



DRUG ALERT

Regional Pharmacovigilance Centre (South)

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Centre's Report

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An Analysis of Adverse Drug Reactions Reported in JIPMER

The National Pharmacovigilance Programme was started on November 2004, by Central Drugs Standard Control Organisation (CDSCO), Ministry of Health and Family Welfare, Government of India. JIPMER is the Regional Pharmacovigilance Centre for the southern region.

Overview of reports

The analysis was done with reports from January 2007 to December 2007. Our centre received a total of 322 adverse drug reaction (ADR) reports during this one year period, from various department of our hospital. Most of the ADR reports were by doctors, followed by MBBS students (Figure 1).

It was observed that, more ADR was reported in males (53.72%) than females (45.96%). The highest number of ADR reports were received from age group 20-29 years (26.70%).

The drug classes causing ADRs are given in figure 2. Antibiotics caused 112 (34.8%) ADRs. Among them ADRs were more in fluoroquinolones (24, 21.43%) followed by cephalosporins (23, 20.54%) and aminoglycosides (17, 15.18%).

Most common drugs associated with ADRs are given in table 1, with their suspected adverse drug reactions. Causality assessment was done by using WHO scale. It shows that 186 (57.76%) were probable reactions, 132 (40.99%) were possible reactions, 3(0.93%) were conditional reactions and only 1(0.31%) reaction was unassessable. The organ systems affected due to ADRs are given in figure 3.

The severity assessment was done by using Hartwig and Seigel scale. It reveals that 235 (73%) ADRs were only moderate reactions (Figure 4).

The occurrence of adverse drug reactions in hospitalized patients can lead to an increase in length of stay and excess cost. In order to prevent the adverse outcome of therapy insight into the occurrence of adverse drug events during hospitalisation is important.

The data given here is only analysis of spontaneous reporting. There is a possibility that many ADRs are either not reported or notified. This may be achieved by more active ADR reporting by all the health care professionals including MBBS students. This will help

Fig 1. ADR Reporter Details

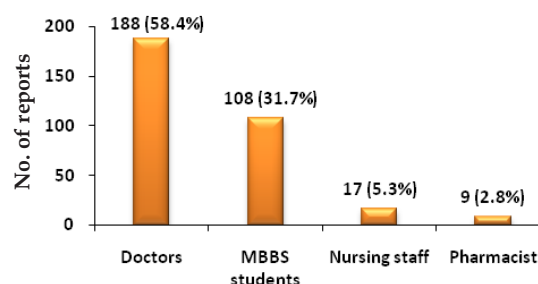


Fig 2. Drugs associated with ADRs

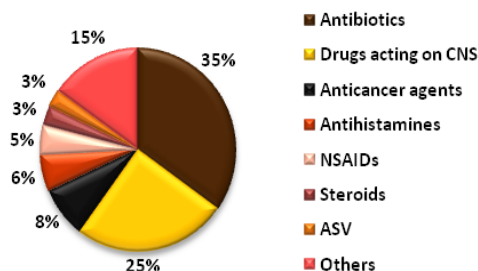


Fig 3. Systems associated with ADRs

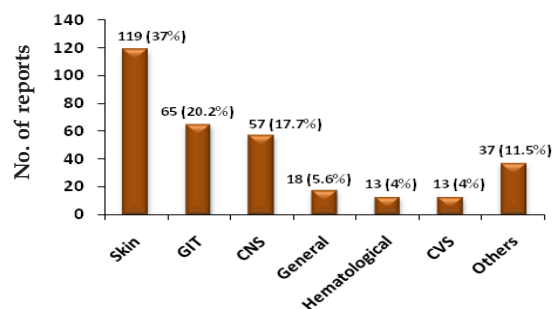


Fig 4. ADR severity assessment scale (Hartwig and Seigel scale)

