INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com
ISSN 2230 – 8407

Review Article

PHARMACOVIGILANCE: NEED FOR INDIAN PHARMA INDUSTRY

Pranay Wal [1]*, Ridhima Mehra [2], Saista Rizvi [2], Rachana Vajpayee [2]
[1]Assistant Professor, Department of Pharmacology, Pranveer Singh Institute of Technology, Bhauti road, Kanpur (U.P) India
[2]Research Scholar, Department of Pharmacology, Pranveer Singh Institute of Technology, Bhauti road, Kanpur (U.P) India
*Corresponding Author Email: pranaywal@gmail.com

Article Received on: 21/09/15 Revised on: 12/10/15 Approved for publication: 20/10/15

DOI: 10.7897/2230-8407.0611144

ABSTRACT

Pharmacovigilance is the science and activities related to the collection, detection and assessment of the adverse event data. The major aim of pharmacovigilance is the evaluation of the benefit-risk profile of the drug for better efficacy and safety for use in patients. Pharmacovigilance has been known to play a key role in the rationale use of drugs by providing information about the adverse drug reactions occurring in patients. Indian Pharma industry is the third largest in the world in terms of the volume and thirteen largest in terms of value. India has also been a hub for clinical research and drug development. With new drug entities, chemical moieties, dosage forms and drugs being discovered and manufactured on a large scale; Indian Pharma industry require a global and standardize pharmacovigilance system for better safety assessment. This review article explains the need of pharmacovigilance in Pharma industry, basic steps related to pharmacovigilance and the current status of the pharmacovigilance in the country.

Keywords: pharmacovigilance, adverse event, drug development, Indian Pharma industry

INTRODUCTION

The Indian pharmaceutical industry is valued at Rs. 90,000 crore and is growing at a rate 12-14% per annum. Exports are growing at a rate of 25% compound annual growth rate. The total export of Pharma products is to extent of Rs. 40,000 crore. India has also emerged as a hub for the clinical trials and drug discovery and development. Further more and more drug entities are being introduced which includes New Chemical Entities, Pharma products, vaccines, dosage forms, new routes of drug administration and new therapeutic claims of existing drug moieties. This is reflected in the fact that total number of applications received & processed at CDSCO HQ; New Delhi has been more than double from 10,000 in the year 2005 to 22,806 in year 2009.This includes increase in New Drug Applications, Clinical Trials, Market Authorization of vaccines and biotech products.[1]

Such rapid increase in introduction of new drug entities and Pharma products has led to the monitoring of Adverse drug Reactions (ADRs) for the pharmaceutical products over a large population base. Every drug has side effects, some of them are known by the clinical trials but still some are unknown even through the drug is in clinical use. It is therefore necessary to determine the known and unknown side effects of the drug for better assessment of benefit-risk ratio of the drug. Pharmacovigilance (PV) is defined as the science and activities relating to the detection, evaluation, understanding and prevention of adverse effects or any other drug related problems.[2]

Pharmacovigilance is mainly related to the detection of adverse drug reaction or ADR which is defined as-"A response to a drug which is noxious and unintended, and which occurs at doses normally used for the prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function."[3] Pharmacovigilance is an important and integral part of clinical research and drug development. With a recent ban by CDSCO on some major drugs like dextropropoxyphene and analgin, pharmacovigilance has now become an important tool for assessing the safety profile of the drugs. Pharmacovigilance is more important for newer drugs as the information obtained from the clinical trials is inadequate to cover all aspects of the drug safety.

A drug has to pass through various phases of clinical trials before it would be marketed for human use. However clinical trials have various limitations like: strict exclusion and inclusion criteria for patients, special population groups like elderly, pregnant woman, children are not included in trials and other factors such as genetic variation, environment factors and drug interactions may have not been studied in trials.[4] There is a need of standardize pharmacovigilance system in each country because of following main reasons:[5]

- While medicines have led to improvement in the control and treatment of disease, they also produce adverse effects on human body
- While many drugs are precisely targeted to the causes and the mechanism of the disease , they may also have distressing effects on other parts of the body , or may interact negatively with other administered drugs
- There are risks in any intrusion to the human body, whether chemical or surgical.
- Efficacy is used to express the extent to which a drug works under ideal circumstances (i.e. clinical trials).

India being a vast country with over 1.2 billion population with vast ethnic variability, different disease pattern, genetic variations and practices of different system of medicines requires a standardized and robust programme for collection of adverse event data and for assuring patient safety. Collecting this information in a systematic manner and analyzing the data to reach a meaningful conclusion on the continued use of these medicines is the rationale to institute this program for India. Since, there are considerable social and economic consequences of ADRs there is a need to engage health-care professionals, in a well-structured programme to build synergies for monitoring ADRs.

