IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 5, Issue 2, January 2025

Pharmacovigilance: A Comprehensive Review

Arti Madhavrao Jadhav[1], Dr. Shivshankar D Mhaske[2], Prof. Satish Gajanan Lodhe[3], Shital Vishnu Mule[4], Nayna Ramesh Khade[5]
Students, B Pharm Final Year, Satyajeet College of Pharmacy, Mehkar, India[1,4,5]
Principal, Satyajeet College of Pharmacy, Mehkar, India[2]
Professor, Satyajeet College of Pharmacy, Mehkar, India[3]
madhavjjadhav9977@gmail.com

Abstract: *Pharmacovigilance is a critical field in healthcare that focuses on the detection, assessment, understanding, and prevention of adverse drug reactions (ADRs) and other drug-related issues. With the increasing complexity of modern pharmacotherapy, pharmacovigilance plays a vital role in ensuring patient safety and the effective use of medications. This review provides a comprehensive overview of pharmacovigilance, highlighting its importance in both pre-market and post-market drug safety. It discusses the key components of pharmacovigilance systems, including ADR reporting, signal detection, risk management, and regulatory frameworks. The review also explores recent advancements, such as the integration of artificial intelligence, big data, and real-world evidence in monitoring drug safety. Challenges in pharmacovigilance, including underreporting, data integrity, and the monitoring of biologics and orphan drugs, are also addressed. Additionally, the review examines the role of pharmacovigilance in special populations, including pediatric, geriatric, and rare disease patients. In conclusion, pharmacovigilance remains an essential discipline in ensuring the continued safety and efficacy of medicinal products, with ongoing advancements enhancing its capabilities.*

Keywords: Pharmacovigilance, Adverse Drug Reactions (ADRs), Signal Detection, Risk Management, Artificial Intelligence, Big Data, Real-World Evidence, Drug Safety, Regulatory Frameworks, Biologics, Orphan Drugs, Pediatric Pharmacovigilance, Geriatric Pharmacovigilance, Reporting Systems, Post-Marketing Surveillance

I. INTRODUCTION

Pharmacovigilance is "defined as the pharmacological science relating to the detection, assessment, understanding and prevention of adverse effects, principally long term and short term adverse effects of medicines. It is an important and integral part of clinical research. India is the world's second most populated country with over one billion potential drug consumers. Although, India is participating in the UMC program, its contribution to the UMC database is very little. This problem is essentially due to the absence of a robust ADR monitoring system & also the lack of awareness of reporting concept among Indian HCP. The specific aims of Pharmacovigilance are to advance patient care and safety in relation to the use of medicines and all medical and paramedical interventions, contribute to the assessment of benefit, harm, effectiveness, and risk of medicines, promising their safe, rational and more effective use, promote indulgent, education, and clinical training in Pharmacovigilance and its effective communication to the public. Pharmacovigilance methods must also be capable to designate which patients are at risk of developing an ADR. A suitably working Pharmacovigilance system is important if medicines are to be used cautiously. It will be advantageous for healthcare professionals, regulatory authorities, pharmaceutical companies and the consumers. It aids pharmaceutical companies to monitor their medicines for risk.

It has been known that world health organization (WHO) has initiated the program of reporting all adverse reactions possessed by the drugs. The further awareness about the adverse drug reactions resulted in the emergence of the practice and science of Pharmacovigilance.[1] Pharmacovigilance is "defined as the pharmacological science relating to the recognition, assessment, understanding and prevention of adverse effects, particularly long term and short term adverse effects of medicines.[2, 3] After discovery & pre-clinical phase the drug typically undergoes trials in human volunteer. Clinical trials are very well regulated & are no longer an overlooked practice by the pharmaceutical

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 5, Issue 2, January 2025

manufacturer. Trails are closely monitored by the investigator & the manufacturing, industrial company and it is a mandatory regulatory requirement to report all the adverse events in a clinical trial setting in a given time frame. At least in the clinical trial setting, "GCP" has moved the Pharmacovigilance word from a reactive to a proactive approach. A robust, well-defined Pharmacovigilance system for monitoring adverse events is in a place for evaluating the safety of the investigational new drug.[4] Moreover, its concerns have been widened to include the herbal drug products; traditional and complementary medicines; blood products; Biologicals; medical devices; and vaccines. In addition, Pharmacovigilance possess various roles like, identification, quantification and documentation of drug-related problems which are responsible for drug-related injuries.

