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A PERSPECTIVE STUDY OF PHARMACOVIGILANCE

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ABSTRACT:
The WHO (World Health Organization) defines PV (Pharmacovigilance) as "the study of medicines and procedures applicable towards the identification, evaluation, feting , evaluation, preventative measures against side goods or any other illness. "Fresh issues relating to medicines. It's essential to making sure that cases get safe specifics. Our understanding of a drug's side. There are several ways to boost revulsions, including robotic reporting, close observation, and database exploration. New procedures scientific and nonsupervisory fabrics are being erected with the intention of enhancing pharmacovigilance. In terms of regulations, two pivotal factors are enhanced patient involvement and translucency. Pharmacovigilance encourages the responsible and safe use of specifics. One pivotal aspect of pharmacovigilance is the unplanned exposure of responses to medicines. Adverse drug reaction (ADRs) are, nonetheless, significantly underreported. In developing nations, adverse drug responses have grown to be a significant issue. Understanding pharmacovigilance could serve as the foundation for enterprise meant to increase ADR reduction and reporting rates.
Keywords : Drug Safety, Adverse Drug Reaction, Clinical Trails, Drug Monitoring

INTRODUCTION:

Pharmacovigilance is especially important for new drug because the information obtained from clinical trials does not have sufficient information to cover all aspects of drug safety. India, a largest country more than 1.2 billion people with different ethnicities, different diseases, genetic difference and different healthcare system, need a reliable and standardized process to collect information on adverse events and ensure patient health. An important and important aspects of clinical research is pharmacovigilance. Safety in post-marketing clinical studies (often referred to as phased studies or post-marketing studies) is important throughout the lifecycle of the product. Based on the number of recent removals of important substances, the pharmaceutical sector and many international RA has raised standards. World Health Organization defines pharmacovigilance as "pharamacovigilance" and methods related to their discovery".

"The evaluation, identification and prevention of adverse reactions due to drugs, or pharamacovigilance, is term that refers to system and orders by which drugs are collected and regulated during the prescription and life of the drug The word "pharmacovigilance" consists of two words. The Greek word pharamkon (medicine) and the latin word vigilare (hour)mean to warm.[12]

MODULE 1

Clinical Research

Clinical trials are procedures developed to assess the security and effectiveness of a specific medication or equipment on human subjects 1 - 2. As per the World Health Organization, a clinical trial is a study that refers people to various health services to evaluate the benefits of a healthy diet. Clinical trials are often conducted without safety and quality data to inform the

drug or product. It was clear from the beginning that the analysis was based on the quality of the product, which affects all stages of the creative process. Researchers first select patients or volunteers. Work in groups for 4-6 tests. When information is safe and accessible, patient numbers increase. Additionally, clinical studies have been conducted in many countries. New drug testing is usually done in four stages. Each stage of the drug approval process can be considered a separate trial. Clinical trials are generally divided into five phases. Pharmacodynamic and pharmacokinetic studies were conducted in Phase H.0, II, III, IV7-8 and I0 studies. Including security level and authentication. Instead, the second step should be to create an experiment. Use the third phase as the final test. 4-6 about the fourth stage after approval. Additionally, researchers evaluated the treatment at the time of evaluation to gather sufficient evidence that the surgery was effective. The stages of drug testing include drug discovery and development, animal testing, and finally human involvement 9 – 10.[4]

PHASES OF CLINICAL TRIALS:-

Preclinical trials:-

Preclinical research encompasses both animal population studies and in vitro (test tube or laboratory) studies. Investigational drugs may be tested in vitro on substrates or in laboratory animals at a variety of doses to yield initial data on pharmacokinetics, toxicity, and efficacy to assist pharmaceutical companies in deciding the value of additional research[1]

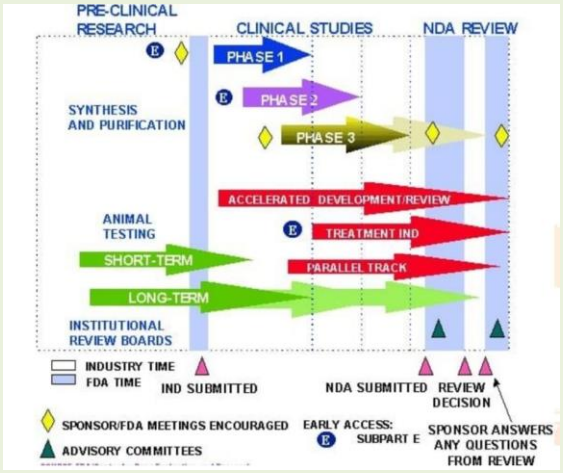

Fig.no.1- Phases of Clinical Trials

Phase 0

Under US regulations, the first study in humans is now called Phase 0. The FDA, which is based in the United States, will examine new drugs through INDs in 2006. Trials Phase 0 is designed to accelerate the development of a drug. Benefiting people by determining early in the research process whether a chemical or drug candidate, drug, or drug will be effective. This is mine. Level 0 testing is characterized by limited restrictions. (10-15 subjects) received a sub-therapeutic dose of study drug.

