



REVIEW ARTICLE

A review of pharmacovigilance

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ARTICLE INFO ABSTRACT



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Introduction: Pharmacovigilance involves more than spontaneous reporting, and is more than just evaluating marketed medications. It has grown from a minor component of drug control to a major activity and expanded its scope to encompass the assistance for patient safety during clinical trials by ensuring adequate informed consent and institutional review boards (ethical committees); development of a safety profile for proper use of a new molecular entity and appropriate communication of that information to a range of relevant stakeholders; selection of the first safe dose for use in humans based on pharmacologic data obtained in animal studies; development of a safety profile. This study implicates the growth of pharmacovigilance in assessing the safety of drugs.

Methods: The subsequent information was obtained by reviewing the data from earlier published material. The obtained information was evaluated, compiled, deconstructed, reassembled, interpreted, and conclusions were reached.

Results: The supply of data necessary for assessing the advantages and dangers of medicines is, first and foremost, a scientific task. Good pharmacovigilance practice must be created to guarantee that data is gathered and used correctly for the intended purpose.

Conclusion: Pharmacovigilance has grown into an essential part of drug control. Signal management protocols ensure that surveillance operations monitor the produced product through collaborative actions with manufacturing specialists, analyze benefit-risk management and inspection readiness maintenance as a corporate culture process.

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Introduction

Pharmacovigilance word comes from the combination of two words- Pharmakon means 'drug'- a substance which shows therapeutic effect and Vigilance means 'keep watching'- to keep an eye on something. Here, it refers to keeping watching the activity/effect of a drug. It includes studying the drug in the background, its adverse effects, and

unwanted effects after launching it in the market. Pharmacovigilance is the science of observing the drug effects (Beninger, 2018).

WHO defines pharmacovigilance as “the study and practice of detecting, assessing, analyzing, and preventing adverse drug reactions”. Pharmacovigilance's particular goals are to enhance patient care and safety in connection to the use of



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medicines and all medical and paramedical treatments, as well as to improve public health and safety about the use of medicines. The particular goals of pharmacovigilance are to contribute to the evaluation of the benefit, harm, efficacy, and risk of medications, as well as to improve understanding, education, and clinical training in pharmacovigilance and its effective communication to the public (Olsson & Harrison-Woolrych, 2018).

Pharmacovigilance is involved in collecting information about a future treatment to analyze its benefits and risks and develop measures to minimize the identified risks to ensure that the expected benefits outweigh the risks. ADR

causality evaluation is a method for determining the strength of the link between drug exposure and adverse reaction incidence (Beninger, 2018). When dealing with ADRs in patients, healthcare practitioners analyze causation informally to make judgments about future therapy. It includes reporting of relationship with the time of drug administration, previous knowledge about drug, dechallenge, and rechallenge. The assessment can be of various kinds like definite, probable, possible, and doubtful (Almandil, 2016). The different pharmacovigilance services have been presented in Figure 1 (van Leeuwen & Edwards, 2021).



Figure 1: Pharmacovigilance Services

Cloud Bernard, a great pharmacologist, stated that "Everything is poisonous, nothing is poisonous." It means that it depends upon the dose of the drug whether it will act as a medicine or poison. That's why no drug is safe and no drug is poisonous. The safety and efficacy of the drug depending upon the dose. There remained some historical events due to which pharmacovigilance came into existence (Martin *et al.*, 2018). The two major events of them are:

Sulfanilamide disaster: S.E. Massengill company, U.S. was selling sulfanilamide for the cure of Streptococcal infection like pharyngitis, tonsillitis, etc. To make it convenient for children, there was a demand for this drug in liquid form. Due to its solubility issue, it became a difficult task. Later, it was found that sulfanilamide was soluble in diethylene glycol. As a result of this, elixir sulfanilamide was manufactured and sold in the market. Gradually, poisonous effects of diethylene glycol were seen and 107 deaths were reported. Due to this, the pharmacist who developed the formula committed suicide and S.E. Massengill company was fined the highest possible amount of the drug (Montané & Santesmases, 2020).

This disaster happened because there were no laws governing the safety of the medicines. It was for the first time that the government felt the need for the safety of medicine. The government of the USA introduced the law namely the Food, Drug, and Cosmetic Act, 1938. The drawback of this law was that the whole world was over the safety of the drug and not efficacy. Only the safety of the drug has to be proved under this law, not efficacy.

Thalidomide Tragedy: A German company, West pharmaceuticals in 1950 introduced a sedative drug, Thalidomide. It is used to induce natural sleep without a hangover on the next day. The drug became popular. Later, animal studies with Thalidomide proved that no highest dose of Thalidomide can kill the animal. Due to this, the company sold the drug by saying that suicide is not possible with Thalidomide and proving it to be the safest drug (Dylan Fernandes *et al.*, 2019).