An adverse event is any untoward medical occurrence in a patient administered a medicinal product & which doesn't necessarily have a causal relationship with this treatment. Adverse drug reactions are noxious & unintended responses to a medicinal product. A reaction, in contrast to an event, is characterized by the fact that a causal relationship b/w the drug & the occurrence is supposed.[7, 8] India is the world's second most populated country with over one billion potential drug consumers. Although, India is participating in the UMC program, its contribution to the UMC database is very little. This problem is essentially due to the absence of a robust ADR monitoring system & also the lack of awareness of reporting conceptamong Indian HCP. With over 1 billion US worth of clinical trials conducted in India, it is very important to focus on the attention of the medical community on the importance of adverse drug reporting to ensure max. benefits for public health and safety. For regulatory reporting purposes, if an event is instinctively reported, even if the relationship is mysterious or unstated, it meets the definition of an adverse drug reaction.

A serious Adverse Effect (SAE) is any untoward medical manifestation, that at any dose:

- Results in death
- Is life-threatening (well-defined as an event in which the subject was at risk of death at the time of the event)
- Requires in-patient hospitalization or causes prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect
- Is an important medical event (defined as an medical event(s) that may not be immediately life-threatening or result in death or hospitalization but, based upon suitable medical & scientific judgment, may require intervention to prevent one of the serious outcomes as listed above).

Aims of Pharmacovigilance are too:

- Advancing patient care and safety in relation to the use of medicines and all medical and paramedical interventions
- Advance public health and safety in relation to the use of medicines
- Contribute to the valuation of benefit, harm, effectiveness and risk of medicines, encouraging their safe, rational and more effective use
- Promote understanding, education and clinical training in Pharmacovigilance and its effective communication to the public.[11]

Under reporting occurs when the medicinal product hits the market after going through all the required authorization processes. Many adverse reactions can be noticed only after the medicinal product has been prescribed for, & used by, a large no. of patients world-wide as this environment, with multiple potential new co-factors of real life, cannot be replicated in clinical trials.

Clinical trials have its own limitations:-

- Conducted in a limited patient population
- Restricted population in terms of age, sex and ethnicity
- Restricted co-medication
- Restricted conditions of use
- Limited co-morbidity as the trial has strict inclusion and exclusion criteria

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 5, Issue 2, January 2025

- Reasonably short duration of exposure and follow-up
- Statistical problems accompanying with looking multiple outcomes
- Knowledge concerning the safety profile of any drug is also limited & cannot be considered complete and accurate.

1.1 Pharmacovigilance Methods

1] Passive surveillance

a) Spontaneous reports

A spontaneous report is a voluntary communication by healthcare professionals or consumers to a company, regulatory authority or other organization that defines one or more adverse drug reactions (ADRs) in a patient who was given one or more medicinal products and that does not originate from a study or any structured data collection scheme.[12] It plays a key role in the identification of safety signals once a medicine is marketed. In various occurrences, spontaneous reports can vigilant a company to rare adverse events that were not noticed in earlier clinical trials or other pre-marketing studies. It can also deliver important information on at-risk groups, risk factors and clinical features of known serious ADRs.

