IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Understanding Pharmacovigilance: A Comprehensive Overview

Ms. Mrunal Mohan Paulbudhe[1], Mrs. Sangita Bhandare[2]

1* Student, Pravara College of Pharmacy (For Women's), Chincholi, Nashik, Maharashtra.

2 Assistant Professor, Pravara College of Pharmacy (For Women's), Chincholi, Nashik, Maharashtra.

Abstract

Pharmacovigilance is an important aspect of clinical research that focusses on detecting, assessing, analysing, and preventing adverse drug reactions (ADRs) throughout the drug's lifecycle. The name is derived from the Greek word "pharmakon" (medication) and the Latin "vigilare" (to watch). Spontaneous reporting of ADRs is critical for early safety data gathering since clinical trials frequently exclude different groups and may not completely account for genetic or environmental factors that influence drug reactions. Historical occurrences, such as the thalidomide catastrophe in the 1960s, highlighted the importance of rigorous drug safety monitoring, prompting global regulatory improvements. In India, the National Pharmacovigilance Program was formed in 2005 to promote the reporting of adverse drug reactions and to include healthcare professionals in safety monitoring. Despite operational issues, the initiative is looking for to serve as a global standard for drug monitoring. Pharmacovigilance aims to find unrecognized ADRs, monitor safety on a regular basis, and provide vital information on drug interactions. Pharmacovigilance is critical for recognising and managing drug-related hazards, and it necessitates coordination among a wide range of stakeholders, including healthcare professionals, regulatory authorities, and the pharmaceutical industry. Effective pharmacovigilance is critical for the safe use of medicines, ensuring that the benefits outweigh any hazards.The future of pharmacovigilance depends in improving mechanisms for detecting adverse drug reactions and data collection approaches. Active surveillance and patient participation in reporting are critical in identifying risk variables linked with ADRs. An effective pharmacovigilance system will benefit healthcare professionals, regulatory agencies, and consumers by increasing transparency and drug safety, ultimately boosting public health. As advances in data analysis and visualisation emerge, the area of pharmacovigilance is poised to make great progress, enhancing the overall safety of medicinal interventions.

Keywords: Pharmacovigilance, Adverse Drug Reactions (ADRs), Safety Monitoring, Reporting, Public Health.

Introduction

Pharmacovigilance is an essential and vital component of clinical research [1]. Clinical trial safety and post-marketing pharmacovigilance are both crucial throughout the product's lifecycle. Drug surveillance is "defined as the pharmacological science relating to the detection, assessment, understanding and prevention of adverse effects, particularly long term and short term adverse effects of medicines"[2]. The word "pharmacovigilance" has two roots: Pharmakon (Greek for 'drug') and vigilare (Latin for 'to keep watch')[3].

The spontaneous reporting of adverse medication reactions and undesirable events is a critical approach to acquiring safety data for early detection. It is widely understood that a medicine must go through several steps of testing to determine its safety and efficacy before it can be commercialised. However, clinical trials have several restrictions, including strict inclusion and exclusion criteria that limit their use to a very select group of patients; special population groups such as children, pregnant women, and mature individuals are not studied during the trials; and other factors causing drug reactions, such as genetic factors, environmental factors, and drug-drug interactions, may not have been studied during the clinical trials [4].

To preserve public health safety, it's crucial to understand new and unusual types of adverse drug reactions (ADRs), as some cannot be avoided. This includes ADRs of new medicinal products. Pharmacovigilance is a continuing process that monitors medication safety and disseminates new information and understanding regarding ADRs. Drug regulators rely on this information to make informed decisions concerning marketed drugs [5]. A drug is considered safe if the benefits outweigh the related risks. To assess the whole safety profile of a treatment or therapy, persistent and continuous monitoring in a broad population is required, which is attainable through Pharmacovigilance (PV). PV is concerned with the comprehensive investigation of drug-related side effects and other issues [6].

