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Review Article

STUDY OF PHARMACOVIGILANCE

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INTRODUCTION:-

Pharmacovigilance was studied to measure the safety of medicine. To measure the adverse effect & problems caused by medicine. Pharmacovigilance is the science & activities relating to the detection, prevention, understanding, assessment of adverse effect or any other medicine related problem. Its aims are to enhance patient care and patient safety and to support public health programmes by providing reliable, balanced information for the effective assessment of the benefit- risk profile of medicines and vaccines.

- **DEFINATION ACCORDING TO WHO:-**

"Pharmacovigilance" (PV) is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problem.

Essentially it is drug safety. It ensures the rigorous testing of clinical drugs to improve patient care & reduce the risk of negative side. It is also called drug safety.

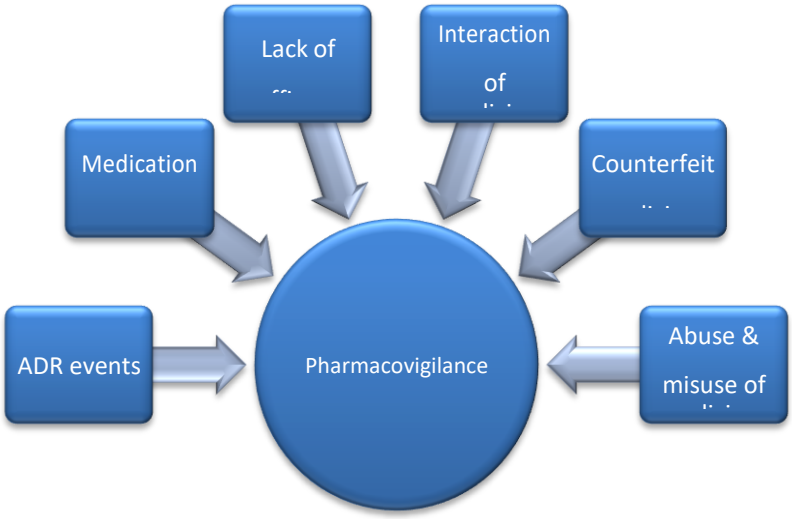
Pharmacon - In Greek- Drug.

Vigilanve – In Latin – To keep watch.

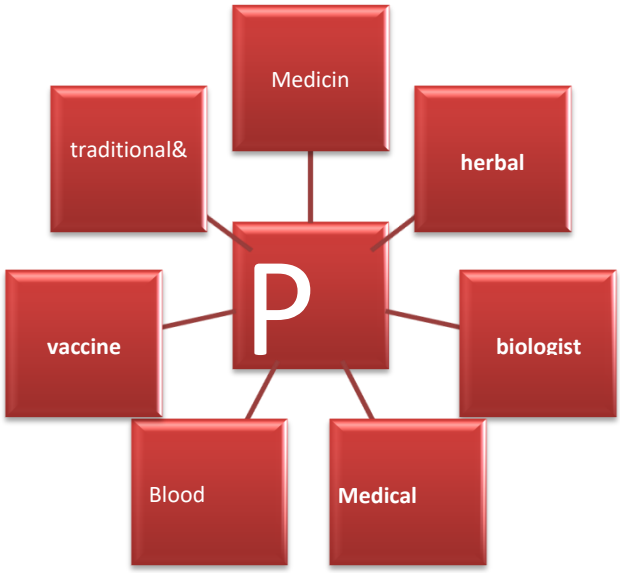
Pharmacovigilance is concerned with the development of science of regulation in the area of drug safety. It is the study of safety of marketed drugs under the practical condition of clinical use in large communities. It can improve the patient care & safety. It can improve the public health & safety& also promote education, clinical training, rational & safe use of medicine.

- **SCOPE OF PHARMACOVIGILANCE:-**

The scope of pharmacovigilance has grown remarkably in recent times & is now considered to include the following domains.



