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History, Current Status And Future Aspects Of pharmacovigilance In India

Kajal Pansare[1*], Ganesh Sonawane[1], Prashant Tapadiya[2], Renu Tapadiya[3], Chandrashekhar Patil[4,5], Jai Singh Vaghela[5], Shekhar Kokate[1]

[1]Assistant Professor, SND College of Pharmacy, Yeola, Maharashtra (India)

[2]Senior Project Manager, Clinical Development Department, Alvogen Pharma (India)

[3]Lecturer, Bhalchandra College of Pharmacy, Pune, Maharashtra (India)

[4]Assistant Professor, Divine College of Pharmacy, Satana, Maharashtra (India)

[5]Bhupal Nobel University, Udaipur, Rajasthan (India)

ABSTRACT

Pharmacovigilance(PV) is defined by the World Health Organization (WHO) as "the research and practices associated to the detection, evaluation, comprehension, and prevention of adverse effects or other important issues caused by drugs."Pharmacovigilance is primarily concerned with the detection of Adverse drug reactions (ADRs) of drugs.Safety of medications is one of the important factors for success of any therapy, along with therapeutic efficacy, in the ever-increasing range and potency of medicines. India is currently a desirable clinical testing locationfor to be launched drug entities.The PV activity is regulated in India by the Indian Pharmacopoeia Commission (IPC) and the National Coordination Committee (NCC) through the Central Drug Standard Control Organization (CDSCO). The Indian government planned and launched the Pharmacovigilance Programme of India in 2010 to establish a potential PV system in India.To enhance regulatory compliance, clinical trial safety, and post-marketing surveillance, the Drugs Controller General of India (DCGI) should act fast to improve PV by implementing Good Pharmacovigilance Practice (GPP) into processes and procedures. If medicines are to be used safely, a well-functioning PV system is essential.This article summarized introduction, history, current status and future aspects of Pharmacovigilance in India.

Keywords: Pharmacovigilance, Adverse drug reaction, Safety, India, Uppsala monitoring center

INTRODUCTION

Pharmacovigilanceis defined by the World Health Organization as "the research and practices associated to the detection, evaluation, comprehension, and prevention of adverse effects or other important issues caused by drugs(1)."Pharmacovigilance is primarily concerned with the detection of Adverse drug reactions of drugs. ADRs are defined as "an unpleasant and unintended response to drugs that occurs at levels normally used for disease prevention, diagnosis and therapy or for the alteration of physiological function." PV is an essential component of clinical trials and medication development(2).Throughout the lifecycle of a product, both clinical trial safety and post-market pharmacovigilance are essential. Pharmacovigilance's main goal is to improve the safe and effective utilization of health products, in part by making information readily available to patients, medical professionals, and the general public. It is critical to detect any side effects of drugs as soon as possible, and data collection is vital(3).During the post-marketing phase of an approved drug, spontaneous adverse drug reaction reporting (SADR) is used to examine and monitor the risk-benefit profile of new pharmaceuticals.The field of Pharmacovigilance deals with reports that raise concerns about the post-marketing safety of drugs that cause adverse drug reactions(4).PV plays a vital part in the evaluation of medication side effects, whether they are induced by oral, parenteral, or intravenous medicines. These medications are tested for adverse drug reactionsbefore they are released globally(5).Pharmacovigilance has expanded its scope throughout time to encompass the monitoring of herbal, traditional and complementary medicines, blood products, medical devices, biological and vaccines, with the purpose of providing patients with the most current information on product risks. Clinical studies now give major pharmaceutical companies with an early warning of risks associated with their products. This kind of signal identification and risk management has added a new dimension to the field of Pharmacovigilance, which is still expanding(6).The drug development process includes the continuum from the identification of a potential pharmaceutical agent to research on possible efficacy and safety through regulatory approval. The drug approval process mainly involves phase I, II, III (pre-marketing), IV (post-marketing) trials. The National Pharmacovigilance Program was inaugurated in November 2004 by the Central Drugs Standard Control Organization of India's Ministry of Health and Family Welfare. It is largely based on the WHO report "Safety Monitoring of Medicinal Products Guidelines for Establishing and Operating a Pharmacovigilance Center(7)".With the goal of improving public safety and welfare in India, on 14 July 2010, the Indian government launched the Pharmacovigilance Programme of India (PvPI) with the National Coordination Center at All India Institute of Medical Sciences (AIIMS) in New Delhi, which was later transferred to the Indian Pharmacopoeia Commission in Ghaziabad, India, in April 2011 to monitor adverse drug reactions in the country and protect public health(8).