Historical background

The safety of drugs was not a major concern in their early history. The thalidomide catastrophe in the 1960s prompted drug regulators and healthcare experts to create measures to ensure medication safety [7,8]. In 1893, The Lancet published the first report of a chloroform-related death, marking a significant milestone in medication safety [7]. Drug safety has since become a global problem, with several countries launching various programs to protect public health. The US Federal Food and Drug Administration (US FDA) Act was first passed in 1906, but it was updated to restrict misbranding of substances and misleading advertising claims following the deaths related with sulphanilamide elixir [7]. The usage of diethylene glycol as a solvent for sulfanilamide elixir resulted in 107 deaths. There were drastic changes in the drug safety issues after the worldwide thalidomide catastrophe, which was initially reported by an Australian physician, William McBride, in 1961[7]. He observed thalidomide-associated "seal limbs" in the newborn, which was utilised pregnancy. This medicine had not been thoroughly tested for teratogenic effects, but comparable deformities were later observed in the rabbit and (at high doses) in the rat. In West Germany, 4000 people were affected. The incident increased global awareness about drug safety, as efficacy was only one measure used to assess drug effectiveness. In 1962, the US FDA legislation was changed to require mandatory premarketing submission of both efficacy and safety data immediately following the tragedy [7]. The UK Medicines Act was enacted in 1968, while safety monitoring through the "yellow card system" was introduced in 1964[7]. Drug safety issues were globalised, strengthened, and systematised after the formation of the World Health Organisation (WHO) Programme for International Drug Monitoring in 1968[9,10]. The International Drug Monitoring program is coordinated by the Uppsala Monitoring Centre (UMC), which is located in Uppsala, Sweden [10].

India joined the World Health Organization's (WHO) Adverse Drug Reaction Monitoring Programme, which is situated in Uppsala, Sweden. This initiative was unsuccessful, thus the WHO-sponsored and World Bank-funded National Pharmacovigilance Program for India became active on January 1, 2005 (Garlapati and Nagandla 2015) [11]. The National Pharmacovigilance was responsible for managing the National Pharmacovigilance Programs, which got underway in January 2005. Advisory Committee based under the Central Drugs Standard Control Organisation (CDSCO) in New Delhi.

Two zonal centres, the South-West zonal centre (located in the Department of Clinical Pharmacology, Seth GS Medical College and KEM Hospital, Mumbai) and the North-East zonal centre (located in the Department of Pharmacology, AIIMS, New Delhi), were to collect information from across the country and send it to the

Committee as well as the Uppsala monitoring centre in Sweden. Three regional centres would report to the Mumbai centre, two to the New Delhi one. Each regional centre would receive reports from many outlying centres[12].The program has three broad aims (Preda, 2013)[12].

- The short-term goal is to promote a reporting culture.
- The intermediate goal is to involve a large number of healthcare professionals in the information distribution process.
- The long-term goal is for the program to serve as a global benchmark for drug monitoring.

Aim of pharmacovigilance

The primary goals of pharmacovigilance have been outlined for human drugs (Stephens, 2000) [13], and these can be easily adapted for veterinary pharmaceuticals:

1. Detection and measurement of previously unknown adverse medication responses.
2. Continuous monitoring of a product's safety in each species for which it is approved, to ensure that the risks and benefits remain acceptable. This should include expanding monitoring to new indications and species.
3.Comparing the adverse reaction profile to that of other products in the same therapeutic class, both within and between species.
4.Additional examination of a medicine or product's toxicological, pharmacological, or microbiological qualities in order to determine, where possible, the causes driving adverse drug responses.
5. Provide adequate information about adverse drug reactions and drug-drug interactions to veterinarians and others involved in animal therapy, such as farmers and other animal owners [13].
6.Pharmacovigilance monitors any adverse effects of medications.
7. Encourage good public communication, pharmacovigilance knowledge, education, and clinical training.
8.Help to assess the benefit, harm, effectiveness, and risk of medicines, promoting their safe, rational, and more effective (including cost-effective) use [14].

Role of pharmacovigilance

Pharmacovigilance is widely recognised as playing an important role in the early detection of drug-related risks. All drugs are tested on a tiny sample of the population before being approved for post-marketing surveillance. Pharmacovigilance plays multiple roles, including identifying, quantifying, and documenting drug-related problems, reducing the risk of drug-related problems in healthcare systems, and improving understanding of the factors and mechanisms that cause drug-related injuries[15].To effectively fulfil pharmacovigilance roles, stakeholders with decision-making power, such as politicians, healthcare administrators, drug regulatory authorities, pharmaceutical companies, healthcare professionals, academic institutions, media representatives, and health insurance companies, must collaborate[16].

