NAAS Score: 4.11; IC Value: 74.82; UGC-India Approved
The Journal of Phytopharmacology 2018; 7(2): 216-221
Online at: www.phytopharmajournal.com

Research Article

ISSN 2320-480X
JPHYTO 2018; 7(2): 216-221
March- April
Received: 21-03-2018
Accepted: 05-04-2018

Shobharam Sahu
Research Scholar, Faculty of Pharmaceutical Science, Sri Venkateshwara University, Gajraula, Uttar Pradesh, India

Poonam Rishishwar
Faculty of Pharmaceutical Science, Sri Venkateshwara University, Gajraula, Uttar Pradesh, India

Chhaya Rathod
Rajiv Gandhi college of Pharmacy, Nautanwa, Maharajganj, Uttar Pradesh, India

Correspondence:
Shobharam Sahu
Research Scholar, Faculty of Pharmaceutical Science, Sri Venkateshwara University, Gajraula, Uttar Pradesh, India
Email: srs2712[at]yahoo.com

Pharmacovigilence practice for safety of medication system in India

Shobharam Sahu*, Poonam Rishishwar, Chhaya Rathod

ABSTRACT

Pharmacovigilance is very essential tool to ensure the safety of drug. It provides safety to patients in case of medication. Activity of pharmacovigilance is coordinates by National pharmacovigilance center in collaboration with international regulatory authorities (WHO, The Uppsala Monitoring center). Under the aegis of Ministry of Health & Family Welfare, Government of India, the Central Drugs Standard Control Organisation (CDSCO), New Delhi, has initiated a nation-wide pharmacovigilance programme, with the All India Institute of Medical Sciences (AIIMS), New Delhi as the National Coordinating Centre (NCC) for monitoring Adverse Drug Reactions (ADR).

Keywords: Pharmacovigilance, India, Uppsala monitoring center, Drug sefty, Adverse drug reaction reporting, CDSCO, NCC, ICSR.

INTRODUCTION

The etymological roots for the word "pharmacovigilance" are pharmacon (Greek) meaning drug and vigilare (Latin) meaning to keep watch [1]. Pharmacovigilance is a system to monitor the safety and effectiveness of medicines and other pharmaceutical product in the real world. Modern therapies of medicines have changed the way in which diseases are controlled and managed. Pharmacovigilance process begins at the initial stage of clinical trial development process of a drug and continue throughout the life cycle of the drug product [2]. According to W.H.O. 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 problems". Pharmacovigilance is particularly concerned with adverse drug which occurs at doses normally used in man for prophylaxis, diagnosis of therapy of diseases, or for modification of physiological function" [3]. In some countries, adverse drug reactions rank among the top 10 leading cause of mortality [4].

AIMS OF PHARMACOVIGILANCE

The aims of pharmacovigilance are [5-6]. Improve patients care and safety in relation to the use of medicine and all medical and paramedical intervention. The identification of sub-groups of patients at particular risk of ADRs and the continued monitoring of the safety of a product, throughout the duration of its use, to ensure that its risks and benefits remain acceptable. This includes safety monitoring following significant newly approved indications. Further identification and quantification of previously unrecognized adverse drug reactions (ADR) and the detection of significant drug–drug interactions between new products and co therapy with agents already established on the market, which may only be detected during widespread use. The comparative adverse drug reaction profile of products within the same therapeutic class. The further elucidation of a product's pharmacological/toxicological properties and the mechanism by which it produces adverse drug reactions and detection of inappropriate prescription and administration.

Pharmacovigilence practice in India

In 2004 India's Drugs Control Department within the Ministry of Health & Family Welfare initiated the establishment of a nationwide network to build a comprehensive pharmacovigilance data system. The National Pharmacovigilance Advisory Committee (NPAC) was created under the chairmanship of the Director General of Health Services and the Drug Controller General of India (DCGI), who functions as the member secretary of the Committee. Based at the Central Drugs Standard Control Organization, NPAC was assigned the primary responsibility of setting up the system to monitor the

pharmacovigilance programme throughout the country. It was on November 23 2004, the CDSCO (Central Drug standard Control Organization) launched a formal National Pharmacovigilance Programme (NPP) and NPP became functional from January 1, 2005. Under this programme, the whole country is divided into zones and regions for perational efficiency. Central Drug Standard Control Organization is at the top of the hierarchy followed by two zonal pharmacovigilance centres viz, Seth GS Medical College, Mumbai and AIIMS, New Delhi. There are 5 regional pharmacovigilance centers located at Kolkata (IPGMR-SSKM Hospitals), Mumbai (TN Medical College & BYL Nair Charitable Hospital), Nagpur (Indira Gandhi Medical College), New Delhi (Lady Hardinge Medical College) and Pondicherry (JIPMER). Twenty eight peripheral centers, spread country-wide, are attached to their nearest peripheral centre.

