Research Article

Pharmacovigilance system and the future challenges in India-A Perspective

***SANDHYA JAIN*, [1]DR VIKAS JAIN, [2]RADHA SHARMA**
*Parul institute of Pharmacy, Vadodara.
[1]Alembic Pharmaceuticals. Vadodara,
[2]Shri Ram College of Pharmacy, Murena, M.P.
Email Id : Sandhya.jain16114@paruluniversity.ac.in

ABSTRACT
PVPI 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. This article provides a brief overview about the current situation and the future challenges of pharmacovigilance in India. The importance of implementing proper pharmacovigilance in the Indian scenario has been analysed the first recognised attempt to start pharmacovigilance activities in India dates back to 1986, when a formal Adverse Drug Reaction (ADR) monitoring system with 12 regional centres for a population of 50 million each, was proposed. However, the system did not come into existence. In 1997, India joined the World Health Organization's ADR Monitoring Programme based in Uppsala, Sweden. The Uppsala Monitoring Centre (UMC) maintains an international database of suspected adverse drug reaction reports from all over the world to support good decision-making regarding the benefits and risks of treatment options for patients taking medicines.

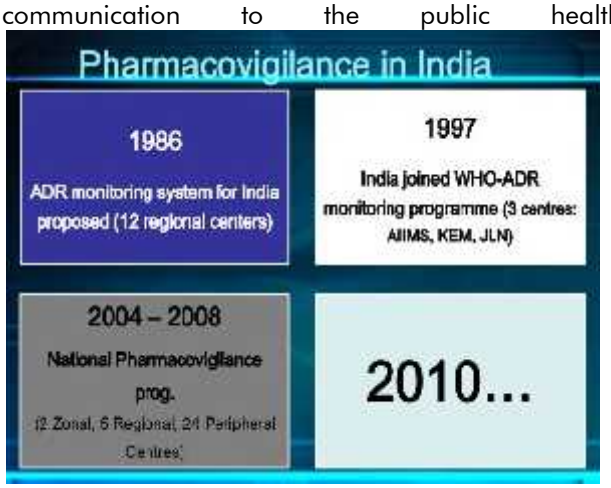
Keywords :Adverse Drug Reaction (ADR), Uppsala Monitoring Centre (UMC), pharmacovigilance programme in India PVP

INTRODUCTION

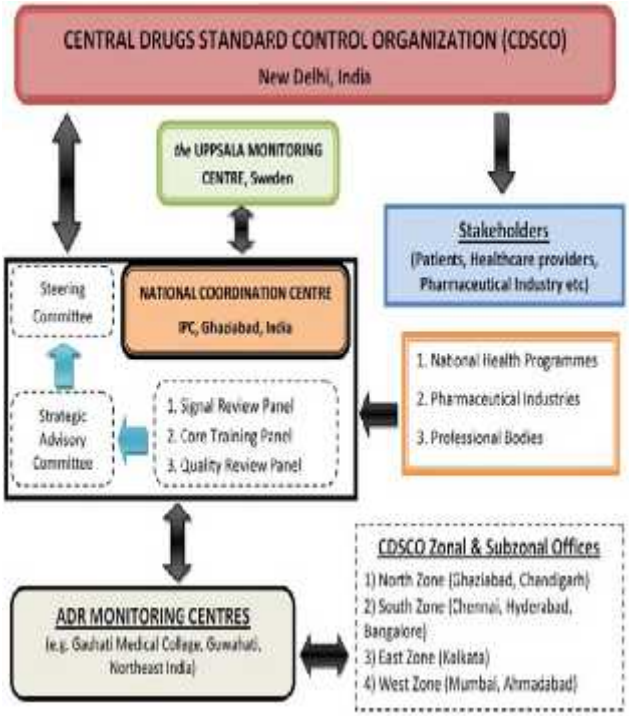
Pharmacovigilance is defined as the pharmacological science relating to the detection, assessment, understanding and prevention of adverse effects, particularly long-term and short-term adverse effects of medicines. Pharmacovigilance is an important and integral part of clinical research. Both, safety of clinical trials and post-marketing pharmacovigilance are critical throughout the product lifecycle. With a number of recent high-profile drug withdrawals, like Cerivastatin, the pharmaceutical industry and regulatory agencies have raised the issue of pharmacovigilance Early detection of signals from both clinical trials and post-marketing surveillance studies have now been adapted by major pharmaceutical companies in order to identify the risks associated with the medicinal product and effectively manage the risks by applying robust risk management plans throughout the lifecycle of the product. Signal detection and risk management has added a new dimension to the field of pharmacovigilance and as an evolving discipline; it requires ongoing refinement in order to increase its applicability and value to public health.