Phase I

The first phase of the research consists of human trials. A small sample of 20 to 80 healthcare professionals was recruited. This phase includes studies evaluating drug pharmacokinetics, pharmacodynamics, tolerability, and safety pharmacovigilance. Studies like these are usually

performed in clinical areas of the hospital where staff can observe each day. In general, various drug half-lives are observed in drug users. Phase I trials (also called escalation trials) often involve injections to determine the best course of treatment. Dosages tested in animal studies are generally harmful. Phase 1 trials usually include healthy participants. However, in some cases real patients are used: B. There is a fatal disease for which there are no other treatment options. In HIV medication trials and oncology (cancer), these exclusions are more frequent. For the time they spend at the event, volunteers are compensated. The price ranges from a minimal sum for temporary lodging up to approximately £4,000, based on how long the engagement lasts.[3]

Phase II

In order to assess the efficacy and safety of the investigational drug, a Phase II trial involving larger groups (20–300 people) was carried out following the establishment of the drug's initial safety in the Phase I trial. Analyze each stage. May proceed to the gender evaluation stage with sizable patient and volunteer cohorts. If the drug development process is not successful, it is usually revealed in the second attempt that the drug has not yet been developed or is problematic. Generally speaking, phase IIA and phase IIB trials are separate from each other. Drug need (i.e., how much to take) is measured in Phase IIA. For toxicity and efficacy trials, some studies offer Phase I and Phase II.

Phase III

Phase III studies are multicenter, controlled trials that are randomised that may include 300–3,000 or more patients, depending on the disease or treatment being investigated, and their goal is to find out how effective the medication is in comparison to the "gold standard" of care. Phase III studies, particularly in long-term clinical settings, are more costly, time-consuming, and challenging to plan and carry out due to their size and duration. Generally, some Phase III trials are conducted pending approval from regulatory agencies. Although this is not necessary in all cases. Generally speaking, a valid Phase III trial must at least demonstrate the safety and effectiveness of the drug in order to get the necessary regulatory body's approval (FDA (US), TGA). Production process, product development and shelf life. This collection of information is a “lawful export” and will be reviewed by relevant regulatory authorities in various countries. According to FDA regulations, most drugs participating in clinical trials in phase III may be marketed using appropriate instructions & warnings, however, should any adverse effects on the market, the drug must be withdrawn immediately. Many drugs on the market regularly enter phase 3 clinical trials, but many companies shy away from this approach.[16]

Phase IV

Post-marketing clinical studies are another name for Phase IV empirical trials. Evaluating the effectiveness of the drug includes monitoring the safety or dosage of the drug and monitoring the continued support of the drug after marketing approval. Phase IV trials may be mandated by a sponsoring company or regulatory agency for competition (such as a new drug on the market) or for other reasons (such as limited testing in certain populations (such as pregnant women). The purpose of safety monitoring is to identify events that are rare or occur in the majority of patients and to conduct trials of longer duration than required by Phase I-III studies. A negative result during IV testing may result in discontinuation or discontinuation of supplementation.

Recent examples include rofecoxib (Vioxx), troglitazone (Rezulin), and cerivastatin (commercial names Baycol and Lipobay) 2.[2]

FUNCTIONS OF DRUG CONTROLLER GENERAL OF INDIA (DCGI):

