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A COMPREHENSIVE STUDY OF PHARMACOVIGILANCE.

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ABSTRACT:

Pharmacovigilance is defined by WHO as the science and activities relating to the detection, assessment, understanding and prevention of the adverse effects of drugs or any other possible drug related problems. Adverse drug reactions (ADRs) are ranked as top 10 leading causes of mortality and morbidity in the world. Pharmacovigilance is concerned about evaluating and monitoring the safety of medicine in clinical practice to improve patient's safety. Pharmacovigilance promotes safety and efficacy of the drug. Pharmacovigilance is concerned about evaluating and monitoring the safety of medicine in clinical practice to improve patient's safety. Pharmacovigilance promotes safety and efficacy of the drug. The preliminary essential steps of pharmacovigilance is the reporting of suspected adverse drug events. PV evidence of medicine related problems like poor quality drugs, treatment failure, drug interaction. The Pharmacovigilance exertion in India is organized by The India Pharmacopoeia Commission and conducted by the Central Drugs Standard Control Organization (CDSCO). The fundamental aim of PvPI is to collect data, method, analyze it and provide necessary interventions to Health care professionals to minimizing the potential risks associated with the drug or blood and blood products. Pharmacists contribute to the drug safety by preventing, identifying, documenting, reporting of ADRs. It plays a key role in ensuring that Patients receive safe drugs. Our knowledge of a drug's adverse Reactions can be increased by various means, including spontaneous, reporting intensive monitoring and database studies.

KEYWORDS: Pharmacovigilance, importance, PvPI. Programme in India. ROLE OF PHARMACIST. pharmacovigilance spontaneous reporting, Transparency.

INTRODUCTIONS:

Pharmacovigilance is defined by WHO as the science and activities relating to the detection, assessment, understanding and prevention of the adverse effects of drugs or any other possible drug-related problems.

These adverse drugs reactions (ADRs) not only add to suffering of patients but also increase morbidity and mortality along with a financial burden on society.

Pharmacovigilance is an important and integral part of clinical research.

Both clinical trials safety and post marketing pharmacovigilance are critical throughout the product lifecycle. Pharmacovigilance is “defined as the pharmacological science relating to the detection, assessment, understanding and prevention of adverse effects, particularly long term and short term adverse effects of medicines.” Pharmacovigilance is still in its infancy in India and there exists very limited knowledge about the discipline.

PV is an important and integral part of clinical research [2]. The under-reporting of adverse drug reactions (ADRs) is the major setback worldwide which may be attributed to the lack of time and report forms. There is a need to monitor the effects of drugs before and after it's successfully tested and launched in the market. Pharmacovigilance involves monitoring and assessing the quality of drugs, detection and preventing of any adverse effects of drugs. Pharmacovigilance involves

evaluating information provided by health care providers, pharmaceutical companies and patients in order to understand the risks and benefits involved with a particular drug.[3]

CONCEPT OF PHARMACOVIGILANCE:

Definition, Objective, Types, components of pharmacovigilance.

Definition Pharmacovigilance –

Pharmaco +vigilance

Derived from greek

Pharmaco-Medicine

Vigilance -To watch

The process of paying and close and continuous attention.

“Pharmacovigilance is the science and activities relating to the Detection, assessment , understanding and prevention of adverse drug reaction or any other possible adverse drug related problems.”

Objective of Pharmacovigilance:

- To improve patient care safety.
- To improve Public health and safety.
- Benefit risk analysis.
- To promote understanding education and clinical training.

TYPES OF PHARMACOVIGILANCE:

- a) Case control study (Retrospective study)
- b) Prospective study (cohort study)
- c) Population statistics
- d) Intensive event report .

Components of Pharmacovigilance:

- a. Adverse event Case management including excited reporting.
- b. Aggregate reporting
- c. Signal intelligences
- d. Risk management

NEED FOR PHARMACOVIGILANCE:

1: Humanitarian concern - Insufficient evidence of safety from clinical trials Animal experiments Phase 1-3 studies prior to marketing authorization.

2: Medicines are supposed to save lives Dying from a disease is sometimes Unavoidable; dying from a medicine is unacceptable.

3: ADR-related cost to the country exceeds the cost of the medications themselves. 4: Promoting rational use of medicines and adherence.

5: Ensuring public confidence.

Pharmacovigilance Programme In India:

Pharmacovigilance Programme of India (PvPI) The Central Drugs Standard Control Organization (CDSCO), Directorate General of Health Services under the aegis of Ministry Of Health & Family Welfare, Government of India in association with Indian Pharmacopeia Commission, Ghaziabad is initiating a nation-wide Pharmacovigilance Programme for Protecting the health of the patients by promising drug safety.