Importance of pharmacovigilance

New medicines marketed without long-term safety trials may not be therapeutically safe or effective, and may cause injury or even death. Previously in India, drug safety evaluations were centred on long-term use. However, this approach proved erroneous and failed to claim 100% safety [17]. Given this reality, numerous Indian organisations or research funding bodies began investing in individual drug research and the development of fresh products. Once a product is produced, fresh information is generated, which may be favourable or negative, and has an impact on the product's risk-benefit profile. To protect the public health, it is necessary to conduct a thorough analysis or assessment of freshly generated information using a PV system.Drug side effects can cause morbidity or mortality, and studying them is critical to minimising risks and maximising benefits. Due to recent high-profile drug withdrawals, pharmaceutical companies and regulatory authorities are placing a strong emphasis on drug safety in the market, sometimes known as PV [18].

Scope of pharmacovigilance

PV is a rapidly growing field that includes chemical, botanical, and biological therapies, as well as medicinal devices [19,20].To successfully communicate undesirable effects and toxicity associated with a medicine, it's important to target an audience with the necessary understanding (Allabi and Nwokirke, 2014) [21].This is the role of pharmacovigilance (PV), which has already been achieved, but more work is needed to fully integrate the discipline into clinical practice and public policy. To meet the PV responsibilities for its marketed medicines as per regulations, a pharmaceutical company in India must primarily conduct operations like as the collection and expedited reporting of major unexpected adverse drug reactions (ADRs) [22].Information regarding the questionable product is gathered from healthcare providers and patients in order to discover and prevent any linked issues.As a result, PV deals with drug side effects, polypharmacy, paradoxical reactions, and serious adverse events. It also addresses immunisation failure, irrational use, ineffectiveness, drug interactions, poisoning, overdose, abuse, prescription errors, and drug misuse [23].

Pharmacovigilance program in India

In India, consideration for ADR surveillance emerged rather late, as the government previously had no idea of medication surveillance. Even though PV is still in its infancy, it is not new in India. It wasn't until 1986 that a few physicians, mostly from academic institutions, urged for more attention to the potential side effects of prescription drugs and sensible prescribing of medications. This resulted in the development of the first ADR monitoring program, which included 12 regional centres covering 50 million people each [24]. In 1997, India participated in WHO's adverse drug reaction monitoring program held in Uppsala, Sweden [25].
The majority of the three ADR monitoring centers—two WHO special centers at Mumbai (KEM Hospital) as well as Aligarh (JLN Hospital, Aligarh) and a National Pharmacovigilance Center housed in the Dept. of Pharmacology at All India Institute of Medical Sciences (AIIMS) in New Delhi—are based in teaching hospitals. These centres were to report ADRs to India's drug regulatory authority. The primary function of these centres was to monitor ADRs to pharmaceuticals marketed in India. However, they were ineffective since prescribers were never informed about the need to report ADRs or the functions of these monitoring centres, and the government did not provide adequate money. This endeavour was unsuccessful, thus on January 1, 2005, the WHO-sponsored and World Bank-funded National Pharmacovigilance Program (NPVP) for India was established [26]. The National Pharmacovigilance Advisory Committee, situated at the Central Drugs Standard Control Organisation, was to manage the NPVP, which was founded in January 2005 [27].The program had three broad objectives. Instilling a reporting culture was the short-term objective; including a significant number of health care experts in information dissemination was the intermediate goal; and the program's long-term objective was to serve as a baseline for global drug monitoring. Regretfully, the program didn't work either [28].

Methods Utilized in the pharmacovigilance

Pharmacovigilance efforts are broadly classified into three categories: regulatory, industrial, and academic. Regulatory Pharmacovigilance aims to ensure that pharmaceuticals have a positive benefit-harm profile for the public. In this context, certain issues concerning regulatory post-marketing surveillance will be explored, followed by a description of the methods utilised to discover new ADRs, as well as a discussion of the benefits and drawbacks of each method [29].

