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A REVIEW ON: PHARMACOVIGILANCE AND IT'S IMPORTANCE

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Abstract:

Pharmacovigilance supports the safe and proper use of drugs. Spontaneous reporting of adverse drug reactions (ADRs) is a vital part of pharmacovigilance. However, there is a lot of underreporting of ADRs. Adverse drug reactions have become a big problem in developing countries. Understanding pharmacovigilance could help improve reporting rates and reduce ADRs. Pharmacovigilance focuses on adverse drug reactions (ADRs). These reactions are any harmful and unintended response to a drug, including cases where the drug does not work as expected for prevention, treatment, or changes in bodily functions. Still, ADRs are often underreported. In developing countries, adverse medication responses are now a major concern. Knowing about pharmacovigilance could lay the groundwork for efforts to boost reporting rates and decrease ADRs.

Keywords:

Pharmacovigilance , Adverse drug reaction , ADR's reporting

Introduction:

The word "pharmacovigilance" comes from two roots: Pharmakon, which means 'drug' in Greek, and vigilare, which means 'to keep watch' in Latin.[2] The World Health Organization defines pharmacovigilance as the science and activities related to detecting, assessing, understanding, and preventing adverse effects or other drug-related issues. This includes both long-term and short-term negative effects of medicines [19]

Adverse responses are a known risk of medication therapy, even with all the benefits of drugs. A common and often preventable cause of illness, disability, and death is an adverse drug response (ADR). One definition describes an ADR as "a significantly harmful or unpleasant reaction that occurs from using a medicinal product. This reaction predicts risks from future use and requires prevention, specific treatment, a change in dosage, or stopping the product [1][.8]. " Post-marketing studies and Phase IV clinical trials are both crucial for ensuring safety are both essential.[3][8] Government entities, such as the FDA or the European Medicines Agency (EMA), have improved their pharmacovigilance initiatives in a number of ways. In the U.S., medications are actively and passively monitored after the marketplace via post marketing surveillance. The primary methods include Phase IV clinical trials, as well as voluntary and mandatory reporting through the FDA's Adverse Event Reporting System (FAERS), Med Watch, and the Institute of Safe Medication Practices Medication Error Reporting System (MERP). Consider Med Watch, which allows the public (both patients and providers) to report suspected or observed ADRs; manufacturers are required to report adverse events, whereas healthcare providers and the public's reporting is voluntary. Because there is an element of volunteerism in this type of reporting and detection of adverse events, timely reporting and incomplete detection is inevitable. Recent studies have highlighted the multitude of limitations related to these spontaneous reporting systems. Researchers have started seeking out other avenues of reporting for ADR monitoring. The objective of pharmacovigilance is to evaluate risks of adverse events for patients taking drugs- bearing in mind that drugs are never without risk- at the time of

regulatory approval for marketing and throughout the product's life cycle. While pharmacovigilance is an important aspect of both patient safety and clinical outcomes, there are certain disease states in which timely, accurate and thorough reports are paramount. Oncology regimens with high toxicity and narrow therapeutic windows are a part of this higher priority group. However, studies of pharmacovigilance and post-marketing surveillance of oncology drugs are limited. Though pharmacovigilance is defined differently, with different systems having different definitions, broadly the goal of pharmacovigilance is to promote patients' care and safety and give reliable and balanced information to inform the assessment of the risks and benefits of medical drugs.[22]

History of pharmacovigilance:

In India, pharmacovigilance started in 1986. There was no significant growth, even though a formal Adverse Drug Reactions (ADR) monitoring system began with 12 regional centers, each serving a population of 50 million. In 1997, India joined the World Health Organization (WHO) program for monitoring ADRs based in Uppsala, Sweden, but it did not succeed. Consequently, the National Pharmacovigilance Programme (NPPV) of India, which has support from the WHO and funding from the World Bank, became operational after 2005.[4][5][6]

Table.2.The sequential Pharmacovigilance development with special Reference to india.[17][18] [19]