The Pharmacovigilance Program of India (PvPI) was launched with a broad objective to safe guard the health of 1.27 billion people of India. Adverse drug Reactions (ADRs) are reported from all over the country to NCC-PvPI, which also work in collaboration with the global ADR monitoring center (WHO-UMC), Sweden to contribute in the global ADRs data base. NCC-PvPI monitors the ADRs among Indian population and helps the regulatory authority of India (CDSCO) in taking decision for safe use of medicines [6].

The Start of the Programme

After understanding the need for a better ADR reporting system in 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 Coordinating Centre was then shifted from the All India Institute of Medical Sciences (AIIMS), New Delhi to the Indian Pharmacopoeia Commission (IPC), Ghaziabad, (U.P.) in April, 2011. Currently, there are more than 170 AMCs in India, with addition of many more every year. The main functions of these AMCs are collection of adverse events as per the standard procedure, following up to the completeness of the ADR reports and uploading of reports in the Vigiflow software. These Individual Case Safety Reports (ICSRs) are collected in the standard suspected ADR reporting form, which consists of 4 sections i.e., patient's information, suspected adverse reaction, suspected medication(s), and reporter's information. These ICSRs are then reported to the National Coordinating Centre (NCC) via the Vigiflow software and the causality assessments of ADRs are performed utilising the WHO-UMC causality assessment scale system.

Important Areas of Pharmacovigilance

The discipline of pharmacovigilance remains a dynamic clinical and scientific discipline. The priority areas of pharmacovigilance at national and international level have been outlined by WHO and included the world Health Organization (WHO) defines a drug/medicine as "any substance in a pharmaceutical product that is used to modify or explore physiological systems or pathological states for the benefit of the recipient." The term drug/medicinal product is used in a wider sense to include the whole formulated and registered product, including the presentation and packaging, and the accompanying information. As per WHO following are the definitions for adverse event/adverse experience (AE) and adverse drug reaction (ADR)

Adverse Event (or Adverse Experience)

'Any untoward medical occurrence that may appear during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with the treatment'. An adverse event (AE) can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding) symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

Adverse Drug Reaction (ADR)

'A response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function.' This definition is a well-accepted definition for the marketed products.

ICH (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) guideline on Clinical Safety Data Management (E2A guidelines) further elaborates the definition of adverse drug reactions during the pre-approval (before marketing of the pharmaceutical product) phase. As per the ICH E2A [7] guidelines: In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not be established: all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. Adverse drug reactions (ADRs) are undesirable effects of medications that lead to large-scale morbidity and mortality in developed countries [8, 9, 10]. However, there is dearth of research that claims ADR presence in developing countries such as India. A few studies have examined the effects of ADRs mainly by looking at hospital readmissions [11, 12]. Serious ADRs are seen in 6.7% patients in India on an average and the number can be as high as 8% in rural South India [13]. In South India, ADRs are responsible for 0.7-3.4% hospital admissions, 3.7% hospital readmissions and 1.3% mortality [12, 13, 14]. ADRs can be detected by yellow card reporting, a cost effective method to monitor safe use of drugs. Yellow card reporting is useful in a number of ways. It identifies unidentified ADRs, risk factors for the occurrence of ADRs, drug safety issues and risk benefit comparisons among medications belonging to different therapeutic classes [15, 16].

Detection of ADRs

Detection and accurate diagnosis of ADRs by healthcare providers and patients. Active surveillance of specific drug(s) through epidemiological methods such as case control studies, record linkage and epidemiological studies. Consideration of special activities and expertise required for the detection of safety concerns related to vaccines, biological, veterinary medicines, herbal medicines, biotechnology products and investigational drugs. Improvement of signal detection systems by facilitating the rapid availability of ADR data that may have international relevance. Revisit the definitions of terms used within the field of pharmacovigilance including the definitions of specific ADRs to ensure reliability and universal understanding of data obtained through ADR reporting systems.

Develop and implement ADR detection systems that could benefit populations with restricted access to health care.

Assessment of ADRs

Further development of automated signal detection systems used in spontaneous monitoring programmes. Improvements in assessment of drug safety concerns that are of international relevance. Foster collaborative links both at local and international level that could allow countries to assess and respond appropriately to drug safety crises. Consider methods by which information on local patterns of drug use can be integrated with pharmacovigilance information during assessment of benefit and harm at a national level.

