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PHARMACY AND PHARMACOVIGILANCE

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ABSTRACT

Pharmacy as a profession has made remarkable progress in the recent years. It has seen a pattern shift from product orientation to patient focus. Pharmacists can extend their role in pharmacovigilance as providers of services which promote drug safety. The meaning of pharmacovigilance is pharmakon (for medication) and vigilare (to keep watch). Pharmacovigilance is the science and activities related to the collection, detection and assessment of adverse event data. Pharmacovigiance is a complex concept which deals with botanical, chemical, biological medicines and medical devices. The primary data regarding suspected product is collected from healthcare professionals and patients to identify and prevent abnormalities associated with it. Pharmacovigilance deals with adverse effects if drug, serious adverse events, poly-pharmacy and paradoxical reactions. PV also includes vaccines failure, drug-drug interactions, irrational use, poisoning, overdose, misuse of drug as well as medication errors.

KEYWORDS: Pharmacovigilance, PvPI, Drug Safety, ADR.

INTRODUCTION

Drugs are used to cure or treat the illness as they capable to alter the physiological function in body. But due to various factors they always pose unwanted or unintended effects are called as adverse drug events.[1] It has been known that WHO has started the program of reporting and recording all adverse reactions processed by drugs.[2] The potential awareness about adverse drug reactions has resulted in the emergence of the practice of pharmacovigilance. Recently, herbal as well as blood products have been included as a part of pharmacovigilance.[3] Pharmacovigilance is an essential and integral part of clinical research.

It is widely accepted that a drug has to pass through clinical trials to establish its safety and efficacy before it launched in the market. Clinical trials offer many limitations like exclusion of some population groups like pregnant women, pediatrics which is not studied during trials. Further some other factors causing ADRs like environmental factor, genetic factor and drug interactions may not have been studied during trials.[4] So, the systemic pharmacovigilance is important to build up valid data on the safety of all category medicines for the developments of guidelines for effective use. The (CDSCO) Central Drugs Standard Control Organization already started a nationwide Pharmacovigilance program under the guidance of (DGHS) Directorate General of Health Services, Ministry of Family and Health Welfare and Government of India. It is necessary to improve communication between healthcare professionals and the public; and educating healthcare professionals well to understand risk/benefits of medicines. Establishing own national database and sharing the data with other regulatory agencies will contribute a lot required data from worldwide information to take the right decision on medicines and other products.[5] Softwares play a crucial role in clinical research. For clinical trial management softwares like Open Clinica, Real time-CTMS were used for patient management, investigator management, regulatory compliance at the study site and (Contract Research Organization) CRO site. Macro, eClinical suite were used in clinical information managements for case report form, designing, CRF Annotation, database designing, data entry, data verification, data validation, discrepancy management and data extraction at sponsor or CRO site. Whereas, pharmacovigilance software such as Argus, ArisGlobal, PvNET were the drug safety databases used duringthe study and VigiBase, VigiFlow were used in post marketing surveillance at the sponsor site to store the adverse event reports and safety profile of the drug.[6]

WHO DEFINATION

WHO defines the Pharmacovigilance (PV) as the pharmacological science relating to activities such as detection, evaluation, understanding and prevention of adverse effects, especially long term and short term side effects of medicines.[7] Pharmacovigilance is an important as well as integral part of clinical research. In General, pharmacovigilance is the knowledge of observing, examining and estimating evidence from patients and health care workers on the effects of drugs, natural products, traditional and herbal medicines with view to:

- Prevention from infectious diseases.
- Reporting essential requirements in special situations.

