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REVIEW ON: PHARMACOVIGILANCE

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ABSTRACT:
Pharmacovigilance is the science & activities involved in identifying recognizing, assessing, checking, & preventing adverse effect of pharmaceutical products. Pharmacovigilance is the science & activities of pharmacists, crucial in maintaining safe &reasonable medicine use. This study examines the perspective of drug store students on pharmacovigilance & ADR Announcement in under graduate drug store education. Clinical Research encompasses the entire process from lab to consumer market, identifying promising drug. Pre-clinical studies or animal studies examine safety, toxicity, & efficacy. Pharmacovigilance is crucial in healthcare, assessing drug interactions & their effect on human. Pharmacogenetics & pharmacogenomics are essential in Clinical Research, as they determine human genome variation & disease susceptibility, aiding early drug discovery. Pharmacovigilance is crucial tool used to monitor the side effects & related problems of medicines & vaccines, ensuring their safety & effectiveness in the market. The relevant details are presented in this Chapter.

Key words: *Pharmacovigilance, Clinical Trials, ADRs, Pharmaceutical Product, pharmacy, Safety, Toxicity, Efficacy, Marketing.*

INTRODUCTION

Pharmacovigilance is the science of erecting, evaluating, understanding goal to provide patients with certainty about their medicines. Clinical Trials are crucial for Drug Development, assessing, safety & efficacy pharmacovigilance is essential for participant safety, focusing on detecting, assessing, understanding & preventing adverse effects. It involves systematic data collection, analysis, reporting & benefit risk balance assessment. This review article highlights the significance of pharmacovigilance in Clinical Trials, focusing on measures like adverse event monitoring, data integrity benefit risk assessment. It highlights the responsibilities of stakeholders & the need for a comprehensive understanding of pharmacovigilance role in enhancing the reliability, integrity & ethical conduct of clinical research ultimately leading to safety therapeutic interventions. PV plays various Roles, such as identification, qualification & documentation of drug relates problem. National PV programs have been introduced to increase public awareness about drugs since 1977. PV is essential in the daily lives of doctors, Patients &the pharmaceutical industry.

MODULE 1: CLINICAL TRIAL

Clinical research is a type of clinical practice. Studies that evaluate the protection and efficacy of drugs, products, medical devices, and medical procedures for human use. Clinical Trials: This studies that evaluate the safety and effectiveness of new treatments or interventions. (such as a drug, food, or product for medical use) in humans. According to World Health Organization “Any prospective study that subject’s people to one or more health interventions for the purpose of evaluating the health effects. Clinical research is scientific study conducted on individuals to assess the safety & effectiveness of new medical, surgical or behavioural interventions. There are following phases of clinical Trials.

1. Phase1: (Evaluation of safety)

Trials on healthy individuals (20-80) assess drug safety, side effects, & dosage, with 70% of drugs moved for further testing. These Trials study small numbers of healthy people.

2. Phase2:

A phase 2 clinical Trials evaluates the effectiveness & safety of new drug or drug combination for specific indication. The trials focus on drug efficacy, Safety, &short-term side effects with 33% of eligible drugs eligible for phase2 trials. More Volunteers (100-300) will participate in phase2.

3. Phase3:

Phase3 Clinical trials compare the safety and effectiveness of new treatments's with existing standard treatments. Phase3 trials gathers safety & efficacy information from voluntarily participating hundreds to 3000 participants. Positive results from the FDA approval with 25-30% of drugs progressing to the next phase.

4. Phase4:

Phase4 Trials, conducted after a drug has been approved by the FDA, involve thousands of participants to assess long safety, effectiveness& identify potential adverse effect.

Role of Drug Administration General of India (DCGI)

DCGI is responsible for maintaining operational standards and quality in manufacturing, sale, import and distribution of medicines in India.

1. The program aims to maintain national reference standard
2. Enforce the Drugs & Cosmetic act uniformly, train drug analyses cosmetic samples from CDSCO.
3. DCGI approves drug licenses sets standard for manufacturing, sale, importation & distribution of pharmaceutical in India.
4. The DCGI approves drug licenses, sets standard for manufacturing, sale, importation & Distribution in India, including blood, vaccines, iv fluids & serum.

