WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 13, Issue 21, 517-527. Review Article ISSN 2277–7105

THE IMPACT OF PHARMACOVIGILANCE ON PUBLIC HEALTH

Maheshwari P. Dakhole*, Nikita V. Mahalle, Harigopal S. Sawarkar, Neha L. Zod and Umesh R. Bansod

Dr. Rajendra Gode College of Pharmacy, Amravati, Maharashtra-444602, India.

Article Received on
13 September 2024,
Revised on 03 October 2024,
Accepted on 23 October 2024
DOI: 10.20959/wjpr202421-34443

***Corresponding Author**
Maheshwari P. Dakhole
Dr. Rajendra Gode College of Pharmacy, Amravati, Maharashtra-444602, India.

ABSTRACT

The impact of pharmacovigilance activities on public health remains under- investigated, and measuring the impact on health of pharmacovigilance activities for a specific safety signal. The aim of pharmacovigilance is to protect public health by identifying, evaluating and minimizing safety issues to ensure that the overall benefits of medicines outweigh the risks. However, the recent withdrawal from the market of certain medicines has focused attention on pharmacovigilance approaches; raised concerns about improving the existing pharmacovigilance framework; and highlighted the need to ensure consistency among international regulations governing the reporting of side effects ("Adverse Drug Reactions" - (ADRs). In drug regulation problems related to the safety and quality of drugs exists in many places. Effective drug regulation is required to ensure the safety, efficacy and quality of drugs, as well as the accuracy and appropriateness of the drug information available to the public. Regulation of drugs encompasses aproblems related to the safety and quality of drugs exists in many places. Effective drug regulation is required to ensure the safety, efficacy and quality of drugs, as well as the accuracy and appropriateness of the drug information available to the public. Pharmacovigilance is crucial for ensuring drug safety and efficacy. This review provides a comprehensive overview of pharmacovigilance in India, encompassing its definition, importance and history. It delves into clinical development, drug regulation, adverse reactions and practical applications. Real-world examples, legislation and implications for public health and patient safety are discussed. This review aims to enhance understanding of pharmacovigilance's vital role in India's pharmaceutical landscape.

KEYWORDS: Pharmacovigilance, Drug regulation, Adverse Drug Reactions, Safety, Efficacy.

INTRODUCTION

What is Pharmacovigilance?

WHO defines pharmacovigilance as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problems.

Brief history of Pharmacovigilance in India

Even though pharmacovigilance is still in its infancy, it is not new to India. It was not until 1986 that a formal adverse drug reaction (ADR) monitoring system consisting of 12 regional canters, each covering a population of 50 million, was proposed for India.[1] However, nothing much happened until a decade later when in 1997, India joined the World Health Organization (WHO) Adverse Drug Reaction Monitoring Programme based in Uppsala, Sweden. Three canters for ADR monitoring were identified, mainly based in teaching hospitals: a National Pharmacovigilance Centre located in the Department of Pharmacology, All India Institute of Medical Sciences (AIIMS), New Delhi and two WHO special canters in Mumbai (KEM Hospital) and Aligarh (JLN Hospital, Aligarh Muslim University). ese canters were to report ADRs to the drug regulatory authority of India. The major role of these canters was to monitor ADRs to medicines marketed in India. This attempt was unsuccessful and hence, again from the 1st of January 2005, the WHO-sponsored and World Bank-funded National Pharmacovigilance Program for India was made operational.[2] The National Pharmacovigilance Program established in January 2005, was to be overseen by the National Pharmacovigilance Advisory Committee based in the Central Drugs Standard Control Organization (CDSCO), New Delhi. Two zonal canters-the South -West zonal centre (located in the Department of Clinical Pharmacology, Seth GS Medical College and KEM Hospital, Mumbai) and the North-East zonal centre (located in the Department of Pharmacology, AIIMS, New Delhi), were to collate information from all over the country and send it to the Committee as well as to the Uppsala Monitoring centre in Sweden. Three regional centres would report to the Mumbai canter and two to the New Delhi one. Each regional canter in turn would have several peripheral centers reporting to it. Presently there are 24 peripheral centers.

The science as it is today had to go through various milestones to reach what it is today. Some of the issues which are important in the historical point of view are[3]

- Elixir of Sulphanilamide (1937) which resulted in poisoning in children. It was identified that it was a formulation defect which led to improvements in pharmaceutical regulation.