- Finding new risks associated with remedies.[8]

AIM OF PHARMACOVIGILANCE IN PHARMACY

Pharmacovigilance has an important role in the assessment of various side effects caused by the drugs. Pharmacovigilance has key role in pharmacy for detection and identification of drugs which caused a ADRs and the mechanism by which it caused the injury.[9]

- Improve public health, safety and patient care regarding use of medicines and all medical and paramedical interventions.[10]
- The Research efficacy of drug and by monitoring the adverse effects of drugs throughout the duration of their use to ensure their benefits/risks remains acceptable.
- The pharmacovigilance keeps track of any drastic effects of drugs.
- Contribute to the benefit, effectiveness, harm and the risk of medicines, encouraging their safe, rational as well as more effective use.
- Promote understanding, clinical trainig and education in pharmacovigilance and its effective communication to public.[11]
- Quantification and identification of previously unrecognized and unexpected adverse drug reactions to the established drugs and even the minor adverse effect to new drugs.
- Detection of groups of patient population at particular risk of ADRs.
- Detection of significant drug-drug interactions between new medicines and co-therapy with products already proven in the market, which may only be detected during widespread use.[5]

NEED OF PHARMACOVIGILANCE IN PHARMACY

Although medicines have led to advancement in the treatment and control of various diseases, they also produce adverse effects on human body. Most of drugs are targeted precisely to the causes and mechanisms of diseases, but they may also have minor effects on the other parts of the body; or interact negatively with the systems of the particular individual or with other drugs or substances they are administering or not work well or at all for some, may or all of those who take them for illness.[5]

Once a drug is marketed, it leaves the protected scientific environment of clinical trials and is free for the consumption by public. At this stage, many of drugs are only have been studied for short term safety and efficacy on a limited number of carefully selected individuals. Here need of pharmacovigilance arises which contains securing the early detection of newer

adverse reactions or the patients groups of exceptional sensitivity and introduces certain measures in order to manage such type of risks.[12]

OBJECTIVES OF PHARMACIOVIGILANCE IN PHARMACY

The important objective of pharmacovigilance involves exhibiting the efficacy of drugs by monitoring their adverse effect profile for many years from laboratory to the duration of the drugs. Pharmacovigilance helps to improves public health and safety in relation to use of medicines. In addition, it provides information to consumers and regulators on the effective use of drugs along with designing programs and procedures for collecting analyzing the reports from the clinicians and patients.[2,13] Pharmacovigilance prevents from drug-induced physical, mental sufferings by patients and it helps to avoid financial risks associated with unexpected adverse effects.[14]

ROLE OF PHARMACIST AS PHARMACOVIGILANCE PRACTITIONER

Pharmacists are one of the major shareholders along with the physicians, patients and other healthcare professionals.[15] Pharmacists play an important role in prevention, monitoring and management of the adverse events of various drugs. Pharmacists should be noted safety related activities of newer drugs by adding consequences when drug comes in direct contact with the patients who may not be involved in the clinical trials for ethical reasons. Pharmacists should investigate drug-drug interactions when newly formed drug is taken in combination with other drug. They should report spontaneous adverse reactions by using spontaneous report tool. Spontaneous reporting is helpful in detection of very delayed or rare reactions that could not be detected during the short period of the clinical trials. Pharmacists should be aware of the potential occurrence of unpredicted adverse reactions and report suspected adverse reactions to the Medicine Regulatory Authorities to facilitate identification and the assessment of drug safety signals. Pharmacists should notice that no medicinal product is entirely safe for all patients, in all places and at all times. They must always practice with some measures of uncertainty.[16]

Pharmacovigilance concept was started around 169 years ago, On Jan 29, 1848 when a young girl (Hannah Greener) from north of England died after receiving chloroform anesthetic before removal of an infected toenail. Mr. James Simpson had discovered that chloroform was a powerful as well as safer anesthetic and he had introduced it in clinical practice. The cause of Hannah's death was investigated but it was impossible to identify what killed her. Probably she died of a pulmonary aspiration or lethal arrhythmia.[17]

As a result of other deaths and alerts raised by clinicians about safety of anesthesia, the Lancet Journal established a commission to report deaths caused by anesthesia. The results were published in the Lancet in 1893.