The Importance of Pharmacovigilance.
(Safety monitoring of medicinal products)
1. Drug monitoring
2. Pharmaceutical preparations – adverse effects
3. Adverse drug reaction reporting
4. Product surveillance, Post marketing
5. Legislation, Drug I. Series.

The specific aims of pharmacovigilance are to:
• improve patient care and safety in relation to the use of medicines and all medical and paramedical interventions.
• improve public health and safety in relation to the use of medicines.
• contribute to the assessment of benefit, harm, effectiveness and risk of medicines, encouraging their safe, rational and more effective (including cost-effective) use.
• promote understanding, education and clinical training in pharmacovigilance and its effective communication to the public health



Recognising the need to re-conceptualise the national pharmacovigilance programme, the framework of the subsequent programme was formulated with more forethought. The programme was renamed the Pharmacovigilance Programme of India (PvPI). The CDSCO, Directorate General of Health Services under the aegis of the Ministry of Health and Family Welfare, Government of India in collaboration with Indian Pharmacopeia commission, Ghaziabad initiated this nation-wide pharmacovigilance programme for protecting the health of the patients by assuring drug safety. The programme is being coordinated by the Indian Pharmacopeia commission, Ghaziabad as a National Coordinating Centre (NCC). The centre will operate under the supervision of a Steering Committee which has the Drug Controller General of India (DCGI) as its exofficio chairman and the Officer-in-Charge (New Drugs), CDSCO, New Delhi as its ex-officio Member Secretary. The goal of the PvPI is to ensure that the benefits of use of medicines outweigh the risks and thus safeguard the health of the Indian population. The PvPI has been operational from mid July 2010.Programme communications are illustrated in the schematic sketches provided below.



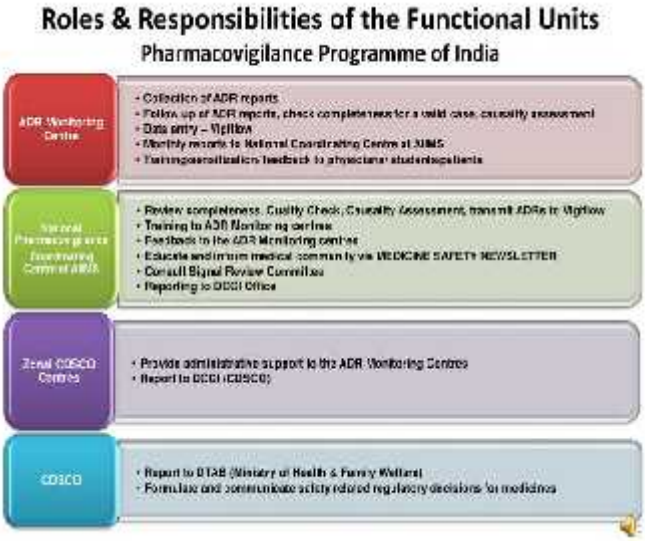
PvPI objectives:

The program has three broad objectives:

The short-term objective is to foster a reporting culture.

The intermediate objective is to involve a large number of healthcare professionals in the system in information dissemination.

Long-term objective is for the program to be a benchmark for global drug monitoring.