Prevention of ADRs

Improves access to reliable and unbiased drug information at all levels of health care. Improves access to safer and more effective medicines for neglected diseases prevalent in developing communities. Integrate pharmacovigilance activities into rational drug use among health professionals and the public. Integrate pharmacovigilance activities into national drug policies and the activities arising from these (e.g. standard treatment guidelines, essential drugs lists etc).

Further incorporation of pharmacovigilance principles into clinical practice and academic medicine. Encourage the principles of product stewardship among the various partners in health care. Improve regulation and pharmacovigilance of traditional and herbal medicines. Develop systems which assess the impact of preventive actions taken in response to drug safety problems.

Communication

Improve communication and collaboration between key partners in pharmacovigilance both locally and internationally. Adoption of the principles of good communication practice in pharmacovigilance and drug regulation. Developement of communication in different countries and regions and the sharing of mutual experience. Development of a better understanding of patients, their expectations of medicines and their perception of risk associated with the use of medicines. Development of sustained and active relationships with the media in order to facilitate effective and accurate communication of drug information to the public. Harmonization of drug regulatory and pharmaovigilance activities by incorporating the wider international community in the development of harmonization policies.

For the purpose of the recording or reporting, it is important that all adverse medical events rather than ADR or side effects are collected, as the term 'ADR' imply that the adverse medical event was caused by drug and, if the recorder is not certain whether the event was caused by a drug then it would not be recorded. The term 'adverse event' or 'adverse experience' is preferable and should be used in clinical trials [17-18] and post marketing [19-20].

Adverse Drug Reactions Reporting: Importance

Adverse drug reaction is important causes of mortality and hospitalization worldwide [21]. As evident from many clinical studies, adverse drug reactions are a major clinical problem. The studies have shown that they account for about 2%-6% of all hospital admissions [22-27]. ADR are important causes of mortality and hospitalization worldwide. A recent meta-analysis has suggested that adverse drug reactions were between the fourth and sixth commonest cause of death in United States [28]. Surveys conducted recently have also shown that adverse drug events are associated with an increased length of stay in hospital of 2 days, thereby leading to an increased cost of approximately $2500 per patient. Adverse drug events decrease patients' quality of life [29] and may reduce their confidence in the whole healthcare system. They also add to the total cost of health care and increase the number of undue investigations as they mimic a disease process [30]. Find out of adverse events helpful to generate a signal for any new adverse event associated with a medicine and also judge the health benefit- risk associated with it depending on the severity and commonness of the adverse event [31]. This may further lead to change in the summary of product characteristic (general uses, contraindications, warnings, and precautions, use in special population) and depending upon its risk-benefit analysis, may also be responsible for withdrawal of a drug from the market. Thus, it is extremely important to increase awareness among health care professionals regarding diagnosis, prevention, and reporting of adverse drug events. In addition to the above mentioned reasons adverse drug reactions may have many other indirect effects, which also provide their importance. The various direct and indirect effects of adverse drug reactions are adverse effect on patient quality of life. Admission to hospitals or attendance in primary health centre. Length of hospital stay gets increased (prolongation of inpatient hospitalization). Cost of patient care gets increased. Patient may lose confidence in their treating doctor. Adverse reactions may mimic disease and result in unnecessary investigations and/or delay in treatment procedures. Adverse reactions may lead to death/ permanent disability/congenital anomaly or birth defects.

Outcome and Impact of Current Pharmacovigilance System

The pharmacovigilance programs have identified potentially dangerous adverse drug reactions. Significant measures and steps have been taken in the past to effectively deal with the adverse drug reaction and withdrawing the potentially harmful drugs from the market. Some recent examples of drug withdrawal and banned (Table 1 and 2) from the market have been given here:

Table 1: Drugs Banned In India [32]

Drug	Reason
Rosiglitazone	Cardiac Problems
Cisapride	Arrhythmias
Sibutramine	Increased Cardiovascular events and Stroke
Phenylpropanolamine	Stroke
Tegaserod	Cardiovascular events
Gatifloxacin	Dysglycemia
Letrozole	congenital anomalies in infants
Pioglitazone	Bladder Cancer Risk
Nimusulide +Paracetamol	adverse effects on liver

Table 2: Drug Safety Alerts In 2017 [33]

