Review Article

A Review on Pharmacovigilance

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ABSTRACT

Pharmacovigilance, defined by the World Health Organization as 'the science and series of activities relating to the detection, evaluation, understanding and avoidance of adverse effects or any other drug-related problem' plays an important role in ensuring that patients be given safe drugs. The knowledge of a drug's Adverse Drug Reactions (ADRs) can be augmented by various means such database studies, intensive monitoring, spontaneous reporting, and other new processes at dictatorial and a scientific level are being developed with the intention of escalation pharmacovigilance. On dictatorial level, these include risk management plans and conditional approval and on scientific level, increased patient involvement and transparency are two vital elements. The main objective of review is to unfold various aspects of pharmacovigilance including new methodological developments.

Keywords: Pharmacovigilance, Adverse Drug Reactions, WHO, Drug safety.

INTRODUCTION

According to the World Health Organization, "Pharmacovigilance is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problem, particularly long term and short term adverse effects of medicines".[1] Pharmacovigilance is also known as Drug Safety and abbreviated PV or PhV.

The etymological roots for the word "pharmacovigilance" are: *Pharmakon* (Greek word for 'drug') and *vigilare* (Latin word for 'to keep watch').[2]

Pharmacovigilance greatly focuses on adverse drug reactions (ADRs) which are defined as any reaction to a drug which is harmful and unintended including lack of efficacy used for the prophylaxis, analysis or therapy of illness or for the modification of physiological function.[2]

History of Pharmacovigilance in India

Pharmacovigilance in India started from 1986. A formal Adverse Drug Reactions (ADR) monitoring system was initiated with 12 regional centres, each covering a population of 50 million.

However, no noteworthy growth was made. Afterward in 1997, India joined the World Health Organization (WHO) and Adverse Drug Reaction (ADR) scrutinizing program based at[2] Uppsala, Sweden but got fail.

Hence, after 2005 WHO supported and World Bank – funded National Pharmacovigilance Programme (NPPV) of India was made operational.[2, 17, 21, 19]

Table 1: The sequential pharmacovigilance developments with special reference to India:[1, 11, 16.]

Year	Developments
1747	Very first known clinical trials by James Lind, proving the usefulness of lemon juice in preventing scurvy.
1937	Death of more than 100 children due to toxicity of sulfanilamide.
1950	Apalstic anemia reported due to chloramphenicol toxicity.
1961	Worldwide tragedy due to thalidomide toxicity.
1963	16th World Health congregation recognize significant to rapid action on Adverse Drug Reactions (ADRs).
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 Adverse Drug Reaction Monitoring Program.
1998	Initiation of pharmacovigilance in India.
2002	67th National Pharmacovigilance Center established in India.
2004 -05	India launched National Pharmacovigilance Program.
2005	Accomplishment of structured clinical trials in India.
2009 -10	Pharmacovigilance Program (PvPI) started.

Need of pharmacovigilance

The forceful marketing of new drug products by pharmaceutical companies and the consequential rapid disclosure over a short period of time of large numbers of patients to them necessitate the formation of a system for global assessment of drug safety concerns. These actions need an effective and efficient pharmacovigilance system that has been realized more than ever to make sure safe use of drugs. There are several rationales for

increasing requirement of pharmacovigilance system. The bases of need are as follows:

1. Untrustworthiness of pre-clinical safety information.
   - Well-controlled environment.
   - Appropriate and precise sample size.
   - Pressure from various systems to decrease time to authorization.
2. Altering pharmaceutical marketing policies.
   - Aggressive marketing
   - Launch the drug in many countries at a time
3. Varying physician's, patient's and other health professional's preferences
   - Increasing use of newer drugs
   - Increasing use of drugs to get better quality of life
   - Shift of manage to self-administered treatment.
4. Easy convenience
   - Growing conversion of prescription drugs to over the counter drugs
   - Easy access to drug information on the Internet.[1,2,11,21]

According to International Conference on Harmonization Efficacy Guidelines 2 (ICHE2E) guidelines pharmacovigilance techniques can be categorized as:

Passive surveillance

(1) Spontaneous reporting system (SRS).

(2) Case series.

