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Review Article

Review; Pharmacovigilance and Drug Safety: A Global Perspective

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A B S T R A C T

A significant and essential component of clinical research is pharmacovigilance. Throughout the product lifecycle, post-marketing pharmacovigilance and clinical trial safety are both crucial. The pharmacological science that deals with the identification, evaluation, comprehension, and avoidance of negative consequences is known as pharmacovigilance. What is known about its advantages and disadvantages, difficulties, and prospects in Indian medicine? Here, the primary emphasis is on the objectives and function of pharmacovigilance in the regulation of medications and their partners. including the short- and long-term negative consequences of medications. In India, pharmacovigilance is still in its infancy, and very little is known about the field. Although the field of pharmacovigilance has made significant strides in western nations, nothing has been accomplished inIndia chose to join the Uppasla Centre for Adverse Event Monitoring at that time. With the help of the media and regulatory bodies, pharmacovigilance has become increasingly important as people have grown more knowledgeable about the risks and benefits of medications. Any unfavourable medical event that may arise when taking a medication but is not always connected to its use is referred to as an adverse event. "An adverse drug reaction is any unpleasant, unexpected, and undesirable side effect of a medication that happens at dosage used in humans for diagnosis, treatment, prevention, or alteration of physiological function." In order to collect safety data for early detection, spontaneous reporting of adverse drug reactions and events is a crucial tool. A growing number of Indian businesses have emerged in recent years. In 2008, this is really recent data and has been used here since most recent and relevant data available are of this year. Available, it was estimated that (ADRS) accounted for 5% of the total amount of reports, thus minimizing the number of times that honest adverse reaction reports were being eliminated

Keywords: Pharmacovigilance, Uppasla Centre, Adverse Event Monitoring, Medications, Emphasis

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INTRODUCTION:

Pharmacovigilance is an important and integral part of clinical research.[1]Both clinical trials safety and post marketing pharmacovigilance are critical throughout the product lifecycle. Pharmacovigilance is "defined as the pharmacological science relating to the detection, assessment, understanding and prevention of adverse effects,What do we know of its benefits and risks, challenges and the future hold for pharmacovigilance in Indian medicine. Here the main focus on the aims and role of pharmacovigilance in medicines regulation and their Partners. particularly long term and short term adverse effects of medicines." Pharmacovigilance is still in its infancy in India and there exists very limited knowledge about the discipline. While major advancements of discipline of pharmacovigilance have taken place in the western countries not much has been achieved in India.Pharmacovigilance is not new to India and has infact been going on from 1998.[2] When India decided to join the uppaslacentre for adverse event monitoring. The importance of pharmacovigilance is withdrawls the regulatory agencies, media; consumers have become more aware about the benefit and risks of medicines. "An adverse event is defined as any un toward medical occurrence that may present during treatment with a drug but which does not necessarily have a relationship with its use." "An adverse drug reaction is any noxious, unintended and undesired effect of a drug, which occurs at a dose used in human for prophylaxis, diagnosis, therapy or modification of physiological function." Spontaneous reporting of adverse drug reaction and adverse

events is an important tool for gathering the safety information for early detection. In recent years many Indian companies are increasing the investment in research and development and are enhancing their capacity to develop and market new drugs with their own research efforts.[3] In 2008, this is really recent data and has been used here since most recent and relevant data available are of this year. Available, it was estimated that (ADRS) accounted for 5% of the total amount of reports, thus minimizing the number of times that honest adverse reaction reports were being eliminated. It accounts for about 200,000 hospitalizations and about 197,000 deaths per year in european union (EU) and its there fore they attract societal cost of €79 billion [4]

HISTORY AND PERSPECTIVE OF PHARMACOVIGILANCE

Thalidomide:

The decisive event for the birth of pharmacovigilance occurred in 1961 when the use of thalidomide during pregnancy caused a 20% increase in congenital malformations in newborns. The drug was tested for two years on 300 patients, without detecting any particularside effects. Therefore, considered safe, it was marketed in over 50 countries starting from 1957. Thalidomide was used primarily as a sedative, antiemetic and hypnotic in pregnant women. Its administration caused a serious anomaly in the development of the foetus: the newborns had serious deformities of the limbs, especially the upper ones, such as the absence (amelia) or reduction of the bones (phocomelia). Approximately 10,000 to 20,0000 children suffered incomplete development.In 1977, the united states food development authority established what is known as the adverse drug reaction reporting system forcing drug producers to report any side effects related to their products..[5][6][7][8][9][10][11]

Chloroform:

The history of pharmacovigilance dates back to 1848, when a series of suspicious deaths occurred in great britain during operations in which chloroform was administered to patients.chloroform was used as an anesthesia starting in 1847. The following year a 15-year-old girl died following its use. This tragic event sparked concern, prompting the lancet journal to set up a commission and urge british doctors to report similar cases. A debate therefore opened on the safety of anesthesia procedures and following various reports, the drug ceased to be used as an anesthesia in 1976. This episode represented the first step towards the establishment of pharmacological safety procedures.[12][13]

Sulfanilamide:

Most consequential mass poisonings of the 20th century. Sulfanilamide an antibacterial drug, was being used safely in the treatment of streptococcal infection a new elixir the elixir sulfanilamide disaster of 1937 was one of the formulation with raspberry flavour was prepared using diethylene (deg) as there was a need for the drug in its liquid form. Deg can be fatal, and unknowingly the company distributed the product across the united states. However, the food and drug regulation (at that time) did not insist on toxicity studies for the new formulation. Hence, the company did not carry out any toxicity studies. Soon after its appearance on the market, the american medical association was made aware of the lethal cases from the administration of this elixir, and though immediate attempts were made to recall it, many died. The elixir was produced by a us pharmaceutical company, s. E. Massengill company. The formulation resulted in the death of 105 patients who consumed the elixir. In reaction to this calamity, the us congress passed the 1938 federal food, drug and cosmetic (FAC) act, which required proof of safety before the release of a new drug. The 1938 law changed the drug focus of the food and drug administration (FDA).[14][15]