The Drugs Control General of India (DCGI) is the flagship of the Central Drugs Standard Control Organization (CDSCO).
Standardisation is also imposed by DCGI on the production, marketing, import, and distribution of pharmaceuticals in India.
8DCGI additionally inspects healthcare devices & drugs.
Whenever there is a dispute regarding the quality of the drug, DCGI will be responsible for the claim.
DCGI develops and maintains national pharmaceutical standards.
DCGI ensures compliance with the D & C Act.
DCGI is in charge of providing pharmaceutical analysts working for other organizations and national pharmaceutical laboratories with training.
DCGI is also responsible for reviewing cosmetic samples received from CDSCO as review samples.
DCGI is also a licensed medical device operator under the Medical Devices Act 2017.[8]
Functions of CDSCO (Central drug standard control organization):
Under the Ministry of Health and Family Welfare, CDSCO is a national regulatory organisation. Licences for specific purposes must be approved by this body. Its headquarters is in New Delhi. CDSCO has six laboratories.
Approval of drugs under the D & C Act.
Develop drug formula.
Carry out clinical research.
Effective control of foreign drugs
Cooperation of national drug regulatory authorities.
List of foreign pharmaceutical and medical equipment manufacturers whose products will be imported into the country.
Issuing licenses to transport medicines to public hospitals or clinics for use by patients.
It is recommended to ban drugs or drugs considered dangerous under Section 26A of the D & C Act.[11]
Types of Regulatory Application for IND application:
Investigator IND Application:
Applications are made under the direct supervision of physicians who modeled and conducted the trial and administered or dispensed the investigational drugs. Doctors can apply for an IND for research; unapproved drugs, products approved for new indications, or products approved in new patients.
Emergency Use IND application:
An FDA can approve the use of an experimental medication by applying under 21 CFR, Part 312.23 or Part 312.20, in emergency circumstances that would not otherwise permit the filing of an IND application. It can also be used in patients who do not follow the current study protocol or do not have an approved study protocol. In this case, the FDA may allow a drug to be submitted for a specific use before an IND application is filed.

TREATMENT IND APPLICATION:

While definitive treatment is underway, clinical trials that have been shown to be promising in diagnosing serious or life-threatening conditions are being submitted and FDA review is ongoing. Drugs not granted permission for the market might be the subject of a serious or immediate dangerous to life conditions among patients who do not have similar or sufficiently high levels of drugs or other treatments.

Screening IND application:

Refer to multiple connections to review preferred connections in your model. Preferred compounds can be developed as separate INDs. It is used to analyze various esters, salts, and other chemical derivatives with dissimilar but comparable characteristics.[17]

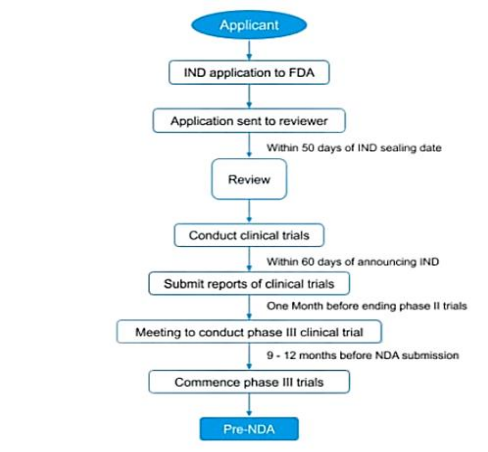

Fig.no.2 -Drug Approval Process

New Drug Application (NDA):-

An NDA application is the vehicle used by a pharmaceutical sponsor to announce FDA approval of a novel medication available for purchase and distribution in the US. The NDA contains information gathered from research conducted on animals and from human clinical trials of novel drugs.

• Do the benefits of the medication outweigh the risks, and is it safe and effective for the intended use?

• The necessity of a prescription and the contents of one.

• The manufacturing method employed for the medication and the existence of controls to verify its identity, potency, excellence, and purity.[15]

Abbreviated New Drug Application:-

Application for a license to sell a generic drug (or replica) that has been approved as a full NDA (i.e. the drug meets regulatory requirements for safety and effectiveness, good job)

Includes Abbreviated New Drug Application (ANDA) Review of generic drug products and their potential Documents submitted to FDA for approval.

Once approved, the applicant can produce and sell pharmaceutical products that are effective, efficient, and at a lower cost than traditional pharmaceutical products. The price of the branded drugs they mention varies.

Generic drug products are products that are equivalent to the innovative drug product in terms of quantity, potency, application method, quality performance features and intended use.[18]

