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A RANDOM STUDY OF ADVERSE DRUG REACTIONS

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Abstract

Objective: To study the incidence of adverse drug reactions (ADRs) in a randomized sample of patients and evaluate the drugs commonly causing ADRs, the age group and sex generally affected and the outcome of the treatment given to the patients for the ADRs. **Methods:** It was a cross sectional study done in a few selected hospitals in Hyderabad, for a period of 8 months (February-October 2010). Patients developing or getting admitted for ADRs in these hospitals were recorded. **Results:** Thirty cases of ADRs were recorded in this study. Chemotherapeutic agents were found to produce ADRs in 63% of patients, NSAIDs in 23% and some miscellaneous drugs in 14% of patients. All age groups were equally affected with a slightly higher incidence in the elderly. Women (56%) had a slightly higher incidence of ADRs than men (44%). **Conclusion:** Adverse drug reactions may vary in severity from mild rashes to severe toxic epidermal necrosis. The doctors should prescribe the safest and minimum number of drugs. Multiple drugs and frequent dosing, incorrect prescriptions, non-therapeutic and irrational use should be avoided. Caution should be taken in the elderly considering their age related kinetics. It is very important that self medication without consulting the doctor be strongly discouraged.

INTRODUCTION

If a drug, when used in man at normal doses, for prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function, results in a reaction which is noxious and unintended it is known as an adverse drug reaction[1] . Adverse drug reactions to drugs are as old as medicine and ancient physicians were well aware of them[2]. Year after year new drugs are launched with limited information on market penetration and on their rational and safe prescribing. The society is paying for promotional excess of the drug industry in the form of adverse drug reactions. In the last two decades attempts have been made in India to monitor ADRs. There still is a need for a national policy and concerted efforts to identify drugs which are not safe for our population[3].

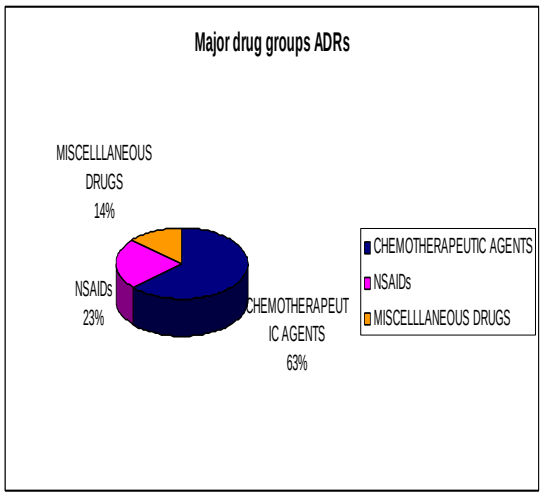
This study was done to evaluate the drugs which frequently produced ADRs, the age group and sex commonly affected and the outcome of the treatment given for the ADR.

MATERIALS AND METHODS

This was a cross sectional study done in a few selected hospitals in Hyderabad, India, from February to October 2010. Patients admitted for or developing ADRs during hospitalization were noted. All cases of ADRs in these hospitals, however, could not be recorded on account of communication problems. The complete history of the cases, treatment given and investigations done were recorded. Follow up was done till the patient got discharged.

RESULTS

Total thirty cases of ADRs were noted in this study. Chemotherapeutic agents were found to be the predominant group of drugs producing ADRs in 63%, NSAIDs in 23% and some miscellaneous drugs in 14% of the patients.