ROLE OF PHARMACOVIGILANCE:

Pharmacovigilance has been widely accepted to possess a significant role in early observation of the risk associated with the drug. All the medicines are tested on a concerned small ratio of population before it is approved for post-marketing surveillance. The pharmacovigilance has been known to possess various roles like, identification, quantification and documentation of drug-related problems; contribution towards reducing the risk of drug-related problems in healthcare systems; and enhancement of knowledge and understanding of factors and mechanisms which are responsible for drug-related injuries. However, in order to fill the various roles of pharmacovigilance, the interactions and influence of many stakeholders in society with decision-making powers has been required, which include, politicians at national, regional and local levels; healthcare administrators; drug regulatory authorities; pharmaceutical companies; healthcare professionals like physicians, dentists, pharmacists and nurses; academic institutions; media representatives; health insurance companies; lawyers; and patient group.Associated with marketed medicines.Other important followers of pharmacovigilance are the health professionals: Originally physicians were the only professionals who observe different kinds of drug related problems by exercising the skill of differential diagnosis. Last of all, the patients form the most important adherent of pharmacovigilance as, a patient knows the actual benefit and harm of a medicine prescribed to him. Vaccines and biological medicines require modified systems of safety monitoring. They are often administered to healthy children. This applies particularly to vaccines used within a national immunization program..[16][17]

CURRENT METHODS OF PHARMACOVIGILANCE:

Spontaneous Reports;

Spontaneous reports' are so-called because they arise during a clinician's normal diagnostic appraisal of a patient, the clinician drawing the conclusion that a drug may be implicated in the causality of the clinical event. As with all diagnoses the certainty of attribution will vary with the skill and experience of the doctor, what confirmatory tests may show, the natural history of the clinical event, and the existence of other plausible explanations. Under-reporting, reports of known reactions, and false causality attribution are the common criticisms of spontaneous reporting systems. [18][19]

Targeted clinical investigations;

Over-all pharmacovigilance methods;

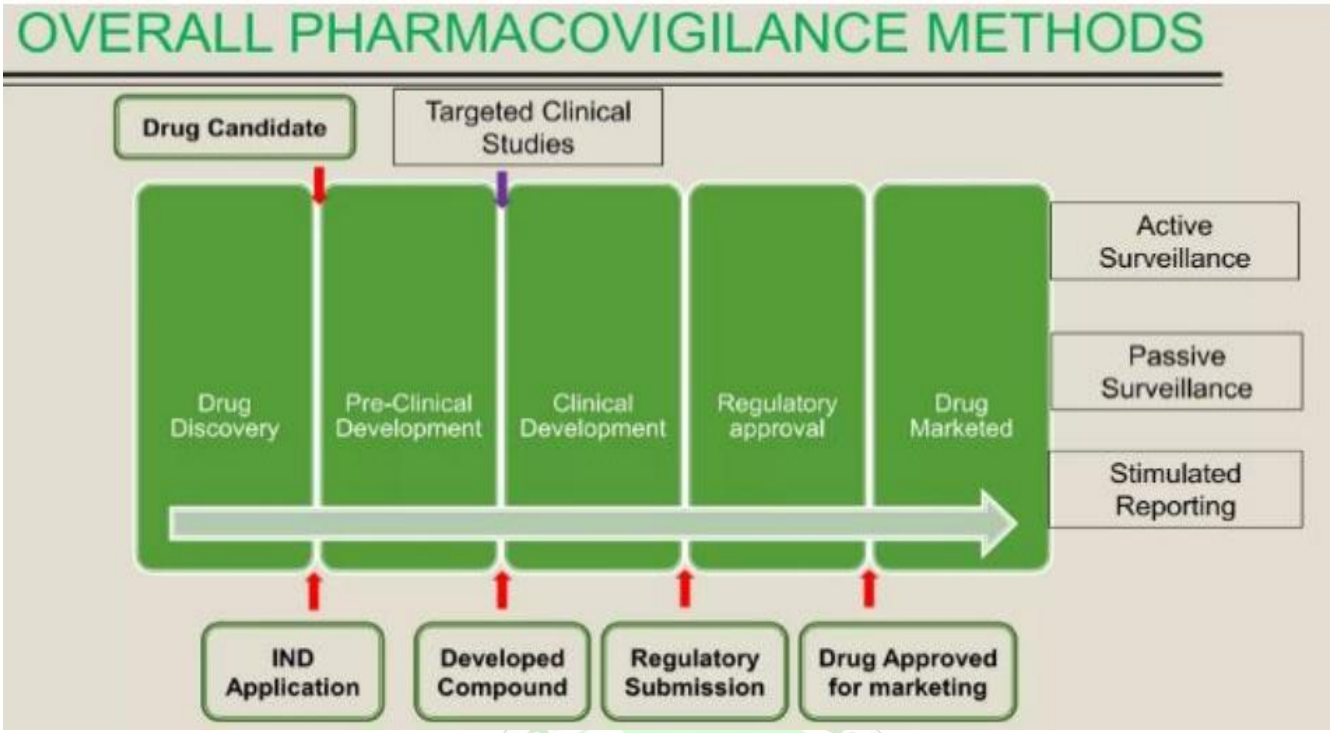

Figure1: Drug development Process

Targeted clinical investigation- • When significant risks are identified from pre-approval clinical trials, further clinical studies might be called for to evaluate the mechanism of action for ADRs This investigation includes- > PK and PD studies > Genetic testing >Interaction studies > Large simplified trial.

