Analyzing adverse drug reaction patterns in a tertiary care hospital of Dakshina Kannada district: A cross sectional study

Prabhakar Adake[1], Kumar Gourav[2], Roopa P Nayak[3*]

[1]Associate Professor, [2]Post graduate/Tutor, [3]Professor & HOD, Dept. of Pharmacology, Yenepoya Medical College, Yenepoya (Deemed to be University), Mangalore, Karnataka, India

***Corresponding Author: Roopa P Nayak**
Email: roopapnayak@yenepoya.edu.in

Abstract
Objectives: To evaluate which group of drug is causing maximum number of adverse reactions and to evaluate which gender/age group of patient is most vulnerable to adverse reactions.
Materials and Methods: This was a retrospective cross sectional study. This study included ADRs reported to Pharmacovigilance cell of Yenepoya Medical College Hospital from 1st January 2017 to 30th August 2019. A total of 100 ADRs were included. The details of ADRs were collected and data was analyzed using IBM SPSS 23 software. The results are expressed in percentages.
Results: A total of 100 ADRs were evaluated. Nearly 81% of ADRs were due to antimicrobials, which is highest among all other groups of drugs. Parenteral drugs contributed highest ADRs (72%) followed by oral formulations (28%). A maximum number of ADRs were observed in 31–60 years of age group (48%). Both the genders contributed almost equal proportions of ADRs, with female being affected in 52% of cases. Most of the reactions were non-serious (80%) i.e maculopapular rash and itching followed by angioedema while serious reactions were only 20%. Based on causality assessment, the probable cases had a higher incidence (93%), followed by possible (4%) and remaining were certain (3%).
Conclusion: The present study calls for the judicious use of the antimicrobial agents and it should be used only when necessary. Moreover, there should be increase in the awareness among the health care professionals about ADR reporting.

Keywords: Pharmacovigilance, Cross sectional study, Antimicrobial agents, Health care professionals.

Introduction
Adverse Drug Reaction (ADR) is any noxious change which is suspected to be due to a drug, occurs at doses normally used in man, requires treatment or decrease in dose or indicates caution in the further use of the same drug. This definition excludes any trivial, expected side effects and poisoning or overdose. Adverse Drug Event (ADE) is any untoward medical occurrence that may present during treatment with a medicine, but which does not necessarily have a causal relationship with the treatment.[1]

Adverse drug reaction (ADR) is one of the leading causes of morbidity and mortality worldwide. The consequences of ADRs burden on the healthcare system are increased cost of therapy and prolongation of hospitalization. It is therefore, imperative to monitor the safety of medicines.

All the drugs are capable of producing adverse reactions. Whenever a drug is given a risk is taken. One has to look for risk benefit ratio before prescribing. Adverse Drug Reactions (ADR) can be classified into 2 types, expected undesirable effects (type A/Augmented) reactions and unexpected undesirable effects (type B/Bizarre) reactions. Predictable reactions are mechanism based adverse effects. It includes side effects, secondary effects, toxic effects and consequences of drug withdrawal. For example CNS depression produced by barbiturates is predictable in a dose dependent manner. Similarly, hypotension produced by nifedipine is related to dose. Tardive dyskinesia, an extrapyramidal motor disorder associated with use of antipsychotic medications is dependent on the duration of exposure.[2] Unpredictable reactions are based on peculiarities of the patient and not of the drug. It includes allergy and idiosyncrasy.[3] Allergic reactions are mediated by the immune system, that results from prior sensitization to a particular chemical or to one that is structurally similar.[2]

Adverse drug reaction is relatively more common among antimicrobial agent. It can cause local irritancy, systemic toxicity and hypersensitivity reactions. Most of the serious adverse effects of penicillins and cephalosporin are due to hypersensitivity. The antigenic determinants like degradation products of penicillins, particularly penicilloic acid and products of alkaline hydrolysis bind to host protein. Allergic reactions include anaphylactic shock, serum sickness–type reactions like urticaria, fever, joint swelling, angioedema, pruritis and a variety of skin rashes. Like penicillins, cephalosporins may elicit a variety of hypersensitivity reactions, including anaphylaxis, fever, skin rashes, nephritis, granulocytopenia, and hemolytic anemia. Vancomycin can cause irritation to the tissue, resulting in phlebitis at the site of injection. Chills and fever may occur. Hypersensitivity reactions (drug fever, skin rashes) due to tetracyclines are uncommon. Most adverse effects of broad spectrum antibiotics are due to alteration of normal microbial flora causing super infection.[4-6]