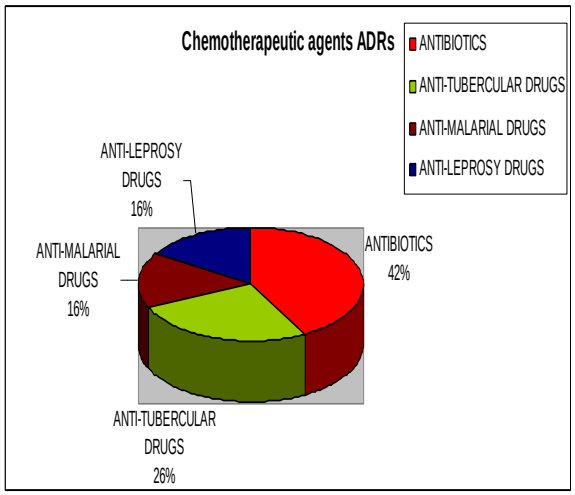


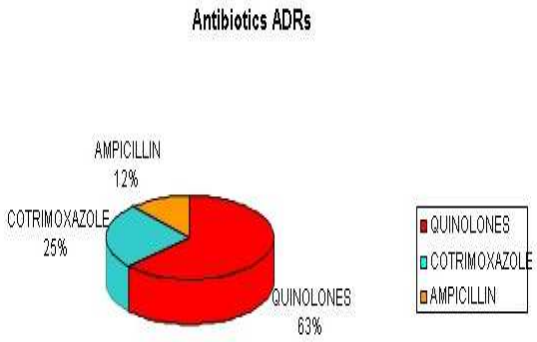
CHEMOTHERAPEUTIC AGENTS

In the chemotherapeutic agents, antibiotics produced ADRs in 42%, anti-tubercular drugs in 26% and anti-leprosy and anti-malarial drugs in 16% of patients each.

ANTIBIOTICS

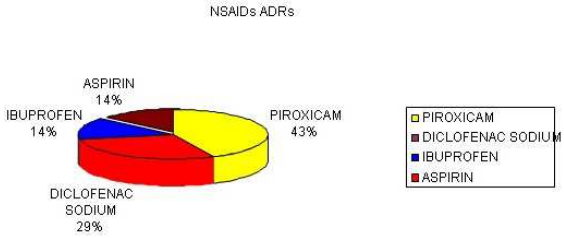
In the antibiotics, quinolones produced ADRs in 63%, cotrimoxazole in 25% and ampicillin in 12% of patients.





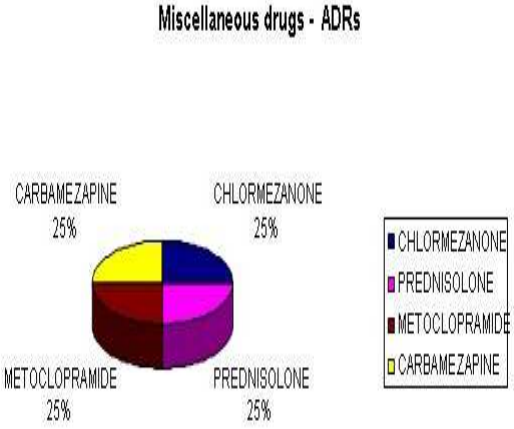
NSAIDs

The NSAIDs formed the second major group producing ADRs in 23% of patients. In the NSAIDs, piroxicam produced ADRs in 43%, diclofenac sodium in 29% and ibuprofen and aspirin in 14% of patients each.



MISCELLANEOUS DRUGS

The miscellaneous group of drugs produced ADRs in 14% of patients. Chlormezanone, prednisolone, metoclorpramide and carbamezapine produced ADRs in 25% of patients each.



INCIDENCE IN MEN & WOMEN

The incidence in women was 56% and in men it was 44% of patients.

INCIDENCE IN DIFFERENT AGE GROUPS

All age groups (excluding pediatric patients) were found to be equally affected with a slightly higher incidence in the older group.

DISCUSSION

In this study thirty patients were observed to develop ADRs. Patients numbered 1 to 5 were prescribed quinolones for various types of infections like upper respiratory tract infection (RTI), urinary tract infection (UTI) and even tuberculosis. This is clearly misuse of newer broad spectrum antibiotics. Norfloxacin is more appropriate for the treatment of UTI in place of ciprofloxacin (patients 3 and 4). Ciprofloxacin was combined with tobramycin for a known case of tuberculosis (patient 2). Ciprofloxacin can be used in the treatment of tuberculosis but only if it is a case of multi-drug resistant tuberculosis. Sparfloxacin, another quinolone was noticed to be combined with an antibiotic (amoxicillin), an antifungal (fluconazole) and an NSAID (nimesulide) to treat an elderly patient for RTI (patient 5). This is over enthusiasm of a physician at a district level in India where polypharmacy is extremely common.