Pk and pd studies;

Pharmacodynamics is the study of how a drug affects an organism, whereas pharmacokinetics is the study of how the organism affect the drug.

Pharmacodynamic and pharmacokinetic studies are conducted to determine whether a particular dosing instruction can put patients at an increased risk of adverse events.[20]

Drug-Drug- Interaction of PD and Pk Studies:

Drug- drug interactions occur when a drug interacts , or interferes, with another drug. This can alter the way one or both of the drugs act in the body, or cause unexpected side effects.

Aspirin + Warfarin Synergism (excessive bleeding Antibiotic + Blood thinner Antagonism (less effect) Codeine + Paracetamol Addition (increased analgesic effect)

Co-hert studies;

He term "cohort" is derived from the Latin word *cohors*. Roman legions were composed of ten cohorts. During battle each cohort, or military unit, consisting of a specific number of warriors and commanding centurions, were traceable. The word "cohort" has been adopted into epidemiology to define a set of people followed over a period of time. W.H. Frost, an epidemiologist from the early 1900s, was the first to use the word "cohort" in his 1935 publication assessing age-specific mortality rates and tuberculosis.The modern epidemiological definition of the word now means a "group of people with defined characteristics who are followed up to determine incidence of, or mortality from, some specific disease, all causes of death, or some other outcome.[21]

Longitudinal Electronic studies;

Collections of longitudinal electronic patient records are extremely valuable but underused in analysing real-world use of medicines. They cover large populations, provide detailed information on extended parts of medical histories and include information on both exposed and unexposed patients. The range of clinical information available may include prescriptions, laboratory test results, hospital referrals and admissions, and notes on symptoms, signs and diagnoses. Ideally, anonymised information is extracted directly from the computer systems in which physicians store patients' data, so that no extra effort is required to provide the information and the risk of omissions is minimised. Privacy protection for patients and physicians is of the utmost importance and needs to be carefully controlled. In the UK, general practitioners' records provide an important source of information and have formed the basis of the General Practice Research Database, , *i.e.*, reports on adrs that are not solely triggered by the expertise and suspicion of a medical expert, but also influenced by other factors, e.g., extensive media coverage of newly suspected adverse reactions after exposure to a certain drug.[22]

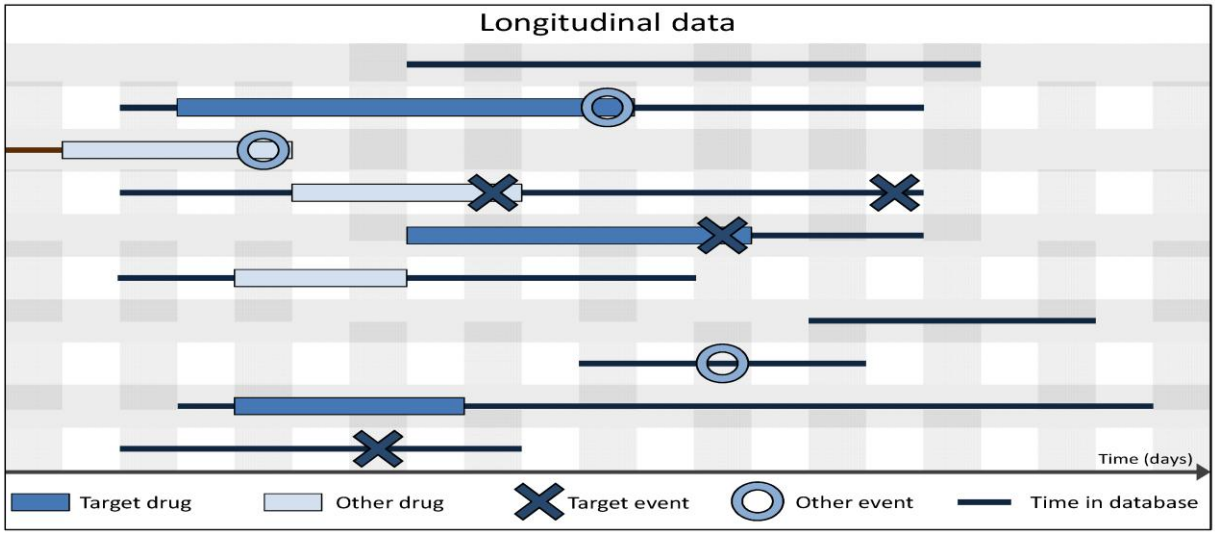

Figure 2: Longitudinal data

Screening Patient Records;

Patient records are already an important resource for confirmatory pharmacoepidemiology studies. In recent years interest has increased in extending their use to exploratory analysis and routine drug surveillance.[31] Many methods focus exclusively on one specific aspect of the drug-event association, such as the time from first exposure to the medicine to the first occurrence of the event or differences in the frequencies of the event in the same patients when exposed and unexposed. However, there is great variation in temporal patterns of potential interest, including those related to:[23][24]

- Suspected ADRS
- Potential beneficial effects of medicines
- Events related to the underlying disease
- Periodic patterns and trends, and
- Medical events that are generally common in exposed patients.