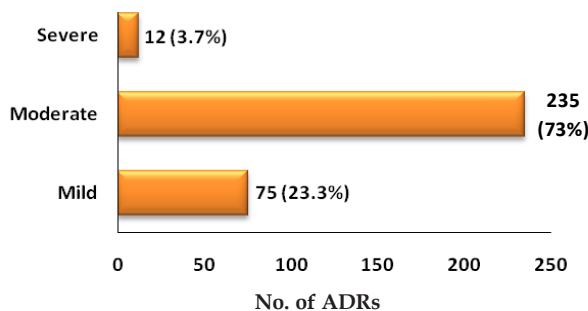


Table 1. Drugs with reported ADRs

Drugs	No. of reports	Suspected Reactions
Ciprofloxacin	23	Leukocytoclastic vasculitis, skin rashes, nausea, metallic taste, itching, maculopapular rashes, facial erythema, tremors, exfoliation, excessive hair loss, neuroleptic malignant syndrome.
Ceftriaxone	15	Urticarial rashes, maculopapular rashes, angioedema, hypotension.
Anti tubercular drugs	15	Vomiting, hepatitis, respiratory distress, cardiorespiratory arrest, rhabdomyolysis with intravascular hemolysis, cardiac events, generalised tonic-clonic seizures.
Vancomycin	12	Thrombocytopenia, itching, loss of hearing, skin rashes, increased serum creatinine level, swelling of face.
Beta lactam antibiotics	11	Abdominal pain, maculopapular lesion, severe pruritis and chest pain, metabolic disorder, dystonia, severe vomiting and hair loss.
Cisplatin	10	Hair loss, vomiting.
Paracetamol	7	Exfoliative dermatitis, fixed drug eruption over lips. toxic epidermal necrolysis, erythematous maculopapular rashes.
Cyclophosphamide	7	Hyper pigmentation of nails, alopecia, severe pancytopenia.
Haloperidol	5	Agitation and dysphoria, marked tremulousness of hands
Prednisolone	4	Diabetes, acniform eruption.
Paclitaxel	4	Vomiting, loss of hair, diarrhea.
Diclofenac	4	Aplastic anaemia, fixed drug eruption.
Rifampicin	3	Vomiting, thrombocytopenia
Sodium Valproate	3	Aggressiveness, emesis
Clonazepam	3	Maculopapular rashes, fixed drug eruption
Anti Snake Venom	3	Rashes, severe pruritis, chest pain.
Factor VIII	2	Chills, giddiness

in the reduction of adverse drug reactions associated economic burden to the patients as well as society.

Moreover in the long run we will have our own ADRs database.

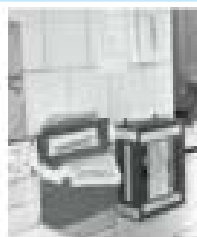
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Achievements: 2006 - 2008

A Simple Initiative

Doctors in Pondicherry, India come up with an idea for improving reporting



UPPSALA REPORTS - 2006



Collage Competition - 2007



Awareness Programme for Senior Health Professional - 2008

Congratulations

Uppsala Prize for young scientist and best paper presentation was awarded to **Akhtar S, Surendiran A and Krishna Kumar D** in the 7th Annual Conference of the Society of Pharmacovigilance in India (SOPI), held on 23-25th November, 2007 at National Institute of Medical Sciences, Jaipur.

New Drug

Entry Inhibitor - Maraviroc in HIV treatment

Maraviroc, an anti retroviral drug is approved for use in combination with other antiretroviral drugs for the treatment of adults infected with CCR5 tropic HIV-1. It can be used in conditions where resistance to other available antiretroviral drugs are encountered.¹

Maraviroc blocks the chemokine co receptor CCR5 and inhibits the interaction between the viral gp 120 and host CCR5 co receptor. Thus the viral entry into the cell is inhibited. The other co-receptor used by HIV-1 CXCR4, is however unaffected.² Resistance to other groups of drug namely NRTIs, NNRTIs, and protease inhibitors do not produce cross resistance to maraviroc. Maraviroc is not recommended for monotherapy or for patients in whom antiretroviral therapy is being started for the first time.^{1,2} When patients with HIV-1 are treated with maraviroc, the X4 tropic viruses seem to emerge. Identification of the viral tropism is essential for treatment with maraviroc.

In adults it has no apparent significant adverse effects. The drug has not been tested in children less than sixteen years and in pregnant women. The effectiveness of maraviroc as a monotherapy for HIV 1 infection and for patients not treated with any other antiretroviral therapy has not been established.

The common adverse events seen during clinical trials were cough, fever, upper respiratory tract infections, rash, musculoskeletal symptoms, abdominal pain, and dizziness. The product label includes a boxed warning about hepatotoxicity. In clinical trials, more

cardiovascular events, including heart attacks, were seen in patients receiving maraviroc as compared to placebo.

Maraviroc is available as 150 mg and 300 mg tablets. It can be given twice daily with or without food. It is metabolized by the enzyme CYP3A4. The dosage for maraviroc depends upon co-administered drugs. When CYP3A4 inhibitors are administered, it can cause increased exposure to maraviroc and requires a dosage of 150 mg BD. In the presence of CYP3A4 inducers it has to be given in higher doses of 600 mg BD as the metabolism of maraviroc is enhanced. With other concomitant medications it can be given in doses of 300 mg BD.²

Maraviroc, is another step forward in the discovery of an effective drug for the treatment of HIV infection. It holds promise for HIV-positive patients who no longer respond to other HIV drugs. Maraviroc has received patent in India and is in the process of registration the drug in India.