Being a sedative drug, it was also useful for pregnant women in morning sickness. So West pharmaceuticals company promoted the drug in pregnant ladies. Very soon, in Nov. 1961, there was a sudden increase in the cases of

phocomelia- upper and lower limbs become short in newborns. It became a serious issue to be addressed at that time.

Meanwhile, an Australian obstetrician, Dr. William McBride, and a German pediatrician, Dr. Widukin Lenz came up with some data and said that the drug Thalidomide is causing phocomelia. After this, subsequently, the animal trials were conducted and proven that the drug which was the safest, became the reason for serious congenital anomalies.

Methods

These drug reactions compelled the government to bring the law, the testing of the drug in animals and humans is part of drug development. The data generated on human beings is in a very small population of patients. But when we conduct clinical trials in 3000-5000 and generate some data and then extrapolate it in the whole population. As with this small number of patients, some of the adverse drug reactions will not be recognized. So, to prevent this and recognize the adverse drug reactions, the licensing authority of India- DCGI & CDSCO compels the marketing agency to give ADR information regarding that new drug (Montastruc *et al.*, 2016).

Earlier clinical trials related to drug development used to be conducted in the USA. The data generated was of the US population only and previously, India used to apply that data to the humans of this country. But, the ethnicity and genetics of the Indian people are different from people of the USA. So, it became mandatory for the government of India to conduct at least phase 2 and phase 3 trials in the Indian population. This is how the PV program became very important in India (Jose & Rafeek, 2019).

PV program is important because once the data is developed from your population, you may be able to give cautions and alerts for use of the drug. Sometimes these reactions are so serious that they can even lead to the withdrawal of the drug. This is why it became important for healthcare professionals to report adverse drug reactions. The information generated by the PV is important in educating the doctors about adverse drug reactions and official regulation of the drug that is used in a large population. The healthcare professionals report adverse drug reactions to the government of India, so that the alerts, controls, withdrawals, change in the labels, change in the indications may be issued (Lihite & Lahkar, 2015). The government of India also allows a common man to report adverse drug reactions and the reporting form by the patient layman is available on the website of PvPI in vernacular languages.

PvPI, the Pharmacovigilance program of India, is conducted by IPC & CDSCO. Both of these institutes are under the Ministry of Health and Family welfare. PvPI is controlled by the IPC & Head of the program in DCGI. The manufacturers, importers of the drug, the marketing

authorization companies, the healthcare professionals, and the common man are the major pillars of PvPI. The objectives of PvPI are to monitor adverse drug reactions, monitor the reporting of adverse drug reactions, educate the healthcare professionals, make them aware about reporting of adverse drug reactions in total drug regulation (Kalaiselvan, Thota & Singh, 2016). If more adverse drug reactions are being reported, the government performs a risk-benefit analysis to evaluate whether to continue or withdraw the drug from the market.

WHO Quality Assurance and Safety

The medical team is in charge of providing medication safety guidelines and support to nations. The team is part of the WHO Health Technology and Pharmaceuticals cluster's Department of Essential Drugs and Medicines Policy. The department's mission is to help save lives and improve health by reducing the vast gap between the promise of critical pharmaceuticals and the reality that medicines are inaccessible, costly, dangerous, or incorrectly utilized by millions of people, particularly the poor and disadvantaged. WHO strives to achieve this goal by offering global guidelines on critical medications and medicines, as well as assisting countries in implementing national drug policies (Manzanera *et al.*, 2018). These are intended to provide equitable access to critical medications, as well as drug quality and safety, as well as sensible drug usage.

The Uppsala Monitoring Centre's main task is to maintain a worldwide database of ADR reports received from National Centers. The efficacy of this system is determined by the size of the database, the quality of reports received from contributing centers, the timeliness of such reporting, and a culture of active and accurate reporting within participating countries. The UMC's function as a communications and training center, as well as a clearinghouse for drug safety information, has grown in recent years (Inacio *et al.*, 2017). The UMC team, in conjunction with the WHO, supports and encourages international collaboration, which was recognized as critical for pharmacovigilance success in 1972. The WHO program's terminology for classifying adverse reactions and medications has been extensively adopted by National Centers, manufacturers, and drug regulators. In industrialized nations, the World Health Organization Adverse Reaction Nomenclature (WHO-ART) has been superseded in recent years by a new terminology known as MedDRA (Medical Dictionary for Drug Regulatory Activities) (Hegerius *et al.*, 2020). Within the International Programme, WHO-ART continues to be the primary means of conveying adverse reactions in the majority of poor countries.