Ghaziabad is initiating a nation wide Pharmacovigilance programmed for protecting the Health of the patients by promising commission Ghaziabad as a National Coordinating centre (NCC). In the year 2010,22 ADR Monitoring centers including AIIMS, New Delhi was set up under this programmed.

Mission-Safeguard the Health of the Indian Population by ensuring that the benefits use of medicine Outweigh the Risk associated with its use.

Vision-To improve safety and Welfare in Indian Population by monitoring the Drug safety and thereby Reducing the Risk associated with use of medicine.

PvPI is one of the integral part of safety program. The fundamental aim of PvPI is to collect Data, method, analyse it and provide necessary interventions to Health care professionals to Minimizing the potential risks associated with the drug or blood and blood products or Medical devices thereby it ensures the safet

Pharmacovigilance Programme of India (PVPI)

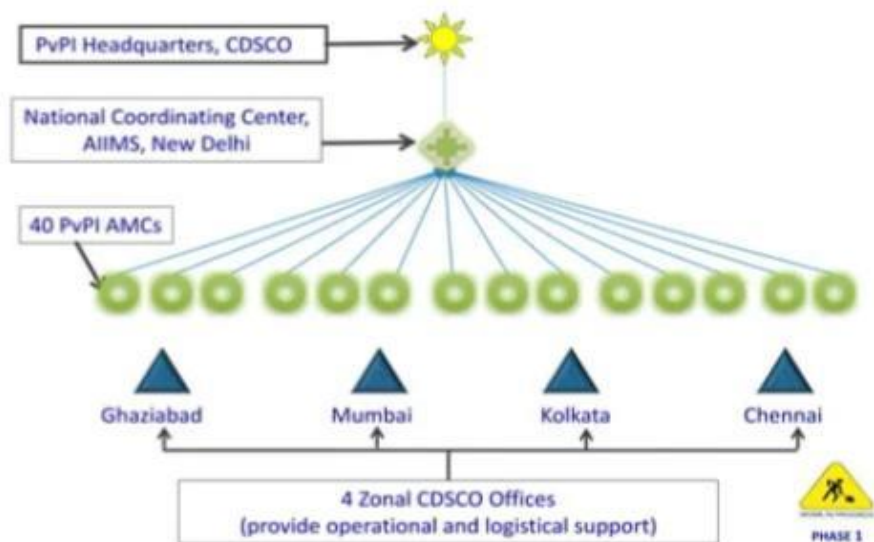


Fig 1: Pharmacovigilance Program of India

Objective:

1. To create a nation wide system for patient safety reporting
2. To identify and analyze the new Signal (ADR) from the reported cases.
3. To analyses the benefit-Risk ratio of marketed medications.
4. To generate the evidence based information on safety of medication.

IMPORTANCE OF PHARMACOVIGILANCE:

When a pharmaceutical drug is introduced in the market there are still a lot of things that are unknown about the safety of the new drug. These medicines are used by various patients for different diseases who might be using several other drugs and must be following different traditions and diets which may adversely affect the impact of medicine in them. Also the same medicine might differ in the manner of their production and ingredients. Additionally adverse drug reactions might also occur when drugs are taken along with traditional and herbal medicines which should be monitored through pharmacovigilance.

In some cases, adverse drug reactions of certain medicine might occur only in one country or region. To prevent all undue physical, mental and financial suffering of patients, pharmacovigilance proves to be an important monitoring system for the safety of medicines in a country with the support of doctors, pharmacists, nurses and other health professionals of the country.[16]The importance of pharmacovigilance is as follows.

- Safety monitoring of medicinal products
- Pharmacoepidemiological studies
- Clinical trials
- Case reports
- Developing case serie

- Analysis of case series
- Use of data mining to identify product -event combination
- Spontaneous reporting [16]

Steps In Pharmacovigilance Programe:

1. Finding the risk of a drug
2. Clinical trials
3. Pharmacoepidemiological study
4. Case report
5. Developing case series
6. Analysis of case series
7. Use of data mining to identify product- event combination
8. Spontaneous reporting.

ACTIVITIES IN PHARMACOVIGILANCE OPERATIONS:

- Case Registry
- Triage
- Registry
- Enrollment
- Processing
- Data Entering
- Coding
- Labelling

Medical Review:

- Serious Case Medical Review
- Non Serious Listing Review
- Aggregate Report Review

Aggregate Reports:

- Analysis And Creation of IND/NDA Reports
- Analysis And Creation of Pader Reports
- Analysis And Creation of Psur & Bridge Reports

PARTNERS IN PHARMACOVIGILANCE :

A complex and vital relationship exists between wide ranges of partners in the practice of drug safety monitoring. Sustained collaboration and commitment are vital if future challenges in pharmacovigilance are to be met in order to develop and

flourish.