- Dangaumou's French Method [30]
- Kramer et al. technique [31]
- Naranjo et al. technique (the Naranjo scale) [32]
- Balanced assessment technique [33]
- Ciba-Geigy Method [34]
- Loupi et al's technique [35]
- Roussel Uclaf's casualty evaluation approach [36]
- Australian Method [37]

Adverse Drug Reactions (ADRs)

An adverse drug (ADR) is defined as AN fortuitous and hazardous to a health product that causes at the doses occasionally or tested for the diagnosis, impediment, or treatment of a disease or the alteration of AN organic function [38,39,40]. However, it is difficult to determine the actuating agent associated with adverse drug reactions (ADRs) encountered because they contain many substances [41]. When deciding whether or not to utilise a specific drug in a given patient, the magnitude of the risk must be considered with the magnitude of the projected medical speciality advantages [42]. Adverse drug reactions (ADRs) are characterised in two

- Foreseeable (Type-A) Reaction
- Unpredictable Reaction (Type-B)

Predictable (Type A) Reaction: These square measure supported pharmacologic aspects of the medicine, such as increased but quantifiable response to the drug, which encapsulate aspect effects, Gyanogenic effects, and the consequences of drug withdrawal [41,44].

Unpredictable (Type-B) Reactions: These are based on the patient's unique characteristics rather than the drug's known effects, such as allergic reactions and specialities. These are less common, non-dose-related, dangerous, and may require medication withdrawal. An inventory of suspected and acknowledged medicine-related side effects [41,43,44]. The recognised drug and its harmful effects are shown in the table no.1 [45].

Table 1: Known Drug and its adverse effects

Drug	Adverse Drug Reactions (ADRs)
Thalidomide	Aspirin/ Indomethacin
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

Clinical Trial

A clinical trial is an analysis research that tries a replacement medical treatment or a replacement method of maltreatment in conjunction with an existing therapy to determine if it will be more effective in stopping and screening for disease diagnosis or treatment [46]. A wide range of doses of the study drug are administered to Associate in Nursing patients or an in-vitro substrate in order to get preliminary efficacy, toxicity, and pharmacokinetic data [47]. Before beginning clinical trials on a medicine, pharmaceutical companies do extensive preclinical investigations [48]. Global pharmaceutical companies have discovered India as a desirable

destination for clinical trials because India's clinical research space and opportunity are particularly appealing [49]. India provides several advantages for clinical trials, including:

- A high level of adherence to international guidelines such as the International Conference on Harmonisation (ICH)/ WHO Good Clinical Practice (ICH-GCP) and US Food and Drug Administration regulations.
- The availability of highly qualified English-speaking research workers, including physicians.
- Ongoing government support and cooperation.
- Lower cost than the west [50].
- An increase in the prevalence of ailments that affect both developed and developing countries.
- Availability of enough infrastructure.
- Changes to patent laws since January 2005 [51]. Indian-born contract research organisations (CROs) have benefits over newer entrants in the industry, including better grasp of the Indian scenario, competitive pricing, and knowledge of investigator sites. India's existing favourable regulatory framework and regulations with worldwide standards, increased knowledge of good clinical practice guidelines, and their adoption by clinicians are some of the primary causes driving the expansion of clinical research in India [52,53]. Figure 1. displays the distribution of clinical trials by therapeutic area, as well as the availability of a diverse patient population throughout India's key therapeutic sectors [54].

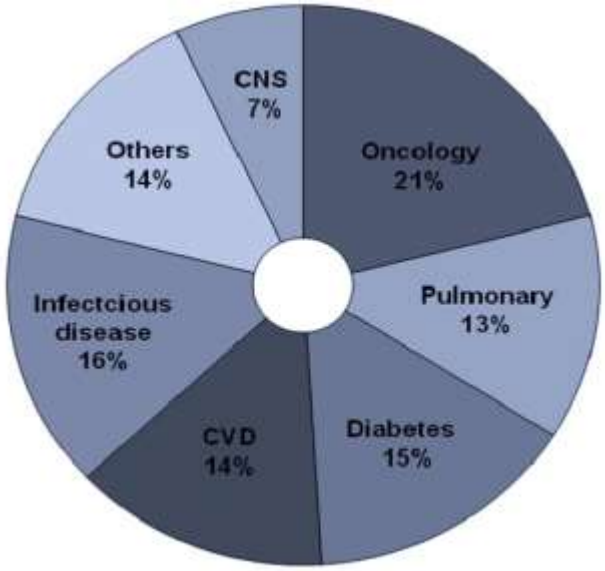

Figure 1. Clinical studies for specific therapeutic areas are being outsourced to India.