Newly, systematic methods for the recognition of safety signals from spontaneous reports have begun to be used. Several of these methods are static in development and their utility for identifying safety signals is being assessed. These methods include the calculation of the proportional reporting ratio, as well as the use of Bayesian and other techniques for signal detection.[17-19] Data mining techniques have also been used to examine medicine-medicine interactions[20], but these techniques should always be used in conjunction with and not in place of, analyses of single case-reports. Data mining techniques facilitate the evaluation of spontaneous reports by using statistical methods to detect potential signals that merit further evaluation. However, this tool does not quantify the magnitude of risk and caution should be exercised when comparing medicines. Further, when using data mining techniques, consideration should be given to the threshold established for detecting signals, since this will have implications for the sensitivity and specificity of the method (a high threshold is associated with high specificity and low sensitivity). Confounding factors that influence reporting of spontaneous adverse events are not removed from data mining. The results of data mining should thus be interpreted with the knowledge of the weaknesses of the spontaneous reporting system and more specifically, the large differences in the ADR reporting rate for different medicines and the many potential biases inherent in spontaneous reporting. All signals should be evaluated while recognizing the possibility of false-positives. In addition, the absence of a signal does not mean that a problem does not exist.

b) Case series

A series of case-reports can deliver sign of an association between a medicine and an adverse event, but they are normally more valuable for producing theories than for confirming a relationship between medicine exposure and outcome.

C) Stimulated reporting

A number of methods have been used to reassure and simplify reporting by health professionals in definite circumstances for new products or for partial time periods.[23] Such systems comprise on-line reporting of adverse events and methodical motivation of reporting of adverse events based on a pre-designed method. While these methods have been shown to advance reporting, they are not invulnerable to the confines of passive surveillance, particularly discriminating reporting and imperfect information. This should be considered as a procedure of spontaneous event reporting and thus data acquired from stimulated reporting cannot be used to make precise incidence rates, but reporting rates can be projected.

II) Active surveillance :-

Active surveillance, in contrast to passive surveillance, pursues to determine the particular number of adverse events through a constant pre-organized process.[24] In common, it is more achievable to acquire wide-ranging data on discrete adverse event reports through an active surveillance system than through a passive reporting system.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 5, Issue 2, January 2025

a) Sentinel sites

Active surveillance can be attained by revising medical records or questioning patients and/or physicians in a section of sentinel sites to guarantee that comprehensive and precise data on reported adverse events are collected from these sites. The selected sites can deliver information, such as data from specific patient subgroups, which would not be accessible in a passive spontaneous reporting system.[25] The major weaknesses of sentinel sites comprise difficulties with selection bias, small numbers of patients and augmented costs. Active surveillance with sentinel sites is most effective for those medicines used primarily in institutional settings such as hospitals, nursing homes and haemodialysis centers. Institutional settings may use certain medicinal products more commonly and can deliver an arrangement for enthusiastic reporting. Intensive monitoring of sentinel sites can also be supportive in recognizing risks among patients taking orphan medicines.

b) Medicine event monitoring

It is a process of active Pharmacovigilance surveillance. Studies using this process are cohort-based and prospective and observational. For medication event monitoring, patients can be acknowledged from electronic or automated health insurance claims. A single prescription or a series might be composed over the period of monitoring. A follow-up questionnaire can then be sent to each prescribing physician or patient at pre-specified intervals to acquire outcome data. Requests for data on patient demographics, indication for treatment, duration of therapy, dosage, clinical events, reasons for termination and applicable past history can be involved in the questionnaires.[26-30] The restrictions of medicine event monitoring can comprise the poor physician and patient reply rates.

c) Registries

A registry is a list of patients presenting with the identical representative(s). This representative can be a disease (disease registry) or a specific exposure (medicine registry). Both types of registrations, which vary only by the type of patient data of interest, can gather a cordless of information using standardized questionnaires in a prospective fashion. Disease registries, such as registries for blood dyscrasias, severe cutaneous reactions, or congenital malformations can help to gather data on medicine exposure and other factors related to a clinical condition. A disease registry might also be used as a veil for a case control study associating the medicine exposure of cases recognized from the registry with controls selected either from patients with another condition within the registry, or from patients outside the registry.