References

1. Kuritzkes D et al. *Nature Review Drug Discov* 2008. 7:15-16.
2. Emmelkamp J et al. *Eur J Med Res* 2007. 12:409-17.

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Case Report

Paclitaxel: Hypersensitivity reactions in a 40-year old woman with ovarian malignancy

A 40 year old woman developed hypersensitivity reactions after receiving paclitaxel for ovarian malignancy.

She was administered paclitaxel in recommended doses for the primary treatment of **ovarian cancer** (135 mg/m² infused over 24 hours). The reactions occurred within the first hour of infusion with dyspnea, flushing, chest pain, tachycardia and generalised rashes over the skin. All the manifestations subsided when paclitaxel infusion was withheld and the woman was treated with antihistamines and steroids. Based on the Naranjo probability scale, it is probable that paclitaxel was the causative agent for these reactions.

Despite premedication with corticosteroids, antihistamines, and H₂-antagonists, hypersensitivity reactions occur frequently in patients given paclitaxel; about 40% of patients may experience a mild reaction and 2% a severe reaction. Fatalities have been reported. There are rare reports of delayed hypersensitivity

reactions with paclitaxel; necrotic ulceration has occurred, without evidence of extravasation.¹ Some consider the cause to be the polyethoxylated castor oil diluent for paclitaxel and docetaxel has been suggested as a suitable alternative.² However, hypersensitivity reactions have also occurred with docetaxel and taxane cross-reactivity has been reported. Although the manufacturers of both drugs consider further use to be contra-indicated after a severe reaction, strategies for continuation of treatment and desensitization have been described.

References

1. Beri R. *Ann Pharmacother* 2004; **38**: 238-41.
2. Markman M et al. *J Clin Oncol* 2000; **18**: 102-5.

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ADR Alert**Known drugs, Unknown ADRs****List of first reports of serious adverse drug reactions recently reported**

Name of the drug	Adverse effect	Reference
Aripiprazole: interaction with haloperidol	QT interval prolongation	Leo R et al. <i>J Clin Psychiatry</i> 2008; 69: 327-8.
Carbamazepine	Eosinophilic esophagitis	Baltsinou C et al. <i>Dig Liver Dis</i> 2008;40:327-8.
Ceftazidime	DRESS syndrome in an elderly patient	Patricio L et al. <i>Allergy</i> 2007;62: 542.
Deferiprone	Henoch-Schoenlein purpura in a child	Unal S et al. <i>Am J Hematol</i> 2008;83:165-6.
Hydroxychloroquine	DRESS syndrome	Vollpe A et al. <i>Clin Rheumatol</i> 2008;27:537-9.
Lisinopril	Dermatitis exfoliativa in an elderly patient	Broski SE et al. <i>J Drugs Dermatol</i> 2008;7:163-6.
Thalidomide	Intestinal perforation	McClay H et al. <i>Br J Hematol</i> 2008;140:360-1.
Vinblastine	Reactivation of hepatitis B in an elderly patient	Miralles CI et al. <i>Gastroenterol Hepatol</i> 2007;30:563.

DRESS- Drug Rash with Eosinophilia and Systemic Symptoms

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Quiz

- The vaccine known to cause intussusception is.....
- The gastrointestinal ADR of clozapine which can be fatal is.....
- The antidiabetic drug which can cause parotid gland enlargement is.....
- The life threatening neurological adverse effect of rituximab is.....
- The adverse effect to be borne in mind while prescribing pioglitazone in a post menopausal women for diabetes is.....
- What is XDR tuberculosis?
- The possible drug related cause of acute abdomen in a patient taking antituberculosis therapy is.....
- The anticancer drug which can cause hepatic veno occlusive disease is.....
- In drug interaction parlance, triple whammy is.....
- The anti epileptic which can cause angle closure glaucoma is.....

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Answers

1. Rota virus oral pentavalent vaccine indicated for viral gastroenteritis. 2. Clozapine induced constipation may be associated with toxic megacolon, intestinal obstruction and bowel perforation. 3. Thiazolidinediones like rosiglitazone and pioglitazone. 4. Progressive multifocal encephalopathy. 5. Increased risk of fractures. 6. The laboratory definition of XDR-TB is: resistance to at least rifampicin and isoniazid from among the first line anti-TB drugs in addition to resistance to any fluorquinolone, and to at least one of three injectable second line anti-TB drugs used in TB treatment (capreomycin, kanamycin, and amikacin). 7. INH induced pancreatitis. 8. Busulfan. 9. The combination of ACE inhibitor, diuretic and NSAID producing acute renal failure. 10. Topiramate.

Drug Information Service

-  Have queries on therapy of disease?
-  Need to know about drug interactions?
-  Want to know the safety of a drug?
-  Searching for information about new drugs?

We are here to help you

Drug Information Centre
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Mobile No: 9791858689; Phone: 2272380; Ext: 3301, 3302.