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problems. The main aim of Pharmacovigilance Programme of India (PvPI) is to safeguard the health of the Indian population by ensuring that the benefits of use of medicines outweigh the risks associated with its use. The Pharmacovigilance

exercise in India is organized by The Indian Pharmacopoeia Commission (IPC) and conducted by the Central Drugs Standard Control Organization (CDSCO). The Programme is coordinated by the Indian Pharmacopeia commission, Ghaziabad as a National Coordinating Centre (NCC). [7]

The Pharmacovigilance Programme of India (PvPI) was started by the Government of India on 14th July 2010 at All India Institute of Medical Sciences (AIIMS), New Delhi as the National Coordination Centre for monitoring Adverse Drug Reactions in the country for safe-guarding Public Health. In the year 2010, 22 ADR monitoring centres (including AIIMS, New Delhi) were set up under this programme. To safeguard implementation of this programme in a more effective way, the National Coordination Centre (NCC) was shifted from the All India Institute of Medical Sciences (AIIMS), New Delhi to the Indian Pharmacopoeia Commission, Ghaziabad, Uttar Pradesh on 15th April 2011.[8-10]

Many new drugs are being introduced in the country, so there is a need to improve the Pharmacovigilance system in order to protect the Indian population from potential harm that may be caused by the drugs. However, there are numerous issues and problems that have prevented building a robust Pharmacovigilance system. Pharmacovigilance systems are not well-funded and systematized for a vast country like India to serve patients and the public. The data obtained in the Zonal centres from various peripheral centres is often poor and not well-analyzed. There is inadequate research on ADRs in India, so the exact incidence of specific ADRs is unknown. Involvement of healthcare professionals (in rural, urban cities and hospitals) and knowledge and motivation for Pharmacovigilance is negligible.[7]

Therefore this present research topic is selected to know the patterns of ADR collected in tertiary care hospital of Dakshina Kannada district which is helpful to the Physicians in their practice.

Objectives of the Study

1. To evaluate which group of drug is causing maximum number of adverse reactions
2. To evaluate which gender/age group of patient is most vulnerable to adverse reactions.

Materials and Methods

The present cross sectional study was carried out after the approval from Institutional Ethics Committee. The study was conductd from 1st April 2019 to 30th September 2019. A total of 100 (n=100) ADR reports were collected from Pharmacovigilance cell of Yenepoya Medical College Hospital, Mangalore which are reported from 1st January 2017 to 30th August 2019. The details of ADRs like age, gender, suspected drug, type of ADR and causality assessment were noted and data is entered in excel sheet and subjected for statistical analysis. While collecting data, patient identity was kept anonymous.

Statistical analysis

The data analysis was done using IBM SPSS 23 software. Descriptive statistics was applied and results were expressed in percentages.

Results

A total of 100 ADRs were evaluated. Out of 100 ADRs, 52% contributed from women and rest 48 % collected from men (Table 1). A maximum number of ADRs (48%) were observed in the patients of 31–60 years of age followed by 26%, 17% and 9% which were observed in 0-18 years, 18-30 years and > 60 years of patients respectively (Table 2). Nearly 78% of ADRs were due to antimicrobial agents, which was highest among all other groups of drugs (Table 3). Parenteral drugs involved in 72% of total ADRs and remaining 28% by oral formulations (Table 4). Based on causality assessment, the probable cases had a higher incidence (93%), followed by possible (4%) and 3 % of certain (Fig. 1). Around 80% of ADRs were non-serious which includes maculopapular rash and itching followed by angioedema while serious reactions were only 20% (Table 6). Fig. 7 shows characteristics of ADRs observed in patients. Most of patients (61%) presented with maculopapular rash or itching, followed by blisters (9%) and angioedema (6%).

Table 1: Gender wise division of ADRs

Gender	No.
Male	48
Female	52
Total	100

Table 2: Division of ADRs based on age groups

Age Group (YRS)	No.
0-18	26
18-30	17
31-60	48
>60	9

Table 3: Division of ADRs based on Pharmacological classification of drugs

Pharmacological classes		No.
Antimicrobial Agents	Sulphonamides (4)	78
	β-lactam antibiotics (35)	
	Tetracyclins (1)	
	Aminoglycosides (4)	
	Macrolides (1)	
	FQs (15)	
	Anti fungal (3)	
	Antiviral (6)	
	Anticancer drug (1)	
	Antiprotozoal/ Anti-amoebic (2)	
	Others (6)	
Gastro intestinal tract	Drugs on peptic ulcer (4)	4
Autocoids	Histamine and Anti-histaminics (2)	7