Exposure (medicine) registries address populations exposed to the medicines of interest to govern if a medicine has a distinct influence on this group of patients. Some exposure (medicine) registries address drug exposures in specific populations, such as pregnant women. Patients can be followed over time and included in a cohort study to collect data on adverse events using standardized questionnaires. Single cohort studies can quantity incidence, but, without a comparison group, cannot deliver proof of association. This type of registry can be very valuable when examining the safety of an orphan medicine indicated for a specific condition. Customary epidemiological methods are a key constituent in the evaluation of adverse events. There are numerous of observational study designs that are valuable in validating signals from spontaneous reports, case series or medicine event monitoring. The most imperative of these designs is cross-sectional studies, case-control studies and cohort studies.

d) Cross-sectional study (survey)

Data collected on inhabitants of patients during a specified interval of time, regardless of exposure or disease status constitute a cross-sectional study. These types of study are principally used to collect data for surveys or for ecological analyses. The major disadvantage of cross-sectional studies is that the temporal relationship between exposure and outcome cannot be straight addressed. These studies are paramount used to scrutinize the prevalence of a disease at one time point or to inspect trends over time, when data for serial time points can be captured. These studies can also be used to observe the crude relationship between exposure and outcome in ecological analyses. Cross-sectional studies are utmost valuable when exposures do not change over time.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 5, Issue 2, January 2025

e) Case-control study

In a case-control study, cases of disease (or events) are recognized. Controls, or patients in whom the disease or event of interest has not happened, are then carefully chosen from the source population that gave rise to the cases. The controls should be selected in such a way that the prevalence of exposure among the controls exemplifies the prevalence of exposure in the source population. The exposure status of the two groups is then paralleled using the odds ratio, which is an estimate of the relative risk of disease in the two groups. Patients can be acknowledged from an existing database or using data collected unambiguously for the purpose of the study. If safety data is sought for special populations, the cases and controls can be stratified according to the population of interest. For rare adverse events, prevailing large population-based databases are a useful and efficient means of providing the necessary data on medicine exposure and medical outcome relatively quickly. Case control studies are predominantly useful when the goal is to examine whether there is a relationship between a medicine (or medicines) and one specific rare adverse event, as well as to identify risk factors for adverse events. Risk factors can include conditions, such as renal and hepatic dysfunction, which might modify the relationship between the medicine exposure and the adverse event. Under particular conditions, a case-control study can deliver the complete incidence rate of the event.

f) Cohort study

In a cohort study, a population at risk for the disease (or event) is monitored over time to record the occurrence of the disease (or event). Information on exposure status is accessible during the followup period for each patient. A patient might be exposed to a medicine at one time during follow-up, but not exposed at another time. Meanwhile the population exposure during follow-up is acknowledged, incidence rates can be calculated. In many cohort studies concerning medicine exposure, appraisal cohorts of interest are selected on the basis of medicine use and monitored over time. Cohort studies are useful when there is a requisite to know the incidence rates of adverse events in addition to the relative risks. Multiple adverse events can also be scrutinized using the similar data source in a cohort study. Conversely, it can be problematic to recruit adequate numbers of patients who are exposed to the medicine of interest or to study very rare outcomes. Similar to case-control studies, patients in cohort studies can be recognized from large automated databases or from data collected precisely for the study at hand. In addition, cohort studies can be used to scrutinize safety issues in special populations through oversampling of these patients or by stratifying the cohort if adequate numbers of patients are included. There are numerous automated databases obtainable for pharmacoepidemiological studies.[35, 36, 37] They consist of databases that contain automated medical records or automated accounting/billing systems. Databases that are fashioned from accounting/billing systems might be connected to pharmacy claims and medical claims databases. These datasets may contain millions of patients. Subsequently, they are fashioned for administrative or billing purposes; they might not have all the detailed and precise information needed for some research, such as authenticated diagnostic information or laboratory data. Even though medical records can be used to establish and authenticate test results and medical diagnoses, one should know about the privacy and privacy regulations that apply to patient medical records.