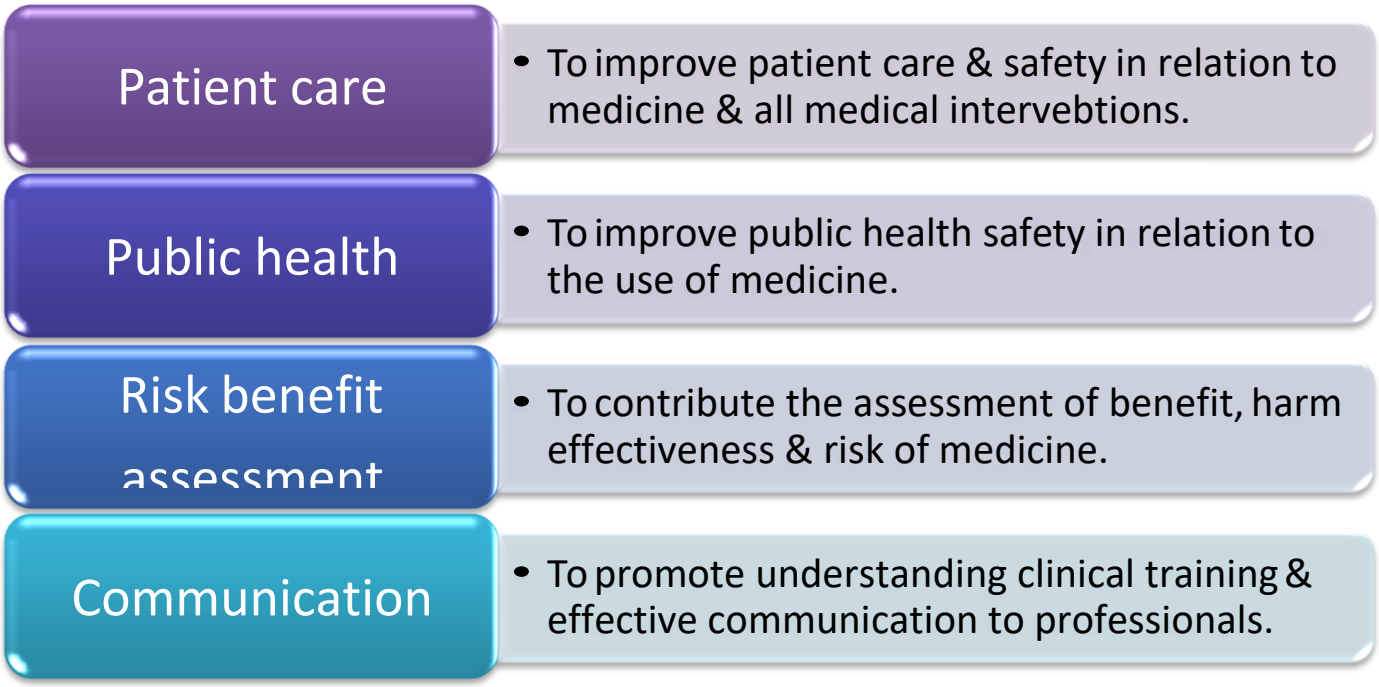
The product under consideration go beyond convectional medicines & also include herbal medicines, other tradition & complementary products, biological vaccines, blood products & possibly medical device.



The pharmacovigilance product considered during the development & use of set of to serve as tools for their monitoring & evaluation. The scope of pharmacovigilance widened allowing for better adjusted information on ADR to the need of regulatory patients for the treatment & managing the ADR's.

Pharmacovigilance should make a shift from the finding new , previously unknown associations & elucidating the frequency of event to analysis of content meaning of ADR for both healthcare professionals & patients.

The concept of pharmacovigilance have developed over time the current playground of pharmacovigilance analysis of reporting of ADR's



- **NEED OF PHARMACOVIGILANCE:-**

a) Insufficient evidence of safety from clinical trials.
b) Medicines are supposed to save lives.
c) To protect people from unnecessary harm.
d) To keep products on the market.
e) To reduce health care expenses.
f) Ensuring public confidence.
g) Promoting rational use of medicine & adherence.
h) Ethical things to do:-
To know of something is harmful to another person who does not know & not telling is unethical.
i) Clinical trials.
j) ADR are expensive.
k) Insufficient evidence of safety form.

