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 drug-related problem, particularly long-term and short-term adverse effects of medicines". 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’). 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.

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 Uppsala, Sweden but got fail.

Hence, after 2005 WHO supported and World Bank – funded National Pharmacovigilance Programme (NPPV) of India was made operational. These early long 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.

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

<table>
<thead>
<tr>
<th>Year</th>
<th>Developments</th>
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<tr>
<td>1747</td>
<td>Very first known clinical trials by James Lind, proving the usefulness of lemon juice in preventing scurvy.</td>
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<td>1937</td>
<td>Death of more than 100 children due to toxicity of sulfanilamide.</td>
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<td>1950</td>
<td>Aplastic anemia reported due to chloramphenicol toxicity.</td>
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<td>1961</td>
<td>Worldwide tragedy due to thalidomide toxicity.</td>
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<tr>
<td>1963</td>
<td>16th World Health congregation recognize significant to rapid action on Adverse Drug Reactions (ADRs).</td>
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<tr>
<td>1968</td>
<td>WHO research project for international drug monitoring on pilot scale.</td>
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<td>1996</td>
<td>Global standards level clinical trials initiated in India.</td>
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<td>1997</td>
<td>India attached with WHO Adverse Drug Reaction Monitoring Program.</td>
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<td>1998</td>
<td>Initiation of pharmacovigilance in India.</td>
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<td>2002</td>
<td>67th National Pharmacovigilance Center established in India.</td>
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<tr>
<td>2004 - 05</td>
<td>India launched National Pharmacovigilance Program.</td>
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<td>2005</td>
<td>Accomplishment of structured clinical trials in India.</td>
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<tr>
<td>2009 - 10</td>
<td>Pharmacovigilance Program (PvPI) started.</td>
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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 (ICH-E2) 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 standardized 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. 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.

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. 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. 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.

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. 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. All drugs are capable of producing adverse drug reactions (ADRs) and whenever a drug is given a risk is taken.

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. 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. Adverse drug reactions (ADRs) have been classified in to two ways:

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.

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.

Table 2: Known drugs adverse effects

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

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. Adverse Event (AE) reporting includes the receipt, triage, data maintaining, evaluation, distribution, reporting of AE data. 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. 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:

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. 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. 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. 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. 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.

REFERENCES

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.


