Pharmaco Vigilance and Adverse Drug Reaction Reporting

A Marthanda Pillai

Ananthapuri Hospitals, Kairali, National Highway, Trivandrum*

ABSTRACT

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Pharmaco vigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug – related problem. Various types of Adverse Drug Reactions are described, its mechanisms explained and the importance of recognizing it is mentioned. Training programmes to help detect ADRs are needed. The method of providing a proper ADR report is provided.

Monitoring of adverse drug reactions is an ongoing, ceaseless and continuing process. Given the limitation of clinical trials in identifying rare and delayed ADR's, and the need for comprehensive safety profiles, the importance of reporting ADR's cannot be over-emphasized. Given the limitation of clinical trials in identifying rare and delayed ADR's, and the need for comprehensive safety profiles, the importance of reporting ADR's cannot be over-emphasized. Most of the time the ADRs mentioned in formularies is based on Western experience. ADR's in Indian population can differ, and it is important that we know ADR's in Indian population and this can be known only if the ADR's are reported.

Keywords: Pharmacovigilance, Adverse drug reactions, Mechanisms, ADR report.

*See End Note for complete author details

Pharmaco vigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug – related problem. The major aims of Pharmaco vigilance are early detection of unknown safety problems, detection of increase in frequency, identification of risk factors, qualifying risks and preventing patients from being affected unnecessarily.

Pharmaco vigilance in India is still in infancy with multiple challenges at varied fronts. It is important that physicians should report adverse drug reactions. Pharmaco Vigilance and adverse drug monitory was started in India in 1982, with Drug Controller of India as chair person. In the first phase All India Medical Institutes like AIIMS, PGI, Chandigarh JIPMER, KGMG Lucknow etc were participating. In the second phase CGHS and other government bodies were included. The third phase with the active involvement of Indian Medical Association general practitioners are being trained to report adverse drug reactions to DCG though IMA.

Adverse Drugs Reactions

Adverse drugs reactions (ADRs), put simply, are noxious, unintended, and undesirable effects that occur as a result of drug treatment at doses normally used in man for diagnosis, prophylaxis and treatment. Although there are many terms indicating the harmful and undesirable effects of drug treatment, the term 'adverse drug reaction' describes them best.

Type of Adverse Drug Reaction

Type – A (Augmented)

Commonest (up to 70%)

1. Dose dependent
2. Severity increases with dose
3. Preventable in most part by slow introduction of low dosages.
4. Predictable by the pharmacological mechanisms
   eg:- Hypotension – Beta – blockers
   - Hypoglycaemia – insulins or oral hypoglycemics
   - NSAID induced gastric ulcers

Type – B (Bizarre)

Rare, idiosyncratic, genetically determined, unpredictable, mechanisms are unknown, serious, can be fatal. Unrelated to the dose

Eg: Hepatitis – Halothane

Corresponding Author:
Dr. A Marthanda Pillai, Sr. Consultant Neuro Surgeon, Ananthapuri Hospitals, Kairali, National Highway, Trivandrum 695 024.
Fax: 0471-2506969 Mobile: 98470 62019. E-mail: ananthapurihri@sancharnet.in

Aplastic anaemia – Chloramphenicol

Type – C (continuous drug use)

Occurs as a result of continuous drug use. May be irreversible, unexpected, unpredictable.

Eg: Tardive Dyskinesias – Antipsychotics
Dementia –Anticholinergic medication

Type – D (Delayed)

Delayed occurrence of ADRs, even after the cessation of treatment.

Eg: Corneal opacities after thioridazine
Ophthalmopathy after chloroquine
Pulmonary / Peritoneal fibrosis by methyserzide

Type – E (End of dose)

Withdrawal reactions. Occurs typically with the depressant drugs.

Eg: Hypertension and restlessness in opiate abstainer Seizures on alcohol or benzodiazepines withdrawal

Type F (Failure of therapy)

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

Accelerated hypertension because of inefficient control

Mechanisms of Adverse Drug Reaction

Common mechanisms are:

1. Abnormal pharmacokinetics due to Genetic factors or Comorbid disease states
2. Synergistic effects between either a drug and a disease or Two drugs

ADR is a Global Problem

In United Kingdom 6.5% hospital admission experience ADR (80%directly due to ADR).4% hospital beds occupancy is due to ADR and annual cost to NHS is $466 million. In USA according to 1998 report 10600Americans die every year due to ADR. This is three times the number of automobiles fatality. It is the fourth highest killer after heart disease cancer and CVA. 39 separate studies found that 3.2 out of 1000 hospitalized patients die due to ADR each year. In India no data is available because of large number of patients, poor doctor – patient ratio, and due to self – medication. Alternative systems of medicine (AYUSH) malnutrition, widespread anaemias, presence of counterfeit drugs and presence of the highest number of drug combinational products in the world.