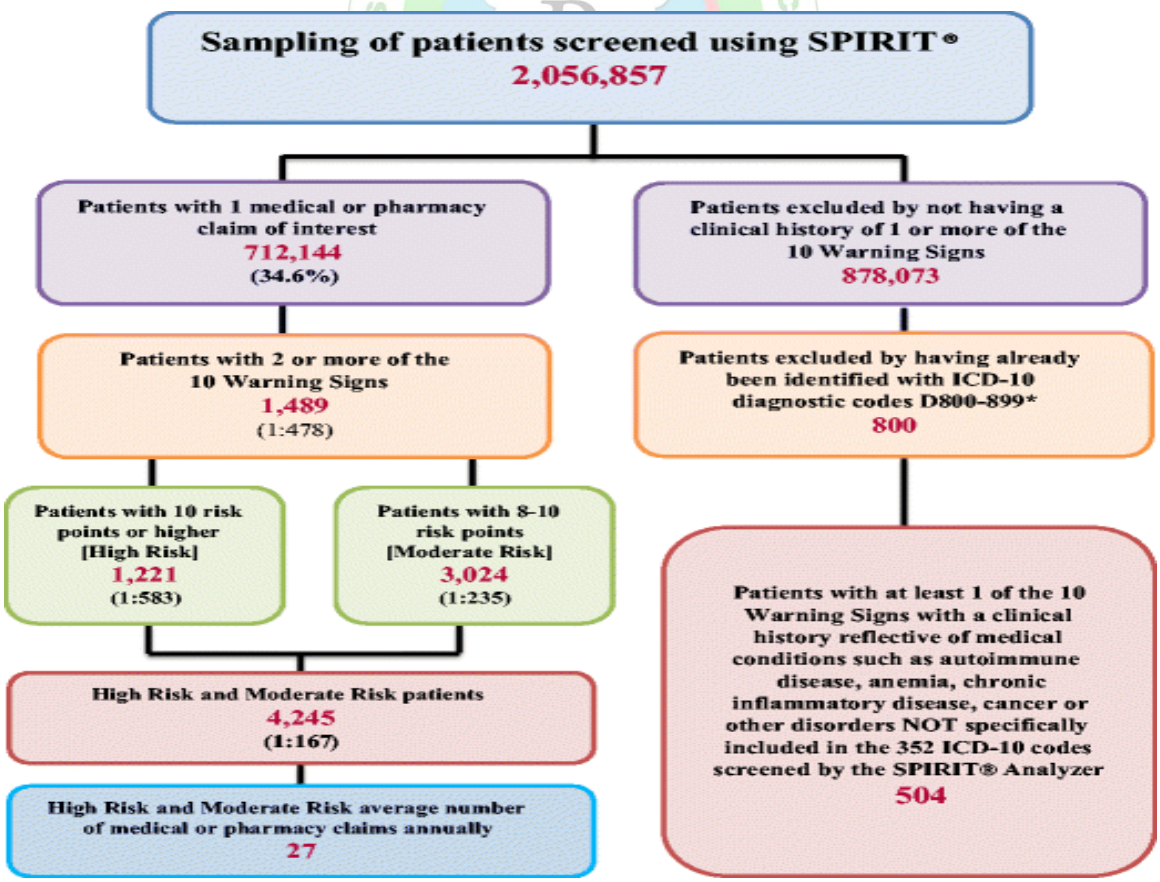

Figure 3: Sampling of Patients Screened Using Spirit

ADVERSE EVENT CASE PROCESSING:

Introduction:

Registries that collect information on specific drugs and medical devices need to anticipate the need for adverse event (AE) detection, processing, and reporting. This chapter addresses the identification, processing, and reporting of adverse events detected in situations in which a registry has contact with individual patients. This document is not a formal regulatory or legal document; therefore, any information or suggestions presented herein do not supersede, replace, or otherwise interpret Federal guidance documents that touch on these subjects. Registry sponsors are encouraged to discuss plans for AE collection and processing with local health authorities when planning a registry. This chapter primarily focuses on adverse events related to pharmaceutical products. Medical devices are significantly different from pharmaceutical products in the manner in which adverse events and product problems (complaints) present themselves, in the etiology of their occurrence, and in the regulation governing the defining and reporting of these occurrences, as well as post approval study requirements. Other sources provide more information about defining and reporting device-related adverse events and product problems, and about post marketing studies (including those involving registries).In pharmacovigilance, case processing is a fundamental activity. It provides data for the analysis of adverse effects that allows to detect new safety concerns and to periodically assess the benefit-to-risk ratio associated with the use of a pharmaceutical product. The precision and quality of safety data processing, also from the medical point of view, is crucial for ensuring correct analysis and undertaking corrective actions in a timely manner, which in turn helps to safeguard the health of the patients and allows safe use of the drug.Or post approval studies financially sponsored by manufacturers.[25][26]

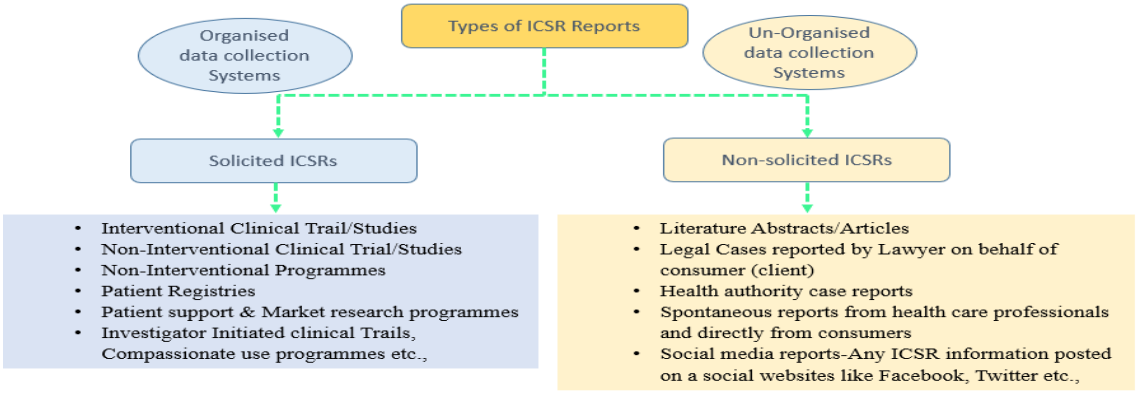

Figure 4: Sources of individual (adverse event) case safety reports

Sources of individual case safety reports;