Quinolones. (Sp. ciprofloxacin) have taken the place of penicillin's of prior days in being the first choice of practicing physician for each and every patient with infection or we can say they are presently being highly misused by prescribing doctors. Where newer broad spectrum antibiotics are commonly being misused we also have general physicians who continue prescribing some older antibiotics like cotrimoxazole despite the availability of safer (ADR profile) and equally effective new antibiotics. Prescribing doctors can replace cotrimoxazole (with a high incidence of ADRs it being a sulpha drug) by some very safe newer antibiotics like azithromycin. Patient number 6 developed the most severe form of ADR, toxic epidermal necrolysis (TEN), when she was given cotrimoxazole for pyrexia by a general practitioner. This was the most unfortunate case of all ADRs in this study as it met with a tragic end.

Cotrimoxazole is also very commonly used by patients in self medication as seen in 7 of this study. Allergic reactions are bound to occur with this antibiotic owing to its chemical structure. All anti tubercular drugs (patients 9 to16) are known to produce adverse drug reactions. Hepatic toxicity is common to nearly all first line anti-tubercular drugs. Treatment of tuberculosis and leprosy requires multiple drugs for a longer duration of time (minimum 6 months). When multiple drugs are used for a longer duration the incidence of toxic effects also increases. It is imperative on the part of the physician to detail all this to the patient before initiating anti-tubercular treatment. The need for regular reviews should be stressed upon. The significance of baseline and regular liver function tests cannot be under estimated here. This aspect has been completely overlooked in all the cases of tuberculosis developing ADRs in this study. As India is an endemic area malaria is extremely common here. Chloroquine has always remained the mainstay of anti-malarial treatment. In the last one decade newer antimalarials like qinghasu derivatives (artemsenin, artether) have also been introduced. The other anti-malarial drugs like, primaquine, mefloquine, pyrimethamine-sulfadoxine combinations are also very useful anti-malarial drugs but each one has its own indication in malaria. Primaquine – for complete eradication of plasmodium species. Mefloquine – for prophylaxis of malaria in travellers. Pyrimethamine-sulfadoxine – for chloroquine resistant cases we have seen in this study (patients 17-19) the erratic use of different anti-malarial drugs in any patient of pyrexia likely to have malaria. NSAIDS currently justify to occupy the leading position in the most misused drugs being prescribed by doctors, nurses, chemists, allied sciences specialists (homeopathy, ayurveda, unani) and even the general population in self medication (patients 20 to 26). It is also a common component of poly-pharmacy. Presently, we have a long list of NSAIDs with newer and safer drugs being added every few years. As the life expectancy of the population is going up there will also be a parallel increase in the incidence of age related musculoskeletal disorders and NSAIDS prescriptions as well. The ADR profile (erosive gastritis, allergic reactions) should be considered before prescribing NSAIDs. The newer and

comparatively safer NSAIDs (selective cox II inhibitors) can be recommended else the older NSAIDS should be prescribed only under the protection of a H_2 blocker, proton pump inhibitor or a prostaglandin analogue.

Patient number 26 is an example of overdosing of aspirin in self medication resulting in an idiosyncratic reaction of tinnitus. In patient number 27 there is overlooking of the age factor (70 year old patient). Simple analgesics like paracetamol are not considered as the first choice of drugs over drugs like chlormezanone. Patient number 28 was a chronic case of bronchial asthma self medicating her during acute attacks with steroids ultimately developing drug induced gastritis and moon facies. Patient number 29 developed Steven Johnson syndrome on using carbamezapine, gabbapentin and tinazidine. As the patient was a diabetic combination of drugs like carbamezapine and gabapentin is not indicated for simple muscular pains. He could have been treated with thiamine tablets for his neuropathy.

The ADR of patient number 30 was an extension of the pharmacological actions of metoclopramide producing muscular dystonias.

MAJOR DRUG GROUPS PRODUCING ADRs TOTAL PATIENTS n=30	
CHEMOTHERAPEUTIC AGENTS	63% PATIENTS
NSAIDs	23% PATIENTS
MISCELLLANEOUS DRUGS	14% PATIENTS

NSAIDS - ADRs TOTAL PATIENTS n=7	
PIROXICAM	43% PATIENTS
DICLOFENAC SODIUM	29% PATIENTS
IBUPROFEN	14% PATIENTS
ASPIRIN	14% PATIENTS