HISTORY

On January 29, 1848, a little girl from the north of England (Hannah Greener) died after receiving chloroform anesthesia before to the removal of an infected toenail, marking the beginning of pharmacovigilance(9).The second major issue arose later, and it was caused by acetylsalicylic acid. On August 12th, 1897, Felix Hoffman, a German chemist working for Bayer, created acetylsalicylic acid, which was better tolerated than sodium salicylate when consumed, and was given the name Aspirin(10).The issue that arose in 1898 was the commercialization of diacetylmorphine, later known as

heroin, which became addicted around the turn of the century. Approximately0.5 million dependent patients were identified in the United States alone. Thalidomide was first sold as an over-the-counter hypnotic/sedative drug in 1957, and it was later used to relieve nausea in pregnant women. This was confirmed the following year, when it was shown that thalidomide was responsible for 20% of the increase in phocomelia and limb agenesis of limb defects(11).The Indian government has changed and amended Schedule Y of the Drug and Cosmetics Rules of 1945, realizing the promise of clinical research for new therapies. Schedule Y establishes a set of clinical trial guidelines and requirements. The Indian Council of Medical Research (ICMR) released the Ethical Standards for Biomedical Research on Human Subjects in 2000, while the CDSCO issued the Indian Good Clinical Practice (GCP) guidelines in 2001(12).When a formal ADR monitoring system with 12 centers was planned in 1986, there was no development or special attention paid to PV activity. In 1997, India actively participated in the WHO's ADR Monitoring Program, which was held in Uppsala, Sweden(13).India has a population of approximately 1.21 billion people, making it the world's second most populous country, according to the 2011 census. The pharmaceutical industry in India is worth 18 billion dollars, and it is expected to develop at a rate of 12-14 % per year. India is being recognized as a growing country for clinical trials, medication discovery, research, and development on a global scale. The most critical step in preventing or minimizing ADRs is for healthcare professionals to report them right away.In India, the ADR reporting rate is less than 1%, compared to a global rate of 5%. One of the explanations for the lower rate in India could be because Indian healthcare workers are more aware of Pharmacovigilance and ADR monitoring(14).Over 65 countries had their own pharmacovigilance facilities in 2002. The WHO Collaborating Center for Worldwide Drug Monitoring, often known as the Uppsala Monitoring Center, coordinates WHO membership for international drug monitoring (UMC). Pharmacovigilance is now firmly based on good scientific principles and is an important part of effective therapeutic approach.To satisfy the public's expectations and the challenges of current public health, the field must evolve further. A resolution was adopted at the Sixteenth World Health Assembly(15).

Table 1. The development of pharmacovigilance over time, with a focus on India(16)

Developments	Year
James Lind conducted the first documented clinical research establishing the effectiveness of lemon juice in scurvy prevention.	1747
More than 100 children have died as a result of sulfanilamide poisoning.	1937
Chloramphenicol poisoning has been associated to aplasticanemia.	1950
Toxicity to thalidomide has caused a worldwide tragedy.	1961
The 16th World Health Assembly recognizes the importance of quick action on adverse drug reactions (ADRs).	1963
The WHO is conducting research for international drug surveillance on a small scale.	1968
In India, clinical trials at the global standard level have started.	1996
India has joined the Adverse Drug Reaction Monitoring Program of the World Health Organization.	1997
Pharmacovigilance is started in India.	1998

In India, the 67th National Pharmacovigilance Center was formed	2002
The National Pharmacovigilance Program was established in India.	2004-05
Structured clinical trials have been completed in India.	2005
PvPI (Pharmacovigilance Program) has started.	2009-10

The National Pharmacovigilance Advisory Committee was established in January 2005 to supervise the National Pharmacovigilance Program. It is based at the Central Drugs Standard Control Organization in New Delhi.Data was collected from around the country and relayed to the Committee and the Uppsala monitoring center in Sweden by the South-West zonal centerand the North-East zonal center.The Mumbai center would report to three regional centers, while the New Delhi center would report to two. Each regional center would be responsible for a number of peripheral centers. There are currently 26 peripheral centers(17).In July 2010, the Ministry of Health and Family Welfare, Government of India, launched a national pharmacovigilance programme, with the All-India Institute of Medical Sciences, New Delhi, serving as the National Coordinating Center for monitoring adverse drug reactions in the country to protect global health.In 2010, 22 ADR monitoring centers (AMCs) were established as part of this programmes, including AIIMS in New Delhi. In April 2011, the National Coordination Center was relocated from New Delhi's All India Institute of Medical Science to the Indian Pharmacopoeia Commission in Gaziabad, Uttar Pradesh, to ensuring that this initiative is implemented more successfully(2).

PRESENT STATUS

In India, which is a vast country, there are over 6,000 licensed medicine manufacturers and over 60,000 branded formulations.India is the world's fourth largest pharmaceutical producer and is increasingly becoming a center for clinical trials. However, in the recent history the time between when a drug is approved for sale and when it becomes available in India has shrunk to the point that longer-term safety data is no longer available. Additionally, through their own research efforts, Indian pharmaceutical companies have improved their ability to develop and commercialize new products, highlighting the importance of establishing acceptable internal pharmacovigilance standards to detect adverse drug events(18).The Drugs Technical Advisory Board (DTAB) had previously proposed that pharmaceutical companies be required to report adverse effects of marketed drugs. Despite the proactive nature of the recommendations, the mandate legislation also was established in March 2016.Since many pharmaceutical companies regard reporting ADRs to be an industry practice, periodic communications and interactive conversations between PvPI and its stakeholders have resulted in progress in receiving ADR reports. As a result, the pharmaceutical industry's ADR reporting rate to PvPI in 2015 was 18.80 percent(13).To promote a more effective implementation of the programme, the NCC was moved from the AIIMS in New Delhi to the Indian Pharmacopoeia Commissionin Ghaziabad, Uttar Pradesh, on April 15th, 2011.The NCC's main goal at IPC is to create independent data on medicine safety that is comparable to worldwide drug safety monitoring standards.PvPI's year-by-year target phases are depicted in Table 2.

