PHARMACOLOGY

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ADVERSE DRUG REACTIONS (ADR)

An adverse drug reaction is a "response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease or for the modification of physiologic function."

CLASSIFICATION- Depending on severity of reaction

Minor	Moderate	Severe	Lethal
No treatment/ antidote/ prolongation of treatment needed	Requires treatment/ change in treatment/ Prolongation by at least 1 day	Life threatening/ permanent damage Which Requires intensive treatment	Directly/indirectly contributes to the death of the patient

CLASSIFICATION- Depending on type of reaction

Type A- Augmented

- Exacerbation of pharmacological effect
- Predicted from the pharmacology of the drug
- Dose dependent
- Alleviated by dose reduction
- Detected in clinical trials
- High incidence, less severe
- High morbidity, low mortality

Anticoagulants → bleeding
Beta blockers → bradycardia

Type B- Bizarre

- Hyper sensitivity reaction
- Cannot be predicted
- Not Dose dependent
- Cannot be detected in clinical trials
- Cannot be alleviated by dose reduction
- Low incidence, more severe
- Low morbidity, high mortality

Penicillin → Anaphylaxis
Anticonvulsant → Hypersensitivity

Type C- Chronic/continuous

- Prolonged exposure to a drug
- Dose& time related
- Exact mechanism unknown
- Irreversible, unexpected & unpredictable

Biphosphonates → Osteonecrosis

Type D- Delayed

- Delayed long after drug exposure
- Diagnosis is difficult
- Uncommon reactions
- Due to drug accumulation

Antipsychotics → Tardive dyskinesia
Chemotherapy → Secondary tumors

Type E-End of Use

- Withdrawal syndrome (abrupt)
- Uncommon
- Can be managed by reintroducing & withdrawing it slowly

Phenytoin → Seizure
Steroid → Adrenocortical insufficiency

Type F-Failure of therapy

- unexpected
- Reduction in drug's efficacy
- By drug interaction

Oral contraceptive + other drugs → pregnancy


PREDISPOSING FACTORS
Polypharmacy
Multiple drug therapy can cause ADR
Diseases
Altered physiological function can cause ADR
Age
Paediatrics & geriatrics are more prone to ADR
Drug charachteristics
Certain drugs have narrow therapeutic range
Gender
Women are more prone to ADR due to hormonal impact
Race & Genetic factors
Genetically predisposed individual can have ADR

SOME OTHER CATEGORIES OF ADR:

Side effects:

Unwanted, but unavoidable effects of the drug at therapeutic dose

Toxic effects:

Excessive pharmacologic action due to over dosage or prolonged dose

Secondary effects:

Indirect consequences of primary action of drug

Intolerance:

Appearance of characteristic toxic effects in an individual at therapeutic doses

Idiosyncracy:

Abnormal reactivity to a chemical (due to unique feature of the individual)

Drug allergy:

immunologically mediated reaction towards the drug given.

SOME OTHER CATEGORIES OF ADR:

Photosensitivity:
Cutaneous reaction resulting from drug induced sensitisation to UV radiation

Drug dependence:
Use of drugs for personal satisfaction rather than basic need

Drug withdrawal reactions:
Sudden interruption of therapy cause certain adverse reactions

Teratogenecity:
Capacity of the drug to cause foetal abnormalities when administered to the pregnant mother

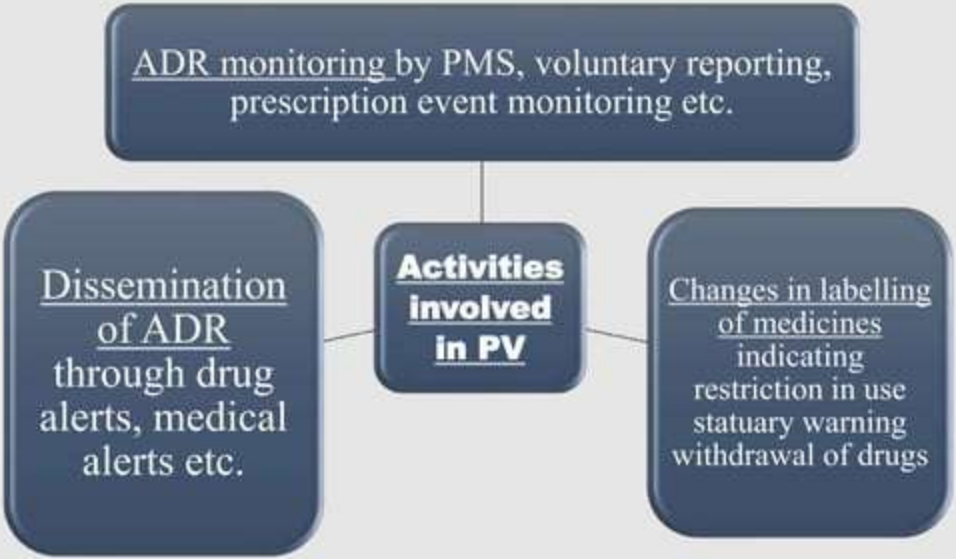
Mutagenecity & Carcinogenecity:
Ability of drugs to alter genes or produce cancer