Role of CDSCO:

The Medicines and Cosmetic Act regulates pharmaceutical companies, sale & distribution, with state authorities primarily responsible central authorities adverse new drug approvals, clinical Trials, drug standard, imported drug quality control & coordination.

The Drug agency approves licenses for certain classes of drugs. He serves as the Health Director of Central Drug Standard Control Organization.

1. CDSCO approves a new drugs & Clinical Trials.
2. Testing of new drugs.
3. Import Registration & license.
4. Prohibition of medicines & cosmetics.
5. Issuance of test licenses, personnel license & NOCs for export.
6. Amendment to D & C laws & Regulation.

Types of Regulatory Application Resources for IND application.

The IND Application may be divided into following categories:

A New drug discovery

An Investigational New Drug (IND) application is a review that supports a request for approval from the FDA for the administration of an investigational drug or biologic for humans, generally in terms of clinical data, safety, and effectiveness, and must have been previously filed. The product is in development and has been submitted to the FDA for expanded approval.

1. Pre-clinical Testing:
Pre-clinical Testing involves animal pharmacology & Toxicology studies to determine the drug's safety for human testing, considering previous human experience with drug.
2. Manufacturing records:
Manufacturing records include pharmaceutical ingredients, manufacturing facilities, and controls used to ensure consistent production and distribution of the drug.
3. Research Data:
Scientists (usually doctors) are evaluated for their suitability to administer clinical trials to research subjects to ensure that they are qualified to play a role in clinical trials.
4. The clinical evaluation process forms the basis of the IND and provides detailed instructions for clinical studies to evaluate risks to participants.
5. Commitment to obtain research approval, IRB review, and, for clinical trials with small numbers of patients or patients, to follow investigator guidance to inform reviewers about the clinical trial based on important facts.

B. New Drug Application:

The Nation Drug Authorization (NDA) is a Crucial document for the FDA to assess the manufacturing method Quality control measures for new drugs identify, strength, quality & Purity.
The FDA's New Drug Application (NDA) is a process where drug sponsors propose a new pharmaceutical for approval, with 30% of initial candidate completing the multiyear Development Process.

Facts required for application include
Patient and product data.
Safety of the drug and its specific benefits when used as recommended (used as directed). • The organization oversees reporting on the design, implementation, and conclusion of successful clinical trials. • Drugs are open to abuse.
Usage instructions and instructions.

C. Abbreviated New Drug Application:
An NDA is a U.S generic drug application submitted to the EDA's office of Generic drugs for review & approval. Electronic submissions have grown by 70% since 2008 but the section IV challenge suppresses new drug innovation. Pharmaceutical products have the same effect as patented products in terms of dosage, strength, application method, effectiveness, efficiency and properties, use planning. It stands for New Drug Use because clinical data and clinical trials are not required, but bioequivalence must be demonstrated by measuring the time it time to take medication to reach the blood vessel.
An ANDA is a data submission to the FDA for the review & approval Of Generic Drugs. These drugs are similar to brand-name drugs in dosage form. In order to receive approval from the FDA ki, they must conduct research to show that their product
effective and "bioequivalent" as the innovative drug, and the generic drug must deliver the same product to the patient's blood vessels.

MODULE 2: EFFECTIVE TREATMENT

Clinical quality is an international standard of ethical and scientific quality that ensures the protection and well-beingness of human subjects.

The principles of the ICH GCP are:

1. Clinical Research must comply with the best practices of the GLP Declaration of Helsinki and other regulatory requirements.

2. Consider the possible risks and the complexity of the desired results for individual subjects before starting the experiment, and only proceed if these results justify the risks.
3. Law, experimental safety and health must take priority over the interests of discipline and insurance.
4. Clinical studies should be supported by unbiased data about the investigational product.
5. The guidelines emphasize the importance of clinical trials being well researched and detailed with clear procedures.

Objectives:
The ICH-GCP guide aims to establish common standard for Japan & US for recognizing clinical data by Regulatory authorities. It outlines good clinical Practices & applies to research in other clinics affecting subject safety & health. Review the positive & negative case studies recognize the implications of non-compliance.

Scope:
This guide outlines the responsibilities, organization, and principles of support managers in planning, conducting, and Reports on clinical evaluation provide guidance to the various countries and institutions that support and collaborate with the International Conference on Good Clinical Practice.