- Government
- Industry
- Hospital and academia[7]
- Poison information centers
- Health professionals[8,9]
- Patients
- Consumers
- Media
- WHO

ROLE OF PHARMACIST:

1. Effective and safe pharmacological treatment process requires a team work of the patient and healthcare professionals. Pharmacists and nurses plays a crucial role in monitoring and identification of drug related problems; thus maintain safe use of medicines.
2. Pharmacists contribute to the drug safety by preventing, identifying, documenting, and Reporting of ADRs.
3. To promote rational use of medicines by identifying whether the patients receive Medicines appropriate to their clinical needs, in doses that meet their own individual Requirements, for an adequate period of time, cost effective etc.
4. Pharmacist plays a vital role in medication safety monitoring.
5. Pharmacists can assure a positive environment to the patients in minimizing the Medication errors, improve patient safety and quality of life during the counselling Session.

ADVERSE DRUG REACTIONS REPORTING:

When the adverse reaction to drugs is potentially serious or clinically important, all health care workers including doctors, pharmacists, nurses and other health experts are requested to clarify it. It is necessary to report an adverse drug reaction to pharmacovigilance.

SPONTANEOUS REPORTING SYSTEM:

1. Regionalization
2. Repossession of further data
3. Access to all important pre and post marketing information
4. Detailed drug utilization data.
5. Standardized Evaluation of causality and significance
6. Encouragement

Documentation of ADRs:

The pharmacovigilance curriculum conveyed worldwide motivate that all suspected drug-Related adverse events should be outlined. It takes interests on reports of the following.

A. Every adverse effect suspected or occurred by new drugs and drugs of current issues.

B. Documentation of various drugs that cause ADRs, which include death, life-threatening Conditions, disability, hospitalization and congenital Abnormalities.

The other facts related to adverse events should be informed within eight days. (Bates et al. 1995: Classen et al 1997). The ADR form can be collected through any pharmacovigilance centre. After reviewing the form, the centre

forwards it to the regional centre and after that, it is propelled to the zonal centre (Goldman 1998: Palaian et al. 2006: Ravi Shankar et al. 2010). The details are then statistically inspected and forwarded to WHO-Uppsala Monitoring committee (UMC).[12]

PROCEDURE FOR REPORTING ADRs.

It is the first duty of any pharmacovigilance centre to report all suspected adverse events of the drug if found. Information regarding ADRs that should be reported and tabulated.

Elements In ADR Reporting	Necessary Information	Others
What should be reported	Adverse reaction of drugs	Adverse reaction of drugs
Who can report	Doctors, Pharmacists, Nurses, Staff	All government and private hospitals
When it can be reported	Any adverse reaction if noticed	--
How to report	Through completely filled yellow form	--
Where it can be reported	Complete field ADR from should be submitted to PvpI.	--

Monitoring of ADRs:

ADR monitoring is the practice of continuously monitoring the undesirable effects caused Using any drug. Pharmacovigilance plays an imperative impersonation in monitoring ADRs.[13]

It is inherent for pharmaceutical regulators to screen their pharmaceutical products in the market and record if any suspected adverse reactions are identified. ADRs can occur by use of various pharmaceutical products, herbal drugs, cosmetics, medical devices, biological etc. Introducing this monitoring procedure intends at warranting that patients to receive safe and beneficial medicinal products. {Karch and Lasanga 1997}.

If any of the adverse events are not stated, it may result in noxious and serious effects of remedial products. Thus properly conducting ADR monitoring programs will help to reduce The harmful effects of therapeutic products.

Benefits of ADR monitoring:

An ADR monitoring and reporting program can furnish following benefits:

1. It caters information about quality and safety of pharmaceutical products.
2. It initiates risk-management plans.
3. It prevents the predictable adverse effects and helps in measuring ADR adherence.
4. It instructs health care team i.e., patients, pharmacists and nurses about adverse drug effects and creates awareness regarding ADR.