- **Their needs :-**

1. **Humanitarian concern :-**

Animal toxicology is often not a good predictor for human effect Evidence of safety from clinical trials is insufficient due to some limitation like limited size, narrow population (age sex specific), narrow indication.

Safe use of medicine :-

It has been suggested that ADR cause 5700 deaths per year in UK.

- **IMPORTANCE OF PHARAMACOVIGILANCE *:-***

  - **Thalidomide tragedy (1961 to 1962) :-**

  The greatest of all drug disasters. Thalidomide has been introduced & effective hypotonic & antiemetic. It rapidly become popular for the treatment of nausea & vomiting in earlier pregnancy. Tragically the drug proved to be a potent human teratogen that caused major birth defects in an estimated 10,000 childrens.

- **OBJECTIVE OF PHARMACOVIGILANCE *:-***

Pharmacovigulance to measure pharmacovigilance drug analysed the data of national drug regulatory authority, international health organization, WHO & clinical practice of pharmacovigilance & other international.

a. To describe the significant characteristics of pharmacovigilance
b. To describe the practice of pharmacovigilance in the pharmaceutical industry.
c. To describe the pharmacovigilance in pediatrics.
d. To describe the drug regulation of pharmacovigilance
e. To monitor the safety if medical products.
f. To create a national wide system for patient safety reporting.
g. To identify & analyse the new signal (ADR) for the report case.
h. To analyse the benefit risk ratio of marketed medication.
i. To support regulatory agency in the decision making process on use of medication.
j. To emerge as a national centre of excellence for pharmacovigilance
k. To collaborate with other national centres for the data management & exchange of information.

- **HISTORY OF PHARMACOVIGILANCE :-**

  - **Thalidomide :-**

  In 1960 thalidomide marketed in 46 countries (hypnotic prevention of nausea in pregnancy) heavily promoted. In 1960 first report on deform infants total more than 20,000 cases.

  - **Sulphanilamide tragedy:-**

  Elixir sulphanilamide was an improperly prepared sulphanilamide medicine that causes mass poisoning in the united state in 1937. It cause death of more than 100 people. The public outré caused by this incident & other similar disasters let to the passing of 1938 federal food, drugs

& cosmetic act. FDA had the authority to review new drug for safety by scrutinizing animal studies & small human voluntary trials for any serious hazardous.

- **Diethylene glycol tragedy :-**

  It was mistakenly used to solubilise sulphanilamide in 1973 & causes death of childrens. In 1962 a new bill amending the 1938 food, drug & cosmetic act to approve new drug & continued marketing of established compounds based on the substantial evidence of the therapeutic efficiency & safety. Around 1980 it become compulsory to record side effect by regulatory authorities. The consequences of this are the post marketing survillance when the product is commercialised as an authorized product over the last 30 years. There have been continued instants or drug recalls or precautionary statements due to the discovery of potential hazards during their use.

  Example:- Practolol & the mucocutaneous syndrome, benoxaprofen syndrome, hepatic disorders or deaths in the ealdely, temafloxacin & haemolytic anaemia, fenfluramine or phentermine & pulmonary.hypertention, terfenadine or cisapride & potential cardiac arrhythemia, cerviastatin (lipobay) & rhabdomyonysis with increased risk of cardiovascular events.