The US Federal food and drug act was formed on June 30, 1906. It established that drugs must be free of any contamination. Furthermore, in 1911 this organization was banned for false therapeutic indication of drugs.[18] In 1937, there were 107 deaths in USA, because of use of sulfanilamide elixir, containing diethyl glycol as the solvent. This solvent was considered cause of deaths but the manufactory companies were not aware about its toxicity at that time.[17,19,20]

The thalidomide tragedy is a milestone in the development of pharmacovigilance. It was introduced in 1957 and prescribed as an apparently harmless treatment for morning sickness and nausea. It was tested in around 300 patients without toxicity. It was soon related to a congenital abnormality phocomelia, which caused severe birth defects in children of women who had been prescribed this medicine during their pregnancy. In 1962, after reports of number of cases of phocomelia, it was discontinued. In the same year, the Kefauver-Harris amendment was accepted, requiring scientific evidences of efficacy as well as safety before drug tests in humans.[21] As means of pooling existing data on ADRs, WHO'S programs for International Drug Monitoring was organized in 1968. Initially a trial project in 10 countries established national reporting systems for ADRs; the network has since developed significantly as more countries worldwide established national pharmacovigilance centers for the recording of ADRs.[21] Currently, 86 countries involved in the program, which is co-ordinate by WHO with its collaborating centre in Uppsala, Sweden. The collaborating center is liable for maintaining the global ADR database. At present the database contains approximately four million ADR reports.[22]

METHODS OF PHARMACOVIGILANCE

Currently, there are many methods of causality assessment but no single algorithm is accepted as a standard because of the shortcomings and discordances that subsist between them. We would explicate them in short list as below:-

- Dangaumou's French method
- Kramer et al. method
- Naranjo et al. method (Naranjo scale)

- Balanced assessment method
- Ciba-Geigy method
- Loupi et al. method
- Roussel Ulcaf causality assessment method
- Australian method
- Bayesian approaches or probabilistic.[23]

Most commonly used methods for monitoring of drug safety are as follows:-

- Spontaneous reporting systems
- Prescription-event monitoring (PEM)
- Risk Management
- Causality Assessment
- Signal Detection
- Risk Managements Plans
- Risk/Benefit profile of Drugs.[24]

STEPS IN PHARMACOVIGILANCE[25]

The basic steps involves in pharmacovigilance are as follows:-

- Safety data management
- Signal detection
- Signal evaluation
- Making decisions with regard to safety issues
- Providing information to all concerned stakeholders or parties
- Actions, including regulatory to protect public health

Other than this safety data management also includes:-

- Data collection and verification
- Coding of ADRs
- Causality assessment
- Coding of drugs
- Timely reporting to authorities

PARTNERS AND COMPONENTS OF PHARMACOVIGILANCE

Partners in pharmacovigilance

Understanding and tackling the constraints which typically include lack of resources, training, political support, and most especially scientific infrastructure are an essential prerequisite for future development of the science and practice of pharmacovigilance.

For monitoring the safety of medicines following key partners are required in pharmacovigilance:-

- Government
- Industry
- Academia and Hospitals
- Pharmaceuticals and medicinal associations
- Medicines and poisons information centers
- Patients
- Health professionals
- Consumers
- The media
- WORLD HEALTH ORGANIZATION

Component of Pharmacovigilance

As important component of a country's ability to monitor pharmaceutical safety is a national pharmacovigilance system that is supported by the drug regulatory authority. The major components of a pharmacovigilance system are data collection, which can be passive, active, or mandatory, and data analysis and reporting. The main component of pharmacovigilance is pharmacogenomics or pharmacogenetics. The sudden change in drug response and drug tolerance can be understood by pharmacogenetics.

According to WHO, pharmacovigilance activities are done to monitor detection, assessment, understanding and prevention of any obnoxious adverse reactions to drugs at therapeutic concentration on animal and human beings.

However, there is also a growing focus among scientists and environmentalists about the impact of drugs on environment and surroundings. The existing term 'Ecopharmacology' is too broad and not even defined in a clinical manner.

The term 'Pharmacoenvironmentology' seeks to deal with the environmental impact of drugs given to humans and animals at therapeutic doses.

