ISSN 2581-6217

World Journal of Pharmaceutical Science & Technology

Journal homepage: www.wjpst.com

Review Article

AN OVERVIEW OF THE WORLDWIDE MASTER KEY FOR PHARMACOVIGILANCE AND ITS ROLE IN INDIA

Mrs. Harshada Shewale[1], Ms. Archana Gawade[2]

1. Clinical research Scholar from Elite institute of Pharma Skills Pune.
2. Managing Director, Elite Institute of Pharma Skills, Pune

Address for correspondence:

Mrs. Harshada Shewale, Clinical research Scholar from Elite institute of Pharma Skills Pune.
E-mail- harshadashewale11@gmail.com

Received: 30-3-2022, Revised: 25-4-2022, Accepted: 5-6-2022

ABSTRACT

Pharmacovigilance plays a key role in the healthcare system through assessment, monitoring and discovery of interactions amongst drugs and their effect in human. Pharmaceutical and biotechnological medicines are designed to cure, prevent or treat diseases; however, there are also risks particularly adverse drug reaction (ADR) can cause serious harm to patients. Today many pharmacovigilance centers are working for drug safety monitoring in this global pitch, however, at the turn of the millennium pharmacovigilance faces major challenges in aspect of better safety and monitoring of drug. Thus, for safety medication ADRs monitoring required for each medicine throughout its life cycle, during development of drug such as premarketing including early stages of drug design, clinical trial, and post-marketing surveillance. Adverse events reported by PV system potentially benefit to the community due to their proximity to both population and public health practitioners in terms of language and knowledge, enables easy contact with reporters by electronically. Hence, PV helps to the patients get well and to manage optimally or ideally, avoid illness is a collective responsibility of industry, drug regulators, clinicians and other healthcare professionals to enhance their contribution to public health. This review summarized objectives and methodologies used in PV with critical overview of existing PV in India, challenges to overcome and future prospects with respect to Indian context.

In this review we will discuss about drug safety, worldwide pharmacovigilance centers and their role, benefits and challenges of pharmacovigilance and its future consideration in healthcare sectors. Hence, PV helps to the patients get well and to manage optimally or ideally, avoid illness is a collective responsibility of industry, drug regulators, clinicians and other healthcare professionals to enhance their contribution to public health. This review summarized objectives and methodologies used in PV with critical overview of existing PV in India, challenges to overcome and future prospects with respect to Indian context.

In this review we will discuss about drug safety, worldwide pharmacovigilance centers and their role, benefits and challenges of pharmacovigilance and its future consideration in healthcare

KEYWORDS: Adverse drug reaction; Clinical trials; Data mining; Indian Pharmacopoeia Commission; Pharmacogenomics; Pharmacovigilance (PV).

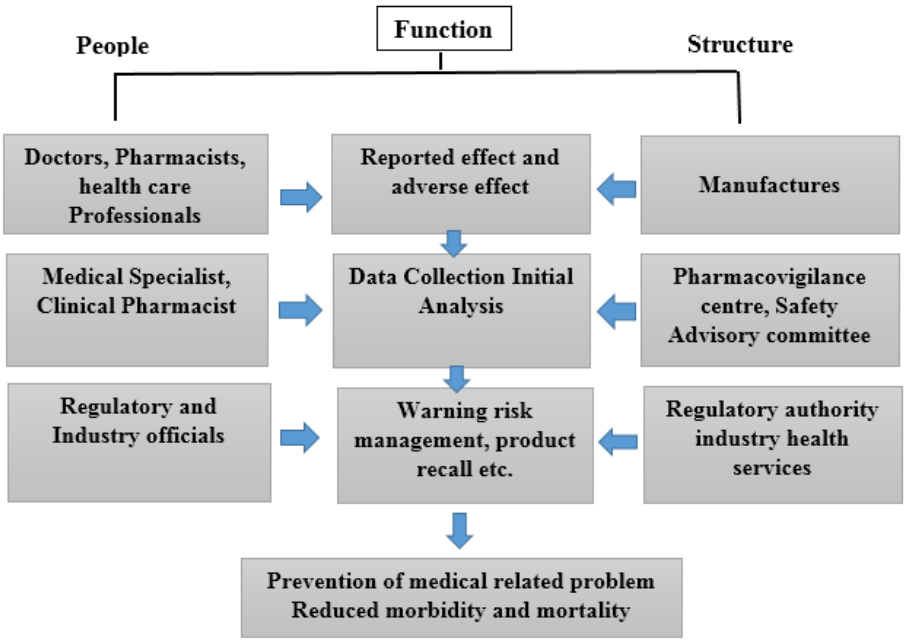
INTRODUCTION:

Pharmacovigilance is science and Activity relating to detection, Assessment, understanding, prevention of adverse drug reaction. Pharmacovigilance (PV) was officially introduced in December 1961 with the publication of a letter (case report) in the Lancet by W. McBride, the Australian doctor who first suspected a causal link between serious fetal deformities (phocomelia) and thalidomide, a drug used during pregnancy: Thalidomide was used as an antiemetic and sedative agent in pregnant women [1].In 1968, the World Health Organization (WHO) promoted the "Programmers for International Drug Monitoring", a pilot project aimed to centralize world data on adverse drug reactions (ADRs). In particular, the main aim of the "WHO Programmers" was to identify the earliest possible PV signals. The term PV was proposed in the mid-70s by a French group of pharmacologists and toxicologists to define the activities promoting "The assessment of the risks of side effects potentially associated with drug treatment" [2]. The overall incidence of ADRs in hospitalized patients is estimated to be 6.7% (range 1.2-24.1%) and that of fatal ADRs 0.32% (0.1-0.85%). [2] Data indicates that in patients who experience ADRs, death rates are 19.18% higher and the length of hospital stay is 8.25% higher. Total medical cost for patients with ADRs are increased by an average of 19.86%. [3].

PV is the science of collecting, monitoring, researching, assessing and evaluating information from healthcare providers and patients on the adverse effects of medications, biological products, blood products, herbals, vaccines, medical device, traditional and complementary medicines with a view to identifying new information about hazards associated with products and preventing harm to patients. The challenge of maximizing drug safety and maintaining public confidence has become increasingly complex. Pharmaceutical and biotechnology companies must not only monitor, but also proactively estimate and manage drug risk throughout a product's lifecycle, from development to post-market [4]. PV is particularly concerned with ADRs, which are drug responses that are noxious and unintended, and which occur at doses normally used for the prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function [4].

SCOPE OF PV

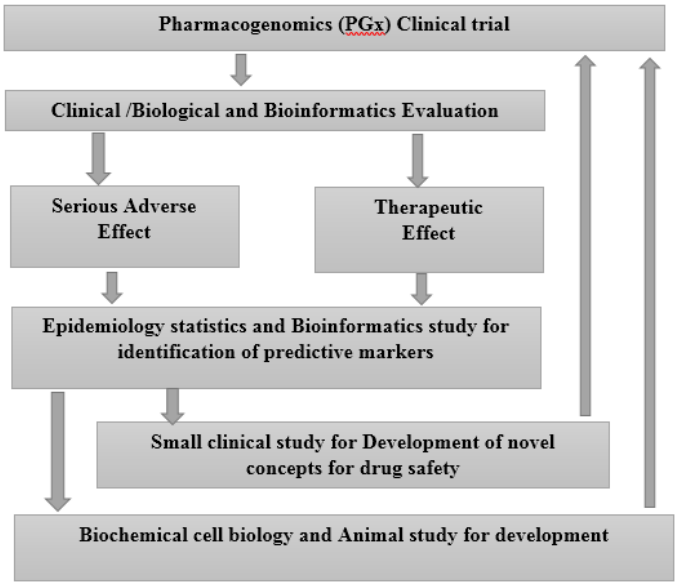
The discipline of PV has developed considerably since the 1972 WHO technical report, and it remains a dynamic clinical and scientific discipline. It has been essential to meet the challenges of the increasing range and potency of pharmaceutical and biological medicines including vaccines, which carry with them an inevitable and sometimes unpredictable potential for harm. The risk of harm, however, is less when medicines are used by an informed health profession and by patients who themselves understand and share responsibility for their drugs. When adverse effects and toxicity appear, particularly when previously unknown in association with the medicine, it is essential that they are analyzed and communicated effectively to an audience that has the knowledge to interpret the information. This is the role of PV, of which much has already been achieved. But more is required for the integration of the discipline into clinical practice and public policy. To fulfill the PV obligations for its marketed products as per regulations, a pharmaceutical company in India has to essentially carry out activities such as collection, and expedited reporting of serious unexpected ADRs [9]. A typical setup for PV studies, including people involved on various levels, organizational units and their functions are shown figure1.