- **LAWS & REGULATION OF PHARMACOVIGILANCE:-**

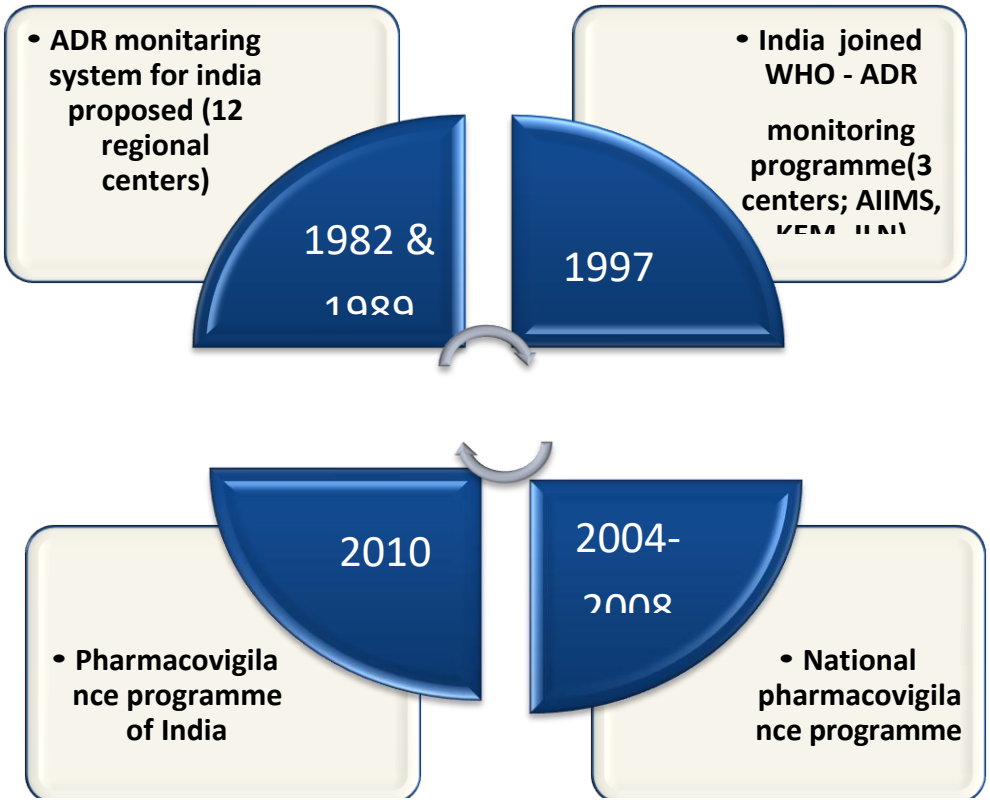
  - **USP:-**

    In 1920 physician concerned about the quality of domestic & imported drugs convened the first USP. The convection wrote guidelines for the information about the formulation of the drug product. In the publication of USP which contain information about drugs including source, physical & chemical properties, test for purity & identification, assay method of storage, category & dosage 1848.

  - **1906 pure food & drug act:-**

    Problem with medicine & foods outraged the public & congress.

- **HISTORY OF PHARMACOVIGILANCE IN INDIA:-**



- **APPLICATION OF PHARMACOVIGILANNCE:-**
  - To improve patient care & safety.
  - To improve public health & safety.
  - To contribute to the assessment of benefit, harm, effectiveness & risk of medicines.
  - To promote rational safe use of medicine.
  - To promote education & clinical training.
  - It can be useful for occupational health surveillance.
  - Useful in national drug policy, clinical practice, regulation of medicines, evaluation of benefit risk balance.

- **STEPS INVOLVED IN PHARMACOVIGILANCE** :-

- **Steps in safety date management are –**
  1. Data collection & verification
  2. Duplicate search
  3. Triage

4. Data entry
5. Case narrative
6. Coding of drug
7. Coding of ADR
8. Case causability assessment
9. Reporting to authorities
   - case processing
   - organization of PV
   - technology of PV

- **Basic steps in Pharmacovigilance case processing**

1. Safety date management.
2. Signal detection for any new altered safety issue.
3. Signal evaluation & making decisions with regard to safety issues.
4. Actions including regulatory to promote public health
5. Informing all concerned parties or stakeholders.

A. Data collection & verification –

Acknowledgement : A valid case needs to have four elements; an adverse event, a reporter, a patient and a drug. Every report needs to be acknowledged, more so the valid reports. Acknowledgement establishes a contact with the reporter for more information whenever required . It builds company image with the stakeholder and also protects from litigation. A consentious reporter may continue to send the same report repeatedly till it is acknowledged, hence this simple action avoids duplication.