Recently the approach of pharmacovigilance has been extended to:
- Herbal medicines
- Traditional medicines
- Biologicals
- Vaccines
- Medical devices
- Blood products

STEPS IN PHARMACOVIGILANCE[6]

The basic steps in pharmacovigilance include:
- Safety data management
- Signal detection
- Signal evaluation and making decisions with regard to safety issues
- Actions, including regulatory to protect public health
- Providing information to all concerned parties or stakeholders

Safety data management: A serious adverse event for a drug may occur during the clinical trial phase or the post marketing phase. It could be a spontaneous report by a physician, healthcare professionals, nurses or pharmacist. Unexpected adverse event may occur anytime during the lifetime of the product, therefore as a part of risk management safety monitoring for a drug is necessary.

The steps in safety data management are:
- data collection and verification
- coding of adverse drug reactions
- coding of drugs
- causality assessment
- timely reporting to authorities

Data Collection and Verification

Acknowledgement: a valid case study consists of four elements: adverse drug reaction, reporter, patient and drug. Every valid case need to be acknowledged as it helps in getting more information from the reporter whenever required.

Duplicate search: Every safety database software has a facility to identify and delete duplicate cases. Certain characteristics of a case such as age, sex, date of drug exposure, clinical trial code, country etc. may be used to identify duplicate reports.

Triage: Triage in safety means prioritizing the case for reporting to authorities. An oversimplification of triage would be to report deaths and life threatening unexpected reports in 7 days and other adverse reactions in 15 days as there are also other occasions where expedited reporting is required.

Data entry: Details of a valid case have to be reported meticulously. Patient information has to follow the HIPPA code for confidentiality. Reporter information has to clear and detailed enough to be able to contact the person if necessary. Drug identifiers like name, formulation and dose have to be captured correctly. Event report has to be detailed enough for the evaluator to decide on the cause of the adverse event. This would include chronological description of the event or events, nature, localization, severity, characteristics of the event, results of investigations and tests, start date, course and outcome, concomitant medications and other risk factors.

Case narratives: It is defined as a summary of a case providing all the relevant information regarding a case. During the course of safety data management, it is seen and used by various groups like case reviewers to decide seriousness, upgrade etc., affiliate companies to triage for their countries, during preparation of PSURs and other summary reports and also by regulatory authorities.

Coding of adverse events: Most commonly used system for coding of adverse events is MedDRA (Medical Dictionary for Regulatory Activities). It is a clinically validated international medical terminology used by pharmaceutical industry and regulatory authorities throughout the entire regulatory process, from pre marketing to post-marketing activities. Use of MedDRA has led to a global standardization across regulatory agencies, across companies & across countries.

Coding of drugs: Both the suspect drug and the concomitant medication need to be coded. Most commonly WHO drug dictionary is used; it is managed by the Uppsala monitoring center Of WHO and entries are updated four times in a year. The dictionary also covers biotech and blood products, diagnostic substances and contrast media. For chemical and therapeutic groupings the WHO drug record number system and ATC classifications are considered.

Causality assessment: Non spontaneous case reports usually indicate whether an adverse drug reaction is suspected due to the administered drug. In these circumstances and even otherwise, a causality assessment is required to be conducted. Various approaches have been developed for the structured determination of the likelihood of a causal relationship between drug exposure and adverse events. These systems are largely based on following considerations:

- The chronology or association in time (or place) between drug administration and event
- current knowledge of nature and frequency of adverse reactions due to the suspect molecule; or the pharmacology
- medical or pharmacological plausibility based on signs and symptoms, laboratory tests, pathological findings, mechanism of action
- Likelihood or exclusion of other causes for the same adverse events; often the disease condition or concomitant medication.

Timely reporting to authorities: This is the end goal for which all the above has to be done in a timely manner. It helps in generation of periodic safety updates regarding the pharmaceutical product.

ROLE OF EFFECTIVE COMMUNICATION IN PHARMACOVIGILANCE [7]

Pharmacovigilance experts from different part of the world have emphasized the role of effective communication in drug safety with the following statements:

- Drug safety information must serve the health of the public
- Education in the appropriate use of drugs, including interpretation of safety information, is essential for the public at large, as well as for health care providers
- All the evidence needed to assess and understand risks and benefits must be openly available
- Every country needs a system with independent expertise to ensure that safety information on all available drugs is adequately collected, impartially evaluated and made accessible to all
- Innovation in drug safety monitoring needs to ensure that emerging problems are promptly recognised and efficiently dealt with, and that information and solutions are effectively communicated

It is believed that these factors might be helpful in assessing the risk-benefit ratio of the drugs and generation of safety information for drugs.