New ICH –Good Practice:
Objectives:
Review GLP(ICH) history
Demonstrate the significance of following ICH GLP when supervising clinical research.
Discuss important aspects of GLP such as patient recruitment, consent, and data confidentiality.
Accept the consequences of noncompliance.
Examine positive and negative research articles.
Scope:
This guide outlines the sponsor's laboratory's responsibilities, organization, and policies for planning, conducting, and reporting inspections.

MODULE 3: CONCEPT ON PHARMACOVIGILANCE

The World Health Organization defines pharmacovigilance as "research and activities related to the observation, evaluation, comprehension and avoidance of side effects and other drug/vaccine-related problems." All drugs and vaccines are extensively tested for protection and efficacy in clinical studies before they are approved for utilize.
Pharmacovigilance (PV) is crucial in healthcare, assessing Drug interaction & their effect on humans. It involves pre marketing to post-marketing. Pharmacogenetics & pharmacogenomics are essential in clinical research, as they determine human genome variation and disease susceptibility, aiding early drug discovery.

Objective:
1. The quality and safety of patients in medical & healthcare settings are crucial parameters that must be improved.
2. Pharmacovigilance aims to demonstrate a Drug's effectiveness by tracking its adverse effects over years from laboratory to monitor to the pharmacy.
3. The goal is to monitor & manage serious drug side effects to ensure public health and safety, promoting safe, rational, and economical drug use.
4. The key to success in pharmacy is a combination of prior knowledge, clinical training, and effective public relations.

History:

India establishes it's pharmacovigilance program in the 1980s, integrating government legislation, a regulator, and research Center as part of the Indian Pharmacopoeia commission, following the Thalidomide scandal in the 1960s.

Constitutional objective of PVPI:

The pharmacovigilance programme of India (PVPI) is an Indian Government Organization established in 2010 to identify and address drug safety issues.

1. The objective is to evaluate the benefit-risk ratio in the medical market and provide evidence-based information on drug safety.
2. The proposed plan involves the establishment of a nationwide system for patient safety reporting and the support of Regulatory authorities in drug use decision-making.
3. The organization aims to educate stakeholders on the safety of its medicine use to minimize risks and establish itself as a national center of excellence in medicine.
4. Collaborate with global pharmacovigilance centers for data exchange and mentoring and analyze new signals.

Adverse Drug Monitoring Centers (AMCs) Nationwide List:

1. The Pharmacy Department of the Medical College located in Guwahati, Assam.
2. The Pharmacology Institute at Madras Medical College in Chennai.
3. Pharmacology Department, SAIMS Medical College, Indore, Ujjain.
4. GSVM Medical College's Department of Pharmacology, Swaroop Nagar, Kanpur, U.P.
5. Pandit Bhagwat Dayal Sharma, Department of Pharmacology, Post Graduate Institute of Medical Sciences, Rohtak, Haryana.
6. Dayanand Medical College and Hospital, Pharmacology Department, Ludhiana, Punjab.
7. Sher-i-Kashmir Institute of Medical Sciences, Srinagar, J&K; Department of Clinical Pharmacology.
8. In Uttarakhand's Dehradun, the Himalayan Institute of Medical Sciences.
9. Santosh Medical University, Santosh Nagar, Ghaziabad; Department of Pharmacology.
10. Pharmacology Department, SMS Medical College, Jaipur.
11. Clinical Pharmacology Department, Christian Medical College, Vellore, Tamil Nadu.

Functions:

1. The goal is to enhance public health and safety while using medicines.
2. The Objective is to identify and address issues related to medication usage, minimize risks, and effectively communicate these observations.
3. The goal is to evaluate the benefits, hazards, effectiveness, and dangers of medicines, aiming to minimize harm and maximize beneficial effects.

4 The aim is to improve understanding of PV education, scientific and clinical education, and effective communication with the public.

MODULE 4: INTERNATIONAL CONFERENCE ON HARMONIZATION (ICH) E2e GUIDELINES

1.This document aims to recommend international standards for safety studies for human clinical trials, promoting harmonization to reduce regional differences, facilitate timely clinical Trials, and reduce animal use and Drug development resources, promoting safe and ethical pharmaceutical development and availability.

2. The revised guidance aims to harmonize non clinical safety studies across Europe, USA and Japan, ensuring a consequence on the Scope and duration of these studies for human clinical trials.