	NSAIDs (5)	
Drug acting on CNS	Anti-epileptics (5)	5
Hormones & Related drugs	Corticosteroids (1)	2
	Anti-thyroid drug (1)	
Drugs acting on blood components	Haematinics (1)	1
Miscellaneous drugs	Snake anti-venom (2)	3
	Omnipaque (1)	

Table 4: Division of ADRs based on route of administration

Route of administration	No.
Parenteral	72
Oral	28
Topical	0

Table 5: Division of ADRs based on seriousness

Serious / Non-serious	No.
Serious ADRs	20
Non-serious ADRs	80

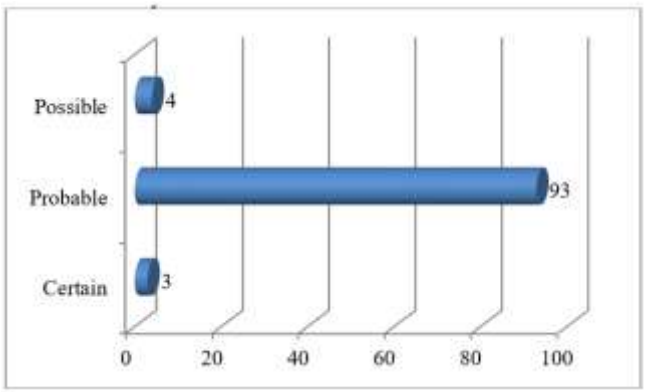

Fig. 1: Division of ADRs based on causality assessment

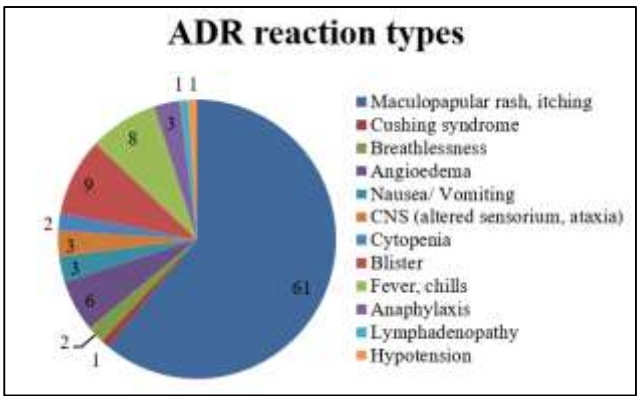

Fig. 2: Division of ADRs based on type of reactions

Discussion

Pharmacovigilance Programme of India (PvPI) is Government of India's flagship health-monitoring programme which collates and analyses drug related adverse events. In 2017-18 NCC-PvPI has received 90,198 Individual Case Safety Reports (ICSRs) through VigiFlow® from various ADR Monitoring Centres (AMCs) enrolled under the umbrella of PvPI. A mobile app "ADR PvPI" for the benefit of all healthcare stakeholders, including common man has been developed indigenously.[11]

In our study, 61% of ADRs were due to involvement of skin and subcutaneous tissue. This finding is similar to the previous study done by Preeti et al and others where maculopapular rashes and itching were the most common reactions.[12] Previous study by R. Jhaj also showed that maculopapular rash is the most common adverse effect.[13] This type of reaction is mainly due to anti microbial agents. The suspected drug was withdrawn in all the cases for the management of the ADRs. Faulty practices like the use of antibiotics in viral infections, too low doses or unnecessarily prolonged duration of treatment and prescribing antibiotics in all fever cases– considered as irrational which actually can do more harm than any benefit.

Moreover, in our study the ADRs were contributed almost equally by both men and women. This finding is similar to the study carried out by Jimmy Jose et al. However, adverse drug reaction was maximum in age group between 30 to 60 which is different from our study findings.[14]

In a similar study conducted by Siraj Sundaran et al. it was found that the drugs most frequently associated with ADRs were antibiotics, antiepileptics and antihypertensives.[15]

The main limitation of our study is small sample size. We could be able to collect only 100 ADRs from our Pharmacovigilance cell. However, effort would be made to include good number of ADRs in future.

Conclusion

The present study calls for the judicious use of the antimicrobial agents and it should be used only when necessary. Moreover, awareness among the health care professionals about ADR reporting is very essential to win the goal of PvPI.

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Conflicts of interest

There are no conflicts of interest.

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