Iatrogenic:
Functional disturbances caused by drugs, which persist even after withdrawal of drugs

PHARMACOVIGILANCE

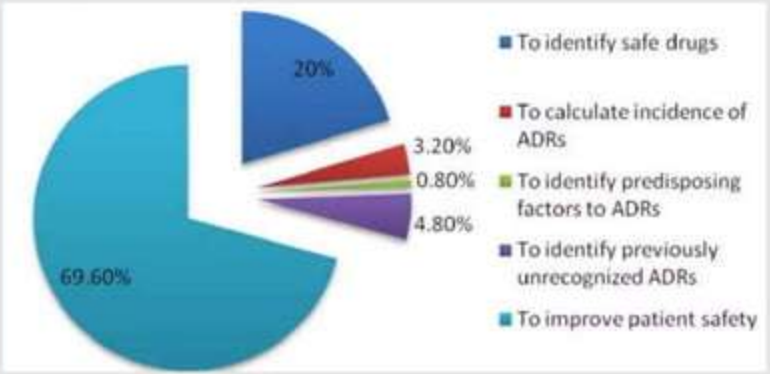
Pharmacovigilance can be defined as the 'science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problems.'

- The **Uppsala Monitoring Centre** (Sweden) is the international collaborating centre.
- In India, the Central Drugs Standard Control Organization (CDSCO) is coordinating the pharmacovigilance programme,
- Under CDSCO, numerous peripheral, regional and zonal monitoring centres have been set up along with a National Pharmacovigilance advisory committee.
- The PV centres collect, communicate and disseminate ADR data by linking with hospitals as well as practitioners
- provide expertise for assessing causality and severity of ADRs by using standard algorithms and rating scales.


ADR monitoring by PMS, voluntary reporting, prescription event monitoring etc.
Activities involved in PV
Dissemination of ADR through drug alerts, medical alerts etc.
Changes in labelling of medicines indicating restriction in use statuary warning withdrawal of drugs

MONITORING OF ADR

NEED:



How can we monitor?

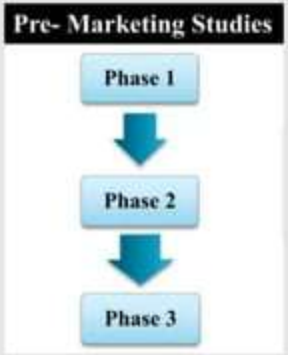
- Patient interview
- Reviewing prescriptions
- Abrupt cessation of medicines
- Obtaining previous medical history

MONITORING OF ADR

METHODS

1. PRE MARKETING STUDIES

- During study in animal models, safety is tested in animal models
- Specific animal studies for carcinogenicity, mutagenecity, teratogenesis, immunotoxicity etc.
- Conducted during 3 phases before drug is being marketed.
- Clinical trials identifies ADRs of frequency 0.5-1.0%



2. POST MARKETING SURVEILLANCE/ STUDIES

SPONTANEOUS ADR REPORTING

- ✓ Health professionals voluntarily submit the ADR
- ✓ Inorder to mitigate the impact of ADR on society

CASE CONTROL STUDIES

- ✓ Individuals affected by ADR is being studied.
- ✓ Both cases & control are investigated for their exposure to possible causative agent

COHORT STUDIES

- ✓ Patient exposed to a particular drug is followed up for ADR .
- ✓ ADR frequencies are compared to unexposed population

3. CAUSALITY ASSESSMENT

- ✓ Method by which extent of relationship b/w a drug and a suspected reaction is established.
- ✓ Once ADR is suspected, assessment starts with collection of all data
    - ✓ Patient demographics
    - ✓ Medication including OTC
    - ✓ Time of onset of action
    - ✓ Duration of onset of action
    - ✓ Treatment of reaction
    - ✓ Outcome of the treatment
    - ✓ Valid reports
- ✓ Assessment is made using different approaches
    - ✓ Opinion of individual experts
    - ✓ Opinion of panel of experts
    - ✓ Formal algorithms like WHO probability scale and Naranjo's algorithm.