PRESCRIPTIONS OF PATIENTS

PRESCRIPTIONS OF CHEMOTHERAPEUTIC AGENTS

PATIENT	TREATMENT TAKEN FOR	PRESCRIPTION GIVEN	ADR DEVELOPED
1	UPPER RESPIRATORY TRACT INFECTION	TAB. CIPROFLOXACIN 500 MGM TWICE DAILY DEXTROMETHORPHAN COUGH LOZENGES	EXFOLIATIVE DERMATITIS
2	TUBERCULOSIS	TAB. CIPROFLOXACIN 500 MGM TWICE DAILY INJ. TOBRAMYCIN 180 MGM DAILY	ERRHYTHEMA MULTIFORME
3	URINARY TRACT INFECTION	TAB. CIPROFLOXACIN 500 MGM TWICE DAILY TAB. PARACETAMOL	STEVEN -JOHNSON SYNDROME
4	URINARY TRACT INFECTION	TAB. CIPROFLOXACIN 500 TWICE DAILY	URTICARIA
5	UPPER RESPIRATORY TRACT INFECTION	TAB.SPARFLOXACIN --- 200 MGM TWICE DAILY CAP. AMOXICILLIN 500 MGM TWICE DAILY TAB. NIMESULIDE 200	STEVEN -JOHNSON SYNDROME

		MGM TWICE DAILY TAB. FLUCONAZOLE 150 MGM DAILY	
6	PYREXIA	TAB. COTRIMOXAZOLE 2 TABS TWICE DAILY TAB. PARACETAMOL 500 MGM TWICE DAILY	TOXIC EPIDERMAL NECROLYSIS
7	URINARY TRACT INFECTION	TAB. COTRIMOXAZOLE 2 TABLETS TWICE DAILY (SELF MEDICATION)	URTICARIA
8	PARAPERISIS	IV FLUIDS CAP. AMPICILLIN 500 MGM TWICE DAILY TAB. MULTIVITAMINS 1 DAILY	ALLERGIC RASH
9	TUBERCULOSIS	TAB. INH 300 MGM DAILY TAB. PYRAZINAMIDE 1000 MGM DAILY TAB. ETHAMBUTOL 800 MGM DAILY CAP. RIFAMPICIN 450 MGM DAILY	HEPATIC ENCEPHALOPATHY
10	TUBERCULOSIS	TAB. INH 300 MGM DAILY	TOXIC EPIDERMAL NECROLYSIS

		TAB. PYRAZINAMIDE 1000 MGM DAILY TAB.ETHAMBUTOL 800 MGM DAILY CAP. RIFAMPICIN 600 MGM DAILY	
11	TUBERCULOSIS	TAB. INH 300 MGM DAILY TAB. PYRAZINAMIDE 1000 MGM DAILY TAB. ETHAMBUTOL 800 MGM DAILY CAP. RIFAMPICIN 450 MGM DAILY	EXFOLIATIVE DERMATITIS
12	TUBERCULOSIS	TAB. INH 300 MGM DAILY TAB. PYRAZINAMIDE 1000 MGM DAILY TAB. ETHAMBUTOL 800 MGM DAILY CAP. RIFAMPICIN 450 MGM DAILY	DRUG INDUCED HEPATITIS
13	TUBERCULOSIS	TAB. OFLOXACIN 200 MGM TWICE DAILY TAB. PYRAZINAMIDE 1000 MGM DAILY TAB. ETHAMBUTOL 800 MGM DAILY	THROMBOCYTOPENIC PURPURA
14	TUBERCULOID	TAB. DAPSONE 100	EXFOLIATIVE

	LEPROSY	MGM DAILY TAB. CIPROFLOXACIN 500 MGM TWICE DAILY TAB. PIROXICAM 20 MGM DAIL	DERMATITIS
15	TUBERCULOID LEPROSY	TAB.DAPSONE 100 MGM DAILY CAP. RIFAMPICIN 450 MGM ONCE A MONTH	THROMBOCYTOPENI C PURPURA
16	LEPROMATOUS LEPROSY	TAB. DAPSONE 100 MGM DAILY CAP. RIFAMPICIN 450 MGM DAILY TAB. CLOFOZAMINE 100 MGM THRICE A WEEK TAB. PREDNISOLONE 20 MGM DAILY TAB.NIMESULIDE 100 MGM DAILY	FULMINANT HEPATITIS
17	PYREXIA	SULPHADOXINEPYRIMETHAMINE COMBINATION 2 TAB. STAT	STEVEN- JOHNSON SYNDROME
18	MALARIA	TAB. CHLOROQUINE 250 MGM THRICE DAILY TAB. PRIMAQUINE 7.5 MGM TWICE DAILY	DRUG INDUCED URTICARIA