Stimulated reporting

I. Active surveillance

(1) Sentinel sites

(2) Drug event monitoring

(3) Registries

II. Comparatives observational studies

(1) Cross sectional study

(2) Case control study

(3) Cohort study

III. Targeted clinical investigations

(1)Descriptive studies

(2) Natural history of disease

(3) Drug utilization study

Pharmacovigilance techniques can be also classified as hypothesis generation techniques and hypothesis testing techniques as follows:

I. Hypothesis generating techniques

(1) Spontaneous ADR reporting

(2) Prescription event monitoring

II. Hypothesis testing techniques

(1) Case control study

(2) Cohort studies

(3) Randomized controlled trials

Most frequently used methods for monitoring of drug safety are as follows**:** [2, 6, 10, 39]

Spontaneous reporting systems (SRSs)

Spontaneous reporting systems involve the recording and reporting clinical observations of a suspected Adverse Drug Reactions (ADRs) with a marketed drug. It is also known as spontaneous or voluntary reporting. There are slight differences in this reporting system among the various countries but the ideology are the same. Safety of medicines is frequently monitored through spontaneous reporting systems (SRSs)**.** [13, 15] Moreover the **s**tandardized forms are used for reporting of alleged adverse drug reactions to the regulatory system by physicians, pharmacists, nurses and consumers as well**.** [2, 3]

Prescription-event monitoring (PEM)

Prescription-event monitoring (PEM) is an observational cohort and non-interventional form of pharmacovigilance. Prescription-event monitoring (PEM) studies are cohort studies in which exposure is collected from a centralized service and outcomes from simple questionnaires finished by general practitioners. Moreover the follow-up forms are used for selected Adverse Events (AE). Prescription-event monitoring (PEM) captures all Adverse Events (AE) and the alleged drug reactions (ADRs)**.** [13, 15] Prescription-event monitoring (PEM) cohorts potentially are different in deference to the distribution of number of Adverse Events (AE) per person depending on the character of the drug under study**.** [2, 3]

National pharmacovigilance system- India

India attached with the World Health Organization's (WHO) Adverse Drug Reaction (ADR) Monitoring Programme based in Uppsala, Sweden in the year 1997. In India, for the monitoring of Adverse Drug Reaction (ADR's) there were three main centres identified**:** [5, 8]

1. A National Pharmacovigilance Centre in the Department of Pharmacology, All India Institute of Medical Sciences (AIIMS), New Delhi.
2. WHO special centers in Mumbai (KEM Hospital).
3. Jawahar Lal Nehru Hospital, Aligarh Muslim University, Aligarh**.** [7, 9]

The mentioned centers monitor the Adverse Drug Reactions (ADRs) of the drugs available in market for sell

on OTC counter.[13] This effort was ineffective and then second time from the 1st of January 2005, the WHO-sponsored and World Bank-funded National Pharmacovigilance Program for India was established.[2]

The National Pharmacovigilance Program (PvPI) recognized in January 2005, and supervised by The Central Drugs Standard Control Organization (CDSCO), Directorate General of Health Services under the aegis of Ministry of Health & Family Welfare, Government of India in collaboration with Indian Pharmacopeia commission, Ghaziabad.[2] Two zonal centers- KEM located in the Department of Pharmacology, AIIMS, New Delhi and the South-West zonal centre located in the Department of Clinical Pharmacology, Seth GS Medical College.[2, 26] Meanwhile established information centres which collate information from all over the country and send it to the Committee as well as to the Uppsala Monitoring centre in Sweden. [5, 9]

Adverse drug reactions (ADRs)

An adverse drug reactions (ADRs) can be defined as an unintended and noxious responses to a health product which causes at the doses usually used or tested for the diagnosis, prevention or treatment of a disease or the alteration of an organic function.[7, 24, 31] Though, it is difficult to recognize the causative agent related with the adverse drug reactions (ADRs) encountered because the medicinal preparations generally contain more than ingredients.[14] All drugs are capable of producing adverse drug reactions (ADRs) and whenever a drug is given a risk is taken.[16]

The magnitude of risk has to be considered along with magnitude of expected therapeutic benefit in deciding whether to use or not to use a particular drug in a given patient. [29] The adverse drug reactions (ADRs) may develop promptly or only after prolonged medication or even after stoppage of drug. Adverse drug reactions (ADRs) are not rare; an incidence of 10- 25% has been documented in different clinical settings and are more common with the multiple drug therapy. [6, 4, 12] Adverse drug reactions (ADRs) have been classified in to two ways; [22]

