinitis
lornoxicam	▼ Xefo®	short term treatment of moderate post-op pain or relief of pain in osteo- and rheumatoid arthritis

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