g) Targeted clinical investigations

When significant risks are identified from pre-approval clinical trials, further clinical studies might be called in to evaluate the mechanism of action for the adverse reaction. In some instances, pharmacodynamics and pharmacokinetic studies might be conducted to define whether a particular dosing instruction can put patients at an increased risk of adverse events. Moreover, based on the pharmacological properties and the predictable use of the medicine in general practice, conducting specific studies to scrutinize potential medicine-medicine interactions and food-medicine interactions might be entitled to. These studies can comprise population pharmacokinetics studies and medicine concentration monitoring in patients and normal volunteers. One drawback of this method is that the outcome measure might be too shortened and this might have an influence on the quality and eventual usefulness of the results of the trial. Large, simplified trials are similarly resource-intensive.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 5, Issue 2, January 2025

Recent development in pharmacovigilance

Pharmacovigilance and the methods used need to continue to develop in order to keep up with the demands of society. In recent years, three publications have been of utmost importance in terms of providing guidance on the future of pharmacovigilance. The first is the Erice Declaration on transparency, which was published in 1997 [57]. In this declaration, pharmacovigilance experts from all over the world, representing different sectors, emphasise the role of communication in drug safety with the following statements:

Drug safety information must serve the health of the public

Education in the appropriate use of drugs, including interpretation of safety information, is essential for the public at large, as well as for health care providers

All the evidence needed to assess and understand risks and benefits must be openly available – Every country needs a system with independent expertise to ensure that safety information on all available drugs is adequately collected, impartially evaluated and made accessible to all

Innovation in drug safety monitoring needs to ensure that emerging problems are promptly recognised and efficiently dealt with, and that information and solutions are effectively communicated

The development of new and effective medicinal products makes a positive contribution to the health and well-being of individuals. However, there is a need to improvepharmacovigilance(PV) systems to more effectively monitor and take action on safety issues associated with medicines to enhance their contribution to public health. This article looks at the current trends driving the development of PV strategies in order to achieve this aim.

It is believed that these factors will help risks and benefits to be assessed, explained and acted upon openly and in a spirit that promotes general confidence and trust. This declaration was followed in 2007 by the Erice Manifesto for global reform of the safety of medicines in patient care [58]. The Erice Manifesto specifies the challenges which must be addressed to ensure the continuing development and usefulness of the science, in particular:

The active involvement of patients and the public in the core debate about the risks and benefits of medicines, and in decisions about their own treatment and health

The development of new ways of collecting, analyzing and communicating information about the safety and effectiveness of medicines; open discussion about it and the decisions which arise from it

The pursuit of learning from other disciplines about how phamacovigilance methods can be improved, alongside wide-ranging professional, official and public collaboration

The creation of purposeful, coordinated, worldwide support amongst politicians, officials, scientists, clinicians, patients and the general public, based on the demonstrable benefits of pharmacovigilance to public health and patient safety

The third article that has had a profound impact on how pharmacovigilance should work in the future is the article published in 2002 by Waller and Evans in which they give their view on the future conduct of pharmacovigilance. The key values that should underpin pharmacovigilance are excellence

(defined as the best possible result), the scientific method and transparency. The paper defines five elements that are considered to be essential for achieving excellence. Three of these are: process-oriented best evidence, robust scientific decision-making and effective tools to deliver protection of public health. The other two elements, scientific development and audit, underpin these processes, recognising that excellence cannot be achieved merely by process [59].

International developments In the past, pharmacovigilance has been most concerned with finding new ADRs, but Waller and Evans suggest that pharmacovigilance should be less focused on finding harm and more focused on extending knowledge of safety [59].

In recent years, regulatory agencies have been reforming their systems in order to keep pace with the developments in pharmacovigilance, with the focus on being more pro-active.