Pharmacovigilance pertains to the activities of adverse effects of drugs at therapeutic doses on animal and human beings. In this context, pharmacoenvironmentology may be extension of pharmacovigilance dealing specifically with the effects pertaining to the environment and ecology of drugs given in therapeutic concentrations.[26]

PHARMACY AND DRUG SAFETY

Safety can be defined as, "relative absence of harm" but that does not mean safety is never doing anything and hoping nothing has happened. In pharmacovigilance, safety means the collection of reports of adverse effects of drugs safety can be generating data and arriving upon a solution to decide further use of drug.

After the thalidomide tragedy that use of opium was deemed necessary to closely control the quality, efficacy and safety of medicines. This basically led to the discipline called pharmacovigilance. Pharmacovigilance is an activity contributing to the protection of public health and patients. It deals with the collection of adverse drug reaction (ADR) reports from stakeholders for monitoring the safety of drugs. ADR is unintended as well as noxious response to medicinal product. ADR may rise from use of the product within or outside the terms of the marketing authentication. A pharmacist knows it better why drugs are non-inclusive of safety profile in entirely before it enters in market. Pharmacists have a main contribution to make with regards to post marketing surveillance. Whether it is prescribed therapy or non-prescribed drug, most drugs accessible to patients are made available through the pharmacists.[16]

Role of pharmacist in drug safety

Erstwhile, pharmacist's key role was only dispensing the drugs. But at present its main role in drug safety, education, as well as in reducing medication error.

Pharmacist's role is not just confined to reporting adverse events but there has to be proactive approach in preventing the drug related adverse events.

ADVERSE DRUG REACTIONS (ADRs)

Sometimes, at normal dose given medications may harm the patients are called as an adverse drug reaction (ADR).[27] Meaning of ADR is different from side effect. In field of pharmacovigilance, the evaluation of adverse drug reaction is most.

Concerning marketed remedies, definition of ADR is as follows:-

In patient at normal doses harmful and unpleasant reaction of drug for treatment and medication of disease or for changes of biological utility.

All drugs are capable for producing adverse reactions and whenever drug is given a risk is taken. The magnitude of risk has to be considering along with magnitude of therapeutic benefit for deciding whether to use or not to use a specific drug in a patient.[28] The ADRs may occur only after prolonged medication or after stoppage of drug. ADRs are common; an incidence of 10- 25% has been documented in different clinical settings. ADRs are more common with multiple drug therapy.[29]

There are mainly two types of ADR which are as follows:-

1. Unlisted/Unexpected/Unpredictable adverse drug reaction:-

An adverse reaction is the nature of drug which is not reliable with the appropriate product data which available at the time of clinical trials. Company is needed help during investigations for an unapproved drug.[30]

2. Listed/Expected/Predictable Adverse Drug Reaction:-

The information about ADR is like specificity and severity of the drug is already recorded.[30]

Adverse drug reactions reporting

When the adverse reaction to drug clinically important, potentially serious, all health care workers, including pharmacists, doctors, nurses and other health experts are requested to clarify it. It is essential to report an adverse reaction of particular or newer drug to pharmacovigilance.[31]

Adverse events (AEs)

An adverse event is not only causal relationship with patient but also its one of the medical incidence with patient. So, adverse event can be critical which is temporally correlated with the use of medication program even if you don’t have all facts or you are unsure that the medicine is definitely responsible for causing the adverse reaction. Adverse event reporting

includes data maintaining, receipt, triage, distribution, evaluation and reporting adverse event data.[29,32]

AE reports may include solicited reports from patient support programs, reports from clinical or marketing studies, spontaneous reports from health professionals, reports from other sources like literature sources, reports from media like social media, websites and reports reported to drug regulatory authorities themselves.[33]

Especially for pharmaceutical companies AE reporting also provides a data that play an important in accessing the benefit-risk profile of a given drug. The following are few elements of AE reporting[34]:-

