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ADVERSE DRUG REACTION REPORTING

Syeda Zuleqa[1], Fazilath Fatima[2]* and Fariya Azeem[3]

[1]Assistant Professor, Deccan School of Pharmacy,
[2,3]Student, Deccan School of Pharmacy (Affiliated to OU),
Department of Pharmacy Practice, Deccan School of Pharmacy, Dar-Us-Salam, Aghapura, Hyderabad-500001, Telangana, INDIA.

***Corresponding Author: Fazilath Fatima**
Student, Deccan School of Pharmacy (Affiliated to OU), Department of Pharmacy Practice, Deccan School of Pharmacy, Dar-Us-Salam, Aghapura, Hyderabad-500001, Telangana, INDIA.

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ABSTRACT
Adverse drugs reactions (Adrs) are toxic, unintended, and undesirable effects which occur as result of drug treatment. The prescribed drugs may produce undesirable effects along with main effect which leads to an adverse drug reactions. Adverse drug reaction are also known as side effects. Most of the adverse drug reactions are curable. Hence, in order to avoid adverse drug reactions one should take only prescribed drugs. The accuracy of safety evaluation depends particular on the quality of the reporting. Adverse drug reactions (ADRs) are considered as the leading causes of death among hospitalized patients. Spontaneous adverse drug reaction reporting form is essential component and a major tool of the pharmacovigilance system of any country. This form is a tool to collect information of ADRs which helps in establishing the causal relationship between the suspected drug and reaction. As different counties have different forms our aim was to study, analyze the suspected drug and the reaction. The current global network of pharmacovigilance centers, coordinated by the Uppsala Monitoring Centre, would be strengthened by an independent system of the review. This would be considered litigious and important drug safety issues that have the potency to affect public health adversely beyond national boundaries. In this review we will discusss about ADR reporting probability scales, ADR reporting centers, in India, role of pharmacist in ADR reporting.

KEYWORDS: Adverse drug reactions, prophylaxis, drug safety, ADR reporting information, pharmacovigilance.

INTRODUCTION

'A response to a drug which is noxious, undesirable and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function'. The study of ADRs is concern with the field known as pharmacovigilance.

TYPES OF ADVERSE DRUG REACTION REPORTING

1)TYPE-A (Augmented) 2)TYPE-B (Bizarre) 3)TYPE-C (Continuous) 4)TYPE-D (Delayed) 5)TYPE-E (End of Dose) 6)TYPE-F (Failure of therapy)

1. TYPE-A (Augmented)

• Dose dependent, severity increases with the dose.
• Preventable in most part by slow introduction of low dosage. Predictable by the pharmacological mechanisms,
• e.g., hypotension by beta-blockers.

2. TYPE-B (Bizarre)

• Rare, genetically determined, unpredictable, mechanisms are unknown, serious, can be fatal; unrelated to the dose,
• e.g. hepatitis caused by halothane.

3. TYPE-C (continuous)

• Occurs as the result of continuous drug use.
• May be irreversible, unexpected, unpredictable.
• e.g., tardive dyskinesias by antipsychotics,

4. TYPE-D (delayed)

• Delayed occurrence of ADRs, even after cessation of the treatment.
• e.g corneal opacities after thioridazine.

5. TYPE-E (End of Dose)

• Withdrawal reactions. Occurs typically with a depressant drugs.
• e.g.,hypertension and restlessness in opiate abstainer.

6. TYPE-F (Failure of therapy)

• Results from ineffective treatment (previously excluded from analysis according to WHO definition),

• e.g., accelerated hypertension because of inefficient control.[1]

HISTORY

In 1922, there was enquiry into the JAUNDICE associated with the use of SALVARSAN, an organic arsenical used. Public and professional concern about these matters first arise in the late 19th century. Every time we give the drug we take a risk. From the early times, pharmaceutical formulations have been recognized as being potentially dangerous.