UNSOLICITIED SOURCES:

Spontaneous reports

An unsolicited communication by a healthcare professional or consumer to a company, regulatory authority or other organization (e.g. WHO, Regional Centre, Poison Control Centre) that describes one or more adverse drug reactions in a patient who was given one or more medicinal products and that does not derive from a study or any organized data collection scheme'(ICH 2003). Spontaneous reporting is by nature a passive approach to pharmacovigilance (PV), relying entirely on the motivation of individuals to report suspected adverse drug reactions (adrs) to a local or national pharmacovigilance centre. Spontaneous reporting systems (SRS) can be paper based (e.g. The UK 'Yellow Card' system) or electronic (online reporting or mobile applications). Single reports from individual patients submitted to pharmacovigilance centres via these systems are known as Individual Case Study Reports (icsrs). Information from multiple icsrs is then used to identify potential 'signals' – suggestions of casual associations between a medicinal product and a previously unknown reaction. Detection and confirmation of these signals, though various methods, can identify previously unknown adverse or beneficial effects of a medication.[27]

SOLICITED SOURCES:

Solicited reports are those derived from organized data collection systems, which include clinical trials, registries, post-approval named patient use programs, other patient support and disease management programs, surveys of patients or healthcare providers, or information gathering on efficacy or patient compliance. Adverse event reports obtained from any of these should not be considered spontaneous. For the purposes of safety reporting, solicited reports should be classified as study reports, and therefore should have an appropriate causality assessment by a healthcare professional or an MAH. Further guidance on study-related issues, such as managing blinded therapy cases, can be found in the ICH E2A guideline.[28]

Regulatory authorities as the sources:

Individual serious unexpected adverse drug reaction reports originating from foreign regulatory authorities are subject to expedited reporting to other authorities by each MAH. Re-submission of serious ADR cases without new information to the originating regulatory authority is not usually necessary, unless otherwise specified.[29]

STANDARDS FOR EXPEDITED REPORTING:

What Should Be Reported?

Serious ADRs Cases of adverse drug reactions that are both serious and unexpected are subject to expedited reporting. The reporting of serious expected reactions in an expedited manner varies among countries. Non-serious adverse reactions, whether expected or not, would normally not be subject to expedited reporting. For reports from studies and other solicited sources, all cases judged by either the reporting healthcare professional or the MAH as having a possible causal relationship to the medicinal product would qualify as ADRs. For purposes of reporting, spontaneous reports associated with approved drugs imply a suspected causal relationship.

Other Observations:

In addtion to single case reports, any safety information from other observations that could change the risk-benefit evaluation for the product should be communicated as soon as possible to the regulatory authorities in accordance with local regulation. Examples include any significant unanticipated safety findings from an in vitro, animal, epidemiological, or clinical study that suggest a significant human risk, such as evidence of mutagenicity, teratogenicity, carcinogenicity, or lack of efficacy with a drug used in treating a life-threatening or serious disease

Lack of Efficacy:

Evidence of lack of efficacy should not normally be expedited, but should be discussed in the relevant periodic safety update report. However, in certain circumstances and in some regions, individual reports of lack of efficacy are considered subject to expedited reporting. Medicinal products used for the treatment of life-threatening or serious diseases, vaccines, and contraceptives are examples of classes of medicinal products where lack of efficacy should be considered for expedited reporting. Clinical judgment should be used in reporting, with consideration of the local product labeling and disease being treated.

Overdose:

Reports of overdose with no associated adverse outcome should not be reported as adverse reactions. Cases associated with serious adverse reactions are considered subject to expedited reporting, unless otherwise specified by local regulation. They should be routinely followed up to ensure that the information is as complete as possible with regard to symptoms, treatment, and outcome. The MAH should collect any available information on overdose related to its products**.**

Minimum Criteria for Reporting:

It is recommended that as much information as possible be collected at the time of the initial report. However, for the purpose of regulatory reporting, the minimum data elements for an ADR case are: an identifiable reporter, an identifiable patient, an adverse reaction, and a suspect product. Lack of any of these four elements means that the case is considered incomplete; however, MAHs are expected to exercise due diligence to collect the missing data elements.[30]

ADR REPORTING:

What to Report PVPI encourages all types of suspected ADRs reporting whether they are known, unknown, serious, or non serious, frequent, or rare regardless of an established causal relationship between a drug and the reaction. ADRs related with the use of allopathic medicines, vaccines, traditional medicines, medical devices, contrast media, etc. can be reported.

Where to Report:

All healthcare professionals (clinicians, dentists, pharmacists, nurses) and patient/consumers can report ADRs to NCC or AMCS. The pharmaceutical companies can also send individual case safety reports for their product to NCC.

How to Report:

Suspected ADR reporting forms for healthcare professionals and consumers are available on the website of IPC to report ADR. To remove language barrier in ADR reporting, the consumer reporting form are made available in 10 vernacular languages (Hindi, Tamil, Telugu, Kannada, Bengali, Gujarati, Assamese, Marathi, Oriya, and Malayalam). ADRs can he also reported via PvPI helpline number (18001803024) on weekdays from 9:00 am to 5:30 pm. The mobile Android application for ADR reporting has also been made available to the public.