PHARMACOVIGILANCE PROGRAMME OF INDIA

The Central Drugs Standard Control Organisation (CDSCO), New Delhi, under the aegis of Ministry of Health & Family Welfare, Government of India has initiated a nation-wide pharmacovigilance programme in July, 2010, with the All India Institute of Medical Sciences (AIIMS), New Delhi as the National Coordinating Centre (NCC) for monitoring Adverse Drug Reactions (ADR) in the country to safe-guard Public Health. In year 2010, 22 ADR monitoring centers (AMCs) including AIIMS, New Delhi had been set up under this Programme. To ensure implementation of this programme in a more effective way, the National Coordination Centre was shifted from the All India Institute of Medical Sciences (AIIMS), New Delhi to the Indian Pharmacopoeia Commission, Ghaziabad, Uttar Pradesh on 15th April 2011.[8]

Objective and purpose of PvPI: The main objective of the pharmacovigilance programmed is to ensure that the benefits of the drugs should outweigh the risk associated with them. The purpose of the PvPI is to collate data, analyze it and use the inferences to recommend informed regulatory interventions, besides communicating risks to healthcare professionals and the public. The broadened patient safety scope of pharmacovigilance includes the detection of medicines of substandard quality as well as the detection of prescribing, dispensing and administration errors.[9]

Implementation of PvPI

IPC understood the need for establishing local hospital based centers across the nation for the better patient safety. It was important to monitor both the known and the unknown side effects of medicines in order to determine any new information available in relation to their safety profile. In a vast country like India with a population of over 1.2 billion and with vast diversity among Indian population, different disease prevalence patterns, practice of different systems of medicines, different socioeconomic status, it was important to have a standardized and robust pharmacovigilance and drug safety monitoring programme for the nation.

Goals of PvPI [9]

Short term Goals

- To develop and implement pharmacovigilance system in India
- To enroll, initially, all MCI approved medical colleges in the program covering north, south, east and west of India
- To encourage healthcare professionals in reporting of adverse reaction to drugs, vaccines, medical devices and biological products
- Collection of case reports and data

Long term Goals

- To expand the pharmacovigilance programme to all hospitals (govt. & private) and centers of public health programs located across India
- To develop and implement electronic reporting system (e-reporting)
- To develop reporting culture amongst healthcare professionals
- To make ADR reporting mandatory for healthcare professionals**.**

Pharmacovigilance is been an effective tool for effective assessment of benefit –risk ratio of the drug and is helpful in generation of safety information, warnings and precautions for the use of the drugs.

Some of the drugs had been banned by CDSCO due to their potential risks to human life. Table 1 contains the list of some of the drugs that have been banned from Indian market and the reason for their ban.[10]

Table 1: Drugs Banned by CDSCO

Drug	Reason for ban
Terfinadine	Caused cardiac arrhythmias
Rofecoxib and its formulations	Myocardial infarction was reported
Valdecoxib and its formulations	Heart attack and stroke occurred
Cisapride	Caused cardiac arrhythmias
Gatifloxacin formulation	Causes hyperglycemia and liver damage
Tegaserod and its formulations	Cardiovascular ischemic events occurred followed by heart attack and stroke
Nimesulide formulations for human use in children below 12 years of age.	Hepatotoxicity
Cisapride and its formulations for human use	Fast heartbeat, convulsions, irregular heartbeat, QT prolongations, torsades de pointes, cardiac arrest
Sibutramine and its formulations for human use.	Cardiovascular risk increases by its use
Dextropropoxyphene and formulations	Cardiac toxicity
Fixed dose combination of Flupenthixol + Melitracen for human use	Potential risk to human life

CURRENT STATUS OF PHARMACOVIGILANCE

Earlier in 2015, the Drugs Technical Advisory Board (DTAB) has recommended mandating pharmaceutical companies to report adverse effects of the marketed drugs. Further, it re-insisted on its 2011 recommendation for setting up pharmacovigilance cells in all Pharma companies which will be managed by a trained medical officer or pharmacist. It also emphasized on sensitizing medical practitioners across the country by involving the Medical Council of India (MCI) and on training medical reps for collecting adverse event reports from doctors.