Suspected Drug	Indication	Adversr Reactions
Lurasidone	Treatment of patients with schizophrenia	Thrombocytopenia
Deferasirox	Treatment of chronic iron overload in patients with non-transfusion dependent thalassemia (NTDT)syndromes	Osteoporosis
Clomipramine	Obsessive-compulsive disorder; panic disorder	Melasma
Ambroxol	All forms of tracheobronchitis, emphysema with bronchitis pneumoconiosis, Chronic obstructive pulmonary disease (COPD), bronchiectasis, bronchitis with bronchospasm	Lacrimation
Etoricoxib	Short term used in acute painful condition	Skin hyperpigmentation
Glimepiride	Type to diabetes mellitus	Lichenoid drug eruption
Levamisole	For the treatment of roundworm and hookworm infestation	Skin Exfoliation
Losartan	Congestive heart failure, hypertension with left ventricular hypertrophy, diabetic nephropathy in type II diabetes	Burning micturition
Cefepine	For serious CRTI, uncomplicated and complicated UTI, Uncomplicated skin &skin structure, infection acute exacerbation of chronic bronchitis & intraabdominal infection	Dermatitis Lichenoid
Metaoprolol	Supraventricular arrhythmia, angina pectoris, hypertension, myocardial infarction, migraine, heart failure, hyperthyroidism,	Lichenoid drug eruption
Amisulpride	For acute and chronic schizophrenic disorders, in which positive symptoms and or negative symptoms are prominent, including patients characterized by predominant negative symptoms	Bruxism

Crisis Management in Pharmacovigilance

In Pharmacovigilance “crisis” is defined as the event which occurs when new information, which could have a serious impact on public health, is received for a marketed product and which requires an immediate action. The crisis is usually provoked by spontaneous reporting and is most likely to occur in a country with a strong and well-developed pharmacovigilance system in place. At the time when crisis is identified the information may not be public however if it becomes public handling of situation with effective communication is crucial as the public confidence is at risk. Immediate measures need to be taken to initiate a pharmacovigilance investigation to either confirm or disprove the signal.

Planning for Crisis Management

The pre-crisis conditions are the major players in deciding the course of action during crisis and post crisis impact. Thus it is important that all organizations think widely well beyond their territory and establish good working relation and communication channels with other supporting organizations which can provide crucial help not only during detection of crisis but also in handling the situation.

Pre crisis planning

The collection of information and evidences as quickly as possible and its subsequent analysis is vital for the recognition of an upcoming crisis. Therefore adequate preparation and planning to facilitate early and accurate recognition of an upcoming event is the first step in the crisis management. The organizations must equip themselves with availability of appropriate sources of information at all times and efficient communication channels to obtain as much information as possible without delay. Availability of staff, which is well informed about their roles and responsibilities at all times, so as to channelize the information correctly and a very efficient system of documentation of all information. Availability of a group of trained managers for prioritizing, analyzing, assessing the information and quick risk identification. and cooperation from all stakeholders and also efficient communication channels to ensure confidence among all stakeholders.

Post crisis review

Crisis planning is a dynamic process and preparedness of the organization at times of no crisis is of immense help during the periods of crisis. Case histories must be written which can be reviewed later by experienced professionals and their opinions can be utilized by making necessary amendments in the existing system or by adding new dimensions to the existing system. All possible technical skills must be utilized with utmost intelligence keeping in mind the emotional sensitivities and at no cost the importance of overall critical review can be undervalued. These activities are essential to further support the crisis management system to create a document of organizational profile giving details of core activities, number of staff, office locations, years in existence, product details and annual productivity figures. This document can be used to provide information to people and groups outside the organization. A document of simple organization chart showing names, contact details and responsibilities of key persons and their deputies and a document showing details of management of previously experienced crisis situations continued in-service training of staff to maintain the awareness and abilities to respond during crisis.