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

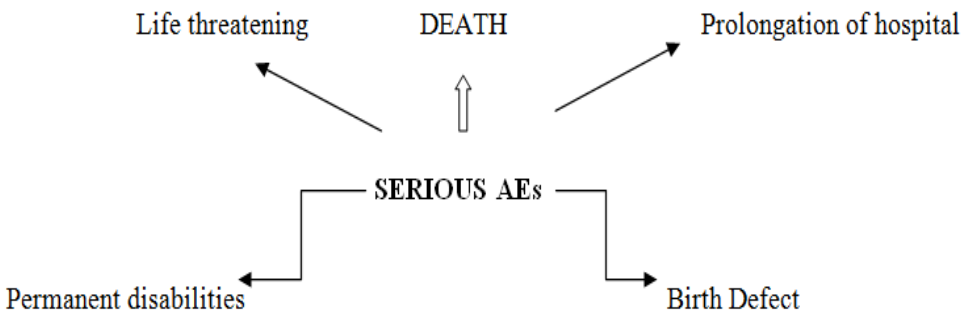

Fig. 1: Effects of serious adverse events.

Spontaneous Reporting Systems in ADRs

- Repossession of further data
- Access to all important pre- and post- marketing information
- Regionalization
- Detailed drug utilization data
- Standard evaluation of significance and causality
- Encouragement.[35]

PHARMACOVIGILANCE REPORTING AND FUNCTIONING

To achieve the pharmacovigilance obligations for its marketed products, a pharmaceutical companies in India has to essentially carry out collection which is included accelerated reporting of serious, unpredicted adverse effects.[36] Pharmacovigilance studies include people involved on various levels, organizational units and their functions which are as follows:-

PEOPLE	FUNCTIONS	STRUCTURE
Healthcare professionals, Doctors, pharmacists	Reporting adverse effects and other effects	Manufactures
Clinical pharmacist, Medical specialist	Initial Analysis, Data collection	Safety Advisory Committee Pharmacovigilance centre
Industry and Regulatory Officials	Warning risk management, Product recall, etc.	Regulatory authority industry Health services

Fig. 2: Chart of pharmacovigilance's function and structure.

The main function of health professionals, clinical pharmacist is to prevent medicines from the particular problem and to reduce mortality and morbidity.

Identification and reporting

The medical practitioner plays vital role in pharmacovigilance to suspect an adverse drug reaction. This is because the medical practitioner is the very first person to who the patient will come with the symptoms.[37] The healthcare professionals report the suspect ADRs which are related to specific medicinal product to the pharmacovigilance center.[38] These reports are in written form, the reports are collected and then verified by pharmacovigilance center and are generally entered in database. This database is used to find to detect the potential signals and analyze the data regarding risk factors, changes in reporting profiles.[39]

Collection and validation

The collection and validation of the initial data that is the data transmitted from reporter to competent authority. For the management of the reports that are transmitted by electronically, the standardized operational procedure should be followed.[40] In European Directives and regulations, only the serious cases reported by healthcare professionals and will be received on an expedited basis. Whereas in India, pharmacovigilance spontaneous report concerns the single case as a one patient, one identifiable reporter, one or more suspected reactions and one or more suspected medicinal products.[41]

IMPLEMENTATION OF PHARMACOVIGILANCE PROGRAMS

IPC (Indian Pharmacopoeia Commission) assumed the need for beginning local hospital based centers across the nation for the patient safety. Monitoring both previously unknown and known serious side effects of medicines is essential to gather any new available data regarding their safety profile. In vast country such as India with a population over 1.2 million and with ethnic diversity, various disease prevalence modes, practice of different systems of medicines, socioeconomic status, it was found significant to have a standardized pharmacovigilance and drug safety monitoring program for the nation.[42]

Short terms goals of PvPI[42]

- To start and implement pharmacovigilance system in India.
- To aware healthcare professionals in reporting of adverse effects of drugs, medicinal instruments, vaccines, biological products.
- To collect case reports and data.
- To enroll, initially, all MCI approved medical colleges in program including south, north, west and east of India.