National pharmacovigilance institutions are currently in charge of most post-marketing surveillance of medications. They have made significant progress in collecting and analyzing ADR case reports, differentiating signals from background "noise," making regulatory decisions related to

strengthened signals, and alerting prescribers, manufacturers, and the general public to new risks of adverse reactions, all in collaboration with the UMC. National Centers' responsibilities have grown to include disseminating information on benefit, harm, efficacy, and risk to practitioners, patients, and the general public. Many regulatory agencies in various parts of the globe have formed strong relationships to communicate safety data acquired on specific drugs and the regulatory choices taken in response to it (Hartman *et al.*, 2017).

Pharmacovigilance has emerged as a clinical field as a consequence of the efforts of clinical pharmacology and pharmacy departments all over the world. In their clinics, wards, and emergency rooms, several medical institutions have created adverse reactions and drug error tracking systems. Case-control studies and other pharmacoepidemiological approaches are increasingly being utilized to evaluate the harm caused by drugs after they have been approved for use (Alwhaibi & Al Aoola, 2020). Drug safety scientific understanding has grown as a result of increased public awareness and academic interest in the area. Teaching, training, research, policy creation, clinical research, ethical committees (institutional review boards), and clinical services provided by academic institutes of pharmacology and pharmacy have all played a significant role (Diesel & Cooles, 2018).

The active engagement of reporters determines whether a spontaneous reporting system succeeds or fails. Although limited patient reporting methods have lately been implemented, health professionals have been the primary source of suspected ADR case reports throughout the history of pharmacovigilance. All segments of the healthcare system, including public and private hospitals, general practitioners, nursing homes, retail dispensaries, and traditional medicine clinics, would need to be included to get a representative image of the truth (Donzanti, 2018). There should be preparedness to notice and report undesired and unexpected medical outcomes wherever drugs are administered. According to certain research, systems for recording patient concerns may be able to detect novel medication safety signals sooner than professional reporting systems alone.

Results

A national culture of drug safety and public faith in medicines are built on sound drug regulatory structures. Clinical trials, the safety of complementary and traditional medicines, vaccines, and biological medicines are among the issues with which drug regulatory authorities must contend, in addition to the approval of new medicines. Other issues include developing lines of communication between all parties with an interest in drug safety and ensuring that they are open and able to function efficiently, particularly during times of crisis. To guarantee that authorities are adequately briefed on safety concerns in everyday practice that may be relevant to future regulatory

action, pharmacovigilance programs must have strong linkages with regulators (Garcia-Doval *et al.*, 2020).

The shifting patterns in clinical trial conduct in recent years provide specific and significant problems for drug regulators, particularly in ensuring that the rights and health of patients and their communities are respected. Regulatory agencies consider the safety and efficacy of new goods under study before approving clinical studies. In collaboration with the relevant institutional review boards, they must also pay attention to the general standards of care and safety for research subjects (Bagheri, Laroche & Montastruc, 2016).

As the research agenda is negotiated with clinical collaborators, sponsors' limitations on the study design, laboratory program, and open sharing of information are progressively affecting the safety of medications in the development stage. While it may help patients comprehend their medications and are in line with the demand for better access to drug information, the lack of dependability and accuracy may jeopardize patient care and safety (Garcia-Doval *et al.*, 2020).

Discussion

The hazards of contemporary living are a source of significant worry in society. Medicinal goods are one of the technical advancements that have brought both enormous advantages and new hazards to humanity. If these risks are to be properly handled, it is necessary to understand how the public perceives them. When it comes to safety, how safe is safe enough? Which risks are you willing to take? When interacting with patients and the general public, these are two essential topics that medical professionals must consider. Recognizing that expert and public perceptions of risk differ, there is a pressing need to examine and comprehend the discrepancies in more depth. The experts' satisfaction with the evidence for safety is insufficient. Effective risk communication is essential for the pharmaceutical business, governments, and healthcare professionals to gain public trust. Only when the public attitude has been analyzed and understood can this be accomplished. Regulators are now required to approach drug regulation, particularly drug safety problems, with a renewed commitment to transparency, involving patients and their representatives in the process (Beninger, 2020).

Conclusions

Pharmacovigilance has evolved into an important aspect of drug control. Even though it is a far from ideal system, it is likely to take the traditional form of spontaneous monitoring in poor nations for the foreseeable future. It is critical to have access to the information that was used to make the initial risk and harm decision to perform effective pharmacovigilance. The monitoring of the safety of commonly used medications should be a standard component of clinical practice. Drug information and poison control centers' communication tools, including

newsletters and other publications, can be used to disseminate drug warnings and other drug safety information to the professionals. There is a trade-off between the benefits and the potential for damage with all medications. To reduce the risk of damage, high-quality, safe, and effective medications must be used sensibly. To do this, it is necessary to promote public health by encouraging patients to have faith in the medications they take, which will eventually lead to trust in the health system as a whole.

Conflict of interest

No conflict of interest.

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