ADRs reporting system

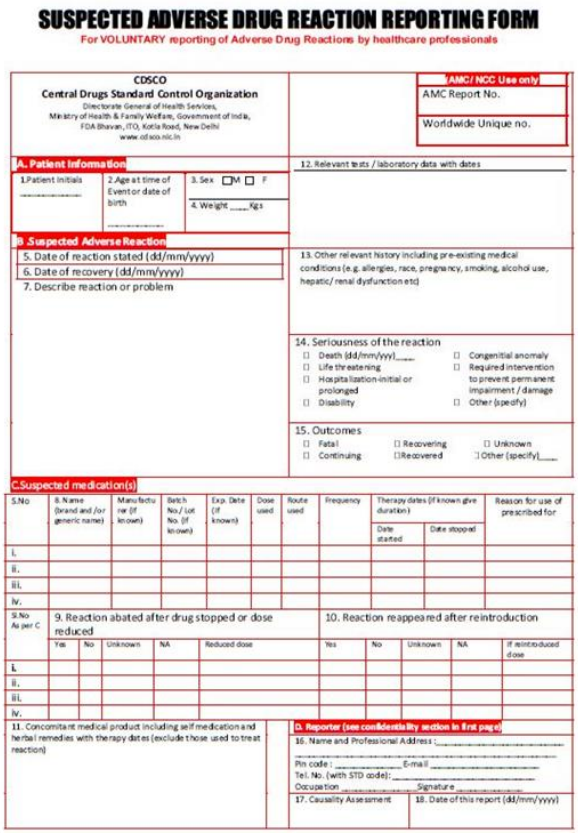
WHAT TO REPORT

The National Pharmacovigilance Programme (NPP) shall encourage reporting of all suspected drug related adverse events, including those suspected to have been caused by herbal, traditional or alternative remedies. The reporting of seemingly insignificant or common adverse reactions would be important since it may highlight a widespread prescribing problem.

The programme particularly solicits reports of all adverse events suspected to have been caused by new drugs and ‘Drugs of current interest’ (List to be published by CDSCO from time to time) and all suspected drug interactions. Reactions to any other drugs which are suspected of significantly affecting a patient's management, including reactions suspected of causing death, life-threatening (real risk of dying), hospitalisation (initial or prolonged), disability (significant,

persistent or permanent), congenital anomaly and required intervention to prevent permanent impairment or damage.

The prescribed 'Adverse Drug Event Reporting Form' shall be used for the purpose of National Pharmacovigilance Programme (Fig.1,2,3).



SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For VOLUNTARY reporting of Adverse Drug Reactions by healthcare professionals

CDSCO
Central Drugs Standard Control Organization
Directorate General of Health Services, Ministry of Health & Family Welfare, Government of India, FDA Bhawan, ITO, Kotla Road, New Delhi
www.cdsco.nic.in

AMC / NCC Use only
AMC Report No.
Worldwide Unique no.

A. Patient Information
1.Patient Initials
2.Age at time of Event or date of birth
3. Sex ☐M ☐ F
4. Weight ____Kgs

B. Suspected Adverse Reaction
5. Date of reaction stated (dd/mm/yyyy)
6. Date of recovery (dd/mm/yyyy)
7. Describe reaction or problem
12. Relevant tests / laboratory data with dates
13. Other relevant history including pre-existing medical conditions (e.g. allergies, race, pregnancy, smoking, alcohol use, hepatic/ renal dysfunction etc)
14. Seriousness of the reaction
☐ Death (dd/mm/yyy)____
☐ Life threatening
☐ Hospitalisation-initial or prolonged
☐ Disability
☐ Congenital anomaly
☐ Required intervention to prevent permanent impairment / damage
☐ Other (specify)
15. Outcomes
☐ Fatal ☐ Recovering ☐ Unknown
☐ Continuing ☐ Recovered ☐ Other (specify)____

C.Suspected medication(s)

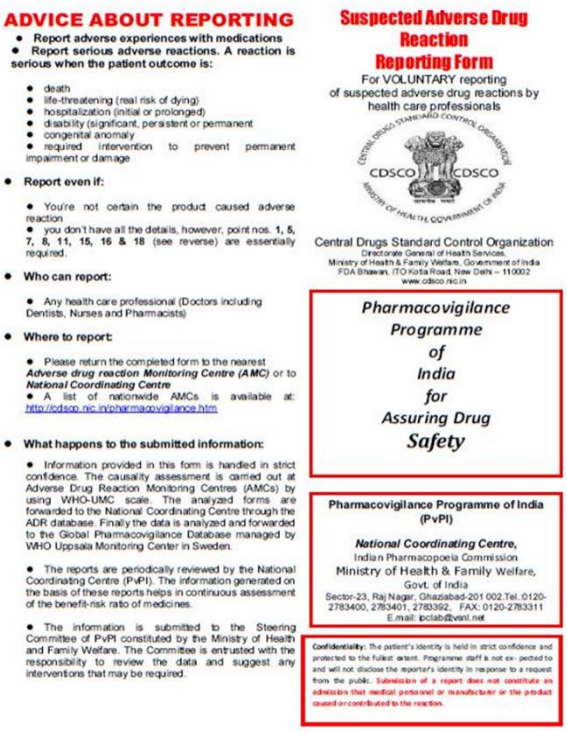
S.No	8. Name (brand and /or generic name)	Manufacturer (if known)	Batch No./ Lot No. (if known)	Exp. Date (if known)	Dose used	Route used	Frequency	Therapy dates (if known give duration) Date started	Date stopped	Reason for use of prescribed for
i.										
ii.										
iii.										
iv.										