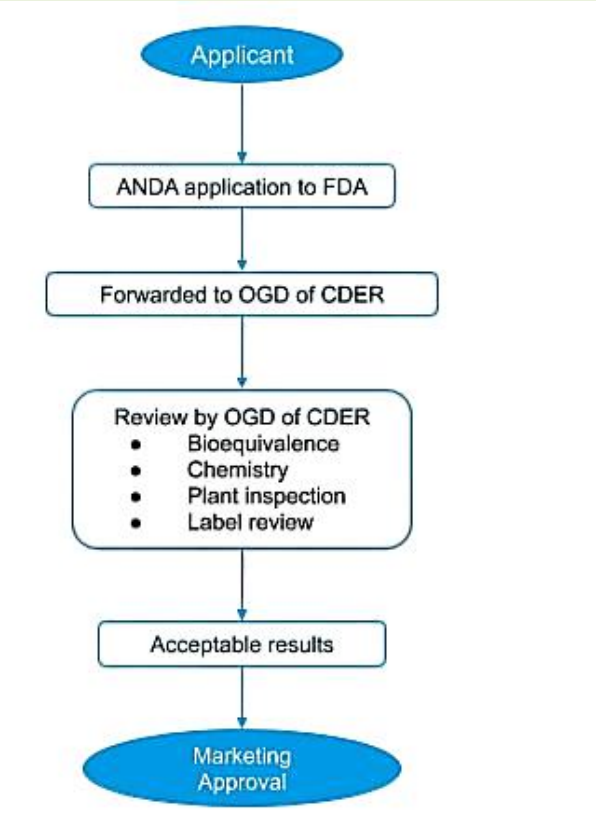

Fig.no.3 -Drug Approval Process in United States

MODULE 2

Good Clinical Practices

International standards regarding ethics and research integrity in the planning, conduct, evaluation, analysis, recording, review and reporting of clinical trials are called Good Clinical Practice (GCP). GCP ensures the fact that the legality, honesty and privacy of trials can be maintained and saved, and that information and reports are reliable and correct. It was completed in 1996 and came into force in 1997, but was not legal until then. The Medicinal Products for Human Use (Medical) Regulations 2004 and the European Union (EU) Good Practice Directive changed the world view. As a result, it is now a legal requirement that all clinical trials involving drug trials in the UK and Europe comply with the GCP.[5]

Objectives:

Clinical research teamwork.

Clinical trial protocol.

Informed consent.

Clinical data management.

Clinical trial monitoring.

Confidentiality.

Foundations of GCP.

An awareness of GCP principles.

Scope:

Trial subjects' rights, integrity and confidentiality are protected.

Results and data are accurately recorded and reported.

Human subjects are protected from investigational products.

Data quality is improved.

New drugs are marketed faster.[14]

Protocol designing for clinical trial:-

The creation of clinical protocols is the first step in any clinical investigation. In addition to guaranteeing test safety and data integrity, a protocol outlines the goal, design, methodology, decision-making process, and organisational structure of a clinical trial. The history, justification, goals, design, procedures, statistical inference, and structure of a medical research project are all described in research methods documents.[7]

As per the ICH Good Practice Guidelines, the following components should be incorporated into the process:

The page title (General Information)

Contextual Data

Goals and Intentions

Study Design

Subject Selection and Exclusion

Subject Treatment

Safety Assessment

Adverse Events

Study Discontinuation;

Statistics

Ethics

Data handling and Record keeping

Publication Timetable/Flowchart

References

Supplements/Appendices

Process of Clinical Trial Application (CTA)

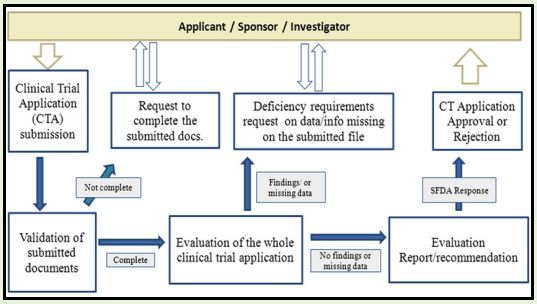

Fig.no.4 - Clinical Trial Authorization Process

MODULE 3

Concept of Pharmacovigilance

The field of research and practice that covers the identification, measurement, awareness of and action to avoid adverse effects and other medication-related issues is called pharmacovigilance. In addition to causing further patient suffering, adverse drug reactions (ADRs) increase morbidity and mortality and increase the economic impact on society. The overall incidence of adverse events in hospitalized patients was 6.7% (range 1.2-24.1%) and ADR leading to death was 0.32% (0.1-0.85%). According to the data, people who experienced adverse events during hospitalization had a higher mortality rate of 19.18% to 8.25%. 19.86%. [3] However, if doctors cannot identify or take responsibility for these adverse drug reactions, they will not treat them appropriately and put patients at risk. Although this may be difficult, communicating the drug combination and adverse events to the patient is important to reduce patient suffering. This includes evaluating relationships and outcomes. By definition, diagnosis is the assessment of the likelihood that recorded side effects are caused by a specific treatment. Evaluates the connection between substance abuse and unfavourable incidents. As a crucial component of pharmacovigilance, helps evaluate the effectiveness of drugs and is an important factor in the evaluation and early warning of adverse drug reactions (ADRs) reported for administration.[19]