Whom to Report:

A reporter can send filled ADR reporting form directly to NCC or their nearest aArthrogryposis multiplex congenita (AMC). In case of AMC, these reports are confirmed by healthcare professionals and entered into Vigiflow and sent to NCC for further assessment. These reports are then finally reviewed at NCC and committed to WHO-Uppsala Monitoring Centre. The obtained information is entered in the drug safety database, analyzed, and assessed by the experts to identify new signals. The submitted ADR report does not have any legal implication on the reporters. The patients' identity are held in strict confidence and protected to the fullest extent. Therefore, healthcare providers are encouraged to report ADRs for better understanding of the risk associated with the use of medicines and to safeguard the health of Indian population.[31][32]

What Should be Reported:

Patient Related Details:

1. Patient details
2. Sex
3. Weight
4. Age at time of reaction or date of birth

Medicine:

1. Name (INN and brand name)
2. Strength
3. Dose, frequency
4. Dosage form
5. Route of administration
6. Indication for use
7. Duration of use
8. Batch number

Suspected Adverse Reaction:

1. Description of the reaction
2. Expectedness of the reaction
3. Date the reaction started, stopped
4. Outcomes
5. Relevant tests/ laboratory data

Reporter's details:

1. Name initials
2. Address
3. Contact details
4. Qualification Above information should be reported during ADR reporting.[33]

Post marketing surveillance:

Post marketing surveillance (PMS) of medications is the process by which marketedmedicines are monitored for adverse drug reactions (ADRs) post clinical trials.1Since most drugs may not reach the market without passing phase III clinical trials, PMS studies are considered to be phase IV studies.[34] The safety and efficacy evaluations of any new medicinal product via clinical trials will provide only limited information on rare ADRs. In addition, discovering 'rare' (1 in 1000) and 'very rare' (1 in 10,000) ADRs usually occurs only in the post marketing phase.[35] This is mainly due to the limited variety of conditions, described as the 'five toos: too few, too simple, too narrow, too median-aged and too brief', referring to the narrow patient selection criteria and sample size along with the short duration of clinical studies. This makes it challenging to attain all the required safety data when relying exclusively on such studies.[46] PMS gives more realistic results as they occur in a more natural setting and afford evidence to safeguard or enhance the safety of approved drugs. As a result of PMS, almost 20% of new medications obtained a black box warning post marketing, and 4% were removed from the market due to safety concerns. An ADR is defined by the World Health Organization (WHO) as: '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' .Each year, millions of patients experience ADRs, especially with the increased use of medicinal drugs .From 2009 to 2012, approximately 47% of people in the United States reported using no less than one prescription medication in the past month and approximately 11% reported using no less than five prescription medications concomitantly. As a result, the amount spent on prescription drugs was estimated to be US$270 billion in 2013 according to the National Center for Health Statistics report in 2014.Lazarou and his colleagues estimated, in a landmark meta-analysis in 1998, that ADRs were associated with over 2,216,000 hospitalization cases annually in USA (admitted because of ADR or suffered ADR while in hospital), leading to more than 106,000 deaths each year. Therefore, ADRs take the place as the fourth to sixth major cause of death, eclipsing pulmonary disease, diabetes, acquired immunodeficiency syndrome and pneumonia.According to the Centers for Disease Control and Prevention, ADRs are responsible for almost 1,300,000 emergency department visits annually.[36]

Post marketing surveillance of suspected ADRs:

Post marketing drug monitoring actions deal with two pharmacology fields: pharmacovigilance and pharmacoepidemiology. Pharmacovigilance, also known as drug safety surveillance, is mainly concerned with the 'timely detection' of 'novel' ADRs that are unique in their 'clinical nature, severity and/or frequency'.[37] Pharmacoepidemiology represents the 'population-based study of drug uses and the risks associated with these uses'. The significance of using pharmacovigilance should be encouraged by highlighting that the life of a drug truly starts post marketing.Nowadays, PMS can be conducted actively, due to technological progress, with the help of computer systems and electronic medical records. This can be achieved when the regulatory authorities, as well as the pharmaceutical companies, have access to electronic medical records database and seek drug-associated ADRs. Three of the main limitations of pharmacovigilance are: under-reporting, difficulty in identifying low risks, and the difficulty or impracticality of quantifying risks.[38] Moreover, ADR reporting is determined by numerous factors, for example how serious or severe an ADR is, how long the drug has been on the market, the experience of the health care professional, and the qualifications of the reporting physician (specialists report more often than general practitioners do). Nevertheless, spontaneous reporting is still the basis of post marketing drug safety surveillance.The fact remains that the main source of data collection for post marketing pharmacovigilance since the 1960s is spontaneous reporting systems (SRSs).[39] They are considered to be a passive approach and are composed of reports of suspected ADRs gathered spontaneously from healthcare professionals, consumers and pharmaceutical companies that are maintained for the most part by 'regulatory health agencies'. As such, PMS is applied in passive national reporting schemes, for example, 'Yellow Card Scheme' in the United Kingdom and 'MedWatch' in the United States. It is also applied as active surveillance, by 'Medicines and Healthcare products Regulatory Agency' (in the UK) and the U.S. Food and Drug Administration (US FDA), which carries out post marketing surveys.[40]
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Spontaneous ADR reporting system:

Spontaneous ADR reporting systems are important since they are a cost-effective method that can lead to the detection of new or rare adrs. Spontaneous reports are collected in databases through different channels (pharmaceutical companies, national and international pharmacovigilance centers or regulatory authorities). These databases belong to different institutes, such as US FDA and EMA, through which adrs are collected and exchanged. Following analysis of the spontaneous reports, signals of unidentified or potential adrs are generated.[45]

Minimum awareness of spontaneous ADR reporting systems:

A study done in Korea on a selected sample from the general population showed that the awareness of an ADR reporting system was quite low, at 8.3%. The main source of information was television/radio (69.9%), then the internet (19.3%), while only 6.1% obtained the information from posters or brochures. These findings indicate that awareness of the importance of ADR spontaneous systems should be boosted by campaigns, to emphasize the importance of this subject. A cross-sectional study done in Ghana on randomly selected doctors showed that less than 30% of the selected doctors were trained in the spontaneous ADR reporting system.[46]

Future prospects of pharmacovigilance:

Pharmacovigilance has clear, well-established goals: to detect ADRs associated with the use of drugs as early as possible, and to avoid risks that may outweigh the benefits of the medication. The evolution of pharmacovigilance has been a slow and steady one.[47] From individual doctors noticing unusual effects in patients and sharing their findings with colleagues to the methods used today to monitor a drug after its release into the market, including spontaneous reports, risk management plans, prospective safety studies, and registries.The main focus of pharmacovigilance has been to detect rare ADRs while giving less attention to the common ones. Recently, however, there has been a climate of change and efforts are now being made to focus on patient-centered pharmacovigilance rather than population-based and regulation-based pharmacovigilance. A study was conducted to evaluate the different aspects of pharmacovigilance currently, and in the future.[48]

CONCLUSION:

Pharmacovigilance continues to play a crucial role in meeting the challenges posed by the ever increasing range and potency of medicines, all of which carry an inevitable and some- times unpredictable potential for harm. When adverse effects and toxicity do appear, especially when previously unknown, it is essential that these are reported, analyzed and their significance is communicated effectively to the audience having knowledge to interpret the information. For all medicines, there is a trade-off between the benefits and the potential for harm. The harm can be minimized by ensuring that medicines of good quality, safety and efficacy are used rationally, and that the expectations and concerns of the patient are taken into account when therapeutic decisions are made. To achieve this is to serve public health, and to foster a sense of trust among patients in the medicines they use that would extend the confidence in the health service in general, ensure that risks in drug use are anticipated and managed, provide regulators with the necessary information to amend the recommendations on the use of the medicines, improve communication between the health professionals and the public and educate health professionals to understand the effectiveness or risk of medicines that they prescribe.

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. Deepa, A. Pharmacovigilance obligations of the pharmaceutical companies in India‟, India J pharmacol, 2008; 40: S13-S16.
4. European Commission. MEMO/08/782, Brussels, 10 December November 2008. Strengthening pharmacovigilance to reduce adverse effects of medicines. http://europa.eu/rapid/press-release_ MEMO-08-782_en.htm?locale=en (2017). Accessed 3 Jul 2017.
5. Miller MT (1991). "Thalidomide Embryopathy: A Model for the Study of Congenital Incomitant Horizontal Strabismus". Transactions of the American Ophthalmological Society. 81: 623–674.
6. Jump up to[a b c d] Loue S, Sajatovic M (2004). Encyclopedia of Women's Health. Springer Science & Business Media. pp. 643–644. ISBN 9780306480737.
7. Sneader W (2005). Drug discovery: a history (Rev. and updated ed.). Chichester: Wiley. p. 367. ISBN 978-0-471-89979-2.
8. Jump up to:[a b c] Cuthbert A (2003). The Oxford Companion to the Body. Oxford University Press. p. 682. Doi:10.1093/acref/9780198524038.001.0001. ISBN 9780198524038.
9. Thomas, Katie (2020-03-23). "The Unseen Survivors of Thalidomide Want to Be Heard". The New York Times. ISSN 0362-4331. Retrieved 2020-03-23.
10. Williams, Roger (September 10, 2012). "The Nazis and Thalidomide: The Worst Drug Scandal of All Time". Newsweek. Retrieved 25 August 2021.
11. Thalidomide Monograph for Professionals". Drugs.com. Retrieved 14 November 2019.
12. Montgomery W. From the New Books (a review of 'Historic South Edinburgh' Vol 2 by CJ Smith), Scots Magazine, 1980; 112: 514. Forrester SD. Scots Magazine, 1980; 113: 122 (L).
13. Smith CJ. Scots Magazine, 1980; 113: 439-40 (L). Smith CJ. Scots Magazine, 1981; 114: 458-9 (L). Broomfield CEo No Women Allowed. Scots Magazine, 1985; 122: 611-4.
14. Ballentine, Carol (June 1981). "Sulphanilamide Disaster" (PDF). FDA Consumer Magazine.^ "Medicine: Post-Mortem". Time. December 20, 1937. Retrieved 2009-07-19.
15. The New York Times. November 26, 1937. Retrieved 2009-07-20.^ Shaw, Leslie M. (2001). The clinical toxicology laboratory: contemporary practice of poisoning evaluation. Washington, DC: AACC Press. ISBN 1-890883-53-0.
16. WHO. Global programme for vaccines and immunization: Expanded Programme on Immunization. Surveillance of adverse events following immunization: Field guide formanagers of immunization programmes. Geneva 1997.
17. Haramburu F, Bégaud B, Moride Y. Temporal trends in spontaneous reporting of unlabelled adverse drug reactions. Br J Clin Pharmacol. 1997;44:299–301. doi: 10.1046/j.1365-2125.1997.t01-1-00573.x.

