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ORIGINAL ARTICLE

Adverse Reactions to Antimicrobials in a Teritary Care Hospital

K BHUVANA, N SARALA, T N KUMAR
Department of Pharmacology, Sri Devaraj Urs Medical College, Kolar, 563101

Introduction

Adverse drug reactions (ADRs) are unwanted consequences of antimicrobial therapy. These reactions can be common but not serious, serious and common, serious, but rare. The reactions will have an important implication on the patient and also the treating physician. Most of the ADRs related to antimicrobials are preventable. Therefore the awareness of these reactions will help us to decrease the occurrence and reduce the patients stay at the hospital and also the cost for the patients. Literature search has shown very few studies. This study will help the clinicians to know the safety profiles of the antimicrobials selected for the hospital antimicrobial formulary and for the patients. Hence the present study was carried out.

Methods

A prospective study was carried out by the department of Pharmacology from January 2006 to August 2006. The details of the patients manifesting with reactions to antimicrobials were collected both from inpatient and outpatient departments of R.L.Jalappa hospital attached to Sri Devaraj Urs Medical College. The parameters included number of patients receiving antimicrobials, their age groups, sex, indications for antimicrobials, type of reaction and the outcome of these reactions. The causality assessment of the ADRs was done as per the directions provided by WHO collaborating centre.

Results

During this 8 months period, 94,852 antimicrobial agents were prescribed. Of these, 31 patients presented with ADRs which accounts to 0.03%. Age distribution is as follows: 16% in pediatrics (0-18years), 80% in adults (19-60years) and 3% in geriatric (>60years) age groups. Males were 12 in number and females 19. Table 1 shows the antimicrobial agents causing both systemic and cutaneous ADRs.

Table 1 Number of patients affected by antimicrobial agents.

Antimicrobial agents	Number of patients
Fluoroquinolones	11
INH	5
Cephalosporins	5
Ampicillin+Cloxacillin	2
Macrolides	2
Amoxicillin	1
Tetracycline	1
Quinine	1
Cotrimoxazole	1
Dapsone	1
Fluconazole	1

The most common indications for the use of these antimicrobials were upper respiratory tract infection followed by fever, urinary tract infection, tuberculosis, bacterial diarrhea, typhoid, leprosy, cerebral malaria, esophageal candidiasis. In the present study we observed both cutaneous and systemic ADRs, which contributed to 77% and 23% respectively. Table 2 shows the type of systemic and cutaneous ADRs and also represents the antimicrobial agents implicated in that reaction.

2 patients presented with vasculitis which subsided by the 4th day and erythema multiforme due to INH subsided by 5 days. The patient with SJS had a hospital stay of 6 days. The lesions subsided gradually and patient was discharged on the 7th day. Insomnia due to ofloxacin subsided when the drug was stopped and alternate drug was given to the patient. INH induced increase in liver enzymes reverted to normal levels when the patient came for follow up after a period of 1 month. One patient had received fluconazole 150mg orally twice daily for a period of 3 days following which patient had bradycardia and ECG showed prolonged QT interval. The drug was stopped and ECG taken subsequently on the 2nd day was normal.

Table 2

Type of reactions	Antimicrobial agents implicated	Number of patients	Percentage
Cutaneous ADRs		**24**	
Maculopapular rash(19)	Fluoroquinolones	24	61
	Cefixime	8	
	Macrolides	4	
	Amoxicillin	2	
	Tetracycline	1	
	Quinine	1	
	Ampicillin+Cloxacillin	1	
Vasculitis (2)	INH	1	7
Stevens-Johnson Syndrome (SJS) (1)	Ampicillin+Cloxacillin	1	
	Ceftazidime	1	
Erythema Multiforme	Cotrimoxazole	1	3
Drug induced photo aggravated melanoderma	INH	1	3
	Dapsone	1	3
Systemic ADRs		7	
Insomnia	Ofloxacin	3	10
Altered Liver function tests	INH	2	7
Increased SGOT/SGPT	INH	1	3
Prolonged QT interval	Fluconazole	1	3

Discussion

Adverse drug reactions in hospitalized patients contribute to 10-20%, 0.3-0.5% of hospital admissions are due to ADRs and deaths in hospitalized patients due to ADRs accounts to 0.24-2.9%. [1] These reactions are common in patients receiving multi drug therapy either because of drug interaction or because of drug-disease interactions. Adverse drug reactions due to antimicrobials can be a result of exaggerated response to the known pharmacological effect, immunological reaction to the drug or its metabolite and idiosyncratic reactions due to the drug [2]

In our study, ADRs due to antimicrobials contributed to 0.03% and we observed both cutaneous and systemic ADRs. 77% of patients had cutaneous reactions, other studies has shown 44.2% [3] and 42.6%. [4] The onset of reaction ranged from few hours to 5 days except in case of INH, the manifestation occurred after 10 days of therapy. The commonest type of reaction in our study was maculopapular rash contributing to 61% which was similar to another study.[5] This subsided by 3 days after stopping the drug. Fluoroquinolones being the commonest cause, followed by cefexime, whereas earlier studies have implicated penicillins and sulphonamides. This change in trend could be due to indiscriminate use of flouroquinolones. Vasculitis which is type III hypersensitivity reaction occurred 3 days after ceftazidime and ampicillin+cloxacillin and subsided 4 days after dechallenge.

SJS was seen in 3% of patients who received cotrimoxazole for urinary tract infection, manifested after 2 days of therapy and subsided 6 days after the drug was discintinued. Earlier study[3] has shown 3.62% contribution. Erythema multiforme occurred in one patient who had received INH for the tubercular osteomyelitis involving the right tibia and the reaction required 5 days to subside. 10% of adverse drug reactions was contributed by ofloxacin causing insomnia. This could be due to the frequent use of the quinolones and insomnia being one of the most common central nervous system adverse effects caused by ofloxacin (4.7%)[6] INH known for its hepatic side effects altered the values of liver function tests in 7% of cases and increased SGOT and SGPT

levels in 3% of patients. Fluconazole was administered for the treatment of oral and esophageal candidiasis and it was detected to have caused bradycardia and prolonged QT interval in the patient and the features disappeared when the drug was withdrawn.

Conclusion

In our study antimicrobials contributed to both cutaneous and systemic ADRs. Cutaneous ADRs were more common followed by systemic.

We observed 11 cases of ADRs were due to fluroquinolones implicating widespread and perhaps indiscriminate us similar to other studies[7-11] and use of sulphonamides has been reduced. Fluoroquinolones contributed to 42% of maculopapular rash which subsided in 2-3 days. Interestingly, systemic unwanted effect observed was insomnia due to ofloxacin. Majority of the reactions were probably due to the drug. Thus a study on the adverse drug reactions caused by antimicrobials both old and new needs to be analysed regularly.

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