B. Duplicate research-

Due to, greater awareness , stringent regulations and multiple reporting sources, duplicate reports is a common phenomenon. Every safety management software has a facility to identify and delete duplicates. . Certain characteristics of a case (sex, age or date of birth, dates of drug exposure, clinical trial code, country, etc.) may be used to identify duplicate reporting. This action is of significance for further processing of the case. The duplicate could actually be follow up information that could alter the seriousness and hence reporting timeline of the case. Missed out duplicates could send misleading information to signal detection systems.

C. Triage –

Collins dictionary defines triage as

a) (Medicine) the principle or practice of sorting casualties in battle or disaster or other patients into categories of priority for treatment
b) (Government, Politics & Diplomacy) the principle or practice of allocating limited resources, as of food or foreign aid, on a basis of expediency rather than according to moral principles or the needs of the recipients

Triage in safety means prioritizing the case for reporting to authorities. An oversimplification of triage would be to report deaths and life threatening unexpected reports in 7 days and other adverse reactions in 15 days as there are also other occasions where expedited reporting is required.

D. Data entry-

A seemingly repetitive and inconsequential step in the process but something that forms the basis of good reporting. The quality of data entry affects the further processing of the case. Details of the four pillars of a valid case have to be reported meticulously. Patient information has to follow the HIPPA code for confidentiality. Reporter information has to clear and detailed enough to be able to contact the person if necessary. Drug identifiers like name, formulation and dose have to be captured correctly. Event report has to be detailed enough for the evaluator to decide on the cause of the adverse event. This would include chronological description of the event or events, nature, localisation, severity, characteristics of the event, results of investigations and tests, start date, course and outcome, concomitant medications and other risk factors .

E. Case narrative -

Provides summary of events to readers who do not have access to original data various groups like case reviewers to decide seriousness, upgrade etc , affiliate companies to triage for their countries, , during preparation of PSURs and other sets. During the course of safety data management, it is seen and used by summary reports and also by regulatory authorities. One should ensure completeness, chronology and sufficient detail in a narrative so that the reader is able to come to a conclusion.

F. Coding of adverse reaction -

This step ensures that everyone is talking the same language and the data can be shared internationally, Most commonly used system is the MedDRA (Medical Dictionary for Regulatory Activities). Use of MedDRA has lead to a global standardization across regulatory agencies, across companies & across countries. This step usually needs oversight by a medically qualified person.

G. Coding for drugs-

Both the suspect drug and concomitant medication have to be coded. The principle is again to be talking the same language across countries, companies and regulatory bodies. Most common dictionary is the WHO Drug Dictionary enhanced. This is provided as a product by the Upsala Monitoring centre of the WHO. Entries are updated 4 times a year. The majority of entries refer to prescription-only products, but some over-the-counter (OTC) preparations are included. The dictionary also covers biotech and blood products, diagnostic substances and contrast media. For chemical and therapeutic groupings the WHO drug record number system and ATC classifications are considered.

H. Casuality assessment –

Non spontaneous case reports usually indicate whether an adverse drug reaction is suspected due to the administered drug. In these circumstances and even otherwise, a causality assessment is required to be conducted. Various approaches have been developed for the structured determination of the likelihood of a causal relationship between drug exposure and adverse events.