SULFANILAMIDE TRAGEDY: In 1937 in USA, 107 people died from taking an Elixir Of Sulfanilamide that contained a Solvent Di-ethylene Glycol. This led to the establishment of Food And Drug Administration (FDA), which was given the task of enquiring into the safety of new drugs before allowing them to be marketed.

THALIDOMIDE TRAGEDY: Major modern catastrophe that changed the professional and public opinion towards medicines was the THALIDOMIDE INCIDENT.[3]

In 1961, it was reported in the West Germany that there was an outbreak of PHOCOMELIA (hypoplastic and aplastic limb deformities) in the new born babies.

The greatest of all drug disaster thalidomide have been introduced and welcome as a safe and effective hypnotic and antiemetic it rapidly became popular for the treatment of nausea and vomiting in early pregnancy.[2]

Pharmacovigilance (**PV** or **Ph.V**), is also known as **drug safety**. It is the pharmacological science relating to *collection, detection, monitoring, and prevention* of adverse effects with pharmaceutical products.**[4]**The etymological roots for the word "pharmacovigilance" is pharmakon and vigilare. As such, pharmacovigilance heavily focuses on adverse drug reactions, which are defined as any response to drug which is noxious and unintended, including lack of efficacy.[5] Medication errors such as overdose, misuse and abuse of drug as well as exposure during pregnancy and breastfeeding, are also of interest, even without an adverse event, because they may result in an adverse drug reaction.[6]

THE NEED OF REPORTING ADVERSE DRUG REACTION:

The need of reporting ADR to reduce the causes of the health damage due to drugs use i.e,

i. Adulteration or inadequate production.

ii. Misuse or abuse of drugs.

iii. Human error such as prescription error or unknown interactions or contra-indication.

Pharmacovigilance is the pharmacological science that deals with the collection, detection, assessment, monitoring and prevention of adverse reactions with pharmaceutical Products. An adverse drug reaction is defined as an effect that is noxious, undesirable and unintended and which occurs at doses used in man for the prophylaxis, diagnosis or the therapy of disease or for the modification of physiological function (Table 1). Pharmacovigilance is essential for safety of patients and also for the rational use of medicines. The people involved in Adverse Drug Reaction reporting are Physicians, Pharmacists, Pharmaceutical companies. Pharmacovigilance will improve patient care, public health in relation to use of medicines, help in risk benefit assessment of medicines and as well as promote effective communication to health professionals and the public about drugs.[7]

Table 1: The following drugs have been withdrawn from the market due to adverse reactions in last few year.

Drug	Year	Reason
Astemizole	1999	Cardiac arrhythmias
Phenylporpanolamine	2000	Stroke
Rapacuronium	2001	Bronchospasm
Troglitazone	2004	Heart attack and stroke
Alatrafloxacin	2006	Liver toxicity
Tegaserod	2007	Heart attack

REPORTING

SCALES

Adverse drug reactions (ADRs) are major cause of morbidity, hospital admission, and even death. Hence it is essential to recognise ADRs and to establish causal relationship between the drug and the adverse event. It is desirable that ADRs should be objectively assessed and presented based on acceptable "Probability Scale." Many causality methods have been proposed to assess the relationship between the drug and an adverse event in a given patient, ranging from short questionnaires to comprehensive algorithms. The causality assessment system proposed by World Health Organization Collaborating Centre for International Drug Monitoring, the Uppsala Monitoring Centre (WHO–UMC), and the Naranjo Probability Scale are the generally accepted and most widely used methods for the causality assessment in clinical practice as they offer a simple methodology. Table 2 summarizes the "Naranjo ADR Probability Scale," which has gained popularity among the clinicians because of its simplicity. Table 3 summarizes the WHO–UMC Probability Scale.[8]

]There are several methods of Pharmacovigilance like Individual Case Safety Reports, Spontaneous Reporting, Cohort Event Monitoring Periodic Safety Update Reports, Electronic Patient Records and Record Linkage. We have The Naranjo Algorithm for Causality Assessment and the Hartwig and Seigels Scale for the Severity assessment.

