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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

Celecoxib: Sulfa Yellow (*Ann. Int. Med.* 2001: **134**: 256)

A 55-year old woman developed severe cholestatic hepatitis 4 weeks after starting treating with celecoxib at 200 mg/day. Liver biopsy was consistent with a drug reaction. Celecoxib was stopped and the woman subsequently recovered. The clinical, biochemical and histologic findings were similar to those seen with sulphonamide-induced cholestatic hepatitis. This woman was allergic to sulfa drugs. The chemical structure of celecoxib includes a sulfonamide group, and because of this celecoxib is contra-indicated in patients with a history of allergic reactions to sulfonamides.

At CSM West Midlands we have received one report of jaundice associated with celecoxib use. An 80-year-old developed cholestatic jaundice shortly after starting treatment with celecoxib 200 mg/day.

Celecoxib has a sulfonamide component and that the presence of an allergy to sulfa-drugs may predispose patients to adverse reactions. We welcome similar reports of any suspected reaction to celecoxib.

Hepatitis B vaccine, arthritis, and sex

(*Clin. Experiment. Rheumatol.* 2000: **18**: 789-90)

A recent analysis of adverse events reported to the Vaccine Adverse Events Reporting System (VAERS) run by the Centers for Disease Control in the US discovered that the 3 major types of arthritic reaction - arthralgia (joint pain), arthritis (joint inflammation), and arthrosis (joint degeneration) - occurred more commonly with hepatitis B vaccine than with any other vaccine in the database. The majority of these reactions were in female patients (female:male ratio = 3.5:1). Most of the reactions occurred in patients in their thirties and within 2 days of receiving a hepatitis B vaccination. The authors suggest that this reaction is immune-mediated.

At CSM West Midlands, we have received 15 reports of joint pain/arthralgia/arthritis associated with hepatitis B vaccine since 1993. Thirteen of these reactions were in female patients. We do not know the proportion of women in those receiving the vaccine.

We welcome any reports of serious reactions to established vaccines and for black triangle (▼) vaccines any reaction, whether trivial or serious.

Spironolactone, better safe than sorry

The use of low dose spironolactone in severe heart failure has increased over the past year following the publication of the Randomised Aldactone Evaluation Study (RALES: *NEJM* 1999; **341**: 709). spironolactone 25 mg a day reduced absolute risk of dying by 11.3%. While the incidence of hyperkalaemia was no higher in the spironolactone-treated grouped in RALES, the trial excluded patients with a serum creatinine concentration above 221 µmol per litre or a serum potassium concentration above 5.0 mmol per litre.

The co-prescribing of ACE inhibitors and spironolactone has previously been avoided because of the risk of hyperkalaemia.

We have received five reports of hyperkalaemia associated with spironolactone since publication of the RALES trial. Four of the cases involved the co-administration of an ACE inhibitor and the other the use of an angiotensin-II receptor antagonist.

It is prudent to monitor serum potassium concentration and renal function in patients taking spironolactone with an ACE-I or angiotensin-II receptor antagonist, especially in the first few months of treatment. The risks and benefits of this combination of drugs should be considered carefully in patients with raised potassium or creatinine concentrations. We welcome reports of serious reactions or interactions to established drugs.

Thalidomide, old drug, old risks (*Brit. J. Derm.* 2001; **144**: 310)

Thalidomide is the classic teratogen, causing serious limb deformities in children born to mothers who had taken it during pregnancy. It is also well established as a cause of severe, and irreversible, peripheral neuropathy. Although its use was largely abandoned in the 1960s, it has re-emerged as a treatment for some dermatological disorders, erythema nodosum leprosum, aphthous ulcers in HIV syndrome and Behcet's disease, rheumatoid arthritis, multiple myeloma, and pain.

A recent survey of consultant dermatologists in Wales showed that 65% had used thalidomide to treat serious skin disorders. Of the women patients treated 58% were of child-bearing age, and none had a pregnancy test prior to the use of thalidomide. In addition, patients received little information about thalidomide and although most prescribers performed nerve conduction studies to detect sub-clinical nerve damage, only 36% of prescribers obtained baseline values.

Adverse effects leading to discontinuation of thalidomide occurred in 20% of patients; 5 patients developed peripheral neuropathy with paraesthesia. The authors of the survey have produced a consent form, information leaflet and checklist for the use of thalidomide following this survey. This has been distributed across Wales. A copy of the consent form, information leaflet and checklist can be found on our website.

We welcome reports of reactions to unlicensed drugs, whether they are minor or serious reactions.

Clopidogrel: bad blood? (*Lancet* 2001; **357**: 446)

Clopidogrel (Plavix®), licensed for the prevention of ischaemic events in patients with a history of symptomatic heart disease, has recently been associated with fatal aplastic anaemia in a 88-year-old man with symptomatic carotid stenosis. Following 5 months of treatment haematological results included: haemoglobin 8.6 g/dl, white-cell count 2.6 x 10^9/L and platelets 30 x 10^9/L.The bone marrow biopsy showed aplastic anaemia. The patient eventually died from pneumonia. No other new drugs had been introduced since clopidogrel.

We have received one report of thrombocytopenia with clopidogrel in a 47-year-old man whose platelets fell from 215 to 144 after treatment, and continued to fall for 45 days before recovering.

Clopidogrel is a black triangle (▼) drug under intensive surveillance and we are keen to receive reports of any suspected reactions to this agent.

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

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.

ADDITIONS TO THE LIST OF INTENSIVELY MONITORED DRUGS

Approved name	Trade name	Indication
almotriptan	▼ Almogran®	acute treatment of migraine attacks
desloratidine	▼ Neoclarityn®	relief of symptoms of seasonal allergic rhinitis
linezolid	▼ Zyvox®	treatment of susceptible infections
lopinavir, ritonavir	▼ Kaletra®	advanced HIV infection
nateglinide	▼ Starlix®	type 2 diabetes
sibutramine	▼ Reductil®	treatment of nutritional obesity

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