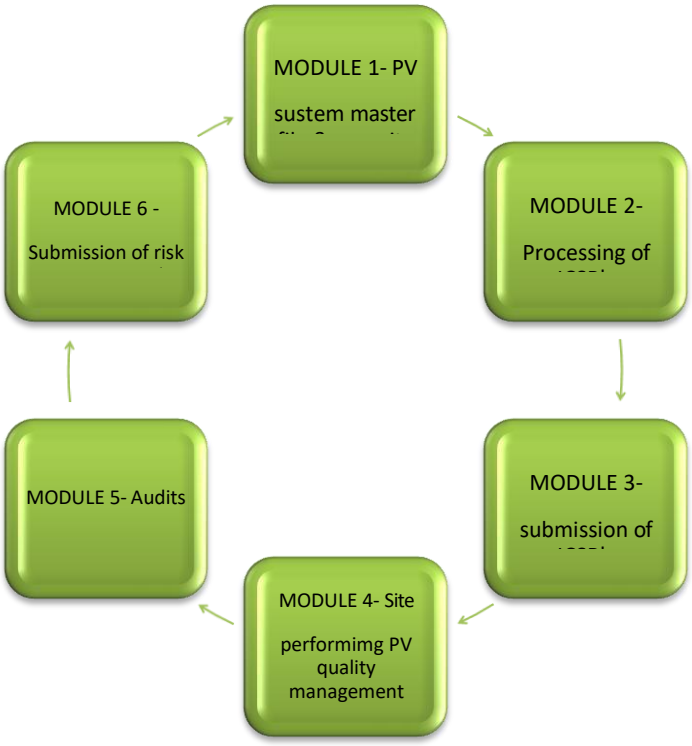
These systems are largely based on following considerations

a) the chronology or association in time (or place) between drug administration and event
b) current knowledge of nature and frequency of adverse reactions due to the suspect molecule; or the pharmacology
c) medical or pharmacological plausibility based on signs and symptoms, laboratory tests, pathological findings, mechanism of action
d) .likelihood or exclusion of other causes for the same adverse events; often the disease condition or concomitant medication.

I. Timeline reporting to authorities -

This is the end goal for which all the above has to be done in a timely manner. The reporting could be by sending data back to the sponsor or by a click of a button based on the software used. The latter will provide an extra couple of days for case processing. Safety data management is the most basic step in pharmacovigilance. This is often outsourced so that internal company resources can focus on the domain related, mentally stimulating activities like signal detection, regulatory responses, information to stakeholders.

- **GUIDELINE OF PHARMACOVIGILANE**



- **ICH guideline of PV :-**

It can be divided into 4 categories –

1. **Q (Quality guideline) :** it include stability, impurity, testing, GMP.
2. **S (Safety guideline) :** it include carcinogenicity, genotoxicity, reprotoxicity.
3. **E (Efficacy guideline) :** it include clinical pharmacogenomics.
4. **M (Multidiciplinary guideline) :** it include medical dictionary for regulatory activities, electronic standards, non-clinical safety studies, common technical documents.

- **CONCLUSION OF PHARMACOVIGILANCE**

For all medicines there is a trade-off between the benefits and the potential for harm. To minimize the harm, it is necessary that medicines of good quality, safety and efficacy are used rationally, and that the expectations and concerns of the patient are taken into account when therapeutic decisions are made. To achieve, this is to serve public health, and to foster a sense of trust in patients in the medicines they use that would extend to confidence in the health service in general

The discipline of pharmacovigilance should be developed considerably day by day, and it remains a dynamic clinical and scientific discipline. It has been essential to meet the challenges of the increasing

range and potency of medicines (including vaccines), which carry with them an inevitable and sometimes unpredictable potential for harm.

The risk of harm, however, is less when medicines are used by an informed health profession and by patients who themselves understand and share responsibility for their drugs. When adverse effects and toxicity appear – particularly when previously unknown in association with the medicine – it is essential that they should be analyzed and communicated effectively to an audience that has the knowledge to interpret the information. There is a realization that drug safety is more than the monitoring, detection and assessment of ADRs occurring under clearly defined conditions and within a specific dose range. Rather, it is closely linked to the patterns of drug use within society. Problems resulting from: irrational drug use, overdoses, polypharmacy and interactions, increasing use of traditional and herbal medicines with other medicines, illegal sale of medicines and drugs of abuse over the Internet, increasing self medication practices, substandard medicines, medications errors, lack of efficiency. This is the role of pharmacovigilance.

- **REFERENCE BOOKS**

1. Textbook of Pharmacology, Nirali publication by S.K Gupta. Pg no- 4.3 to 4.4
2. Textbook of Pharmacovigilance Practical, Page No – 99,102-110
3. Strom B. Pharmacoepidemiology, 4thEdition 2005. Chichester, UK.; Page No - 137