The Health Ministry in March,2015 approved the 'Materio Vigilance Programme of India' (MvPI) which would monitor Medical Device associated Adverse Events (MDAE) and be coordinated by the Indian Pharmacopoeia Commission (IPC) in collaboration with the Central Drug Standard Control Organisation (CDSCO). MvPI cells are to be established initially in 10 medical colleges in order to monitor the benefit-risk profile of medical devices. The MvPI was formally launched on 6 July, 2015 at IPC, Ghaziabad by DCGI. Similar programmes for Biovigilance and Haemovigilance were launched in 2012. Recent initiatives undertaken by PvPI include the provision of a toll-free number and introduction of AE reporting forms in different regional languages to encourage consumer reporting. Global pharmaceutical companies and the pharmacovigilance outsourcing industry have shown interest to work with PvPI. It is worth mentioning that the pharmacovigilance outsourcing industry in India has grown by leaps and bounds in the past 8 years, with the number of pharmacovigilance professionals in the country amounting to almost 15,000 people. Ranging from basic case processing activities to complex functions such as signal detection and analysis; the spectrum of pharmacovigilance capabilities available in India has been expanding.[11]

CONCLUSION

Indian pharmaceutical industry is third largest industry in terms of volume and thirteen largest in term of value. The market is dominated mainly by branded generic drugs which contribute nearly 70-80% of the market. It has also emerged as a hub for the clinical trials and drug development process with a frequent increase in new drug delivery system, devices and chemical entities. Therefore we need a standard

pharmacovigilance system for the monitoring of the adverse effects of drug and assuring patient safety. Despite of all the efforts made by CDSCO for the establishment of a global pharmacovigilance system for the country a lot of challenges need to be overcome for successful implementation of pharmacovigilance like lack of awareness among pharmacists, nurses, patients and shortage of technical staff for reporting ADRs. The need of the hour is to educate the physicians, pharmacist and nurses to encourage them to report ADRs that occur in patients. Standard guidelines for pharmacovigilance in India, inspired by the good pharmacovigilance practices devised by EMA, will truly serve the purpose of ensuring safety of our patients and establishing a global system for drug safety monitoring.

REFERENCES

1. Pharmacovigilance Programme of India (PvPI); [cited on 25/07/2015]; Available at URL: http://cdsco.nic.in/forms/contentpage1.aspx?lid=1752
2. WHO; Importance of Pharmacovigilance. 2002; [cited on 25/07/2015]: Available from URL: http://apps.who.int/medicinedocs/en/d/Js4893e
3. Effective communications in Pharmacovigilance. The Erice Report. International Conference on Developing Effective Communications in Pharmacovigilance, Erice, Sicily, 24-27 September 1997, at which a policy statement was drawn up known as The Erice Declaration
4. Mann RD and Andrews EB (eds.) Pharmacovigilance, John Wiley & Sons Ltd. Chichester, 2002
5. Rashmi arora, Ramit Kapoor, NS Gill, Amit Aggarwal, AC Rana. Pharmacovigilance: A way for better tomorrow, Int Res J Pharm, 2011, 2(12), 43-46.
6. Basic steps in Pharmacovigilance Case Processing [cited on 30/7/2015]; Available at URL:http://www.pharmawisdom com/Basic-steps-in-Pharmacovigilance-Case-Processing.html
7. Härmark L, Van Grootheest AC. Pharmacovigilance: Methods, recent developments and future perspectives. European Journal of Clinical Pharmacology 2008, 64:743–752
8. Indian Pharmacopoeia commission: Pharmacovigilance Programme of India (PvPI); [cited on 1/08/2015]; Available at: ipc.nic.in/write read data/link images/pvpi-2611733527.pdf
9. Pharmacovigilance Programme of India; [cited on 5/08/2015] ;Available from: URL: http://www.ipc.gov.in /PvPI/pv_orginv.html.
10. List of banned drugs in the Country - Central Drugs Standard and Control Organisation [cited on 6/08/2015]Available from URL: cdsco.nic.in/.../drugs%20banned% 20in%20the%20country2.pdf
11. Dr J. Vijay Venkatraman; Current status of pharmacovigilance in India: [cited on 7/08/2015]; Available from URL:http:// www.pharmabiz.com/PrintArticle

Cite this article as:

Pranay Wal, Ridhima Mehra, Saista Rizvi, Rachana Vajpayee. Pharmacovigilance: Need for Indian pharma industry. Int. Res. J. Pharm. 2015; 6(11):740-743 http://dx.doi.org/10.7897/2230-8407.0611144

Source of support: Nil, Conflict of interest: None Declared