Current trends

in recent times, pharmacovigilance has started gaining importance in the media as the number of stories on drug recalls increases. Since clinical trials involve only smaller numbers and selected groups of patients, less common adverse events are often unknown at the time when a drug enters in the market. Also, use of drugs in organ-impaired patients and use in special populations like pregnant women and children are not studied extensively in clinical trials because of ethical limitations. Post marketing pharmacovigilance gains much importance, since it uses tools such as data mining and investigation of case reports to identify the relationships between drugs and ADRs. India is now coming to understand that the benefit-risk ratio of pharmaceutical products is a dynamic variable and that it has to be continuously monitored. Early detection of signals from both clinical trials and post-marketing surveillance studies are done by global pharmaceutical companies in order to identify the risks associated with the medicinal products and effectively manage the risks by applying proactive risk management plans throughout the life cycle of the product. Indian pharmaceutical companies with international presence have understood these changes in the global scenario and are also starting to apply the same strategies.

Signal detection and risk management have added new dimensions to the field of Indian pharmacovigilance and as evolving disciplines, they require ongoing refinement in order to increase their applicability and add value to the public health aspect in India.

With the Indian pharmaceutical industry entering into a good number of joint ventureswith multinational pharmaceutical companies and considering the phenomenal increase in export of Indian-made drugs to the developed world, the pressure is mounting on the Indian pharmaceutical companies to invest in pharmacovigilance either by setting up

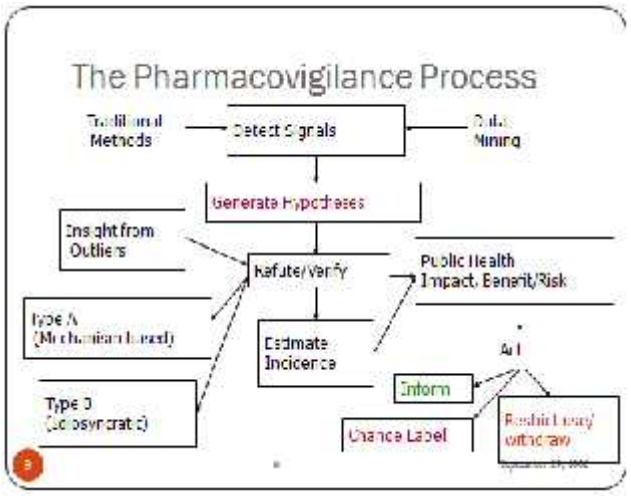
their own team completely or outsourcing parts of it to contract research organisations. Till recently, the Indian drug market has mostly seen the launch of only those products that were already approved and marketed in the regulated markets. For assessing the benefit-risk profile of a drug and to take appropriate corrective actions, the Indian pharmaceutical companies as well as the regulators have been depending on the experiences gained from these markets. Due to this reason, pharmacovigilance was considered to be non-vital and little emphasis was placed on establishing an India-specific pharmacovigilance system. However, with drugs getting global approvals almost simultaneously, the lead time Indian regulators used to get before deciding on the approval of a drug has decreased so much that the longer-term safety data from the regulated markets is no longer available. The capability that Indian drug companies have built in getting close to bringing their own research molecules to the market has indicated that implementing sufficient internal pharmacovigilance standards to detect adverse drug events is something that they cannot ignore any more. Moreover, with Indian companies launching bio similar which cannot be considered as replicas of the innovators' molecules due to their complex structure and high molecular weight, special pharmacovigilance planning is needed for this set of drugs. With expansion of the medical devices market in India and augmented awareness of Adverse Events Following Immunisation (AEFI) through the media, the significance of the pharmacovigilance of medical devices and vaccines is now being realised. Thus, globalisation seems to have played a major role in breaking the 'innovator company – generic company' divide.

Another point to ponder is that most of the high-profile drugs that have been recently withdrawn were available in Indian market. In such cases, the Indian regulatory agency could not count on the experience of other regulated markets to assess the benefitrisk balance of the said drug.

In fact, we are not even sure as to whether those drugs harmed Indian patients to a lesser extent or if they did so more seriously. This point stresses the importance of developing our own adequately designed pharmacovigilance system for India. All these factors have drawn the attention of the Indian regulators and the pharmaceutical companies toward the inadequacy of pharmacovigilance systems in India.

Major challenges are:

1) Globalization. The globalization of drug distribution and the increased exposure of massive populations to large volumes of medicines. These include novel chemical entities used for symptomatic relief and lifestyle modification as well as medicines used in developing countries to curb the prevalence of pandemic diseases such as HIV/AIDS, malaria and tuberculosis.