3.The process of providing recommendations for non-clinical safety studies for drug marketing approval, including safety pharmacology, repeated toxicity, Pharmacokinetic and intellectual pharmacokinetic studies, conceptive studies, genotoxicity studies and evaluation of cancer-causing potential. It also discusses the need for case-by-case studies and their relation to human clinical trials. The guideline emphasizes the need for

scientifically and ethically appropriate animal safety studies and human clinical trials for biotechnology-derived products.

Component of Non-Clinical and Clinical Safety Practices Non-Clinical Safety Practices:
Specific instructions should describe safety findings such as toxicity, general treatment, pharmacodynamic interactions, and other poisonous-related information.
Limitations on human protection, uneducated population during the pre-approval period, and adverse events/incidents should be discussed.
Epidemiological studies should consider prevalence, mortality, and prevalence of indicators such as age, gender, and race/ethnicity. These issues need to be discussed clearly in order to predict the safety of the product in the market.

Identification and evaluation of risks including drug-drug interactions and drug food interaction:
The Pharmacovigilance plan should include detailed information on identified risks and adverse events (AEs/ADRs), including serious or frequent ones that may impact the product's benefits and risks. These risks should be discussed, including casual relationships severity, seriousness, frequency, reversibility and at-risk groups. Risk factors should be explained using evidence that supports the conclusions. Identification and potential interactions, including food-medicine and drug-drug interactions, should be discussed, including general education and health risks to the public.

MODULE 5: ASSESSMENT OF ADR BY NARANJO SCALE

The Naranjo algorithm, also known as the Adverse Drug Reaction Probability Scale, is a tool developed in 1991 by Naranjo and colleagues at the University of Toronto to model the evaluation of adverse drug reactions. There are 10 questions in the scale, each of which is given scores ranging from -1 to +2.

A simplified version of the 10 questions is given below
1. Is there a clear message behind this attack?
2. Are there any side effects after taking the medicine?
3. Is there a better effect after stopping the drug or applying specific antagonists?
4. Do side effects reoccur after repeated use?
5. Is there anything else that could cause this?
6. Are there any side effects after taking the placebo?
7. Are there toxins in the blood or other body fluids?
8. Do reactions become more severe as the dose increases?
9. Are reactions less common after the dose is reduced?
10. Has the patient used any medicine or other preparations similar to this medicine in the past?
11. Is the adverse event supported by other objective evidence?
12. The scale is easy to use but has high sensitivity and specificity in determining causality in case of drug-induced liver injury.

Even after a drug has been given the go ahead to be sold on the market, pharmacovigilance remains an essential component of determining its safety and effectiveness. For assessing the safety, effectiveness and dosage of a novel chemical entity, clinical studies are crucial. The ethical awareness, trial idea and procedures, public Safety, research and development cost effectiveness, data recognition, and marketing structure are all improved by ICH GCP. The article discusses emerging trends in pharmacovigilance in clinical trials, these include electronic data capture systems, real-world evidence sharing, statisticians, robotics, expert systems for error detection Challenges include global harmonization, ethical considerations, transparency, and communication. Future directions include real-time monitoring, proactive pharmacovigilance and data sharing for improved safety and drug safety.

In conclusion pharmacovigilance is crucial for trial participant safety. Researchers, Regulatory bodies, and stakeholders can improve the safety and Efficacy of investigational medications, ultimately leading to better healthcare outcomes, by adopting efficient pharmacovigilance methods, addressing issues and embracing future directions.

CONCLUSION

1. Drug -drug interaction background:

This study evaluates current practices for the identification and treatment of drug-drug interactions and identifies opportunities to increase Prevention and reduce adverse events in primary care physicians due to aging populations and polypharmacy.

Drug-drug interactions (DDIs) are a global health problem causing approximately 770,000 deaths and significant medical costs. DDIs account for 20% of adverse events in the United States; This problem is caused by the elderly, polypharmacy and nutritional supplement use. Polypharmacy involving more than one drug is associated with an 80% risk of DDI. Taking supplements with prescription drugs puts you at risk.