History:
1747 James Lind published the first clinical study showing the effectiveness of orange juice in preventing scurvy in 1937.
107 children died from sulfonamide poisoning.
1950 Aplastic Anemia Chloramphenicol Report.
In 1961, the toxicity of thalidomide caused a global disaster.
The December World Health Assembly in 1963 recognized the importance of urgent action to combat ADR.
1968 World Health Organization International Drug Monitoring Pilot Program International drug monitoring was started in India in 1996.
India became a member of the WHO Adverse Drug Reaction Surveillance Programme Pharmacovigilance started in India in 1998.
India established its 67th National Pharmacovigilance Center in 2002.
India launched its National Pharmacovigilance Program in 2004.
Start of clinical trials in India in 2005 2009-2010: PVPI started.[6]
Lists of National Adverse Drug monitoring Centers (AMCs)
1. Department .of Pharmacology, all India Institute of Medical Science, New Delhi.
2. Department of Pharmacology, Therapeutic & Toxicology, Govt. Medical College, Bakshi Nagar, Jammu.

3. Department of Pharmacology PGIMER, Chandigarh.

4. Department of Pharmacology R.G. Kar Medical college, Kolkata.

5. Department of Pharmacology Lady Hardinge Medical College, New Delhi.
6. Department of Clinical Pharmacology, Seth GS Medical College & KEM Hospi, Parel, Mumbai.
7. Department of Clinical & Experimental Pharmacology, School of Tropical Medicine, Chittaranjan Avenue, Kolkata.

8. Department of Pharmacology, JIPMER, Pondicherry.
9. Department of Clinical Pharmacy, JSS Medical College Hospital, Karnataka.
10. Department of Pharmacology, Medical College, Guwahati, Assam.
11. Institute of Pharmacology, Madras Medical College, Chennai.
12. Department of Pharmacology, SAIMS Medical College, Indore-Ujjain.
13. Department of Pharmacology, GSVM Medical College, Swaroop Nagar, Kanpur, U.P.
14. Department of Pharmacology Pandit Bhagwat Dayal Sharma, post Graduate Institute of Medical Sciences, Rohtak, Haryana.
15. Department of Pharmacology, Dayanand Medical College and Hospital Ludhiana, Punjab.
16. Department of Clinical Pharmacology, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, J& K.
17. Himalayan Institute of Medical Sciences, Dehradun, Uttarakhand.
18. Department of Pharmacology, Santosh Medical University, Santosh Nagar Ghaziabad.
19. Department of Pharmacology, SMS Medical College, Jaipur.
20. Department of Clinical Pharmacology, Christian Medical College, Vellore Tamilnadu.[13][10]

CONCLUSION

The only method to guarantee the drug's safety throughout use is through pharmacovigilance its lifespan. This is important due to the limitations of clinical trials in identifying rare and rare drugs. The amount of knowledge and information currently available about drug safety demonstrates why drug regulators must make good decisions to protect public health and welfare. ADR reports are usually made by medical professionals. But there is a lot of negative publicity in international media. This is the main problem we face right now. Despite these drawbacks, reports may be the most effective way to report adverse drug reactions (ADRs) and can identify rare and rare ADRs. If all doctors viewed negative feedback as a vital and ethical responsibility, we could make the world a safer place than it already is. Any report by a physician is important, but it is more important to focus on non-serious ADRs. With the emergence of this concept, pharmacovigilance studies have developed and we are getting closer to our destiny every day. We have this. Responsible for ensuring the effectiveness of pharmacovigilance. Physicians should view ADR reporting as a primary rather than an additional medical responsibility to ensure the use of safe medicines worldwide.

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14.Pharmacovigilance Organizations: Organizations dedicated to pharmacovigilance, such as the International Society of Pharmacovigilance (ISOP) or the drug Information Association (DIA), may provide resources and publications related to pharmacovigilance practice

15.World Health Organization (WHO): The WHO provides guidelines and resources on pharmacovigilance, including those specific to clinical trials. Their website offers access to publications, reports, and guidelines related to drug safety and pharmacovigilance.

16.Clinical Trial Registries: Clinical trial registries, such as ClinicalTrials.gov, may include information about pharmacovigilance procedures and safety monitoring in specific trials. While they may not provide comprehensive guidelines, they can give insights into how pharmacovigilance is implemented in different studies.

17.Pharmacovigilance Textbooks: Textbooks on pharmacovigilance may cover topics related to participant safety in clinical trials. Examples include “Pharmacovigilance: Principles and Database Systems” by Patrick Waller and “Pharmacovigilance: A Practical Approach” by RonaldD. Mann.

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