S.No As per C	9. Reaction abated after drug stopped or dose reduced					10. Reaction reappeared after reintroduction				
	Yes	No	Unknown	NA	Reduced dose	Yes	No	Unknown	NA	If reintroduced dose
i.										
ii.										
iii.										
iv.										

11. Concomitant medical product including self medication and herbal remedies with therapy dates (exclude those used to treat reaction)

D. Reporter (see confidentiality section in first page)
16. Name and Professional Address :
Pin code : E-mail
Tel. No. (with STD code): Occupation Signature
17. Causality Assessment
18. Date of this report (dd/mm/yyyy)

Figure 1: Adverse Drug Event Reporting Form



ADVICE ABOUT REPORTING

- Report adverse experiences with medications
- Report serious adverse reactions. A reaction is serious when the patient outcome is:
  - death
  - life-threatening (real risk of dying)
  - hospitalization (initial or prolonged)
  - disability (significant, persistent or permanent
  - congenital anomaly
  - required intervention to prevent permanent impairment or damage
- Report even if:
  - You're not certain the product caused adverse reaction
  - you don't have all the details, however, point nos. 1, 5, 7, 8, 11, 15, 16 & 18 (see reverse) are essentially required.
- Who can report:
  - Any health care professional (Doctors including Dentists, Nurses and Pharmacists)
- Where to report:
  - Please return the completed form to the nearest *Adverse drug reaction Monitoring Centre (AMC)* or to *National Coordinating Centre*
  - A list of nationwide AMCs is available at: http://cdsco.nic.in/pharmacovigilance.htm
- What happens to the submitted information:
  - Information provided in this form is handled in strict confidence. The causality assessment is carried out at Adverse Drug Reaction Monitoring Centres (AMCs) by using WHO-UMC scale. The analyzed forms are forwarded to the National Coordinating Centre through the ADR database. Finally the data is analyzed and forwarded to the Global Pharmacovigilance Database managed by WHO Uppsala Monitoring Center in Sweden.
  - The reports are periodically reviewed by the National Coordinating Centre (PvPI). The information generated on the basis of these reports helps in continuous assessment of the benefit-risk ratio of medicines.
  - The information is submitted to the Steering Committee of PvPI constituted by the Ministry of Health and Family Welfare. The Committee is entrusted with the responsibility to review the data and suggest any interventions that may be required.

Suspected Adverse Drug Reaction Reporting Form

For VOLUNTARY reporting of suspected adverse drug reactions by health care professionals

CDSCO

Central Drugs Standard Control Organization
Directorate General of Health Services, Ministry of Health & Family Welfare, Government of India, FDA Bhawan, ITO Kotla Road, New Delhi – 110002
www.cdsco.nic.in

Pharmacovigilance Programme of India for Assuring Drug Safety

Pharmacovigilance Programme of India (PvPI)

National Coordinating Centre,
Indian Pharmacopoeia Commission
Ministry of Health & Family Welfare,
Govt. of India
Sector-23, Raj Nagar, Ghaziabad-201 002.Tel.:0120-2783400, 2783401, 2783392, FAX: 0120-2783311
E.mail: pcilab@vsnl.net

Confidentiality: The patient's identity is held in strict confidence and protected to the fullest extent. Programme staff & not ex- pected to and will not disclose the reporter's identity in response to a request from the public. Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the reaction.

Figure 2: Adverse Drug Event Reporting Form

WHO CAN REPORT

Any health care professionals (Doctors including Dentists, Nurses, and Pharmacists) may report suspected adverse drug events. The Programme shall not accept reports from lay members of the public or anyone else who is not a health care professional.

WHERE TO REPORT

After completion the form shall be returned / forwarded to the same Pharmacovigilance Centre from where it was received. Reporting can be done to any one of the country vide Pharmacovigilance Centres nearest to the reporter. (Complete list of Pharmacovigilance Centres is available at www.cdsco.nic.in).In case of doubt the form may be sent to the National Pharmacovigilance Centre at: Central Drugs Standard Control Organisation, Directorate General of Health Services, Ministry of Health & Family Welfare, Nirman Bhawan, New Delhi 110 011.