Europe

In 2005, a document was drafted by the Heads of the Medicines Agencies called ‘Implementation of the Action Plan to Further Progress the European Risk Management Strategy’. In July 2007, the EMEA published a document in which they discussed the achievements booked to date. These achievements included the implementation of legal tools for monitoring the safety of medicines and for regulatory actions. Particular emphasis was placed on:

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 5, Issue 2, January 2025

1. Systematic implementation of risk management plans
2. Strengthening the spontaneous reporting scheme through improvements of the Eudra Vigilance database
3. Launching the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) project to strengthen the monitoring of medicinal products
4. The conduct of multi-centre post authorisation safety studies
5. Strengthening the organisation and the operation of the EU Pharmacovigilance system In the course of the next 2 years, two main areas will be covered by the European Risk Management Strategy:

further improving of the operation of the EU Pharmacovigilance System and strengthening the science that underpins the safety monitoring for medicines for human use [60, 61].

In December 2007, a public consultation 'Strategy to Better Protect Public Health by
Strengthening and Rationalising EU Pharmacovigilance' was published on behalf of the European Commission. This document contains legislative strategy and key proposals for legislative changes within the European Union. Areas where legislative changes are needed include: fast and robust decision-making on safety issues, clarification of roles and responsibilities for industry and regulators, strengthening of the role of risk-management planning, improvement of the quality if of non-interventional safety studies, simplification of ADR reporting, including introducing patient reporting, strengthening of medicine safety, transparency and communication, including clearer safety warnings in the product information to improve the safe use of medicines [50]. The USA In the USA, the FDA has had a difficult time since the withdrawal of rofecoxib. The main concern is that the FDA is not able to protect the public from drug risks as efficiently as it might. In February 2007, on the basis of the IOM report, the FDA announced several initiatives designed to improve the safety of prescription drugs [26]. These initiatives fall into four main categories. The first is increasing the resources for drug safety activities. Perceiving the agency as being overly dependent on industry funding, some observers propose eliminating user fees. The second category of proposed reform is new authority for the FDA; the agency needs regulatory tools to help assure drug safety. This authority would be exercised through a required risk.

Factors behind the development of current trends

- Globalization of the pharmaceutical market.
- Development of innovative products.
- Increasing public awareness and changing expectation with regards to the safety of medicines.
- Large costs associated with drug safety.

Integrated Pharmacovigilance

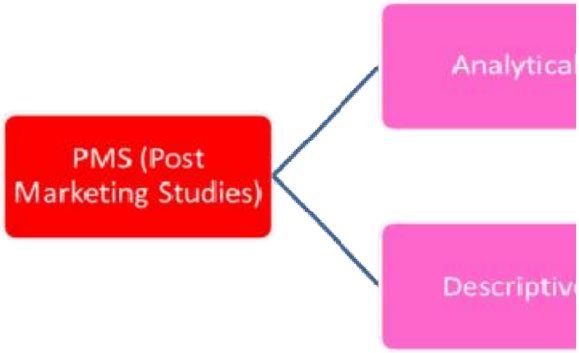
In the past, PV has concentrated primarily on post-marketing safety surveillance. In recent years, it has been shifted towards systematic PV throughout the product life cycle (preclinical studies to post marketing surveillance) as recommended by the CIOMS V Working Group. The effective PV system needs to integrate input from all stakeholders, both within an organization and externally.

Effective integrated PV also includes preclinical and clinical operations,clinical data management, statistics, medical writing, regulatory authorities/activities, IT and medical information, sales and marketing, and public relations.

Current Trends

The main method currently used to gather information on a drug in the premarketing phase is by conducting clinical trials.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 5, Issue 2, January 2025



1.2 Recent Developments

Data Mining Technology in Spontaneous Reporting System

In the past, signal detection in spontaneous reporting has mainly occurred on the basis of case-by-case analyses of reports. Recently, the reports are validated by 'data mining'.

The term 'data mining' refers to the principle of analyzing data from different perspectives and extracting the relevant information.

Algorithms are often used to determine hidden patterns of associations or unexpected occurrences, i.e. signals in large databases.