A. Predictable (Type-A) Reactions

These are based on pharmacological properties of drug like augmented but quantitatively normal response to the drug which include side effects, toxic effects and consequences of drug withdrawal. [6, 14]

B. Unpredictable (Type-B) Reactions

These are based on peculiarities of patient and not on drug's known actions; include allergy and idiosyncrasy. They are less common, often non dose related, generally more serious and require withdrawal of drug. A list of some suspected and known drugs associated with adverse effects is given in Table 2.[6, 14]

Table 2: Known drugs adverse effects[37]

Drug	Adverse Drug Reactions (ADRs)
Thalidomide	Phocomelia, Multiple defects
Methotraxate	Multiple defects, Foetal death
Androgen	Virilization, limb, esophageal, cardiac defects
Progestins	Virilization of female foetus
Stilboestrol	Vaginal carcinoma in teenage female offspring
Tetracyclines	Discolored or deformed teeth, retarded bone growth
Warfarin	nose, eye and hand defects, growth retardation
Phenytoin	Various malformations
Lithium	Foetal goiter, cardiac and other abnormalities
Aspirin/ Indomethacin	Premature closer of ductus arteriosus

Adverse Drug Reactions (ADRs) Reporting/ Adverse Event (AE) Reporting

Adverse Drug Reactions (ADRs) Reporting/ Adverse Event (AE) Reporting is the most commonly associated with Pharmacovigilance (PV) and consumes a considerable amount of resources of government agencies or drug regulatory authorities or drug safety departments in pharmaceutical organizations.[13] Adverse Event (AE) reporting includes the receipt, triage, data maintaining, evaluation, distribution, reporting of AE data.[12, 19, 21] The foundation of AE reports may include solicited reports from patient support programs, reports from clinical or post-marketing studies, spontaneous reports from healthcare professionals or patients or other intermediaries, reports from literature sources, reporting is a regulatory requirement in most countries, reports from the media including social media and websites and reports reported to drug regulatory authorities themselves.[8] For pharmaceutical companies AE reporting also provides data that play an important in assessing the risk-benefit profile of a given drug. The following are several elements of Adverse Event (AE) Reporting: [2, 3]

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

CONCLUSION

India's pharmaceutical industry is now the third largest in the world in terms of volume, 14th in terms of value and now emerging as an important clinical trial hub in the world.[11] With the introduction of new drug molecule a strong pharmacovigilance structure is require in our country to guard the inhabitants from the impending harm and adverse effect.[9] Pharmacovigilance plays an

essential role in convention the challenges posed by the ever rising range and effectiveness of medicines. But the pharmacovigilance system in our country is still need development.[12] Despite of recent implementation of a well structured pharmacovigilance program in India in agreement with the recommendations and objectives of WHO by CDSCO, desired success is still a distant dream.[2, 27] However augmented awareness and training of medical professionals' and public, framing of strong policies for reporting of adverse drug reactions (ADRs), effective execution and mutual efforts between government, pharmaceutical companies, health care professionals, regulatory officials and patient may lead to an effective pharmacovigilance system in India.[2, 13, 22, 28]