- Thalidomide tragedy (1961) which resulted in phocomelia (absence of limbs) in the children of mothers who took this apparently 'safe drug', led to National and international collections of ADR reports and resulted in the introduction of yellow card system initiated in the UK in 1964.

- Ethnic susceptibility and drug use issues were raised and early work on Pharmacogenetics began after new clinical syndrome SMON (Sub acute nouropathy) reported following use of clioquinol (1969).

- Realization that spontaneous reporting will not pick up 'events' that are not easily recognized as caused by drugs after the new clinical syndrome, oculo-mucocutaneous reaction with the use of Protocol (1975) recognized by UK experts led to Prescription event monitoring (PEM).

- One of the most important milestones is the establishment of WHO collaborating center for Drug Monitoring, which is called the Uppsala Monitoring Center (UMC), in 1978, which led to National collaboration enhanced under the WHO programme. This also led to standardizing Adverse Drug Reaction Terminology (ART), WHO-DD (World Health Organization Drug Dictionary) etc., which are updated periodically.

The above issues are recommended for drug safety and monitoring in drug regulation, i. e. Pharmacovigilance plays an important role in drug regulation in medicine world.

Why is Pharmacovigilance Necessary?

The steps in the clinical development process of medications is depicted in Figure 1. after being placed on the market, a medication departs from the safe and secure research setting of clinical trials and is permissibly released for public consumption populace. Currently, the majority of medications will only have been examined for effectiveness and short-term safety on a small group of people who were carefully chosen. In 500 individuals in certain circumstances, but seldom more than 5000, will have obtained the item before its release. For

this reason, it is imperative that fresh and Medicines that are currently developing are kept an eye out for their safety and efficacy in post-release real-world scenarios. Therefore, it is imperative that novel and still-evolving medical therapies be watched for Modes: For good reason, therefore, it is essential that new and medically still evolving treatments are monitored for their effectiveness and safety under real-life conditions post release. More information is generally needed about use in specific population groups, notably children, pregnant women and the elderly, and about the efficacy and safety of chronic use, especially in combination with other medicines. Experience has shown that many adverse effects, interactions (i. e. with foods or other medicines) and risk factors come to light only during the years after the release of a medicine (see table 1).

Therefore, it is imperative that novel and still-evolving medical therapies be watched for their safety and efficacy in post-release real-world scenarios. More details are typically required information regarding usage in particular demographic groups, such as kids, expectant mothers, and the elderly, as well as the effectiveness and security of long-term use, particularly when taken with other medications. Experience has demonstrated that many side effects, interactions (e.g., with foods or other medications), and risk factors only become apparent years after a medication is released (see table 1).[4,5]

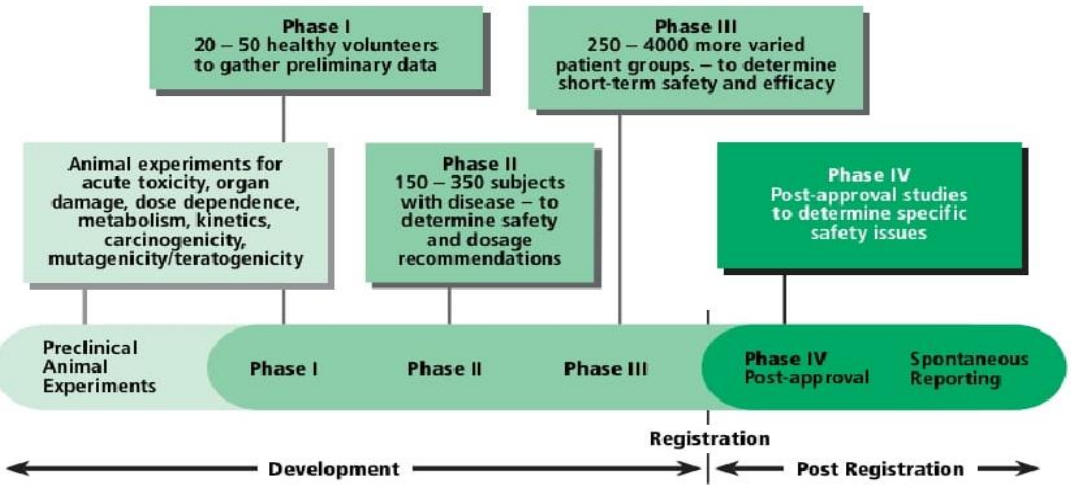

Figure 1: Clinical development of medicines.