YEAR	DEVELOPMENT
1747	Very first known clinical trials by James Lind, proving the usefulness of lemon juice in preventing scurvy.
1937	Death of more than 100 children due to toxicity of sulfanilamide.
1950	Apalstic anemia reported due to chloramphenicol toxicity
1961	Worldwide tragedy due to thalidomide toxicity.
1963	16th World Health congregation recognize significant to rapid action on Adverse Drug Reactions (ADRs).
1968	WHO research project for international drug monitoring on pilot scale.
1996	Global standards level clinical trials initiated in India.
1997	India attached with WHO Adverse Drug Reaction Monitoring Program.
1998	Initiation of Pharmacovigilance in India.
2002	67th National Pharmacovigilance Center established in India.
2004-05	India launched National Pharmacovigilance Program.
2005	Accomplishment of structured clinical trials in India.
2009-10	Pharmacovigilance Program (PvPI) started.

Objective:

1. Monitoring Adverse Effects: On-going vigilance to identify and assess adverse drug reactions (ADRs) associated with drug use.
2. Assessment of Risks and Benefits: Assessing the risk benefit ratio for drugs to determine if the therapeutic benefits outweigh risks or potential adverse effects.
3. Data Collection and Analysis: systematically collecting and analyzing data on medication safety, including information from health care providers, patients, and clinical trials.
4. Risk Management and Mitigation: To create methods to manage and mitigate drug-related harm when there are risks associated with medications like updating labeling, risk minimization strategies, or even withdrawing medications from the marketplace.
5. Promoting Safe Use of Medications: Educating health care professionals and patients to use drugs safely and effectively, which includes proper dosing, administration, and monitoring.
6. Facilitation of Safety Information: Facilitation of safety information to health care providers, regulatory agencies, and the public. The goal would be to support skilled decision-making regarding drug use based on the most current information.
7. Regulatory Compliance: Compliance monitoring and reporting related to drug surveillance.[7][8]

Aim:

1. Adverse Effects Monitoring: Maintain vigilance to detect and assess adverse drug reactions (ADRs) that occur with prescribed drug use.

2. Risk and Benefit Assessment: Assessing the risk-to-benefit ratio of a drug, to ensure that therapeutic benefits outweigh the potential risks or side effects associated with a drug.

3. Data Gathering and Analysis: systematically collect and analyze information on medication safety, including reports from patients and healthcare practitioners, or information from trials.

4. Risk Management and Mitigation: Managing and mitigating the risks associated with medications would include the development of risk mitigation plans, changing label instructions, or even removing medications from the market.

5. Encouraging Safe Medication Use: Teaching patients and healthcare providers about the proper administration, dosage, and other aspects of using medications in a safe and efficient manner

Adverse drug reaction (ADR's):

Adverse Drug Reactions (ADRs) An adverse drug reaction (ADRs) can be defined as an unintentional and harmful response to a health product causing at the doses is usually recommended or tested for the diagnostic, prevention or treatment of a disease or the modification of an organic function.[9][10][11]

A. Predictable (Type A) Reaction; These are based on the drug pharmacological properties which might be an exaggerated but dose appropriate reaction to the pharmacological properties of the drug, which include unwanted effects, toxic effects, or withdrawal symptoms.

B. Unpredictable (Type-B) Reactions ; These are based on patients idiosyncratic responses to the drugs rather than the known pharmacological effect of the drugs; allergy and idiosyncrasy would be examples. They are less common or infrequent, less frequently related to the dose, usually more serious, and require drug discontinuation [12][13]

Table .2. Known drug adverse Reaction.[20]

Thalidomide	Multiple defects
Lithium	Foetal goiter, cardiac and other abnormalities
Methotraxate	Multiple defects, Foetal death

Anndrogen	Virilization, limb, esophageal, cardiac defects
Progestins	Virilization of female foetus
Stilboestrol	Vaginal carcinoma in teenage female offspring
Tetracyclines	Discolored or deformed teeth, retarded bone growth
Warfarin	nose, eye and hand defects, growth retardation
Phenytoin	Various malformations
Aspirin/ Indomethacin	Premature closer of ductus arteriosus

Adverse drug reaction reporting:

A study examining healthcare professionals' knowledge and attitudes towards pharmacovigilance and ADR reporting established training as a key factor for increasing rates of ADR reporting. It was decided to conduct a workshop which would i) provide training in sensitizing healthcare professionals to the importance of pharmacovigilance and ii) effect an increase in ADR reporting from understanding the importance of the 'Pharmwatch' pharmacovigilance programme. The workshop participants reported that the workshops motivated them to report ADRs. These results indicate good evidence that training of healthcare professionals can have a positive impact on rates of ADR under-reporting. There requires more education and training.[16]

AE reports can be based on solicited reports from patient support programs, reports from clinical or post-marketing studies, spontaneous reports from health care practitioners or patients or other intermediaries, reports from literature sources, because reporting is a legal requirement in most countries, reports from media outlets including social media and websites and reports for drug regulatory authorities themselves.

For pharmaceutical companies, AE reporting also generates data that helps in determining the risk-benefit/ratio of a particular drug. The following are several elements of Adverse Event (AE) Reporting.[19] [16] [21]

- An identifiable patient.
- An identifiable reporter.
- A suspect drug.
- An adverse event.

Monitoring of ADRs:

The process of continuously monitoring adverse drug reactions (ADRs) is known a ADRs monitoring. Pharmacovigilance is crucial to the role of ADR Monitoring,safety continues throughout a drug's lifecycle.[14] Pharmaceutical companies with worldwide operations have created large global systems to continuously monitor, investigate, and assess adverse drug events for their products, and will report these to regulatory authorities worldwide. When a physician fills out adverse event report (AER) forms s/he is making a small, but important contribution to this global effort. S/he is indeed a continuous surveillance resource for these products, and carries the responsibility for patient safety. The company can evaluate AEs from reporting for relatedness and this may result in a change in labeling, if necessary.

Advantages of ADR's monitoring:

• It gives information about the reliability, and safety, of medicinal products.

• Strategies for risk management are initiated.

• It facilitates the assessment of ADR compliance, and prevents any anticipated adverse events.

• It increases awareness of the ADRs, and educates the health care team regarding adverse drug reactions (including patients, pharmacists, and nurses).

The key objectives of ADR monitoring is to discover the risk factors that may result in adverse reactions and to also provide the type, magnitude, and frequency of ADRs

ADR Monitoring Centre :

Table 3: ADR Monitoring centres.[15]

New delhi	Department of pharmacology, All India Institute of Medical Science.
Chandigad	Department of pharmacology, PGIMER .
Kolkatta	Department of Clinical Pharmacology, Lady Hardinge Medical College.
Karnataka	Department of Clinical Pharmacy, JSS Medical College Hospital.
Chennai	Institute of pharmacology, Madras Medical College.
Indore-Ujjain	Department of pharmacology, SAIMS Medical College Indore-Ujjain.

Functions:

1. Identify:

Identifying adverse drug reactions (ADRs)

involves recognizing unexpected, harmful effectsof drugs. Causality assessment determines the relationship between a drug and suspected reaction,often using tools like the WHO causality assessment criteria.

2. Documentation:

Documentation of ADRs include recording essential details like patient information,drug details, reaction description, and relevant medical history. Accurate documentation aids incomprehensive analysis

3. Report:

Reporting serious ADRs topharmacovigilance centers of ADR regulating authorities is crucial. This involves submitting detailedreports that contribute to the ongoing monitoring andevaluation of drug safety.[15]

clinical Trials:

Preclinical studies consist of in vitro (i.e., test tube or lab) studies and studies conducted on animal populations. Wide-ranging dosages of the study drug are given to either the animal subjects or to an in vitro substrate, in order to obtain preliminary efficacy, toxicity and pharmacokinetic information, and to allow pharmaceutical companies to make decisions on whether to proceed to further testing or not.

Phase 0:

Phase 0 is a new designation for exploratory, first-in-human studies that are carried out according to the U.S. Food and Drug Administration's (FDA) 2006 Guidance on Exploratory Investigational New Drug (IND) Studies. Phase 0 studies are intended to accelerate the development of promising drugs or imaging agents by demonstrating very early on, if the drug or agent acts in human subjects as anticipated from the previous studies preclinical studies. The components of a Phase O study are characterized by administering a single sub therapeutic dose of the study drug to a small number of subjects (10 to 15) to collect preliminary information regarding the agent's pharmacokinetics (how the body handles the medication) and pharmacodynamics (how the agent acts in the body

Phase 1:

Phase 1 trials are the earliest testing stage in humans. Usually, groups are small (20-80) and selected from healthy volunteers.