19	PYREXIA	TAB. MEFLOQUINE 250 MGM DAILY PARACETAMOL SYRUP THRICE DAILY	ALLERGIC RASH

NSAIDs – PRESCRIPTIONS

PATIENT	TREATMENT TAKEN FOR	PRESCRIPTION GIVEN	ADR DEVELOPED
20	OSTEOARTHRITIS	TAB. PIROXICAM 20 MGM DAILY TAB. OXYPHENBUTAZONE 100 MGM DAILY TAB. BETAMETHASONE 0.5 MGM ONCE IN 3 DAYS	URTICARIA
21	MYALGIA	INJ. PIROXICAM 40 MGM TWICE DAILY	EXFOLIATIVE DERMATITIS
22	FRACTURE NECK FEMUR	TAB. PIROXICAM 20 MGM DAILY TAB. DICLOFENAC SODIUM 50 MGM TWICE DAILY	EROSIVE GASTRITIS
23	OSTEOARTHRITIS	TAB. IBUPROFEN	GASTROINTESTINAL

		400 MGM THRICE DAILY	BLEEDINGMALAENA
24	PYREXIA	TAB. DICLOFENAC SODIUM 50 MGM 2 TAB. STAT (SELF MEDICATION)	URTICARIA
25	PYREXIA	TAB. DICLOFENAC SODIUM 50 MGM TWICE DAILY (SELF MEDICATION)	ERRHYTHEMA MULTIFORME
26	MIGRAINE	TAB. ASPIRIN 325 MGM 2 TAB STAT (SELF MEDICATION)	TINNITUS

MISCELLANEOUS DRUGS PRESCRIPTIONS

PATIENT	TREATMENT TAKEN FOR	PRESCRIPTION GIVEN	ADR DEVELOPED
27	MYALGIA	TAB CHLORMEZANONE 100 MGM THRICE DAILY	STEVEN JOHNSON SYNDROME
28	BRONCHIAL ASTHMA	TAB PREDNISOLONE 20 MGM TWICE DAILY TAB THEOPHYLLINE 200 MGM TWICE DAILY TAB SALBUTAMOL 4 MGM TWICE DAILY	GASTRITIS
29	DIABETIC NEUROPATHY	TAB CARBAMEZAPINE 100 MGM TWICE DAILY	STEVEN JOHNSON SYNDROME

	TAB GABAPENTIN
	300 MGM THRICE DAILY
	TAB TINAZIDINE
	2 MGM THRICE DAILY

ADRs IN DIFFERENT AGE GROUPS

n=30

1-10 years	7%
11-30 years	30 %
31-50 years	30 %
51-70 years	33 %

TOTAL PATIENTS NUMBER OF PATIENTS

n=4

WOMEN	56%
MEN	44%

CHEMOTHERAPEUTIC AGENTS (ADRs)

TOTAL PATIENTS n=19

ANTIBIOTICS	42% PATIENTS
ANTITUBERCULAR DRUGS	26% PATIENTS
ANTIMALARIAL DRUGS	16% PATIENTS
ANTILEPROSY DRUGS	16% PATIENTS

ANTIBIOTICS -ADRs TOTAL PATIENTS n=8	
QUINOLONES	63% PATIENTS
COTRIMOXAZOLE	25% PATIENTS
AMPICILLIN	12% PATIENTS

MISCELLANEOUS DRUGS - ADRs TOTAL PATIENTS n=4	
CHLORMEZANONE	25% PATIENTS
PREDNISOLONE	25% PATIENTS
METOCLOPRAMIDE	25% PATIENTS
CARBAMEZAPINE	25% PATIENTS

REFERENCES

1. World Health Organization. WHO Technical Report No. 498. Geneva: World Health Organization, 1972.

2. Davies DM: 2000 years of Adverse drug reactions. Adverse Drug Reaction Bulletin 1999; 199:759-762

3. Singhal U. From the desk of editor. International workshop on Adverse Drug Reaction monitoring, November 1998.