➢ Role of Pharmacovigilance

- Pharmacovigilance in Drug Regulation
  a. Clinical trial Regulation
  b. Post marketing safety monitoring
  c. International harmonization of drug regulatory requirement
  d. Requirement of National Regulatory Authority

- Pharmacovigilance in clinical practice
  a. Education, training, and Access to reliable information
  b. Communication with health Professional
  c. Linking clinical finding with research and policy.



PHARMACOVIGILANCE IN INDIA

India has more than half a million qualified doctors and 15,000 hospitals having a bed strength of 6,24,000. It is the fourth largest producer of pharmaceuticals in the world. It is emerging as an important trial hub in the world. Many new drugs are introduced in our country. Therefore, there is a need for a vibrant pharmacovigilance system in the country to protect the population from the potential harm that may be caused by some of these new drugs. Clearly aware of the enormity of task the Central Drugs Standard Control Organization (CDSCO) has initiated a well-structured and highly participative National pharmacovigilance program. It is largely based on the recommendations the WHO document titled "safety monitoring of medicinal products- Guidelines for setting up and running a pharmacovigilance centre".[5]

➢ Future aspects of pharmacovigilance in India

With more and more clinical trials and other clinical research activities being conducted in India, there is an immense need to understand the importance of pharmacovigilance and how it impacts the life cycle of product. Given this situation, the DCGI should act quickly to improve pharmacovigilance so as to integrate good pharmacovigilance practice in to the processes and procedures to ensure regulatory compliance and enhance clinical trial safety and post marketing surveillance. A properly working pharmacovigilance system is essential if medicines are to be used safely. It will benefit all parties including health care professionals, regulatory authorities, pharmaceutical companies and the consumers. It helps pharmaceutical companies to monitor their

medicines for risk and to devise and implement effective risk management plans to save their drugs in difficult circumstances.

HISTORICAL PERSPECTIVES OF WHO - DRUG SAFETY MONITORING

In 2002, more than 65 countries have their own pharmacovigilance centers. Membership of the WHO for International Drug Monitoring is coordinated by the WHO Collaborating Centre for International Drug Monitoring, known as the Uppsala Monitoring Centre (UMC).

Pharmacovigilance is now firmly based on sound scientific principles and is integral to effective clinical practice. The discipline needs to develop further to meet public expectations and the demands of modern public health. The Sixteenth World Health Assembly adopted a resolution (WHA 16.36) [6] that reaffirmed the need for early action in regard to rapid dissemination of information on adverse drug reactions and led later to creation of the WHO Pilot Research Project for International Drug Monitoring. The purpose of this was to develop a system, applicable internationally, for detecting previously unknown or poorly understood adverse effects of medicines. [7]

➢ Pharmacovigilance and International Health

The current global network of pharmacovigilance centers is coordinated by the Uppsala Monitoring Centre, would be strengthened by an independent system of review. This would consider contentious and important drug safety issues that have the potential to affect public health adversely beyond national boundaries. The Erice Declaration provides a framework of values and practice for collection, analysis and subsequent communication of drug safety issues. Today, the burden of ADRs on public health despite the progress in pharmacovigilance that has been made, the burden on public health of ADRs remains significant. [8] Pharmacoecono microscopic studies on the costs of adverse reactions suggest that governments pay considerable amounts from health budgets towards covering costs associated with them [9]. However, it has become increasingly clear that the safety profile of medicines is directly linked with socio-political, economic and cultural factors that in turn affect access to medicines, their utilization patterns and public perceptions of them. [10,11]