The Hartwig and Seigel's Scale is.

Mild ADRs are self-limiting and do not contribute to increase in the hospital stay.

Moderate ADRs require therapeutic intervention or hospital admission or the prolonged hospital.[7]

Table 2: Naranjo ADR probability scale—items and score[7]

Question	Yes	No	Don't know
Are there previous conclusion reports on this reaction?	+1	0	0
Did the adverse event appear after the suspect drug was administered?	+2	–1	0
Did the AR improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0
Did the AR reappear when drug was re-administered?	+2	–1	0
Are there alternate causes [other than the drug] that could solely have caused the reaction?	–1	+2	0
Did the reaction reappear when a placebo was given?	–1	+1	0
Was the drug detected in the blood [or other fluids] in a concentration known to be toxic?	+1	0	0
Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0
Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0
Was the adverse event confirmed by objective evidence?	+1	0	0

Scoring for Naranjo algorithm: >9 = definite ADR; 5–8 = probable ADR; 1–4 = possible ADR; 0 = doubtful ADR.

Table 3: WHO – UMC casuality categories.[7]

Causality term	Assessment criteria (all points should be reasonably complied)
Certain	• Event or laboratory test abnormality, with plausible time relationship to drug intake • Cannot be explained by disease or other drugs • Response to withdrawal plausible (pharmacologically, pathologically)
Probable/likely	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Unlikely be attributed to disease or other drugs • Response to the withdrawal clinically reasonable
Possible	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Could also be explained by diseases or other drugs
Unlikely	• Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable • Disease or other drugs will provide plausible explanation
Conditional/unclassified	• Event or the laboratory test abnormality • More data for proper assessment to be needed, or • Additional data under examination

PROCEDURE FOR REPORTING ADVERSE DRUG REACTION

Health care professionals should bear in mind when reporting an ADR that ADR reports are, for the most part, only suspected associations that a drug has caused a particular adverse event. However, in doubtful case it is better to report than not to report.

1. WHAT TO REPORT: The minimal standard information to be provided for proper assessment of ADR case reports are.

1. Patient information
2. Adverse reactions description include laboratory results if available
3. Information related to the suspected drug(s)
4. Information on management of the adverse reactions
5. Information about the reporter.

2. WHO SHOULD REPORT: Submission of a report does not constitute an admission that a health care professional or drug or the product caused or contributed to the ADR in any way as all reports are termed as the suspected. The following should provide reports of any case of the suspected ADRs when encountered to the patient as part of their professional responsibility.

1. All health care professionals including specialists, doctors, dentists, pharmacists, nurses, assistant medical officers, clinical officers, pharmaceutical technicians, pharmaceutical assistants, traditional medicine practitioners and others health care providers.

2. All government and private hospitals, health centres, dispensaries private clinics, private pharmacies and private nursing homes have obligation to report all ADR cases encountered or reported to them by the patients. Incharge of following facilities; government and private hospitals, health centres and dispensaries they are required to nominate a focal person who will coordinate the ADRs collection and reporting within the facility.

3. WHEN TO REPORT: Any suspected ADRs should be reported as soon as possible. Delay in reporting will make reporting not accurate and unreliable. If possible, report while the patient is still in the health facility this gives a chance to the reporter to clear any ambiguity by re-questioning or examining the patient.

4. HOW TO REPORT: Reporters should send accurate information to achieve a better and the efficient program on ADRs monitoring.

1. Send the report in a standardised form for reporting ADRs. The reporting form is self adhesive to postage paid "yellow form"
2. Use a separate form for each patient
3. A completed ADRs case report form should immediately be sealed and mailed within three days or through other reporting centres for onward transmission to the TFDA
4. Reports can also be submitted online by going to website http://www.tfda.or.tz and clicking on "adverse drug reaction reporting" on the bottom-right.