2) Web-based sales and information. The Internet, in addition to its many benefits, has also facilitated the uncontrolled sale of medicines (including herbal and traditional medicines) across national borders

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5) Monitoring of established products. The generic sector of the pharmaceutical industry has not fully recognized its responsibility to continuously monitor the safety of its products throughout the world. There is the erroneous belief that generic drugs are inherently safe even when they interact with other medicines. The generic sector is the largest supplier of essential drugs

6) Developing and emerging countries. Outside the OECD countries, the pharmaceutical industry has not been committed to pharmacovigilance activities, particularly the drug safety issues involving medicines used in communities with overburdened health care systems, different patterns of drug use and different comorbid conditions. Other problems to be tackled include: • irrational and potentially unsafe drug donation practices, and • widespread manufacture and sale of counterfeit and substandard medicines

7) Attitudes and perceptions to benefit and harm. These trends have dramatically changed the way in which medicines are used by society. Healthcare providers, patients and the public have responded in different ways to these changing trends as has been described in previous chapters. Their perception of

benefit and harm and the level of acceptable risk for medicines in the face of these rapid developments have not been considered in a meaningful way. The harm caused by medicines has been shown to be significant. Morbidity and mortality from drug-induced diseases are only recently being recognized as an important item on the public health agenda in developed and developing countries

. 8) Outcomes and Impact. Along with increased public awareness over safety of medicines, there is an increasing public gaze on the performance of the health professions, industry and regulators. Increased accountability must lead to more research into the effectiveness of pharmacovigilance and its place in improving public perception. A major focus approval. Though the PSURs are not directly linked with the PvPI, interactive sessions are being conducted by the CDSCO and the PvPI with an aim to discuss these PSURs and issues involved in reporting the same.

There are many countries where patients are not allowed to do ADR reporting . However, PvPI started the ADR reporting by patients on 1st August 2014. The patients can have the following options to report ADRs:

• Use the phone helpline mentioned above;

•Email the same to pvpi.compat@gmail.com;

Resent advancement process by the PvPI

The Materiovigilance Programme of India (MvPI) was established by the PvPI in 2015 to monitor the adverse events associated with medical devices in the country .The members of MvPI met recently at the IPC in May 2017 to discuss plans to gauge the progress of the ambitious programme. It was decided that biomedical engineers with experience will be recruited and PvPI will provide them with the necessary training. The MvPI members also suggested that the medical devices manufacturers should be involved in interactive sessions with them. It was also decided that steps will be taken by the MvPI to increase the awareness of the programme and encourage reporting of Medical Devices Adverse Events (MDAEs).

Conclusion

Monitoring the safety of medicines is a continuous process, starting from the earliest clinical studies and extending throughout the post-marketing period. By the nature of the discipline, pharmacovigilance activities are conducted in real time to ensure early identification of safety signals. Regulatory agencies worldwide require sponsors of clinical trials and marketing authorization holders to submit reports of adverse drug reactions according to regulations and guidelines. Due to the growing importance ofpharmacovigilance, some contract research organizations have established reputable pharmacovigilance groups. These groups are used by pharmaceutical companies to process product safety data to ensure compliance regulations and to establish quality safety databases for effective safety must be to empower health practitioners and patients themselves with useful information that improves individual therapy, aids the diagnosis and management of medicine-induced disease, and generally leads to a reduction of iatrogenic diseases.

Periodic Safety Update Reports (PSURs) are an important way by which the regulatory authorities in India keep a tab on the marketed medicines in the country. According to the rule by the central drug authority in India which is named the Central Drugs Standard Control Organisation (CDSCO), the Marketing Authorization Holders (MAHs) need to prepare PSURs and see to their submission to the CDSCO twice in a year for the first 2 years and annually for another 2 years after getting marketing monitoring. Pharmacovigilance is an important tool to ensure that a marketed drug is safe. PvPI was launched with the main objective of knowing the ADRs associated with the marketed drugs in India so that the necessary steps can be taken, if needed. The members of PvPI are striving hard to increase its reach in India and to fortify the steps for capacity building. Multiple recent steps have been taken by PvPI which prove that pharmacovigilance is moving in the right direction.

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