Food-drug interaction:

Drug interactions can vary in effect due to interactions with other drugs, food, beverages, dietary supplements or other diseases. These effects may occur due to improper use or lack of knowledge about the active ingredients. Food-drug interactions can alter the body's ability to use the drug or cause serious side effects. A change in the drug product may affect the parent drug. Patients should follow their medical prescription to minimize food-drug interactions for maximum advantage. Data mining can help doctors and pharmacists prescribe medications and provide proper nutrition. Medications are essential for treating health issues, but proper use is crucial for safety and effectiveness. Ideal drugs should be specific, predictable, non-toxic, linear and require only a single dose for permanent cure. Drug interactions involve substances affecting the activity of a drug, affecting its effects or producing new ones. These can occur between drugs, food and herbs and can be influenced by diet and lifestyle.

Drug-drug interactions can negatively impact safety, efficacy and patient nutritional status. To prevent this effect, patients should inform their physicians and pharmacists about food and nutritional products. Because pharmaceutical foods have not been extensively tested, they may interact with prescription or over-the-counter medications. It is important to avoid this interaction.

3 Design and conduct of investigation:

Observational study designs, also known as epidemiological designs, evaluate potential causal relationships for social benefit and prevention impact. They consist of potential cohorts, cross-sectional, case-control, case-crossover, and sustainable design. Diagnostic study design evaluates the advantages and disadvantages of diagnosis that affect the standard, conduct, and analysis of epidemiology.

Observational and Interventional Research Major types of research include observation and survey; Here, observational research looks at the relationship between events and outcomes, while diagnostic research is a different group. Research designs can be retrospective; While retrospective studies capture historical data and provide less bias, prospective studies track participants overtime, providing strong evidence of cause and effect.

REFERENCE

1.Regulatory Guidelines: Regulatory authorities like the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), and other national regulatory bodies provide guidelines on pharmacovigilance practices in clinical trials. You can refer to their official websites for specific guidance documents.

2.International Conference on Harmonization (ICH): The ICH provides guidelines on various aspects of pharmaceutical development, including pharmacovigilance. The ICH E2A guideline, titled "Clinical Safety

Data Management: Definitions and Standards for Expedited Reporting," provides recommendations for safety reporting in clinical trials.
3 Journal Articles: Scientific and medical journals often publish articles on pharmacovigilance in clinical trials. You can search databases like PubMed or other online resources to find relevant articles on the topic.
4.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
5.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.
6.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.
7.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 Ronald D. Mann
8.Pharmaceutical Industry Associations: Industry associations such as the Pharmaceutical Research and Manufacturers of America (PhRMA) or the European Federation of Pharmaceutical Industries and Associations (EFPIA) often publish guidelines and recommendations on pharmacovigilance practices in clinical trials. Their websites may provide relevant resources.
9. Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO). International Ethical Guidelines for Biomedical Research Involving Human Subjects. CIOMS & WHO: Geneva, Switzerland, 2002.
10.https://www.who.int/teams/regulation-prequalification/regulation-andsafety/pharmacovigilance
11.https://www.ema.europa.eu/en/human-regulatory/overview/pharmacovigilance-overview
12.https://www.hopkinsmedicine.org/research/understanding-clinical-trials/clinicalresearch-what-is-it.html
13. https://www.nia.nih.gov/health/what-are-clinical-trials-and-studies.
14.https://simplifiedupsc.in/drug-controller-general-of-india-dcgi
15.https://www.fda.gov/vaccines-blood-biologics/development-approval-processcber/investigational-new drug applications-indscber-regulated-products
16.https://www.fda.gov/drugs/types-applications/new-drug-application-nda
17. https://www.fda.gov/drugs/types-applications/abbreviated-new drugapplicationanda#:~:text=An%20abbreviated%20new%20drug%20application
18.Ankur Rohilla*, Nishant Singh, Vipin Kumar, Mohit Kumar Sharma, Amarjeet Dahiya, Ashok Kushnoor; Published by Journal of Advanced Pharmacy Education & Research; Published on Oct-Dec 2012; Vol.2.
19https://ichgcp.net/scope-of-the-guideline-definitions
20. Duvvuru Ashok Kumar, Languluri Reddenna, Shaik Ayub Basha; Pharmacovigilance Programme of India; 2015, Vol. 6, No. 1, Article
21. http://www.pharmabiz.com/PrintArticle.aspx?aid=63422&sid=18