Medicine	Adverse reaction
Aminophenazone (amidopyrine)	Agranulocytosis
Chloramphenicol	Aplastic anaemia
Clioquinol	Myelooptic neuropathy (SMON)
Erythromycin estolate	Cholestatic hepatitis
Fluothane	Hepatocellular hepatitis
Methyldopa	Haemolytic anaemia
Oral contraceptives	Thromboembolism
Practolol	Sclerosing peritonitis
Reserpine	Depression
Statins	Rhabdomyolysis
Thalidomide	Congenital malformations

Table 1: Classical example of serious and unexpected adverse reactions.

Adverse drug reactions: the example of thalidomide

In 1957, thalidomide was first prescribed widely. as a purportedly risk-free morning sickness remedy and queasy feeling. It was quickly connected to a congenital anomaly which resulted in serious birth abnormalities in female children who had been given this medication while expecting a child. Thalidomide was taken off the market by 1965 in the majority of nations. Nevertheless, it was still in use for the purpose of treating leprosy, and more recently, its signals now cover a far larger spectrum of health issues. These uses are only permitted in accordance with stringent oversight and professional guidance. Despite these measures, the Latin American Collaborative Study of Congenital Malformations recorded 34 occurrences of thalidomide embryopathy in leprosy endemic areas of South America between 1969 and 1995.[6]

Pharmacovigilance in the regulation of medicines

Pharmacovigilance in the control of pharmaceuticals Strong regulatory frameworks serve as the cornerstone for both public trust in pharmaceuticals and a national ethos of medicine safety. In order for drug regulatory authorities to be effective, their mandate must cover a wider range of matters related to medication safety than just approving new drugs. These matters include

• Clinical trials.

• The safety of biological, complementary, and traditional medicines.

• The development of channels of communication between all parties interested in medication safety, ensuring that they can operate effectively and morally, especially during emergencies.

Pharmacovigilance programs and drug regulatory bodies need to work together to accomplish their respective goals.

In order to ensure that drug regulatory authorities are informed about safety issues in routine clinical practice, whether these issues are pertinent to upcoming regulatory action or to public concerns, pharmacovigilance programs must, on the one hand, maintain strong ties with these authorities. On the other hand, regulators must recognize the unique and crucial role that pharmacovigilance plays in guaranteeing the continued safety of pharmaceuticals.

Practical pharmacovigilance: cerivastatin as an example

In 1997, cerivastatin was originally licensed as a lipid-regulating medication. The WHO Collaborating Centre for International Drug Monitoring, located in Uppsala, Sweden, received reports of 549 occurrences of rhabdomyolysis linked to the use of cerivastatin by the year 2000. As a result, a warning was sent out about a possible link between rhabdomyolysis, myopathy, and cerivastatin. Prescription information was updated to include a contraindication for the combination of cerivastatin and gemfibrozil, another lipid-regulating medication, in November 1999 in the United States and March 2000 in Canada. In February 2001, a similar measure was implemented in Australia, along with a notice to prescribers about the potential for rhabdomyolysis to occur with any statin. A European-wide regulatory action was implemented in June 2001 to prohibit the co-administration of cerivastatin and gemfibrozil. Cerivastatin's maker voluntarily removed the drug from the market on August 8, 2001, citing a higher risk of rhabdomyolysis, especially when used with gemfibrozil.[7]

Pharmacovigilance in clinical practice

Clinical practice should include safety monitoring for commonly used medications. How well clinicians understand the principles. pharmacovigilance, and practice according to they have a significant impact on the quality of health care. Education and training for healthcare professions in medicine safety, exchange of information national pharmacovigilance centers, the coordination of this exchange, and the connection of clinical experience of medicine safety through study and All health policies serve to increase successful patient care. A steady flow and interchange of information this strategy implies that national pharmacovigilance Programmes are ideally positioned to discover gaps our understanding of medically generated disorders.[8]