The main objective of ADR monitoring is to disclose the quality and frequency of ADRs and To identify the risk factors that can cause the adverse drug reaction. [14]

Serious Adverse Event:

A serious adverse event (SAE) in human drug trials are defined as any untoward medical Occurrence that is caused at any dose

- (a) Results in death
- (b) Is life threatening
- (c) Require in-patient hospitalization
- (d) Prolongation of existing hospitalization
- (e) Causes congenital anomaly/birth defect.[11]

Investigators in human clinical trial are obligated to report these events in clinical study Reports. Research suggests that these events are often inadequately reported in publicly Available reports.[15]

Future aspects of pharmacovigilance in India.

With more and more clinical trials and other clinical research activities being conducted in India, there is an immense need to understand the importance of pharmacovigilance and how It impacts the life cycle of product. Given this situation, the DCGI should act quickly to Improve pharmacovigilance so as to integrate good pharmacovigilance practice ito the Processes and procedures to ensure regulatory compliance and enhance clinical trial safetyAnd post marketing surveillance. A properly working pharmacovigilance system is essential if Medicines are to be used safely. It will benefit all parties including health care professionals, Regulatory authorities, pharmaceutical companies and the consumers. It helps pharmaceutical Companies to monitor their medicines for risk and to devise and implement effective risk .Management plans to save their drugs in difficult circumstances.

The following proposals must be followed:

- Building and maintaining a robust pharmacovigilance system
- Making pharmacovigilance reporting mandatory and introducing pharmacovigilance Inspections
- High-level discussions with various stake holders
- List all new drugs/ indications by maintaining a standard data base for every Pharmaceutical company.
- Collaborating with Pharmacovigilance organizations in enhancing drug safety with Advancements in information technology there has been the emergence of new Opportunities for national and internationa.
- Building a network of pharmacovigilance and pharmacoepidemiologists in India.

Developments:

- Drug safety information must serve the health of the public.
- Education in the appropriate use of drugs, including interpretation of safety information, Is essential for public at large, as well as for health care providers.
- All the evidence needed to assess and understand risks and benefits must be openly available.
- Innovation in drug safety monitoring needs to ensure that emerging problems are promptly recognized and efficiently deals with and that information and solutions are effectively communicated.

Phase of clinical trial:

“Clinical research is a branch of Healthcare science that determine the safety and effectiveness of Medication for, devices, diagnostic product and treatment regimens intended for human use.”

Definition and phase of clinical trials

Definition-A clinical trial is defined as prospective study comparing the effect and value of intervention (s) Against a control in human beings.