Clinical trials in Phase I assessments that evaluate the safety (pharmacovigilance), tolerability, pharmacokinetics, and pharmacodynamics of a drug. Generally completed in patient clinics, where subject can be monitored by full-time staff.

Phase 1 trials generally also have dose-ranging (dose escalation) studies in addition to the assessments, in order to evaluate the appropriate dose for therapeutic use to be identified. The doses tested will be usually drastically lower than the doses which cause harm in animal testing. Phase I trials are also generally done with healthy volunteers.

Partly, compensation is made in an pain-in-the neck figure for time spent at the pain-in-the neck centre. Amounts of compensation range from a small amount of money for a short period of discomfort, to a bigger amount of over for a long period of participation in the inconvenience..

Phase 2:

After confirming the baseline safety of a study drug in a Phase 1 trial, Phase 2 trials are conducted in larger samples (20-300) to determine how well the drug works continuing safety from Phase 1 in a larger sample of levels and cases.

An unsuccessful development process for a new drug would typically occur during a Phase 2 trial when it is discovered that the drug does not work as intended, or has toxic effects Phase 2 studies can sometimes be divided into Phase 2A and Phase 2B

Phase 2 A is designed for testing dosing parameters (what dose of drug should be given) and Phase 2 B is designed to test efficacy (how well the drug works at the intended dose(s)). Some trials combine Phase I Phase 2 and test both efficacy and toxicity

Phase 3:

Phase 3 trials are the most valuable, time- consuming and complicated to design and execute, owing to their scale and relatively long durations, particularly in curatives for habitual medical conditions.

After the satisfactory completion of Phase 3 trials medicine are usually summarized into a large Reports, including descriptions of the styles and results of clinical, mortal and beast trials, the manufacturing process, expression details and shelf life.

Such reports make up the nonsupervisory submission for review to the applicable nonsupervisory authorities, in multiple countries.

Although most medicinal a companies would rather avoid this, it is fairly common to see the completion of prescriptions undergoing Phases 3 clinical trials in the request.

Phase 4 :

Phase 4 is also known as Post Marketing Surveillance Trial.

Phase 4 trials involve the safety surveillance(pharmacovigilance) and ongoing specialized support of a medicine after it receives authorization to be sold to the public.

Phase 4 studies may be called for by regulatory authorities or may be voluntary by the sponsor company for competition(laying claim to a new market for the medicine) or other reasons(For example, the medicine may not have been studied for interactions with other medicines, or on some population groups such as pregnant women, who are unlikely to subject themselves to studies).

Table 5**:Clinical Trial Phases:**

Phase :0	Phase:1	Phase:2	Phase:3	Phase :4
Micro-dosing study	Human pharmacology and safety	Therapeutic exploratiom and dose ranging	Therapeutic confirmatoin or comparision	Post marketing survillance
Subject: 10-15[healthy volunteer]	Subject : 20-100 healthy volunteer	subject : 100-500 patients	subject: 500-3000 patient multicetered trials	subject : it involves children pregnant and lacteting women eider patients
to acess doses selection	To acess safety to lerabilityband safer clinical dose for human volunteers	Carried out at 2-4 centers to assess safety efficacy and dose range	To assess safety and tolarability on wider scale	Assess efficacy acceptability and adverse drug reaction in a population

Conclusion :

in conclusion, pharmacovigilance is critical in ensuring medicinal safety by monitoring, assessing and preventing adverse effects. Active vigilance and strong reporting systems are key for detecting and addressing the possible risks for consumers and improving public health. The majority of adverse drug reactions (ADRs) are reported by health professionals; however, there is an enormous amount of worldwide under-reporting. It is the most important and current problem. Despite its weaknesses, the spontaneous reporting system remains the most widely used method of reporting adverse events and is capable of producing signals for rare and extremely rare types of ADRs. If all medical care professionals.

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