5. WHERE TO REPORT: Report any suspected ADRs for pharmaceutical products to the appropriate channels as follows.

1. Preferably directly to TFDA through online or by post.
2. Via Zonal Drug Information Centres at Muhimbili National Hospital (MNH), Mbeya Consultant Hospital, Bugando Medical Centre (BMC) and at Kilimanjaro Christian Medical Centre (KCMC), for onward transmission to TFDA.
3. Via a focal person in the following health facility; government and private hospitals, health centres, dispensaries for onward transmission to TFDA.

Reporting form

The ADR reporting form is obtained free of charge by;

1. TFDA offices
2. The website of TFDA, downloaded at http://www.tfda.or.tz
3. Zonal Drug Information Centres [NIMS] in Hyderabad.
4. Regional hospital, district hospitals and ADRs focal persons in hospitals, health centres etc[9]

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For VOLUNTARY reporting of Adverse Drug Reactions by Healthcare Professionals

INDIAN PHARMACOPOEIA COMMISSION

(National Coordination Centre-Pharmacovigilance Programme of India)

Ministry of Health & Family Welfare, Government of India

Sector-23, Raj Nagar, Ghaziabad-201002

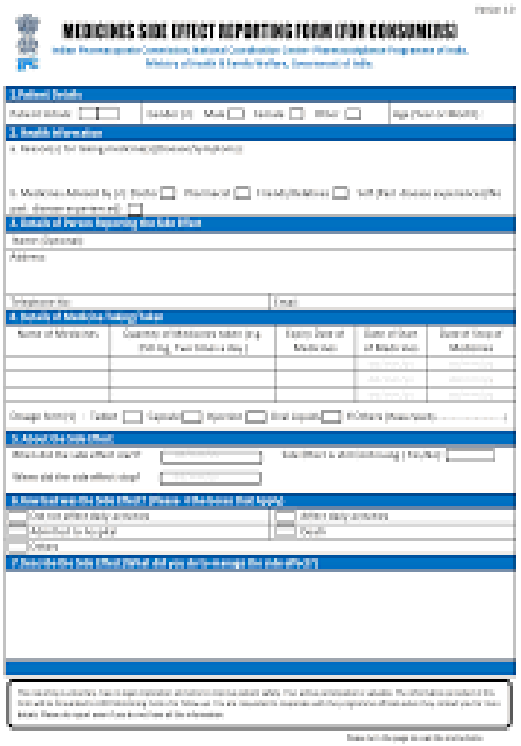
FOR AMC/NCC USE ONLY

A. PATIENT INFORMATION

B. SUSPECTED ADVERSE REACTION

C. SUSPECTED MEDICATION(S)

D. REPORTER DETAILS



ROLE OF A PHARMACIST IN ADR REPORTING

As seen through various studies and the basic concept of pharmaceutical care, pharmacist plays a pivotal role in the identification, detection, prevention and management of drug-drug interactions, drug-food interactions and ADRs. Pharmacist can carry out these activities in

inpatient setting, while taking part in viewing charts during ward rounds and during medication management while dealing with prescriptions. Since pharmacists have a vast knowledge on drugs and the therapeutics, their ability to discover and deal with ADRs is quite important. However, the expertise of pharmacist about a drug, especially if newly marketed, plays important role in ADRs reporting to the authorities which helps in either with drawing the product from market or cause labelling changes. In a community pharmacy, a pharmacist may not have a direct and definite patient list but the patients coming to same pharmacy to refill their prescription gives the pharmacist an opportunity to detect a possible ADR that the patient might be experiencing and can help in the management and the reporting of the said ADR. [10]

CONCLUSION

Research in pharmacovigilance will strengthen clinical pharmacist's role in more clinically valued output. Educational training programs and workshops can clarify and enhance the knowledge of ADR reporting and how causality assessment of ADR is done. HLs will enable the pharmacists to play a prominent role in reporting ADRs and patient safety in the future.

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