Why is the number of ADRs so high

The number of drugs prescribed are high, the ever–increasing number of new drugs in the market and the lack of a formal system for monitoring adverse drug reactions

ADR in Special Group of Patients

Children

All suspected ADR in children under 18 years should be reported

Elderly

- Multiple medicines, Metabolism not efficient and
- More sensitive to drugs contribute to more ADR‘s

Pregnancy and Congenital Anomalies

It is vital to report suspected cases during pregnancy. Babies born with congenital anomalies or where pregnancy results in malformed or aborted foetus which is suspected to be due to ADR should be reported with full information about the medication during the pregnancy

Why is ADR Monitoring needed?

Clinical Trials: are funded mostly by pharmaceutical industry. Since clinical Trial is expensive, the period of trial is kept shortest possible using smallest no. of subjects needed for statistical validity. Highest tolerable dose of medication is required to arrive at an answer in reasonable short period. Conclusion of trials based on specific condition which describe age and genders. Life style, ethnicity or co-morbid conditions are either omitted or not considered. Short term studies on longer term illnesses create ethical dilemmas eg: Six month study of values of drugs in treatment of Alzheimer‘s diseases (where diseases progression itself takes 10-15 years.

What Constitutes an ADR REPORT?

1. **All adverse drug reactions to both older and newer drugs:**
   a. Unexpected, severe and serious reactions to established drugs and minor ones to the newer ones
   b. ADRs to established drugs :
      Chloramphenicol induced aplastic anaemia
      ACE inhibitor induced ARF in bilateral renal

artery stenosis.

Antithyroid drugs induced granulocytopenia.

Cisapride induced cardiac rhythm disturbances.

Phenyl propanolamine induced cerebral haemorrhage

c. ADR stonewerrugs :

Upper gastrointestinal haemorrhage to COX - 2 selective NSAIDs.

Hepatitis by insulin receptor sensitizers – eg Trogliatazone. Adrenal suppression and growth retardation by budesonide, Teratogenesis by both newer and older drugs and their safety in paediatric and geriatric population should be reported whenever encountered or systematically studied

2. Previously obscure adverse reactions,

eg : Hallucinations caused by fluoroquinolones

- Constipation by clozapine
- Pedal oedema by selective COX – 2 inhibitors
- Tracheoesophageal fistula caused by conventional NSAIDs
- Hyperthyrodism and hypothyroidism by lithium in the same patient

3. Unexpected therapeutic benefits that can occur to either newer or established drugs and can accidentally be discovered by careful clinical observations,

eg: Lipid lowering effects of paracetamol

NSAIDs reduced the risk of Alzheimer's disease

Amantidine reduced the manifestation of Parkinson's disease.

Minoxidil produced hair growth

Sildenafil caused penile erection

Lithium increased neutrophil counts in the patients with bone marrow suppression

4. Proof positive ADRs (ADRs that not only occur once a drug is given and subside on discontinuation, but reappear on re-administration – positive re–challenge

- Pencillin cephalosporin allergy
- Bronchial asthma by NSAIDs in susceptible patients
- Extrapyramidal disturbances by antipsychotics

5. Experiences of educational value

- Ampicillin induced rashes in patients with Infectious Mononucleosis
- Indians are less prone to the bone marrow suppressing actions of Thiacetazone
- Asians require lesser doses of antipsychotics than the Caucasian in the management of schizophrenia

CONCLUSION

Monitoring of adverse drug reactions is an ongoing, ceaseless and continuing process. Given the limitation of clinical trials in identifying rare and delayed ADR's, and the need for comprehensive safety profiles, the importance of reporting ADR's cannot be over-emphasized. Most of the time the ADRs mentioned in formularies are based on western experience. ADR's in Indian population can differ, and it is important that we know ADR's in Indian population and this can be known only if the ADR's are reported.

END NOTE

Author Information

Dr. A Marthanda Pillai, Sr. Consultant Neuro Surgeon, Ananthapuri Hospitals, Kairali,
National Highway, Trivandrum 695 024.

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