Future Prospect

As future opportunities become better and PV systems able to identifying new ADRs and enforcing regulatory actions will be essential to protect public health. There has been little emphasis on generating information that can help a healthcare provider or a patient make a decision. Gathering and communicating this information is an essential purpose of PV. Information on the safety of drug active surveillance is required. When developing new approaches for active post marketing surveillance, keep in mind the importance of gathering comprehensive and accurate data on each Serious reported occurrence. Spontaneous reporting is a useful technique in signal generation, but the comparatively low number of reports collected for a specific association makes it less useful in identifying patient features and risk factors. PV techniques must also be able to identify patients who are at risk of experiencing an adverse drug reaction (ADR). As a source of information, the PV approach is congruent with the increased patient involvement in drug safety (Flower, 2013) [55].

The PV could help identify individual risk factors for the incidence of specific ADRs. In the future, PV must focus on patients as a source of information in addition to more traditional groups, such as healthcare professionals. At the moment, the DCGI should work fast to improve PV in order to incorporate Good Pharmacovigilance Practice (GPP) into processes and procedures, thereby ensuring regulatory compliance and improving clinical trial safety and post-marketing surveillance. A well functioning PV system is required if medicines are to be used safely. It will benefit healthcare providers, regulatory bodies, pharmaceutical

businesses, and consumers. It enables pharmaceutical companies to monitor their drugs for potential risks. Post-marketing PV is now a difficult and time-consuming procedure, not only for the sector but also for regulatory agencies (Ghewari, 2014) [56]. GlaxoSmithKline has recently developed a strong new approach to PV by combining classic, case-based PV methodologies with disproportionality and data visualisation tools. These technologies exist within a system structure that allows for in-stream review, safety issue monitoring, and knowledge management [57]. This very unique technology and methods will contribute to the advancement of PV by increasing efficiency and providing new analytical capabilities. Pharmaceutical companies may use a similar approach to quickly detect and analyse ADRs. Transparency and communication would improve consumer reporting, which are significant steps towards increasing consumer participation in PV (Kalaiselvan, 2014) [58].

Conclusion

Pharmacovigilance is critical for assuring drug safety throughout a medication's lifecycle, from clinical trials to post-marketing surveillance. Its goal is to discover, evaluate, and prevent adverse drug reactions (ADRs), particularly those that were not identified during pre-marketing trials. Historical occurrences, such as the thalidomide disaster, illustrate the importance of effective monitoring systems and regulatory frameworks to protect public health. Despite advances, obstacles persist, particularly in developing a culture of reporting and incorporating patient data into safety assessments. The future of pharmacovigilance depends in enhancing active surveillance systems, boosting stakeholder communication, and harnessing emerging technology to better monitor drug safety. A well-functioning pharmacovigilance system is critical for reducing risks and maximizing the benefits of drugs, resulting in more informed healthcare decisions and safer patients.

References

[1] Pipasha, B. , Arun , K.B.,„Setting standards for proactive pharmacovigilance inIndia : The way forward", Indian J pharmacol , 2007; 39(3): 124-128.

[2] Kumanan, R., Sudha, S., Vijayashre, P., Charumath, S., Gowridevi, K.C., Mahesh, M. „Imperative Approach on pharmacovigilance in Indian systems of medicines", International journal of pharma sciences and Research (ijpsr), 2010; 1(9):378-390.

[3] Shuka SS, Gidwani B, Pandey R, Rao SP, Singh V, Vyas A,
Importance pharmacovigilance in Indian Pharmaceutical Industry, Asian Journal of Research in Pharmaceutical Science 2012; (2): 04-08.

[4] Mann RD, Andrews EB,eds. John Wiley & Sons Ltd, Pharmacovigilance, Chichester. 2002.

[5]Netdoctor.Available at http://www. netdoctor.co.uk/medicines/100004446.html (accessed Mar 8th,2011).

[6] World Health Organization (1984) World Health Organization Collaborating Centre for International Drug Monitoring, Geneva.

[7] Routledge P. 150 years of pharmacovigilance.Lancet 1998; 351(9110):1200-1.

[8] Lawson DH. Pharmacovigilance in the 1990s. Br J Clin Pharmacol 1997; 44(2):109-10.

[9] World Health Organization. The importance of pharmacovigilance.Geneva. 2002.

[10] Uppsala Monitoring Centre. Available at http://www.who-umc.org/DynPage.aspx?id=100653&mn1=7347&mn2=7252&mn3=7322&mn4=7442 (accessed May 2nd, 2011)

[11] Garlapati S, Nagandla S. Risk management Plan Its Importance and emphasis on pharmacovigilance activities. Advances in Pharmacoepidemioogy. Drug Safety 2015; 4:128-130.