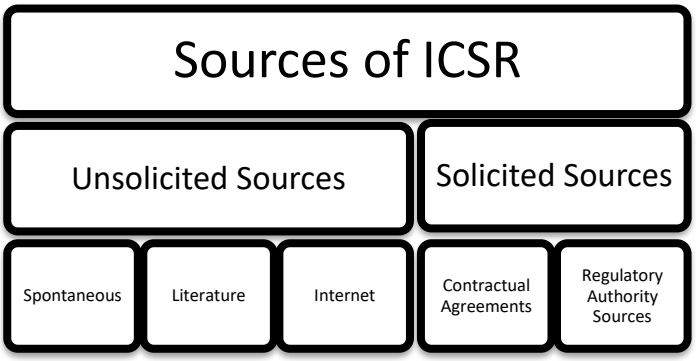
WHAT HAPPENS TO THE INFORMATION SUBMITTED

The information in the form shall be handled in strict confidence. Peripheral Pharmacovigilance Centres shall forward the form to the respective Regional Pharmacovigilance Centres who will carry out the causality analysis. This information shall be forwarded to the Zonal Pharmacovigilance Centres. The data will be statistically analysed and forwarded to the global Pharmacovigilance Database managed by WHO Uppsala Monitoring Centre in Sweden.

The final report based on the analysed data will be periodically reviewed by the National Pharmacovigilance Advisory Committee constituted by the Ministry of Health and Family Welfare. The Committee is entrusted with the responsibility to review data and suggest any regulatory interventions that may be required with respect to the drug/drugs or class of drugs

Individual Case Study Report ICSR

Individual Case Study Report (ICSR) is an adverse event report for an individual patient and is source of data in pharmacovigilance. The minimum criteria for reporting a valid case are an identifiable patient and a suspect drug or active substance. A suspected ADR as well as an identifiable and contactable reporter.



The main focus of ICSRs (individual case safety reports) is reports from healthcare providers and patients in member countries of the WHO Programme. A WHO global individual case safety report database (VigiBase) is maintained and developed on behalf of the WHO by the UMC [30].

Development of Drug and Adverse Events

Indian pharmaceutical industry is estimated growing at an average rate of about 20 % compound growth rate over the next five years. It is further estimated the healthcare market in India to reach US$31.59 billion by 2020 [34]. This includes the introduction of new chemical entities, biological products, vaccines, new dosage formulations, new routes of administration, and new uses of existing drugs. A drug during its evaluation in clinical trials is only exposed to few thousands of population excluding pregnant, lactating women, patients with hepato renal dysfunction, patients with concomitant illnesses and medications. The drug approval process therefore represents a tradeoff between minimizing delays in access to new medications and our ability to fully define the safety of medications prior to widespread use. But once in the market, the drug is exposed to a large patient population with varied characteristics [35]. Here, it becomes necessary to fully understand their long term safety profile and monitor the behavior of a new drug, as many common, uncommon, rare and very rare adverse drug events may come up in the real world post marketing period.

CONCLUSION

The article gives brief overview about safety of medicine as well as Adverse Drug Reactions reporting system of Pharmacovigilance in India. Pharmacovigilance is an important tool to ensure that the safety of marketed drugs and it is a potential source of ADRs has attained a significant role in health care system all over the world for human beings. 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. If all healthcare professional including physicians, dentist, nurses, pharmacist and others including the patient report all ADRs then regulatory authority can take action as soon as possible, and it will be helpful to overcome the complication. Until we have this information, patients and clinicians need to be aware of the gaps the exist in safety data when evaluating the risk to benefit ratio of systemic therapies. The members of PvPI are striving hard to increase its benefit, reach in India and to fortify the steps for capacity building. Various important recent steps have been taken by PvPI which prove that pharmacovigilance is moving in the right direction which will be build up large ADRs database and help to prevent and monitor further ADRs incidence. The CDSCO must formulate a detailed pharmacovigilance guideline and it shall be in tune with the current international norms, so as to support India's growth.