REFERENCES

1. World Health Organization. The importance of pharmacovigilance – safety monitoring of medicinal products. World Health Organization, Geneva, 2002.
2. Shuka SS, Gidwani Bina, Pandey R, Rao SP, Singh V and Vyas Amber, "Importance of Pharmacovigilance in Indian Pharmaceutical Industry", Asian Journal of Research in Pharmaceutical Science, 2, 2012, 04-08.
3. Elkalmi Ramadan Mohamed, Mohamed Azmi Hassali, Mohamed Izham M., Ibrahim Widodo Riyanto T, Efan Qais MA and Muhammad Hadi Abdul, "Pharmacy Students' Knowledge and Perceptions about Pharmacovigilance in Malaysian Public Universities", American Journal of Pharmaceutical Education, 2011.
4. Nainwal P, "Pharmacovigilance of Herbal Medicines: An Intangible Approach", International Journal of Pharmaceutical Sciences and Research, 1, 2010, 60-65.
5. Vora Mukesh kumar B., Paliwal Narendra P., Doshi Vikas G., Barvaliya Manish J. and Tripathi C.B., "Knowledge of Adverse Drug Reactions and Pharmacovigilance Activity among The Undergraduate Medical Students of Gujarat", International Journal of Pharmaceutical Sciences and Research (IJPSR), 3, 27 April, 2012, 1511-1515.
6. Rohilla Ankur, Kumar Vipin, Sharma Mohit Kumar, Dahiya Amarjeet and Kushnoor Ashok, "Pharmacovigilance: Needs and Objectives", Journal of Advanced Pharmacy Education & Research, 2, Oct-Dec 2012, 201-205.
7. Bhosale Uma, Jaiswal Shruti, Yegnanarayan Radha and Godbole Gouri, "A Pharmacovigilance Study of Anti-Asthmatic Agents in Patients of Bronchial Asthma at a Tertiary Care Hospital", Journal of Clinical & Experimental Research, 1, May-August 2013, 26-30.
8. Kothari Miral, Sadaria Priti and Dave Nehal, "Data mining in pharmacovigilance – to reduce Adverse Drug Effects (ADRs)", International Journal of Computer Applications & Information Technology, II, January 2013, 01-04.
9. Patel Avani, Giles D, Thomas Vidhya, Gurubasavarajaswamy P.M. and Patel Riddhi, "Pharmacovigilance: A Review", International Journal of Pharmaceutical & Biological Archives, 2, 24 Oct 2011.
10. Sharda Anisha, Patel Ruchi, Patel Naishi, Vyas Hiral and Dixit Payal, "Regulatory Aspects of Pharmacovigilance along with Comparison in United States and Europe", 2, 21st June 2013, 1756- 1767.
11. Ghosh Rupanwita, Bhatia M.S. and Bhattacharya S.K., "Pharmacovigilance: Master Key to Drug Safety Monitoring and its Status in India", Delhi Psychiatry Journal, 15, October 2012, 412-415.
12. Kumar M. Rupesh, Bodhanapu Surendra, Mani T. Tamizh, Phaneendra P. and Rahiman O.M. Fasalu, "Pharmacovigilance and its importance in drug regulation: An Overview", Scholars Research Library, 3, 2011, 165-179.
13. Reddy V.Lokesh, Pasha S.K. Javeed, Dr. Rathinavelu Mohanraj and Dr. Reddy YP, "Assessment of Knowledge, Attitude and Perception of Pharmacovigilance and Adverse Drug Reaction (ADR) Reporting among the Pharmacy Students in South India", IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS), 9, Mar-Apr. 2014, 34-43.
14. Maiti Bodhisattwa, Nagori B.P., Singh Rambir, Kumar Pragati and Upadhyay Nishant, "Recent Trends in Herbal Drugs: A Review", International Journal of Drug Research and Technology, 1, 2011, 17-25.
15. Sharma Sanjeev, Phadnis Pradeep and Gajbhiye Sapna, "Pharmacovigilance: Its Awareness and Impact Care Teaching Medical College in Central India", International Journal of Pharmaceutical Research and Bio-Science, 2, 2013, 234-247.
16. Kulkarni M.D., Baig M.S., Chandaliya K.C., Doifode S.M., Razvi S.U., Sidhu N.S., "Knowledge, Attitude and Practice of Pharmacovigilance among Prescribers of Government Medical College and Hospital, Aurangabad (Maharashtra), international journal of pharmacology and therapeutics, 3, 2013, 10-18.
17. Jadhav Sudhakar and Chakraborthy Guno, "Pharmacovigilance in India: Need of Hour", Journal of Advances in Pharmacy and Healthcare Research (JAPHR), 1, 2011, 01-03.
18. Chaudhary Anand, Singh Neetu and Kumar Neeraj, "Pharmacovigilance: Boon for the safety and efficacy of Ayurvedic formulations", Journal of Ayurveda & Integrative Medicine, 1, October 2010, 251-256.
19. Muraraiah Sushma, Rajarathna Kavitha, Sreedhar Divyasree, Basavalingu Deepashri and Jayanthi C.R. "A questionnaire study to assess the knowledge, attitude and practice of Pharmacovigilance in a paediatric tertiary care centre", Journal of Chemical and Pharmaceutical Research, 2011, 416-422.
20. Biswas Pipasha, "Pharmacovigilance in Asia", Journal of Pharmacology and Pharmacotherapeutics, December 2013, 4, S7-S19.
21. S Amarnath, S Jaikumar, S Basalingappa, M Thulasimani and S Ramaswamy, "Pharmacovigilance for Health Care Professional Students", Research Journal of Pharmaceutical, Biological and Chemical Sciences (RJPBCS), 4, January-March 2013, 1204-1217.
22. Rama.P, Prudence A Rodrigues and Georgy Archana, "Pharmaovigilance: Perspectives and Future Challenges in Indian Scenario", Asian Journal of Pharmaceutical and Clinical Research, 4, 2011, 01-04.
23. Majagi Suneel and Patil PA, "Pharmacovigilance", Recent Research in Science and Technology, 3, 2011, 33-34.