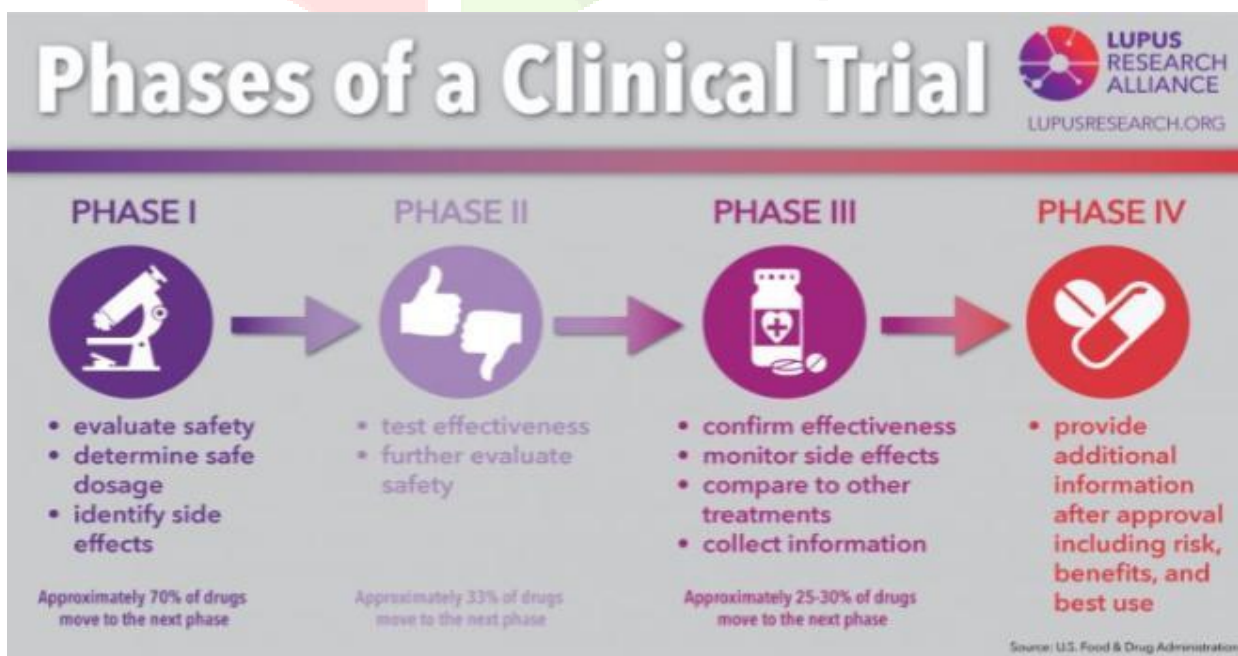


Fig 2: Phase of clinical trial

- **Phase 1:** his phase typically consists of 50 to 100 healthy volunteers. During phase 1, researchers assess the drug's safety, determine the side effects, and evaluate how the drug should be taken.
- **Phase 2:** Typically, 100 to 300 patients with the condition for which the medicine, device, product, or treatment has been developed participate in this next phase. Researchers look to assess the short-term safety and effectiveness of the drug, find the dose at which it works best with the least side effects, and conduct a small-scale placebo comparison.
- **Phase 3:** In phase 3, the pool of volunteers must be must larger. Typically, between several hundred and several thousand patients participate, so researchers can confirm the drug's safety and effectiveness and compare the new drug to other compounds (e.g., a placebo or other therapies).
- **Phase 4:** Finally, after the drug is approved researchers look to study the effectiveness of The drug in a wide variety of patients as well as monitor the safety in a large group and Enable the development of new uses for the compound. These studies often involve Thousands of patients and can inform future research and development.

FUNCTION OF CENTRAL DRUG STANDARD CONTROL ORGANIZATION:

- a) It is headed by Drugs Controller General Of India.
- b) Approval of new drug and clinical trial.
- c) Import Registration and licensing.
- d) It responsible for standard of Drugs, Clinical trials cGMP.
- e) It responsible for Market Authorization.

Function of Drug Controller General of India:

- Preparation and maintain of National reference standard.
- To bring about the uniformity in the enforcement of the Drug and Cosmetics act.
- Training of Drug Analysis deputed by State Drug Control Laboratories and other Institutional analysis of Cosmetics received as survey sample from CDSCO.

GOOD CLINICAL PRACTICE:

“Good clinical practices are an international ethical and scientific quality standard for designing recording and reporting trials that involve the participation of human subject.”

Objective and scope of “ICH-Good clinical

Objective:

- Protect the patient.
- Avoid trial duplication (saving, time, money, resource).
- To provide a unified standard for the EU, Japan and the US to facilitate the mutual acceptance of clinical data by regulatory authorities in these jurisdictions.

Scope:

- Improve ethical awareness.
- Cost effectiveness of research development.
- Public safety.
- Data recognition and marketing structure.

Clinical Trial Application:

A clinical trial application provides comprehensive information about the investigational medicinal products (s) and planned trial, enabling regulatory authorities to assess acceptability of conducting study.

CONCLUSION:

Pharmacovigilance looks at all available information to assess the safety profile of a drug. Pharmacovigilance should also take the benefit of the drug in account. Pharmacovigilance Required for systematically identifying and correlating drugs and side effects and taking Corrective actions.

Pharmacovigilance act as a safeguard to the public health regarding the use of medicine. PV promotes medicine safety by collecting and managing the ADRs, medication errors. It ensures quality, safety and efficacy of all marketed products. It plays an important role in drug regulation as it collects adverse event information, assessment of clinical data and reporting of clinical data.

Pharmacovigilance programme in India will collect data, method, analyze the adverse effects and make necessary interventions to minimize the risks related to the medicine. The major challenge of PvPI is the underreporting of ADR. Pharmacist promote rational use of drugs by monitoring, identifying and evaluate the ADR and other drug related problems. Pharmacist provides communication materials to the health care professional and public.

Pharmacovigilance is the only way to ensure the safety of the drug throughout the life cycle. It is very much crucial as the clinical trials have limitation to detect the rare and very rare ADRs. The knowledge and information available regarding safety of any drug is very much important to take appropriate decision by drug regulators to safe guard public health. Health care professionals are the main reporters of the ADRs. However there are high percentages of under-reporting reported globally. It is the major challenge of today. In spite of those limitations, spontaneous reporting system remains as a most widely used method to report ADRs and is able to generate signal of rare and very rare types of ADRs. If all the health care professionals take ADR reporting as an ethical obligation and a major responsibility, we can make our world safer than what is today. It is likely that many stakeholders would benefit from the creation of a de-identified and open

patient EHR database. For example, this active pharmacovigilance system would assist pharmaceutical companies in their risk profile construction and could be used to collect data on their products within widely diverse clinical contexts including those involving patients with comorbidities,

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