

Pharmacovigilance: A Review

Mahewashsana A. Pathan

Department of Pharmaceutics, SSJP's R.P. College of Pharmacy, Osmanabad 413 501, Maharashtra, India

Abstract- The safe use of medicines is perhaps the single most important criteria that any regulatory authority within a given country has to ensure in order both to protect the public health and the integrity of its health care system. For the same purpose pharmacovigilance was established. According to WHO, Pharmacovigilance is the science and activities related to the collection, detection, and assessment of ADR's. It promotes the systematic, rational use and assures the confidence for the safety of drugs. It improves patient care and safety. Significance of pharmacovigilance is growing as the patients or consumers have become more responsive about the advantage and hazard of medicines. Pharmacovigilance is a complex process and a robust system is essential to undertake the activity. A good pharmacovigilance system will identify the hazard aspects in the short period of time. This review article tries to explain the some basic principles, history and developments, methods and some scope of this developing field i.e. Pharmacovigilance in India.

Index terms- Pharmacovigilance, Adverse Drug Reaction, WHO, Post marketing surveillance

INTRODUCTION

The Indian pharmaceutical industry is valued at Rs. 90,000 crore & is growing at a rate of 12 -14% annually. 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 administration and new therapeutic claims of existing drug moieties. Such rapid increase in introduction of new drug entities and pharma products has led to monitoring of ADR's for the pharmaceutical products over a large population base. Every drug has effects, some of them are known by the clinical trials but still some are unknown even though the drug is in clinical use.

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. India being a vast country with over 1.2 billion population with vast ethnic variability, different disease patterns, genetic variations, and practices of different system of medicines require a standardized and robust program for collection of adverse events data and for assuring patient safety.

Pharmacovigilance is a very important and inseparable part of clinical research. Both clinical trials safety and post-marketing pharmacovigilance (popularly known as post marketing studies or phase 4 clinical trials) are critical throughout the product life cycle. With the reasonably high number of recent high profile drug withdrawals, both the pharmaceutical industry and various regulatory agencies across the globe have raised the bar.

According to WHO, Pharmacovigilance is defined as, "The pharmacological science and activities concerned with the detection, assessment, understanding and prevention of adverse reactions to medicines or Pharmacovigilance is the name given to the mechanisms and controls that together map and ensure the safety of a medicine throughout its life span – from test tube to patient."

Pharmacovigilance word is derived from two words pharmakon (Greek for drug) and vigilare (Latin for to keep Watch).

AIM OF PHARMACOVIGILANCE

1. Expand precaution for patient.
2. Increase public protection from the new products.
3. To contribute the knowledge of value, detriment, efficiency and hazard of medicines.
4. Encourage edification and clinical training.
5. Endorse healthy communication to the community.

6. To promote rational and safe use of medicines.

Adverse Drug Reactions (ADR's):

“ADR is any response to a drug that is noxious and unintended and that occurs in doses used in man for prophylaxis, diagnosis, therapy of disease or for modifications of physiological functions.” ADR's are of two types:

Type A ADR's / Augmented / Attenuated or normal response ADR's

Type B ADR's / Unpredictable / Bizarre response

Table no 1: Some known adverse effects

Sr.No.	Drug	Adverse drug reactions
1	Thalidomide	Phocomelia, multiple defects
2	Methotrexate	Multiple defects, Fetal death
3	Warfarin	Nose, eye & hand defects, growth retardation
4	Aspirin/ Indomethacin	Premature closure of ductus arteriosus
5	Insulin	Severe hypoglycemia
6	Penicillin's	Hypersensitivity reactions

History of Pharmacovigilance:

Table no 2: The sequential pharmacovigilance developments with special reference to India.

Year	Developments
1937	Death of more than 100 children due to toxicity of sulfanilamide.
1950	Aplastic anaemia reported due to chloramphenicol toxicity.
1961	Worldwide tragedy due to thalidomide toxicity.
1963	16 th world health congregation recognize significant to rapid action on ADR's.
1968	WHO research project for international drug monitoring on pilot scale.
1996	Global standards level clinical trials initiated in India.
1997	India attached with WHO ADR's monitoring program.
1998	Initiation of pharmacovigilance in India.
2002	67 th National Pharmacovigilance Center established in India.
2004-05	India launched National Pharmacovigilance Program.
2009-10	PvPI started.

ADR's reporting:

Adverse drug reaction reporting involves the receipt, triage, data entering, assessment, distribution, reporting and archiving of adverse event data and documentation.

The source of ADR's report may include:

1. Spontaneous reports from healthcare professionals or patients.
2. Solicited reports from patients support program
3. Report from clinical and post marketing studies.
4. Reports from literature sources
5. Reports from media (including social media and websites).
6. Reports reported to drug regulatory authorities.

There are four elements of ADR case:

1. An identifiable patient.
2. An identifiable reporter.
3. A suspect drug.
4. An adverse reaction

If one or more of these four elements is missing, the case is not a valid ADR report.