[12] Preda A. Pharmacovigilance in the New Millennium: Challenges, Opportunities and New Directions. Journal of Pharmacovigiance. 2013; 1:106-107.

[13] Stephens K. Pharmacovigilance future prospective. Journal of Pharmacovigilance. 2000; 2:23-29

[14] WHO, Pharmacovigilance: ensuring the safe use of medicines, Geneva: WHO 2004.

[15] Pharmacovigilance. Mann RD, Andrews EB, eds. John Wiley & Sons Ltd, Chichester, 2002

[16]The Importance of Pharmacovigilance, WHO 2002.

[17] Report E, Effective Communications in PV (1997) International Conference on Developing Effective Communications in Pharmacovigilance, Erice, Sicily, pp: 24-27.

[18] Grady C (2005) Payment of clinical research subjects. J Clin Invest 115: 1681.

[19] Kumar S, Baldi A (2013) Pharmacovigilance in India:Perspectives and Prospects. J Drug Deliv Sci Technol 3: 237-246.

[20] Ghewari P, Salunke S, Bhatiya N, Killedar S (2014) Strategies and current scenario of pharmacovigilance in India. JADD 1:122-134.

[21] Allabi AC, Nwokirke JA. Situational analysis of pharmacovigilance system in republic of benin. Journal of Pharmacovigilance. 2014; 2:136-138.

[22] Naik P. The Future consideration of Pharmacovigilance. Journal of Pharmacovigilance. 2015; 3:158-162.

[23] Ruhoy IS, Daughton CG (2008). Beyond the medicine cabinet: An analysis of where and why medications accumulate. Environ Int 34: 1157-1169.

[24] Kulkarni RD. 1986. Reporting system for rare side effects of non-narcotic analgesics in India: Problems and opportunities. Med Toxicol. 1, 110-13. PubMed

[25] Fujimoto M, Higuchi T, Hosomi K, Takada M. Association of statin use with storage lower urinary tract symptoms: Data mining of claims database. Journal of Pharmacovigilance. 2014; 2:147-149.

[26] Moride Y, Haramburu F, Requejo A, Begaud B. 1997. Under-reporting of adverse drug reactions in general practice. Br J Clin Pharmacol. 43(2), 177-81. PubMed

[27] Adithan C. 2005. National pharmacovigilance programme. Indian J Pharmacol. 37, 347. http://dx.doi.org/10.4103/0253-7613.19069

[28] Biswas P, Biswas AK. 2007. Setting Standards for Proactive Pharmacovigilance in India:The Way Forward. Indian J Pharmacol. 39, 124-28. http://dx.doi.org/10.4103/0253-7613.33431

[29] Zarin DA, Young JL, West JC, Challenges to evidence based medicine: a comparison of patients and treatments in randomized controlled trials with patients and treatments in a practice research network. Soc Psychiatry Psychiatr Epidemiol, 2005; 4027–35.

[30] Dangoumau J, Evreux JC, Jouglard J, Mehtod for determination of undesirable effects of drugs, Therapie,1978; 33(3):373-81.

[31] Kramer MS, Leventhal JM, Hutchinson TA, Feinstein AR, An algorithm for the operational assessment of adverse drug reactions:I. Background, description, and instructions for use. JAMA, 1979; 242(7):623-32.

[32] Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, A method for estimating the probability of adverse drug reactions.ClinPharmacolTher1981; 30(2):239-45.

[33] Lagier G, Vincens M, Castot A, Imputability in drug monitoring: Principles of the balanced drug reaction assessment method and principal errors to avoid. Therapie,1983; 38(3):303-18.

[34] Venulet J, Ciucci A, Berneker GC, Standardized assessment of drug-adverse reaction associations – Rationale and experience. Int J ClinPharmacolTherToxico, 1980; 18(9):381-8.

[35] Loupi E, Ponchon AC, Ventre JJ, Evreux JC, Imputability of a teratogenic effect. Therapie, 1986;41(3):207-10.

[36] Danan G, Benichou C, Causality assessment of adverse reactions to drugs--I. A novel method based on the conclusions of international consensus meetings: Application to drug-induced liver injuries, J ClinEpidemiol, 1993; 46(11):1323-30.