Pharmacovigilance in disease control public health programmes: Monitoring

Pharmaceutical safety in nations without regulatory systems or in distant places with limited healthcare access. surveillance or infrastructure, has been identified. A cause for concern. Problems are especially obvious in scenarios that entail the use of drugs in specific populations, such as for the treatment of tropical diseases like malaria, leishmaniasis, and schistosomiasis, as well as HIV/AIDS and tuberculosis. In some contexts Several disease control projects, including the administering medicines to vast communities are implemented within the same population. With little knowledge of, or respect for, how these Various medications may interact with each other. Pharmacovigilance should be a priority for all countries with public health disease control programs.[9]

Malaria: an example of pharmacovigilance in public health

Due of resistance to current antimalarial medications, some countries have adopted artemisinin derivative combinations. Malaria treatments include both first- and second-line options. The change. Artemisinin combination treatments (ACTs) have provided a timely moment to implement pharmacovigilance. system in countries that previously had no established Systems for monitoring the safety of medications. In 2003, Participants from five African nations received training in basic approaches of drug safety monitoring with a view To facilitate the introduction of a common system of Pharmacovigilance of novel antimalarial therapies. Since Then, two of these countries formally constituted a pharmacovigilance center; others are also making. Antimalarial monitoring has progressed.[10]

Medication error

Medication Error Monitoring Questionnaire

An analysis based on a questionnaire was used to evaluate the pharmacovigilance centers' capacity to identify, evaluate, and stop drug mistakes. The investigation made clear how important it is to create and improve methods for identifying, analyzing, and preventing pharmaceutical errors.[11]

Workshop on Medication Errors

Ten national pharmacovigilance centers (Morocco, Kenya, Iran, New Zealand, Thailand, Spain, Switzerland, Nigeria, Brazil, and Tunisia) as well as patient safety organizations from the UK and Canada attended a workshop on drug errors in safety databases in 2011. The workshop produced a revised ICSR form with additional fields to maximize medication error detection, a terminology list of terms and definitions commonly used by patient safety

organizations and pharmacovigilance centers, and an evaluation tool (P method) to gauge how preventable medication errors are.[12] The latter was examined using ICSRs that the centers supplied that were linked to drug mistakes. The national pharmacovigilance centers that were involved subsequently conducted additional testing on the approach. The World Health Organization released a manual in 2014 detailing the function of pharmacovigilance centers in identifying and averting pharmaceutical errors.[13]

Follow-Up Questionnaire on Medication Error Monitoring

Some of the pharmacovigilance centers represented at the workshop reported later modifications to their processes to improve medication error monitoring as part of their regular pharmacovigilance activities in response to a follow-up questionnaire distributed in August 2014. These included changing reporting forms or definitions, revising the terminology used to describe ADRs, using uniform approach to determine if an ADR is preventable, providing training to prospective reporters, and cooperating with other organizations engaged in the prevention of medication errors. Certain pharmacovigilance centers have disclosed that they have detected novel indicators of preventable patient harm.

New pharmacovigilance legislation and the impact on real-life studies

The study of drug use and effects/side effects in large populations is known as pharmacoepidemiology. It studies drug use and consequences using epidemiological methodologies, with a focus on the period after drug marketing, Pharmacoepidemiology aims to improve health outcomes by promoting the population's rational and economical medication usage (rational use, efficacy, tolerability, effects on the population).[14] It is the process of determining the advantages and disadvantages of a product and then creating, putting into practice, and reviewing plans to improve the overall ratio of those advantages and disadvantages. Consequently, the scientific foundation of medicinal risk management is pharmacoepidemiology Pharmacoepidemiologists will have additional chances as a result of the new pharmacovigilance laws. A new pharmacovigilance law mandates that every new medication have an RMP. Data collection and risk planning for post-authorization risk reduction will follow from this. There will undoubtedly be an increase in the number of research carried out by academics or pharmaceutical corporations, in addition to studies that the health authorities require. When substantial uncertainties about a product's effectiveness persist or when advancements in clinical practice or illness understanding could materially alter earlier efficacy assessments, MAHs may be required to do PAS(E)S.A noninterventional