DATA MINING FOR PV

PV, also known as drug safety surveillance, is the science of enhancing patient care and patient safety regarding the use of medicines by collecting, monitoring, assessing, and evaluating information from healthcare providers and patients. In that view, PV can be divided into two stages such as premarketing surveillance – information regarding ADRs is collected from pre-clinical screening and phases I to III clinical trials; and post-marketing surveillance – data accumulated in the post approval stage and throughout a drug's market life shown in Figure 4 [12].PV has relied on biological experiments or manual review of case reports; however, due to the vast quantities and complexity of data to be analysed, computational methods that can accurately detect ADRs in a timely fashion have become a critical component in PV. Large-scale compound databases containing structure, bioassay, and genomic information, as well as comprehensive clinical data sets

such as electronic medical record (EMR) databases, have become the enabling resources for computerized ADR detection methods [13].

- **Premarketing surveillance**

PV at the pre-marketing stage has been devoted to predict or assess potential ADRs early in the drug development pipeline. One of the fundamental methods is the application of preclinical in vitro Safety Pharmacology Profiling (SPP) by testing compounds with biochemical and cellular assays. The hypothesis is that if a compound binds to a certain target, then its effect may translate into possible occurrence of an ADR in humans. However, experimental detection of ADRs remains challenging in terms of cost and efficiency. There have been numerous research activities devoted to developing computational approaches to predict potential ADRs using preclinical characteristics of the compounds or screening data. Most of the existing research can be categorized into protein target based and chemical structure-based approaches. Others have also explored integrative approach [14].

- **Post-marketing surveillance**

Although a drug undergoes extensive screening before its approval by the Food and Drug Administration (FDA), many ADRs may still be missed because the clinical trials are often small, short, and biased by excluding patients with comorbid diseases. Premarketing trials do not mirror actual clinical use situations for diverse (e.g. inpatient) populations, thus it is important to continue the surveillance post market. PV plays an essential role in the post-market analysis of newly developed drugs [15,16]. Pharmaceutical companies' competition along with rigorous regulatory evaluation procedures empowers a complex research and development process before launching a new drug into the market. Several unique data sources are available for post marketing PV [17]. PV, also known as drug safety surveillance, is the science of enhancing patient care and patient safety regarding the use of medicines by collecting, monitoring, assessing, and evaluating information from healthcare providers and patients. In that view, PV can be divided into two stages such as premarketing surveillance – information regarding ADRs is collected from pre-clinical screening and phases I to III clinical trials; and post-marketing surveillance – data accumulated in the post approval stage and throughout a drug’s market life shown in Figure 3 [18].

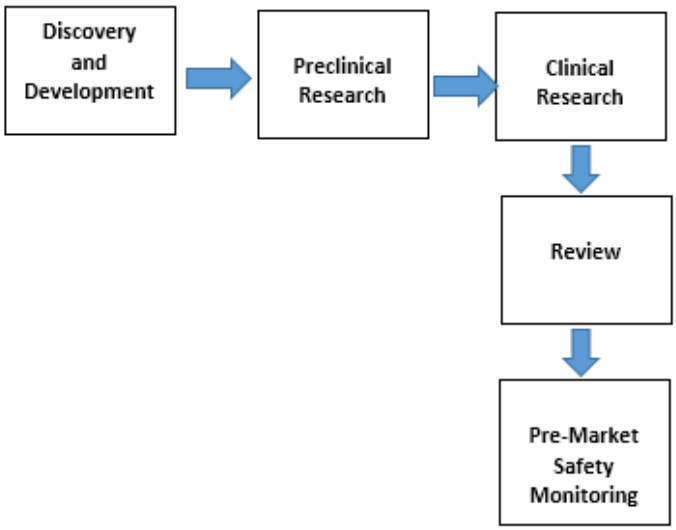


Figure 3. Pharmacovigilance at different stages of drug development

DETECTION AND REPORTING

A healthcare professional or marketing authorization holder reports suspected ADRs related to one or more medicinal products, to a PV centre. Reports are made on writing report forms, by telephone, electronically, or by any other approved way [19]. Reports are collected and validated by the PV centre and are usually entered into a database. Serious reactions should be handled with the highest priority. The database is used to identify potential signals and analyse data in order to clarify risk factors, apparent changes in reporting profiles etc [20]. A typical ADR reporting form is shown Figure 4. Systematic methods for the detection of safety signals from spontaneous reports have been used. These methods include the calculation of the proportional reporting ratio, as well as the use of Bayesian and other techniques for signal detection. Data mining techniques have also been used to examine drug-drug interactions [21].