Causality is assessed on the basis of:

Temporal relationship	• How the time-sequence of the event is related to drug administration.
Previous knowledge	• Whether the drug is known to produce the event in earlier recipients with a certain degree of consistency.
De-challenge:	• Whether the event subsided on stopping the drug.
Rechallenge:	• Whether the event reappeared when the drug was administered again after a gap during which the event had subsided. • Many times rechallenge is unethical/dangerous, and is not done.

4. COMMUNICATING ADRs

Knowledge about safe and rational use of drug should be provided

- ✓ During basic training of healthcare professionals
- ✓ Through continuous education programmes to health care professionals
- ✓ By specifically designed drug information centres
- ✓ Through packaged inserts as well as patient counselling

5. POSTAL SURVEY METHOD

- Consists of specific drug related questionnaire
- Primarily for ADR monitoring of new drugs
- Asks for details of the drugs, usage, dose, brand, number of patients given treatment
- Common ADRs seen with drug are mentioned at the end of the questionnaire
- Questionnaire, along with a prepaid envelope is sent to the practitioners who are likely to use the drug.

REPORTING OF ADR

WHO CAN REPORT?

- Doctors
- Clinicians
- Pharmacists
- Consumers
- Nurses

WHERE TO REPORT?

- Local / Peripheral centre
- Regional PV centre
- National PV centre
- WHO Collaborating Centres
- Manufacturers

WHAT REACTIONS SHOULD BE REPORTED?

- Serious & life threatening reactions
- Fatal reactions
- Permanent harm/ disabilities
- Increased healthcare costs
- Any reactions to newer drugs
- Newer reactions to any drugs
- Rare & uncommon reactions

REPORTING OF ADR

INFORMATION TO BE INCLUDED

- Patient demographics
- Description of ADR
- Suspected drugs
- Dose, ROA of suspected drug
- Onset of ADR
- Description of ADR
- ADR Management details
- Concomitant diseases
- Current drug therapy details, along with OTC drugs
- Details of the reporter

HOW TO REPORT?

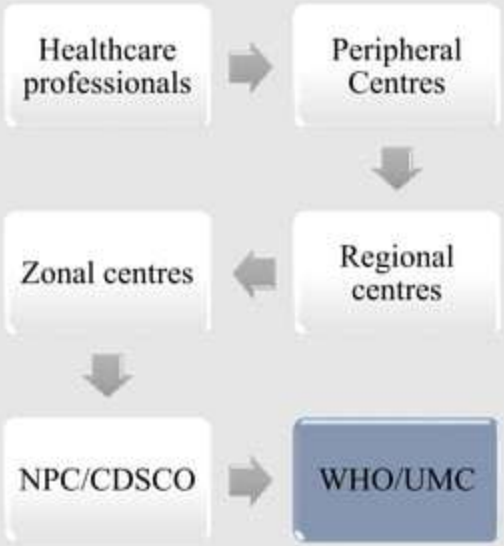
- ✓ Reporting form/ phone call/ vigiflow/ tollfree number/ e-mail/mobile application.
- ✓ Should be on a standard form
- ✓ Use separate form for each patient
- ✓ fill the complete information
- ✓ The completed form must be returned to the nearest ADR Monitoring Centre / National Coordinating Centre
- ✓ Any follow-up information of an already reported ADR can either be filled in a new form or communicated via phone / e-mail

TYPES OF ADR REPORTING FORMS

- **Suspected ADR Reporting Form**
  (For voluntary reporting BY Healthcare professionals)
- **ADR Reporting form for consumers**
  (For consumers)
- **Transfusion Reaction Reporting Form**
  (Haemovigilance Program of India)
- **Medical Device Adverse Event Reporting Form**
  (Materiovigilance program of India)


SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

FATE OF ADR REPORTS




THANKYOU