Three Current Approaches in Data Mining Methods

- **Proportional Reporting Ratios (PPRs)**: This method compares the proportion of reports for a specific Adverse Drug Reaction (ADR) reported for a drug with the proportion for that ADR in all other drugs. The calculation is analogous to that of relative risk. Using the same information, it is also possible to calculate a 'reporting odds ratio'.
- **Bayesian Confidence Propagation Neural Network (BCPNN)**: This approach uses Bayesian statistics to analyze all reported ADR combinations. Strong relationships in the data are highlighted relative to general reporting of suspected adverse effects. The WHO Collaborating Centre for International Drug Monitoring uses this method for data mining.
- **Multi-Item Gamma Poisson Shrinker (MGPS)**: It is used by the FDA for data mining of their spontaneous report's database. The MGPS algorithm computes signal scores for pairs, and for higher-order (e.g. triplet, quadruplet). The significant more frequent combinations of drugs and events would predict.

REFERENCES

[1]. WHO Policy Perspectives on Medicines. Geneva: WHO; 2004. Geneva: World Health Organization. Looking at the Pharmacovigilance: ensuring the safe use of medicines.
[2]. Klepper MJ. The periodic safety updates report as a Pharmacovigilance tool. Drug Saf 2004; 27: 569-78.
[3]. Livio F, Renard D, Buclin T. Pharmacovigilance. Rev Med Suisse, 2012; 8: 116-9.
[4]. WHO, Safety of medicines in public health programmes: Pharmacovigilance an essential tool, WHO, 2006.
[5]. Skalli S, Soulaymani Bencheikh R. Safety monitoring of herb-drug interactions: acomponent of pharmacovigilance. Drug Saf, 2012; 35: 785-91.
[6]. Arnott J, Hesselgreaves H, Nunn AJ, Peak M, Pirmohamed M, Smyth RL, et al. What can we learn from parents about enhancing participation in pharmacovigilance?. Br J Clin Pharmacol 2012; in press.
[7]. WHO, Pharmacovigilance: ensuring the safe use of medicines, Geneva: WHO. 2004.
[8]. WHO, Safety of medicines in public health programmes: pharmacovigilance an essential tool, WHO, 2006.
[9]. WHO Medicines Strategy: Framework for Action in Essential Drugs and Medicines Policy, 2000-2003.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 5, Issue 2, January 2025