Data mining techniques should always be used in conjunction with, and not in place of, analyses of single case reports. Data mining techniques facilitate the evaluation of spontaneous reports by using statistical methods to detect potential signals for further evaluation.

CONCLUSION:

- The PV in India has become an important public health issue as regulators, drug manufacturers, consumers, and healthcare professionals are faced with a number of challenges.
- The PV in India continues to grow, evolve, and improve.
- To achieve this is to serve public health, and to foster a sense of trust among patients in the medicines they use that would extend the confidence in the health service in general.
- This also enhances the knowledge of prescribers about drug-related events, and thus appropriate modification in the treatment can be done to benefit the patients

REFERENCE:

1. McBride WG. 1961. Thalidomide and congenital abnormalities. *Lancet*. 278, 1358. http://dx.doi.org/10.1016/S0140-6736(61)90927-8
2. 2. Lazarou J, Pomeranz BH, Corey PN; Incidence of Adverse Drug Reactions in hospitalized patients. JAMA, 198; 279: 1200-1205.
3. 3. Bord CA, Rachi CL; Adverse Drug Reactions in United States Hospitals. Pharmacotherapy, 2006; 26(5): 601-08. 3. WHO. The Importance of Pharmacovigilance, Safety Monitoring of medicinal products. World Health Organization 2002.
4. Report E. Effective communications in Pharmacovigilance. International Conference on Developing Effective Communications in Pharmacovigilance, Erice, Sicily 1997; 24-27
5. P.Biswas, A. K. Biswas setting standards for proactive pharmacovigilance in India: the way forward. Indian Journal of pharmacology, 2007; 39: 124-128
6. Geneva: World Health Organization. 1973. Handbook of resolutions anddecisions of the World Health Assembly and Executive Board.Availablefrom: http://whqlibdoc.who.int/wha_eb_handbooks/9241652063_Vol2.pdf [Last cited on 2009 Dec 26.
7. Lared NL. Pharmacists' role in reporting adverse drug reactions in an international perspective. 2003. Availablefrom: http://www.lareb.nl/documents/pds2004_1291.pdf [last cited on 2010 Jan 28] [PubMed]
8. Lazarou J, Pomeranz BH, Corey PN. Incidence of ADRs in hospitalized patients: A meta-analysis of prospectivestudies. *J Am Med Assoc.* 1998; 279:1200–5. [PubMed] [Google Scholar]
9. White TJ, Arakelian A, Rho JP. Counting the costs of drug-related adverse events. *Pharmacoeconomics.* 1999; 15:445–58.
10. Avorn J, Solomon DH. Cultural and economic factors that (mis)shape antibiotic use: The non-pharmacologic basis of therapeutics. *Ann Intern Med.* 2000; 133:128–35.
11. Ball LK, Evans G, Bostrom A. Risky business: Challenges in vaccine risk communication. *Pediatrics.* 1998; 101:453–8.
12. Berlin JA, Glasser SC, Ellenberg SS. 2008. Adverse Event Detection in Drug Development: Recommendations and ObligationsBeyond Phase 3. *Am J Public Health*. 98, 1366-71. 10.2105/AJPH.2007.124537.
13. Kahn MG, Ranade D. 2010. The impact of electronic medical records data sources on an adverse drug event qualitymeasure. *J Am Med Inform Assoc*. 17, 185-91. 10.1136/jamia.2009.002451.
14. Whitebread S, Hamon J, Bojanic D, Urban L. 2005. Keynote review: in vitro safety pharmacology profiling: an essential toolfor successful drug development. *Drug Discov Today*. 10, 1421-33. 10.1016/S1359-6446(05)03632-9 [PubMed]15. McClure DL. 2009. Improving Drug Safety: Active Surveillance Systems Should be Paramount. Pharmaceutical Medicine. 23,127-30. 10.1007/BF03256760