Long terms goals of PvPI

- To develop pharmacovigilance system to all hospitals and centers of public health programs located aross India.
- To start and implement (e-reporting) electronic reporting system.
- To develop reporting culture in healthcare professionals.
- To make ADR reporting compulsory for the healthcare professionals.

PHARMACOVIGILANCE IN INDIA

Aim

Safeguard the health of Indian public by ensuring that the benefits of use of medicine outweigh the risk associated with its use.

The Need

In India the clinical trials are being started in 1996 in global market, year of landmark for industry was 2005. The studies of clinical trials are supervised, structured where the safety of newer drug or therapy is tested in an effort to begin new treatments that will help afflicted with targeted condition. For conducting the global clinical trials, Indian clinical market provides an opportunity of availability of highly educated talents, large patient populations,

low operation cost, a wide favourable economic and spectrum of disease. For the approval, well organized, and supervised clinical trials have to be necessarily conducted as per ICH GCP guidelines with the defined rules of the country in which the trials are planned. It is very important as the patients are studied during condition of the phase of pre-marketing which don't necessarily reflect the way the medicine will be used in general practice once it is marketed.[43]

The pharmacovigilance program is coordinated by the Indian Pharmacopeia Commission, Ghaziabad as a (NCC) National Coordinating Center. The main function of IPC is to maintain the quality and to ensure the safety of medicines. The purpose of pharmacovigilance program is to collect primary data, process and analyze it and use inferences to recommend regulatory interventions, besides communicating risks to public as well as healthcare professionals as well as to create a country wide system patient drug monitoring. The motive Of PvPI is to develop evidence based information on safety of medications.[44]

The Development

India joined the WHO ADR monitoring program which is in Uppsala, Sweden in 1997. For monitoring ADRs the three main centers were identified, which are mainly based in teaching hospitals. Mainly, the ADR of the medicines which are marketed for sell in OTC centers are monitored by these centers.[45] The three centers are as follows:-

- The National Pharmacovigilance Centre located in Department of pharmacology and all India Institute of Medical services[AIIMS]
- New Delhi and two WHO centers located in Mumbai(KEM) hospital
- Aligarh [JLN Hospital, Aligarh Muslim University]

The Chronological developments in field of the pharmacovigilance with reference to India are as follows.[46]:-

YEAR	EVENT
1747	First reported clinical trials by James Lind, proving the effectiveness of lemon juice in Preventing scurvy.
1937	Death of 107 children due to sulfanilamide toxicity.
1950	Aplasticanemia caused due to chloromphenicol.
1961	Global tragedy due to thalidomide toxicity.

1963 16th world health assembly recognize important to rapid action of adverse drug reaction.

1968 WHO pilot research project for the international drug monitoring.

1996 Clinical trials of global standards started in India.

1997 India joined WHO adverse drug reaction monitoring programs.

1998 Pharmacovigilance initiated in India.

2002 67th National Pharmacovigilance center developed in India.

2004-05 National Phgarmacovigilance Program established in India.

2005 Conduct of structure clinical trials in India.

2009-10 PvPI initiated.

Pharmacovigilance guideline for India[47,48]

Many more countries have framed their own pharmacovigilance guidelines with a purpose to have a systematic process of drug safety monitoring. India has schedule Y related to drug safety, which when viewed in light of contemporary global practice. There is a robust need that the CDSCO must formulate a detailed pharmacovigilance guideline. Such type of guideline shall cover all relevant areas of pre and post marketing safety, guideline shall be in line with present international scenario so as to support India's growth if any participant in multinational clinical trials.

The International conference on Harmonization contains around six guidelines involving different aspects of drug safety:-

E2A-Clinical Safety Data Management: Standards and Definitions for the expedited reporting.

E2B-Clinical Safety Data Management: Data contents for transmission of single case safety reports.

E2C- Clinical Safety Data Management: Spontaneous safety update reports for the marketed drugs.

E2D- Post Approval Safety Data Management: Definitions and Standards for expedited reporting.

E2E- Pharmacovigilance planning.

E2F- Development of Safety Update Report.