[10]. Olsson S. The role of the WHO Programme for International Drug Monitoring in coordinating worldwide drug safety efforts. Drug Saf, 1998; 19: 1-10.
[11]. WHO, Pharmacovigilance: ensuring the safe use of medicines, Geneva: WHO, 2004.
[12]. ICH Guideline E2D; Post-approval safety data management: definitions and standards for expedited reporting, 3.1.1 Spontaneous reports 2004. International Conference on Harmonisation.
[13]. Pinkston V, Swain EJ. Management of adverse drug reactions and adverse event data through collection, storage, and retrieval. In: Stephens MDB, Talbot JCC, Routledge PA, eds. Detection of new adverse drug reactions. 4th ed. London, MacMillan Reference Ltd, 1998; 282.
[14]. Faich GA, U.S. adverse drug reaction surveillance 1989-1994. Pharmacoepidemiology Drug Safety, 1996; 393-398.
[15]. Goldman SA. Limitations and strengths of spontaneous reports data. Clinical Therapeutics, 1998; 20(Suppl C): C40-C44.
[16]. Hartmann K, Doser AK, Kuhn M. Postmarketing safety information: How useful are spontaneous reports. Pharmacoepidemiology and Drug Safety, 1999; 8: S65-S71.
[17]. Waller PC, Arlett PA. Responding to signals. In: Mann RD, Andrews E, eds. Pharmacovigilance. Chichester, John Wiley and Sons Ltd, 2002; 105-128.
[18]. DuMouchel W. Bayesian data mining in large frequency tables, with an application to the FDA Spontaneous Reporting system. The American Statistician, 1999; 53: 177-190.
[19]. Bate A, Lindquist M, Edwards IR. A Bayesian neural network method for adverse drug reaction signal generation. European Journal of Clinical Pharmacology, 1998; 54: 315-321.
[20]. Van Puijenbroek E, Egberts ACG, Heerdink ER, Leufkens HGM. Detecting drug-drug interactions using a database for spontaneous adverse drug reactions: An example with diuretics and non-steroidal anti-inflammatory drugs. European Journal of Clinical Pharmacology, 2000; 56: 733-738.
[21]. Venning GR. Identification of adverse reactions to new drugs. III: Alerting processes and early warning systems. British Medical Journal, 1983; 286: 458-460.
[22]. Edwards IR. The management of adverse drug reactions: from diagnosis to signal. Thérapie, 2001; 56: 727-733.
[23]. 1Strom BL (ed.) Pharmacoepidemiology, 3rd ed. New York, NY, John Wiley and Sons, Ltd, 2002.
[24]. Mitchell AA, Van Bennekom CM, Louik C. A pregnancy-prevention program in women of childbearing age receiving isotretinoin. New England Journal of Medicine, 1995; 333: 101-106.
[25]. Task Force on Risk Management. Report to the FDA Commissioner. Managing the risks from medical product use: Creating a risk management framework. Part 3. How does FDA conduct postmarketing surveillance and risk assessment. May 1999.
[26]. Shakir SAW. PEM in the UK. In: Mann RD, Andrews EB, eds. Pharmacovigilance Chichester, John Wiley and Sons, 2002; 333-344.
[27]. Coulter DM. PEM in New Zealand. In: Mann RD, Andrews EB, eds. Pharmacovigilance. Chichester, John Wiley & Sons, 2002; 345-362.
[28]. Coulter DM. The New Zealand intensive medicines monitoring programme in pro-active safety surveillance. Pharmacoepidemiology and Drug Safety, 2000; 9: 273-280.
[29]. Mackay FJ. Post-marketing studies. The work of the Drug Safety Research Unit. Drug Safety, 1998; 19: 343-353.
[30]. Garcia Rodriguez LA, Perez Gutthann S. Use of the UK General Practice Research Database for Pharmacoepidemiology. British Journal of Clinical Pharmacology, 1998; 45: 419-425.
[31]. Meyboom RHB, Royer RJ. Causality classification in pharmacovigilance centres in the European Community. Pharmacoepidemiology and Drug Safety, 1992; 1: 87-97.
[32]. Edwards IR, Biriell C. Harmonisation in pharmacovigilance. Drug Safety, 1994; 10: 93-102.

[33]. Strom BL (ed.) Pharmacoepidemiology, 3rd ed. New York, NY, John Wiley and Sons, Ltd, 2002.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 5, Issue 2, January 2025

[34]. Shakir SAW. PEM in the UK. In: Mann RD, Andrews EB, eds. Pharmacovigilance Chichester, John Wiley and Sons, 2002; 333-344.

[35]. Strom BL (ed.) Pharmacoepidemiology, 3rd ed. New York, NY, John Wiley and Sons, Ltd, 2002.

[36]. Shakir SAW. PEM in the UK. In: Mann RD, Andrews EB, eds. Pharmacovigilance Chichester, John Wiley and Sons, 2002; 333-344.

[37]. Mackay FJ. Post-marketing studies. The work of the Drug Safety Research Unit. Drug Safety, 1998; 19: 343-353.

[38]. Psaty BM, Burke SP (2006) Protecting the health of the public– Institute of Medicine recommendations on drug safety. N Engl J Med 355:1753–1755

[39]. European Commission Enterprise and Industry Directorate-general and rationalising EU pharmacovigilance. European Commission Enterprise and Industry, Brussels communication in drug safety. Drug Saf 29:91–93

[40]. Adis International (2007) The Erice Manifesto: for global reform of the safety of medicines in patient care. Drug Safe. 30:187–190

[41]. Waller PC, Evans SJ (2003) A model for the future conduct of on the implementation of the European risk management strategy. Cited 18 Dec 2007