research or a clinical trial could be a post-authorization investigation. Directive 2001/20/EC[15] and Volume 10 of The Regulations Governing Medicinal Products in the EU will be applicable if the PASS is a clinical study. However, if PASS is non-interventional and is started, managed, or funded by an MAH in compliance with duties imposed by a national competent authority, the Agency, or the Commission in accordance with Directive 2001/83/EC (Articles 21a, 22a) and Regulation (EC) No 726/2004 (Articles 10, 10a), then Good Pharmacovigilance Practices (GVP) Module VIII[16,17] shall apply. A lot of the recently mentioned pharmacovigilance laws' new requirements, such RMP and PASS/PAES, call for access to pertinent data that necessitates the necessary authorization(s). Since data for non-interventional research are gathered from pre-existing population databases or hospital medical records, patients are typically involved in an indirect capacity. According to Directive 95/46/EC[18], access to these data should only be permitted with authorization from the appropriate data protection committee. The study's completion was delayed as a result. If patients in real life are treated with a hazardous medication that is kept on the market longer than necessary due to needless administrative delays, there may be potential harm to them. Given the potential rise in PASSes required to comply with the new requirements of the pharmacovigilance Act, it is critical that the requisite authorizations for access to data be finalized as soon as feasible.[19]

CONCLUSION

Pharmacovigilance is indispensable for safeguarding patient health and promoting responsible pharmaceutical practices in India. Key takeaways include

1. Pharmacovigilance's critical role in detecting and preventing adverse reactions.
2. Importance of clinical development, drug regulation and post-marketing surveillance.
3. Lessons from historical cases (Thalidomide, Vioxx, Cerivastatin).
4. Need for enhanced reporting, monitoring and patient counselling.
5. Pharmacovigilance's impact on public health programs and medication error prevention.

FUTURE DIRECTIONS

1. Strengthening regulatory oversight.
2. Enhancing transparency and accountability.
3. Leveraging technology for improved surveillance.

RECOMMENDATIONS

1. Interdisciplinary collaboration.

2. Continuous education and training.
3. Patient-centric approaches.

REFERENCE

1. R.D. Kulkarni; Med Toxicol., 1986; 1: 110-3.
2. Protocol for National Pharmacovigilance Program, CDSCO, Ministry of Health and Family Welfare, Government of India, November 2004.
3. www.edocfind.com/en/ebook/pharmacovigilance%20in%20drug%20regulation-1.html
4. Castilla EE et al. Thalidomide, a current teratogen in South America. Teratology, 1996; 54: 273-277.
5. Lazarou J et al. Incidence of ADR in hospitalized patients: a meta-analysis of prospective studies. Journal of the American Medical Association, 1998; 279: 1000-1005.
6. Linquist AM. Seeing and observing in international pharmacovigilance. Uppsala, World Health Organiza- tion Collaborating Centre for International Drug Monitoring, 2003.
7. WHO Safety monitoring of medicines. Guidelines for setting up and running a pharmacovigilance centre. Geneva, World Health Organization, 2000.
8. WHO. Aide Memoire for a national strategy for safe drugs and their appropriate use. Essential Medicines and Medicines Policy. Geneva, World Health Organization, 2001. (http://www.who.int/medicines/library/qsm/aidemem_drug_safety.pdf; accessed 15 October 2004).
9. WHO. Safety of medicines. A guide to detecting and reporting adverse drug reactions. Geneva, World Health Organization, 2002 (WHO/EDM/QSM/2002.2).
10. WHO. Safety monitoring of medicinal products The importance of pharmacovigilance. Geneva, World Health Organization, 2002.
11. Benabdallah G, Benkirane R, Khattabi A, Edwards IR, Bencheikh RS The involvement of pharmacovigilance centres in medication errors detection. A questionnaire-based analysis. Int J Risk SafMed., 2011; 23: 17–29.
12. Benkirane R, Soulaymani-Bencheikh R, Khattabi A et al. Assessment of a new instrument for detecting preventable adverse drug reactions. Drug Safety. doi:10.1007/s40264-014-0257.
13. World Health Organisation. Reporting and learning systems for medication errors: the role of pharmacovigilance centres. Geneva: WHO Press; 2014. Edited by: Strom BL, Kimmel SE, Hennessy S. Pharmacoepidemiology. Fifth Edition. John Wiley & Sons, Ltd., 2012.

14. Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member State relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use., L 121/34. Sect. 34., 2001.
15. Guideline on good pharmacovigilance practices (GVP) Module VIII – Post authorisation safetystudies.PDFdocument.http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2012/06/WC500129137.pdf [Accessed: November 15th, 2012]
16. Annex to GVP module VIII – Post-authorisation safety studies. PDF document. http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2012/06/WC500129147.pdf [Accessed: November]