INTERNATIONAL SOCIETY OF PHARMACOVIGILANCE (ISOP)

The International Society of the Pharmacovigilance is international non-profit scientific organization which aims to promote the pharmacovigilance in both scientifically and educationally and improves all aspects of the safe and the proper use of medicines in all the countries. In 1992 it was established as the European Society of the Pharmacovigilance.[49]

INTERNATIONAL COLLABORATIONS

The principles of international collaborations in pharmacovigilance are main basis for the WHO International Drug Monitoring Program, through which around 90 to 100 members nations have the systems in place that encourages healthcare personnel to record as well as report the adverse events of drugs in their patients. The Uppsala Monitoring Center located in Uppsala, Sweden. This centre works by collecting, assessing and communicating the data from the member countries the national pharmacovigilance programs related to effectiveness and risks of drugs.[50] The Council for the International Organizations of the Medical Sciences (CIOMS), through its working groups provides the guidance on the safety of drug related problems. It is the part of WHO and the prepared reports are used as the expanding the future policies of drug regulatory.[51]

Europe

The National Competent Authorities (NCAs) conduct as well as coordinate the (EMA) European Medicines Agency. The pharmacovigilance database consists of all suspected serious adverse reactions are balanced and expanded by the EMA in the European Community and the system is known as Eudravigilance.

Japan

Pharmaceuticals and Medical Devices Agency (PMDA) and Ministry of Health, Labour and Welfare (MHLW) regulate the pharmacovigilance system in Japan.

United States

There are mainly three primary branches of pharmacovigilance in U.S. which includes the FDA, the pharmaceutical manufacturers, and the academic or non-profit organizations.

Serbian

To achieve the optimum number of 2000 spontaneous reports per year, regular contact with healthcare professionals and then finally good pharmacovigilance practice is the final aim of the Serbian pharmacovigilance.[51]

CURRENT STATUS OF PHARMACOVIGILANCE

In 2015, (DTAB) the Drug Technical Advisory Board has recommended mandating pharmaceutical companies to report and record the adverse drug events of newly marketed drug. Further it re-insisted on 2011 recommendation for setting up pharmacovigilance in all pharma companies which will managed by well trained medical pharmacist or officer. It also emphasized on sensitizing physicians and pharmacists across the country by involving MCI (Medical Council of India) and on training medical reps for assembling adverse reaction reports from healthcare professionals.[52]

The Health Ministry in March 2015 approved the MvPI (Materio Vigilance Program of India) which would supervise Medical Device which is associated with adverse events (MDAE) and be coordinated by IPC in collaboration with CDSCO. MvPI are to be started initially in 10 medical colleges in order to detect the risk-benefit profile of medical devices. The MvPI was formally launched on 6 July, 2015 at Indian Pharmacopoeia Commission, Ghaziabad by DCGI; similarly the programs for Biovigilance and Haemovigilance were launched in 2012.[53] Current, initiatives undertaken by PvPI consists of provision of toll-free number as well as introduction to adverse event reporting forms in different languages to encourage consumer reporting.

Pharmaceutical companies and the pharmacovigilance outsourcing industries have shown interest to work with PvPI. It is worth mentioning that the pharmacovigilance outsourcing industries in India have grown in the past 8 years, with the number of pharmacovigilance professionals in the country amounting around 15,000 people. Ranging from the primary case processing activities to complex functions like signal (adverse events) detection and analysis, the spectrum of pharmacovigilance capabilities available in India has been expanding.

India is the 4th largest producer of pharmaceutical products in the world. Many new drugs are being introduced in India, so pharmacovigilance system should improve itself to protect Indian people from various drug events. India is a vast country and there is an abundance of various drug brands over 6,000 licensed drug manufacturers and more than 60,000 branded

pharmaceutical formulations.[54] In recent years India based pharmaceutical companies have increased their capacity to develop and launch newer drugs through their own research efforts. This has heightened the significance of developing adequate internal pharmacovigilance standards to identify adverse drug events. The pharmacovigilance system needs a pharmacovigilance advisor to effectively implement the systems and policies on pharmacovigilance.

