Adverse drug reaction monitoring in a tertiary care teaching hospital

Sir,

Adverse drug reaction (ADR) contributes to the burden of drug-related morbidity and mortality.[1] The incidence of ADRs in inpatients of hospital has been reported to be in between 1.7% to 25.1%.[2] ADRs are seen frequently in hospitals due to a combination of factors such as, complexity of diseases, drug interactions, polypharmacy, and possible negligence. The aim of this study was to undertake ADR monitoring in various departments of a tertiary care government hospital

and to cultivate the culture of ADR reporting among fellow physicians.

This was a prospective spontaneous reporting study conducted by the Department of Pharmacology, Maulana Azad Medical College, New Delhi, on inpatients of Lok Nayak Hospital, a tertiary care teaching hospital in New Delhi. ADRs in patients admitted in these wards during the period of 8 months from June 2008 to Jan 2009 were noted. All suspected spontaneous ADRs were initially assessed by the respective consultants and subsequently the information was collected and analysed by the pharmacologists for causality assessment.

Detailed drug and clinical history, and relevant information about suspected reaction, its onset, duration, temporal association with drug intake if any, were recorded in an ADR reporting form. The causality relationship among ADR and drug was assessed using WHO ADR causality assessment criteria.[3]

A total of 207 ADRs were reported from July 2008 to June 2009. The mean age of patients who experienced ADRs was 32, although ADRs were observed in both gender but slight male preponderance was seen (59%).Type of ADRs experienced and drug associated are mentioned in Table 1.

Cutaneous manifestations which included rash, urticaria, dermatitis, Steven Johnson syndrome, Toxic epidermal necrolysis etc were most common ADRs with an incidence of 42%. These side effects were more commonly observed with anti convulsant drugs like carbamazepine, phenytoin and valproate. Out of total 87 skin reactions 40(45.9%) were rash related ADRs, 25(28.7%) were Steven Johnson syndrome, 14(16%) were urticaria, 6(6.8%) cases of toxic epidermal necrolysis, and 2(2.2%) were hyper pigmentation reactions.

The next most common ADR belong to gastrointestinal system which included hepatotoxicity, gastric erosions, dyspepsia, pancreatitis etc accounting for 28.5% of total ADRs. [Table 1] Gastrointestinal side effects including hepatotoxicity were mainly seen in cases who consumed Non steroidal anti inflammatory drugs (NSAIDs) and Anti tubercular therapy (ATT). Febrile neutropenia was observed in 18.3% of total 207 cases. It was observed with most of the drugs given for treatment of cancer, peripheral neuropathy was also seen with paclitaxel and vincristine administration.

Extrapyramidal side effects were seen in patients receiving antipsychotic drugs (2.8%).One of this drug like olanzapine and antidepressant mianserin were associated with weight gain. Nephrotoxicty was mainly observed in patients receiving antifungal and antibiotic treatment accounting for 1.9% of total cases. Anaphylaxis was seen with intravenous administration of ceftriaxone, ciprofloxacin and phenytoin [Table 1]. 41.9% of the total ADRs were associated with polypharmacy wherein 3 or more drugs were prescribed. We also observed that 36.5% of ADRs were seen in patients receiving drugs through intravenous route.

Causality assessment was undertaken based on WHO criteria.[3] It was seen that out of total 207 ADRs, 47.3% were found to be Probable and almost similar number i.e. 47.8% were considered as Possible where as only 0.9% were classified as Certain. ADRs were also categorized according to severity, 24.1% were found to be mild, 38.6% and 37.1% were classified under moderate and severe category respectively [Table 2]. Most of the ADRs in severe category were of Steven Johnson syndrome due to unknown drug wherein the patient reported taking drug from private practioner without prescription. Main indication for which these unknown drugs were given were pyrexia of unknown origin and epilepsy.

In our study, as in accordance of previous reports the most common systems associated with ADRs were skin and gastrointestinal.[4] We also observed that the drugs implicated

Table 1: Category of adverse drug reactions detected and implicated drugs

Types of ADRs (number of ADRs)	Drugs implicated in order of frequency
Cutaneous# (87)	Unknown, carbamazepine, phenytoin, ceftriaxone,valproate, vancomycin, ciprofloxacin, NSAIDs*, ATT** , dapsone, teicoplanin
Gastrointestinal© (38)	NSAIDs, ciprofloxacin tinidazole combination, opioids, chloroquine, ATT, diacerin, amoxicillin
Hepatotoxicity (21)	ATT
Nephrotoxicity (4)	Amphotericin B, vancomycin, gentamicin, tazobactam/piperacillin
Chemotherapy induced febrile neutropenia (38)	Cisplatin, adriamycin, 5-FU, cyclophosphamide,paclitaxel, carboplatin, ifosfamide, vincristine, bleomycin, etoposide
Anaphylaxis (3)	Ceftriaxone,ciprofloxacin,phenytoin
Tremor (5)	Lithium carbonate, salbutamol
Extrapyramidal side effects (6)	Risperidone, haloperidol. trifluoperazine
Peripheral neuropathy (2)	Vincristine, Paclitaxel
Weight gain (2)	Olanzapine, mianserin
Myopathy (1)	Atorvastatin

Rash, exfoliative dermatitis, urticaria, erythroderma, Steven Johnson syndrome, toxic epidermal necrolysis, hyperpigmentation and fixed drug eruptions; ©diarrhoea, vomiting, gastritis, gastric erosions, oral ulcers and hematemesis; * Non-steroidal anti-inflammatory drugs (diclofenac, ibuprofen and piroxicam); ** Anti tubercular therapy (isoniazid, rifampicin, pyrazinamide and ethambutol);

Table 2: Causality assessment and severity of ADRs

Probability scale	Number of ADRs (%)
Certain	2 (0.9)
Probable	98 (47.3)
Possible	99 (47.8)
Unlikely	1 (0.4)
Unassessable	7 (3.3)
Severity of ADR	
Mild	50 (24.1)
Moderate	80 (38.6)
Severe	77 (37.1)

in skin reactions were valproate, carbamazepine, vancomycin and ciprofloxacin. Our findings are similar to earlier published reports.[5] We observed that as expected gastrointestinal side effects and hepatotoxicity were mainly associated with anti tubercular drugs and NSAIDs (diclofenac and ibuprofen).

We also observed that quite a number of adverse drug reactions were with unknown drugs which could be herbal, ayurvedic or belonging to alternative medicine. ADRs observed with these drugs were of moderate to severe category. Drug induced neutropenia was seen in 18.3% of cases. It was observed that side effects with drugs administered through intravenous route were of severe category.

The limitations of our study were its short duration with less number of ADRs and we did not assess preventability of ADRs. We conclude that anticonvulsants, analgesics, antimicrobials and anti cancer drugs are responsible for most of the ADRs. The problem of underreporting of ADRs is much bigger issue and should be addressed immediately.

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