18. Rawlins MD. Pharmacovigilance: paradise lost, regained or postponed? The William Withering Lecture 1994. J R Coll Physicians Lond. 1995;29:41–49. [published erratum appears in J R Coll Physicians Lond 1995; 29: 118]
19. S.K Gupta Textbook of pharmacovigilance 2nd edition .Jaypee brothers medicals publishers.2019.
20. Elizabeth B ,Andrews Nicholas moore mann's pharmacovigilance 3rd edition wily Blackwell 2024.
21. Borton cobert ncobert,s manual pg drug safety and pharmacovigilance 2nd edition jones and b arlett learning 2022.
22. Wood L, Martinez C. The general practice research database: role in pharmacovigilance. Drug Saf 2004;27:871–81.
23. Norén GN, Bate A, Hopstadius J, Star K, Edwards IR. Temporal pattern discovery for trends and transient effects: its application to patient records. In: Proceeding of the 14th ACM SIGKDD International Conference on Knowledge Discovery and Data Mining, 24–27 August 2008, Las Vegas, Nevada, USA.
24. Hocine MN, Musonda P, Andrews NJ, Farrington C. Sequential case series analysis for pharmacovigilance. J R Stat Soc Ser A (Statistics in Society) 2009; 172:213–36. 10.1111/j.1467-985X.2008.00555.x
25. Baim DS, Mehran R, Kereiakes DJ, et al. Postmarket surveillance for drug-eluting coronary stents: a comprehensive approach. Circulation. 2006 Feb 14; 113(6):891–7.
26. U.S. Food and Drug Administration. Medical Device Reporting. [August 15, 2012].
27. Gross TP, Witten CM, Uldriks C, et al. A view from the US Food and Drug Administration. In: Frank E, Johnson KSV, editors. The Bionic Human: Health Promotion for People with Implanted Prosthetic Devices. Vol. 5. Totowa, New Jersey: Humana Press, Inc.; 2006. pp. 61–87.
28. Current Challenges in Pharmacovigilance: Pragmatic Approaches (Report of CIOMS Working V), Geneva 2001
29. Rules Governing Medicinal Products in the European Union, Volume 9, Pharmacovigilance: Medicinal Products for Human Use, 2001 http://pharmacos.eudra.org/F2/eudralex/vol-9/home.htm
30. Safety Reporting Requirements for Human Drug and Biological Products, Proposed Rule, Food and Drug Administration, March 2003 5. Notification No 421 on Enforcement of the Law Revising Partially the Pharmaceutical Affairs Law, the Director General, Pharmaceutical Affairs Bureau, Ministry of Health and Welfare, March 1997
31. Current Challenges in Pharmacovigilance: Pragmatic Approaches (Report of CIOMS Working V) Rules Governing Medicinal Products in the European Union, Volume 9, PHARMACOVIGILANCE: Medicinal Products for Human Use,
32. Guidance for Industry: Postmarketing Safety Reporting for Human Drug and Biological Products Including Vaccines, Food and Drug Administration, (draft) Safety Reporting equirements for Human Drug and Biological Products, Proposed Rule, and Drug Food Administration,
33. Notification No 421 on Enforcement of the Law Revising Partially the Pharmaceutical Affairs Law, the Director General, Pharmaceutical Affairs Bureau, Ministry of Health and Welfare,
34. Vlahović-Palčevski V, Mentzer D. Postmarketing surveillance. In: Seyberth H, Rane A, Schwab M. (eds) Pediatric clinical pharmacology. Berlin: Springer-Verlag, 2011, pp.339–351.
35. Hartzema AG, Porta MS, Tilson HH, et al. Adverse drug events: identification and attribution. Drug Intell Clin Pharm 1987; 21: 915–920.
36. Zhang X, Zhang Y, Ye X, et al. Overview of phase IV clinical trials for postmarket drug safety surveillance: a status report from the ClinicalTrials.gov registry. BMJ Open 2016; 6: e010643.
37. Faillie JL, Montastruc F, Montastruc JL, et al. Pharmacoepidemiology and its input to pharmacovigilance. Therapie 2016; 71: 211–216.
38. Lafond J. Pharmacovigilance implemented by patients: a necessity in the 21st century. Therapie 2016; 71: 245–247.
39. 39. Sharrar RG, Dieck GS. Monitoring product safety in the postmarketing environment. Ther Adv Drug Saf 2013; 4: 211–219.
40. Varallo FR, Planeta CS, Mastroianni PD. Effectiveness of pharmacovigilance: multifaceted educational intervention related to the knowledge, skills and attitudes of multidisciplinary hospital staff. Clinics 2017; 72: 51–57.
41. Pain J, Levacher J, Quinqunel A, et al. Analysis of Twitter data for postmarketing surveillance in pharmacovigilance. In: Proceedings of the 2nd workshop on noisy user-generated text, Osaka, Japan, 2016, pp.94–101.
42. Bahri P, Tsintis P. Pharmacovigilance-related topics at the level of the international conference on harmonisation. In: Mann RD, Andrews EB. (eds) Pharmacovigilance 2nd ed. Chichester: John Wiley & Sons, 2007:51–62.
43. Uppsala Monitoring Centre. Annual report: July 2018–June 2019,.
44. Goldman SA. Limitations and strengths of spontaneous reports data. Clin Ther 1998; 20(Suppl. C): C40–C44.
45. AlShammari TM, Almoslem MJ. Knowledge, attitudes & practices of healthcare professionals in hospitals towards the reporting of adverse drug reactions in Saudi Arabia: a multi-centre cross sectional study. Saudi Pharm J 2018; 26: 925–931.
46. Pham D, Le BK, Ho TB, et al. System pharmacology: application of network theory in predicting potential adverse drug reaction based on gene expression data. In: 2016 IEEE RIVF international conference on computing & communication technologies, research, innovation, and vision for the future (RIVF), 7 November 2016, pp.241–246. Hanoi, Vietnam: IEEE. [Goo
47. Krebs K, Milani L. Translating pharmacogenomics into clinical decisions: do not let the perfect be the enemy of the good. Hum Genomics 2019; 13: 39.
48. Alanazi H, Abdullah A, Qureshi K. A critical review for developing accurate and dynamic predictive models using machine learning methods in medicine and health care. J Med Syst 2017; 41: 69.