REFERENCES

1. https://en.wikipedia.org/wiki/Pharmacovigilance (10 June 2016)
2. Mann RD, Andrews EB. Introduction: Basis of Pharmacovigilance. In Pharmacovigilance (Ed Ronald D. Mann and Elizabeth B. Andrews), John Wiley and Sons, LTD 2002; pp.3-10.
3. World Health Organisation Available at: http://www.who.int/medicines/areas/quality_safety/safety_efficacy/pharmvig/en(10 June 2016)
4. Jason Lazarou, Bruce H Pomeranz, Paul N Corey. Incidence of Adverse Drug Reactions in Hospitalized Patients: A Meta-analysis of Prospective Studies. JAMA. 1998; 279(15):1200-1205.
5. Talbot JCC, Nilsson BS. Pharmacovigilance in the pharmaceutical industry. British Journal of Clinical Pharmacology 1998; 45(5):427-431.
6. Moore N. The Role of the Clinical Pharmacologist in the Management of Adverse Drug Reactions. Drug Safety. 2001; 24(1):1-7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11219484.
7. http://www.ich.org(22 June 2016).
8. Pharmacovigilance, World Health Organization 2017.
9. Van Grootheest K. The Dawn of Pharmacovigilance. Int J Pharmaceut Med 2003; 17:195-200.
10. www.who.umc.org. Available from: http://www.who.int/medicines/areas/quality_safety/safety_efficacy/pharmvigi/en/(July 07 2016).
11. Lihite RJ, Lahkar M. An update on the Pharmacovigilance Programme of India. Front Pharmaco 2015; l6:194.
12. Kalaiselvan V, Prakash J, Singh GN. Pharmacovigilance programme of India. Arch Pharm Pract 2012; 3:229-232.
13. Kalaiselvan V, Thota P, Singh GN. Pharmacovigilance Programme of India: Recent developments and future perspectives. Indian J Pharmacol 2016; 48:624-628.
14. Pharmacovigilance Programme of India, Indian Pharmacopoeia Commission. 2015.
15. Van Grootheest K, de Graaf L, de Jongvan den Berg LT. Consumer adverse drug reaction reporting: A new step in pharmacovigilance? Drug Saf. 2003; 26:211-217.
16. De Langen J, van Hunsel F, Passier A, de Jongvan den Berg L, van Grootheest K. Adverse drug reaction reporting by patients in the Netherlands: Three years of experience. Drug Saf 2008; 31:515-524.
17. Kegg S, DCG, Doll R. The case for recording events in clinical trials. Br Med J 1977; 2:1523-24.
18. Weintraub M. Recording events in clinical trials. Br Med J 1978; 1:581.
19. Simpson RJ, Tiplady B, Skegg DCG. Event recording in a clinical trial of a new medicine. Br Med J 1980; 280:1133-1134.
20. Anon. Lessons from the benoxaprofen affair. Lancet, 1982; 529.
21. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: A meta-analysis of prospective studies. JAMA 1998; 279:1200-5.
22. Einarson TR. Drug related hospital admissions. Ann Pharmacotherapy 1993; 27:832-40.
23. Bates DW, Boyle DL, Viliet MVV, Schenieder J, Leapse L. Relationship between medications errors and adverse drug events. J Gen Intern Med 1995a; 10:199-205.
24. Bates DW, Cullen DJ, Laird N, Petersen LA, Small SD, Servi D, Laffel G, *et al*. Incidence of adverse drug events implications for prevention. J Am Med Assoc 1995b; 274:29-34.
25. Bates DW, Spell N, Culen DJ, Burdick E, Laird N, Petersen LA, *et al*. The cost of adverse drug events in hospitalized patients. J Am Med assoc 1997; 277:307-11.
26. Clasen DC, Pestotnik SL, Evans RS, Lloyds JF, Burke JP. Adverse drug events in hospitalized patients. Excess length of stay, extra costs, and attributable mortality. J Am Med Assoc 1997; 277:301-6.
27. Dhikav V, Singh S, Anand KS. Adverse Drug Reaction Monitoring In India. J I A C M. 2004; 5(1):27-33.
28. Wayne EJ. Problems of toxicity in clinical medicine in Walpole AL. Spinks A editors. the evaluation of drug toxicity London: J&A Churchill Ltd. 1958; 1-11.
29. Sloot S, Boland J, Snowden JA, Ezaydi Y, Foster A, Gethin A, *et al*. Side effects of analgesia may significantly reduce Quality of life in symptomatic multiple myeloma: A cross-sectional prevalence study. Support Care Cancer. 2015; 23:671-8.
30. Kaushal R, Bates DW, Franz C, Soukup JR, Rothschild JM. Costs of adverse events in intensive care units. Crit Care Med. 2007; 35:2479-83.
31. Suke SG, Kosta P, Negi H. Role of pharmacovigilance in India: An overview. Online J Public Health Inform. 2015; 7(2):e223.
32. Drugs banned in India. http://cdsco.nic.in/html/drugsbanned.html(27 July2017)
33. IPC, Government of India. http://www.Ipc.nic.in. 2017 (17July 2017).
34. A Brief Report on Pharmaceutical Industry in India; July, 2015. Available from: http://www.cci.in/pdf/Pharmaceutical-Industry-in-India.pdf.(20 July 2017)
35. Suvarna V. Phase IV of drug development. Perspect Clin Res. 2010; 1:57-60.

HOW TO CITE THIS ARTICLE
Sahu S, Rishishwar P, Rathod C. Pharmacovigilence practice for safety of medication system in India. J Phytopharmacol 2018; 7(2):216-221.