Table no. 3: Drugs banned by CDSCO

Drugs	Reason for ban
Terfenadine	Cardiac arrhythmia
Rofecoxib	Myocardial infarction
Valdecoxib	Heart attack and stroke
Cisapride	Cardiac arrhythmia
Gatifloxacin	Hyperglycemia and liver damage
Sibutramine	Cardiovascular risk increases
dextropropoxyphene	Cardiac toxicity
adderall	addiction

Methods of Pharmacovigilance:

1. Passive Surveillance
 - a. Spontaneous reports
 - b. Case series
2. Stimulated Reporting
3. Active Surveillance
 - a. Sentinel sites
 - b. Drug event monitoring
 - c. Registries
4. Comparative observational studies
 - a. Cross-sectional studies
 - b. Case – control studies

- c. Cohort studies
- 5. Targeted clinical investigations
- 6. Descriptive studies.

WORK FLOW AND DATA PROCESSING IN PHARMACOVIGILANCE

- Pharmacovigilance knowledge is built by accumulation of individual case safety reports and their subsequent analysis.
- Increased knowledge further influences reporting which leads to new data and better information.
- As shown in fig no. 1, data processing can be seen as a series of loops, linked together in a chain.

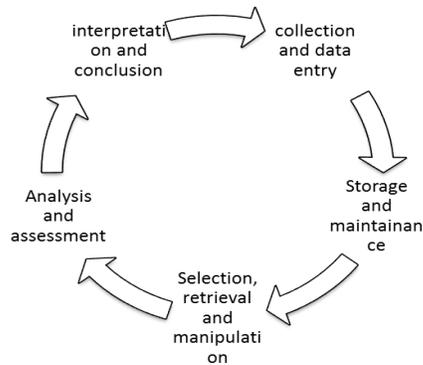


Fig no 1: Data processing in Pharmacovigilance

Data processing in pharmacovigilance is complex, the process involve many players, from different settings and with different interests, such as-

1. Data producers
2. Data collectors
3. Data custodians
4. Data output producers
5. Data consumers

Activities in Pharmacovigilance:



Fig no.2: Activities in Pharmacovigilance

INTERNATIONAL COLLABORATIONS

- 1) World health organization (WHO): More than 100 member nations have system in place.
- 2) International council on harmonization (ICH)
- 3) Council for International Organizations of Medical Sciences (CIOMS): Is a part of WHO, is a globally oriented think tank that provides guidance on drug safety related topics through its working groups.
- 4) International Society of Pharmacovigilance (ISoP): This is an international non-profit scientific organization, which aims to foster pharmacovigilance both scientifically and educationally.

CAREER OPPORTUNITIES IN PHARMACOVIGILANCE

Persons trained in Pharmacovigilance and clinical trials research will found good job options in following:

1. Clinical research associate
2. Clinical research investigator
3. Study co-ordinator
4. Data manager
5. Regulatory affairs manager
6. Clinical trials auditor
7. Clinical project manager
8. Clinical research manager
9. Drug safety associate
10. Medical writer
11. Clinical data manager.

CONCLUSION

Indian pharmaceutical industry is third largest industry in terms of volume and thirteen largest in terms of value. The market is dominated mainly by branded generic drugs which contribute nearly 70-80% of the market. Therefore we need a standard pharmacovigilance system for the monitoring of ADR's of drug and assuring patient safety. Reporting of ADR after marketing should be actively encouraged and should involve all those concerned including doctors, pharmacists, nurses and pharmaceutical companies.

REFERENCES

- [1] Avani Patel, D Giles, Vidhya Thomas, Gurubasvarajaswamy PM, Riddhi Patel, Pharmacovigilance: A Review, International Journal of Pharmaceutical and Biological Archives. 2011.
- [2] Rajkumar Soni, Bikrant Kesari, A Review on Pharmacovigilance, International Journal of Pharmaceutical Sciences Review and Research.
- [3] Pranay Wal, Rhidhima Mehra, Saista Razvi, Rachna Vajpayee, Pharmacovigilance: Need for Indian Pharma Industry, International Research Journal of Pharmacy, 2015.
- [4] Wanmali VV, Brahmane RI, Gupta R, Shinde B, Pharmacovigilance in India : the way ahead.
- [5] Marie Lindquist, Data Quality Management in Pharmacovigilance, Uppasala Monitoring Centre, WHO collaborating centre for International Drug Monitoring, Uppasala, Swedan.
- [6] Priyanka R, Scope of Pharmacovigilance, Research and Reviews: Journal of pharmacology and toxicological studies.
- [7] ICH Harmonised Tripartite guideline, Pharmacovigilance planning E2E, 18 Nov 2004.
- [8] Professor Meir Pugatch, Dr. David Torstensson and Ma'ayan Laufer. The Evaluation of Pharmacovigilance.
- [9] Pharmacovigilance, European Medicines Agency, 2015, from www.ema.europa.eu.
- [10] P.J. Bousquet et al, Pharmacovigilance of drug allergy and hypersensitivity using ENDA-DAHD database and the GA2LEN platform, the Galenda project.
- [11] Sayed K. Ali, Pharmacovigilance analysis of adverse event reports of aliskerin hemifumarate, a first in class direct rennin inhibitor, Dovepress, 2011.
- [12] List of 90 ADR monitoring centers under pharmacovigilance program of India (PvPI).
- [13] List of drugs banned in India.