24. Sharma Sanjeev, Phadnis Pradeep and Gajbhiye Sapna "Pharmacovigilance: Its Awareness and Impact Care Teaching Medical College in Central India Impact- Study in a Tertiary care Teaching Medical College in Central India", International Journal of Pharmaceutical Research and Bio-Science (IJPRBS), 2, 2013, 234-247.

25. Dr. Gupta Pankaj, Dr. Udupa Aaditya, "Adverse Drug Reaction Reporting and Pharmacovigilance: Knowledge, Attitudes and Perceptions amongst Resident Doctors" Journal of Pharmaceutical Science & Research, 3, 2011, 1064-1069.

26. Ghosh A. K., De A and Bala N.N., "Current Problems and Future Aspects of Pharmacovigilance in India", International Journal of Pharma and Bio Sciences, 2, Jan-Mar 2011, 15-28.

27. Alhat Babita Ravindra, "Pharmacovigilance: An Overview", International Journal of Research in Pharmacy and Chemistry (IJRPC), 1, 2011, 968-974.

28. Kumar Sumit and Baldi Ashish, "Pharmacovigilance in India: Perspectives and Prospects", Journal of Drug Delivery & Therapeutics, 3, 2013, 237- 246.

29. Chakraverty Raja and Banerjee Anindya, "Emerging Issues in Pharmacovigilance of Herbal Medicines in India", International Journal of Pharmaceutical Sciences Review and Research, 20, May – Jun 2013, 40-42.

30. Muthiah NS, Elumalai M, Murali NP and Hazra R., "Pharmacovigilance: A Tool for Health Safety", Indian Journal of Multidisciplinary Dentistry, Jan 2012, 2, 374-376.

31. Padmavathi G. V., Beere Nagaraju, Divakara P., Suresh Kumar P., Surendranath A. and Sunil R. Patel, "Screenplay of pharmacovigilance among nursing staff in Bangalore", 2, February 2013, 365-370.

32. Brahmachari Ballari, Fernandes Melanie and Bhatt Arun, "Pharmacovigilance for clinical trials in India: Current practice and areas for reform", Perspectives in Clinical Research (PICR), -2, April, 2014, 49- 53.

33. L.Härmark and A.C.VanGrootheest, "Pharmacovigilance: methods, recent developments and future perspectives", European Journal of Pharmacology, June 2008.

34. Chinenye J. U. and Michael O. U., "Health Workers and Hospital Patients Knowledge of Pharmacovigilance in Sokoto, North-West Nigeria", Nigerian Journal of Pharmaceutical Sciences, 1, September, 2012.

35. Mishra H. and Kumar V., "Pharmacovigilance: Current Scenario in a Tertiary Care Teaching Medical College in North India", Journal of Pharmacovigilance, 1, 2013.

36. Tripathi K.D., Essentials of Medical Pharmacology, 5th Edition, Jaypee Brothers Medical Publishers (P) Ltd. New Delhi, 60-61.

37. Leon Lachman, Herbert A. Liberman, Joseph L.Kanig, 3rd Edition, Varghese Publishing House, Hind Rajasthan Building Dadar, Mumbai, 239-240.

38. John M. Beale, John H.Block, Organic Medical and Pharmaceutical Chemistry, 12th Edition (2003), Lippincott Williams & Wilkins Michigan, 312-313.

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