Table 2. Targets for the Pharmacovigilance Program in India (13)

Each Financial year target for the five phases of PvPI	
2010-11	Developing system and procedure Enroll forty medical institute Start data collection from AEFI Establishing a training center PV Human Resource Training Linkage with UMC Sweden and the World Health Organization Started developing software for the NDSD. Zonal workshop for drug safety public awareness News-letter publication of drug safety
2011-12	Enroll again sixty medical college Training of PV human resource Identify gaps and fulfill them with adequate training. UMC, WHO provide training on PV software supply. Software development and validation Zonal workshop of drug safety public awareness The publication of a drug safety bulletin
2012-13	Enroll additional hundred medical institute PV human resource training On a zonal basis, workshops on drug safety for the general public are held. News-letter publication of drug safety
2013-14	Enroll again more hundred medical college Interaction with international PV bodies PV human resource training The publication of a drug safety bulletin
2014-15	Create a PV center of excellence in the Pacific.

Pharmaceutical companies are required by Good Pharmacovigilance Practices (GPPs) and applicable regulations to continuously assess the benefits and risks of their medications. Throughout the year, the NCC-PvPI is actively involved in offering training to established pharmacovigilance professionals, on the fundamentals and regulatory aspects of pharmacovigilance, as well as young pharmacy, medical, and paramedical professionals. The NCC-PvPI IPC in Ghaziabad was also recognized a WHO Collaborating Center for Pharmacovigilance in Public Health Programs and Regulatory Services on October 30th, 2017(19).The Materiovigilance Programme(MvPI) of India was established by the PvPIin 2015 to evaluate adverse incidences associated with medical devices in India. MvPI members recently gathered at the IPC in May 2017 to discuss strategies for monitoring the ambitious program's success.It was determined that experienced biomedical engineers would be hired, and PvPI would provide them with the necessary training(20).

FUTURE ASPECT

A strong pharmacovigilance system capable of detecting novel ADRs and implementing regulatory steps to protect public health is needed in the future. The creation of data that can assist a healthcare practitioner or a patient in making a decision has received little attention. Pharmacovigilance's primary purpose is to collect and communicate this information. It is vital to have information on the safety of drug active surveillance(21).In addition to more traditional groups such as health professionals, PV will have to focus on patients as a source of information in the future.To enhance regulatory compliance, clinical trial safety, and post-marketing surveillance, the DCGI should act fast to improve PV by implementing Good Pharmacovigilance Practice (GPP) into processes and procedures.If medicines are to be used safely, a well-functioning PV system is essential. Healthcare experts, regulatory authorities, pharmaceutical businesses, and consumers will all benefit from it(3).With so many clinical trials and other clinical research activities taking place in India, it's vital to understand the value of pharmacovigilance and how it influences the life cycle of a product. DCGI has put in a lot of work to create a reliable and effective pharmacovigilance system. However, more work and strategic planning are required to meet the demands of a growing population while also ensuring that all data is recorded and processed. To address the issues of inexperience and a lack of trained personnel, the DCGI might take a step ahead and hire commercial firms to teach and set up an effective pharmacovigilance system(22).

After considering the issues and obstacles that India has in developing an effective pharmacovigilance system, the following suggestions may be made:

1. Establishing and maintaining an effective pharmacovigilance system.
2. Introducing PV inspections and making its reporting mandatory.
3. Discussions at a high level with a variety of stakeholders.
4. Expand the number of trained scientific and medical assessors in the Drug Control General of India office for PV.
5. Creating a single adverse event reporting form that can be used by everyone in any country.
6. A clinical trial and post-marketing database for SAEs/SUSARs and ADRs is being built for signal detection and access to all relevant data from different stakeholders.
7. Keep track of all new medications and indications in a standard database for each pharmaceutical company.
8. Medical students, pharmacists, and nurses receive pharmacovigilance education and training.
9. Collaborating with pharmacovigilance groups to improve medication safety as information technology advances, new potential for national and worldwide collaborations to improve postmarking surveillance programmes and improve drug safety have emerged.
10. In India, establishing a network of pharmacovigilance and pharmacoepidemiologists(23).

CONCLUSION

The awareness of PV system regarding ADR reporting has increased in India. Various international companies have been outsourcing PV system activities to India, which is fostering a positive PV culture.Various universities of India have implemented the PV courses in the curriculum. The government should work on raising pharmacist awareness and improving their expertise, as well as providing them with facilities and power to conduct PV activities.A specific PV cell should be installed in

every hospital to detect and report ADRs.In the near future, India will be the hub and outsourcing center for global PV activity, due to population, talent, interest of healthcare providers, and present development in the PV sector.

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