[37] Mashford ML, The Australian method of drug-event assessment: Special workshop – regulatory. Drug Inf J, 1984; 18(3-4):271-273.

[38] Bhosale U, Jaiswal S, Yegnanarayan R, Godbole G, A Pharmacovigilance Study of Anti- Asthmatic Agents in Patients of Bronchial Asthma at a Tertiary Care Hospital, Journal of Clinical & Experimental Research,1May-August 2013; 26-30.

[39] Sharma S, Phadnis P, Gajbhiye S, 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), 2013; 2:234-247.

[40] Padmavathi GV, Beere N, Divakara P, Suresh KP, Surendranath A, Patel RS, Screenplay of pharmacovigilance among nursing staff in Bangalore,2 February 2013; 365-370.

[41] Maiti B, Nagori B.P., Singh R, Kumar P, Upadhyay N, Recent Trends in Herbal Drugs: A Review, International Journal of Drug Research and Technology, 2011; 117-25.

[42] Chakraverty R, Banerjee A, Emerging Issues in Pharmacovigilance of Herbal Medicines in India: International Journal of Pharmaceutical Sciences Review and Research, 20 May -Jun 2013; 40-42.

[43] Rama P, Prudence AR, Georgy A, Pharmaovigilance: Perspectives and Future Challenges in Indian Scenario, Asian Journal of Pharmaceutical and Clinical Research, 2011; 4:01-04.

[44] Rohilla A, Kumar V, Sharma KM, Dahiya A, Kushnoor A, Pharmacovigilance: Needs and Objectives, Journal of Advanced Pharmacy Education & Research, 2 Oct-Dec 2012;201-205.

[45] Leon L, Herbert A. Liberman, Joseph L. Kanig, Varghese Publishing House, Hind Rajasthan Building Dadar, Mumbai, 3rdEdition, 239-240.

[46] Information about clinical trial. Available from :URLhttp://www.temple.edu/pascope/about-trials.html

[47] Clinical trial wikipedia, the free encyclopedia: Available from, URLhttp://en.wikipedia.org/ wiki/clinical_trial Jan 28 2008;

[48] Kulkarni SK, Hand Book of Experimental Pharmacology, 3rd ed. Vallabh Prakashan New Delhi, 2004; P21.

[49] Strom BL. Overview of automated databases in pharmacoepidemiology (ed). Pharmacoepidemiology Chichester. UK, John Wiley & Sons. 2005;p.219–22.

[50] Butlen S, Ducuing F. 2010. European medicines agency support mechanisms fostering orphan drug development. Drug News Perspect. 23, 71-81. PubMed
http://dx.doi.org/10.1358/dnp.2010.23.1.1437303

[51] Giezen TJ. 2009. Evaluation of post-authorization safety studies in the first cohort of EU risk management plans at time of regulatory approval. Drug Saf. 32, 1175-87. PubMed
http://dx.doi.org/10.2165/11318980-000000000-00000

[52] Herret E. 2010. Validation and validity of diagnoses in the general practice research database. J Clin Pharmacol. 69, 4-14. PubMed http://dx.doi.org/10.1111/j.1365-2125.2009.03537.x

[53] Abenhaim L. 1996. Appetite-suppressant drugs and the risk of primary pulmonary hypertension. N Engl J Med. 335, 609-16. PubMed
http://dx.doi.org/10.1056/NEJM199608293350901

[54] Kaufman DW. 2001. Signal generation and clarification: Use of case-control data. Pharmacoepidemiol Drug Saf. 10, 197-203. PubMed http://dx.doi.org/10.1002/pds.571

[55] Flower DR. Pharmacovigilance, drug repositioning and virtual screening. Journal of Pharmacovigilance. 2013; 1:103-104.

[56] Ghewari P, Salunke S, Bhatiya N, Killedar S. Strategies and current scenario of pharmacovigilance in India. Journal of Pharmacovigilance. 2014; 1:122-134.

[57] IOM. Institute of Medicine. Emerging safety science: Workshop summary. Washington, DC: The National Academies Press. Chapter 8: Pharmacovigilance. 2008; pp74–84.

[58] Kalaiselvan V, Prasad T, Bisht A, Singh S, Singh GN. adverse drug reactions reporting culture in pharmacovigilance programme of India. Indian Journal of Medical Research. 2014; 5:114-117.