The data obtained to date in zonal centers from various peripheral centers is not well-analyzed and poor. There is inadequate research on adverse drug reactions in India, so the exact incidence of particular ADR is still unknown. The reporting forms used by many people who are engaged in various pharmacovigilance works are different from the reporting form used by the PvPI which makes it difficult to transport information to national database. Understanding by healthcare professionals especially in rural areas knowledge and motivation for pharmacovigilance concept is almost negligible.[55] The DCGI should act quickly to improve pharmacovigilance so as to integrate good pharmacovigilance practice into the procedures and processes to help ensure regulatory compliance and enhance post marketing surveillance and clinical trial safety.

FUTUIRE ASPECTS OF PHARMACOVIGILANCE IN INDIA

Pharmacovigilance is a complex concept which deals with botanical, chemical, biological medicines and medical devices.[56] The primary data regarding suspected product is collected from healthcare professionals and patients to identify and prevent abnormalities associated with it. Pharmacovigilance deals with adverse effects if drug, serious adverse events, poly-pharmacy and paradoxical reactions.[57] PV also includes vaccines failure, drug-drug interactions, irrational use, poisoning, overdose, misuse of drug as well as medication errors.[58]

Pharmacovigilance practice is essential for all systems of medicines in India that ensures patient's safety. Following are certain future aspects where more emphasis is essential for better pharmacovigilance practice in ASU system of medicine.[59]

- Strengthen the roles of pharmaceutical manufacturers as the main body of ASU (Ayurveda, Siddha, and Unnani) drugs.
- Improve training, education and publicity.
- Strengthen the pharmacovigilance system for ASU drugs

- Prioritize the basis of ASU drug safety surveillance.
- Encourage the healthcare professionals for rational use of ASU drugs.
- Develop an international coordinating database for adverse events as well as adverse reaction reporting and promote signal detection.
- Communicate safety data to the relevant agencies for cooperation to detect the nature of the ADRs.

A strong pharmacovigilance system is necessary if medicines are to be intended rationally or safely. This will helpful for all healthcare professionals, pharma companies, regulatory authorities and the consumers. It is also beneficial to pharmaceutical industries to supervise their medicines for risk and to implement effective risk management plans to protect their drugs in serious conditions. In order to overcome the issues, problems and challenges facing the growth of robust pharmacovigilance system for India, the following proposals may be helpful[60]:-

- Building and maintaining a robust pharmacovigilance system.
- Making the pharmacovigilance reporting compulsory.
- Initiating pharmacovigilance inspections.
- High-level discussions with various stakeholders.
- Improving the DCGI with the well trained medial evaluators for pharmacovigilance.
- Creating a single country adverse event reporting, recording form which can be used by all.
- Creating post marketing database for ADRs for signal detection.
- Listing of all new drugs for maintaining a standard database for each and every pharmaceutical industry.
- Focused education and training for all healthcare professionals in the area of pharmacovigilance.
- Collaborating with pharmacovigilance organizations in order to improve drug safety.
- Building a network of phartmacovigilance related to pharmacopeidemiologists, pharmacoenvironmentologists and academicians.

CONCLUSION

Pharmacovilgilance concept is necessary for all systems of medicines to check the safety of drugs. It is beneficial to improve public health. In India, Pharmacovigilance system has increased awareness in people regarding ADR reporting. The problems in underreporting are

resolving due to availability reporting like reporting form is available in vernacular languages as well as use of social media for reporting ADRs.

More clinical trials are now being conducted in India. The healthcare professionals should appreciate that there is a specific system in India to report, collect and evaluate the adverse events data. Various companies are started outsourcing the pharmacovigilance activity in India which is helpful for robust pharmacovigilance culture.

Still government needs to focus on enhancement of pharmacist's knowledge and giving them facilities and power to initiate and conduct the pharmacovigilance programs. Considering the Indian population, talent, efforts and interest in HCPs as well as recent developments in pharmacovigilance system, India will be outsourcing centre for global pharmacovigilance system in future.

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