WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Pharmacovigilance: Future Challenges and Opportunities

[1]Rohit Sushil Bairagi, [2]Snehal Ashok Naik, [3]Sakshi Vasant Parhad

[1,2,3]Anuradha College of Pharmacy, Chikhli, Dist–Buldana (MS) India 443201

ABSTRACT

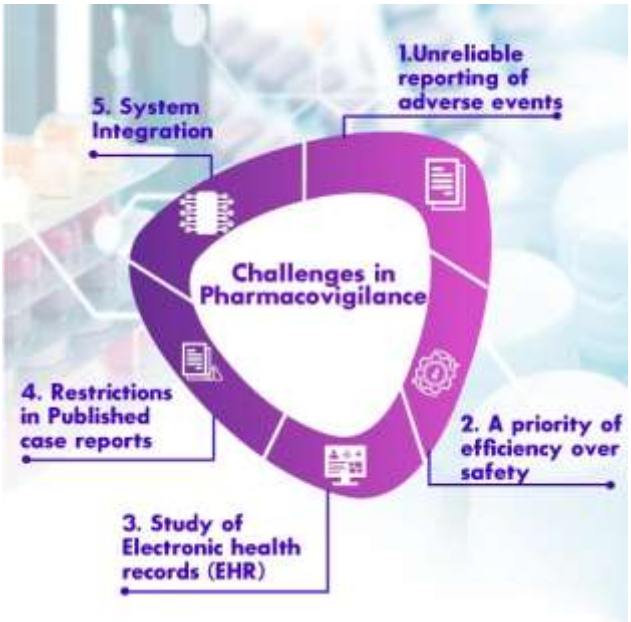
Medicines and vaccines have transform the prevention and treatment of disease. In addition of the benefits, medicinal product may also have side effects, some of which may be undiserable or unexpected. Pharmacovigilance is the science and activity relating to the detection , assessment , understanding and prevention of adverse effect of any medicine/vaccine related problem. All medicines and vaccines undergo rigious testing for safety and efficacy through clinical trials before they are authorized for use. However, the clinical trial process involves studying these products in a relatively small number of selected individuals for a short period of time.

Keywords: pharmacovigilance, pharmacoepidemiology, real-world data, drug safety, regulatory science

Introduction:

Pharmacovigilance is an important and integral part of clinical research. 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, 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 displine of pharmacovigilance have taken place in the western countries not much has been achieved in India. There is an immense need to understand the importance of pharmacovigilance and how it impacts the life cycle of the product. This will enable integration of good pharmacovigilance practice in the process and procedures to help ensure regulatory compliance and enhance clinical trials safety and post marketing surveillance.

Further India is becoming a hub for clinical research activities due to its large population, high enrolment rate and low cost. Moreover, the lag period when a drug is placed for the first time on the market in USA, Europe, and Japan or somewhere in the world and its subsequent availability in India has decreased considerably. As a result, for such drugs the long term safety data is not available and the time of their marketing in India. This is clear by the fact that all the high profile drugs that have been recently withdrawn were available in Indian market. In such cases, the Indian regulatory agencies cannot count on the experience of other market to assess benefit risk balance of a drug



Historical Perspective of WHO: Drug Safety Monitoring

In 2002, more than 65 countries have their own pharmacovigilance centers. Membership of the WHO for International Drug Monitoring is coordinated by the WHO Collaborating Centre for International Drug Monitoring, known as the Uppsala Monitoring Centre (UMC). Pharmacovigilance is now firmly based on sound scientific principles and is integral to effective clinical practice. The discipline needs to develop further to meet public expectations and the demands of modern public health. The Sixteenth World Health Assembly adopted a resolution (WHA 16.36)[5] that reaffirmed the need for early action in regard to rapid dissemination of information on adverse drug reactions and led later to creation of the WHO Pilot Research Project for International Drug Monitoring. The purpose of this was to develop a system, applicable internationally, for detecting previously unknown or poorly understood adverse effects of medicines.

The Erice Declaration:

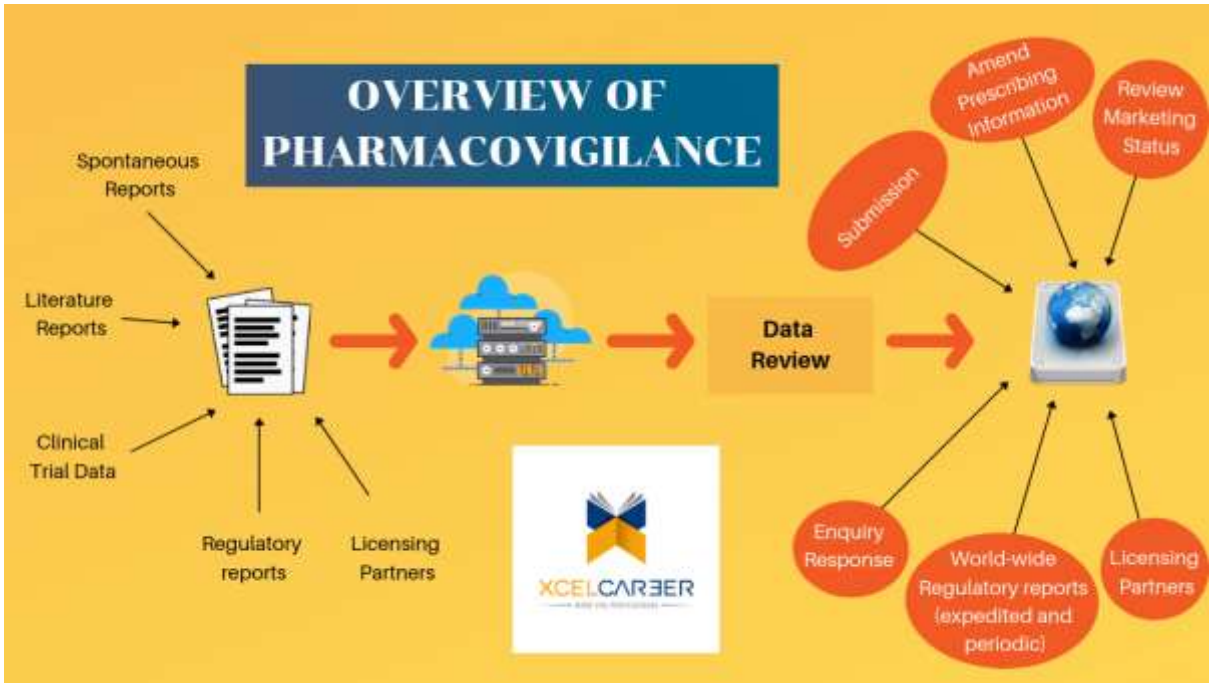
The Erice Declaration represented significant progress in the light of these changes for pharmacovigilance The Declaration challenges all the players like public health administration, health professionals, the pharmaceutical industry, government, drug regulators, the media, consumers to strive towards the highest ethical, professional and scientific standards in protecting and promoting safe use of medicines. The Declaration urges governments and others involved in determining policies relating to the benefit, harm, effectiveness and risk of medicines to account for what they communicate to the public and patients.

There are several challenges facing pharmacovigilance programmes in achieving the aspirations of the Erice Declaration. Like The difficulties and risks in communicating conflicting or contentious messages to the public. For instance, during the course of immunization programmes, communication of new safety concerns associated with the vaccine(s) or with programmatic errors may result in a dramatic fall in coverage. Nonetheless, an approach of secrecy in such circumstances is likely to erode public trust and confidence, and it fails to respect the rights of the public to participate in decision-making. Not only do facts and figures need to be shared with the public, but also the process by which the data is assessed and how decisions are made should be shared openly. Another challenge is Communication between national drug regulatory authorities and national pharmacovigilance centers needs to be improved so that regulatory decisions with possible international implications are rapidly communicated to regulators, to avoid widespread public concern or panic.

Artificial Intelligence in Pharmacovigilance

The availability of healthcare data has been tremendously increasing over the last years and will further increase in the near future thanks to massive marketing of digital tools collecting patient-derived data. Huge amounts of electronic data present an opportunity to apply artificial intelligence (AI) techniques to improve drug safety assessment. Information extraction, using natural language processing (NLP) techniques and text mining to gather relevant insights from available, largely unstructured sources, has been gaining importance within the field of clinical research. As regards pharmacovigilance, text mining and NLP methods can be very useful to gather information on adverse drug reactions (ADRs) and drug-drug interactions from various textual sources, supporting researchers and clinicians in monitoring drug safety . Indeed, both public and private entities are currently trying to develop AI tools that can allow to automatically process ADRs (Basile et al., 2019). Artificial intelligence and machine learning may also be useful in pharmacovigilance for

1) the automatic execution of tasks associated with case report entry and processing.
2) the identification of clusters of adverse events representing symptoms of syndromes.



3) the conduction of pharmacoepidemiological studies.
4) data linkage, through the conduction of probabilistic matching within datasets.
5) the prediction and prevention of adverse events through specific models using real-world data (Bate and Hobbiger, 2021)

The advanced therapy of medicinal products

Advanced therapy medicinal products (ATMPs) are medicines for human use that are based on genes, cells or tissue engineering (European Medicines Agency, 2021). ATMPs provide new opportunities to restore, correct or modify physiological functions or make a medical diagnosis. Due to their high innovativeness, these medicines usually benefit from accelerated assessment and accelerated approval pathways, thus highlighting the need to generate post-marketing evidence about their benefit-risk profile. However, uncertainties concerning the safety profile of new ATMPs cannot be ascribed only to regulatory pathways. As these medicines often target rare diseases, pre-marketing evidence is generally weak because of inherent limitations of clinical trials due to small number of recruited patients, use of surrogate endpoints and single-arm design . Therefore, post-marketing studies play a key role in generating long term evidence about the safety of these medicines and to fill the knowledge gap of pre-marketing studies. The detection of safety issues should start early and continue throughout the development of the ATMP in order to prevent or minimize the risk when possible. In some cases, the use of ATMPs is expected to be a once in a life-time treatment, therefore the sustainability of efficacy over time is a question that can only be answered by long-term efficacy follow-up. The objectives of the safety and efficacy follow-up will depend on the characteristics of the product (European Medicines Agency, 2018a). In the case of chimeric antigenic therapies (CAR-T) routine risk minimization measures have to be supplemented with additional risk minimization measures under relevant important risks (e.g., cytokine release syndrome, infections and serious neurological adverse reactions)

Pharmacovigilance Safety Monitoring

Pharmacovigilance is majorly referred to as drug safety. it's a main integral a part of clinical research. Throughout the merchandise life cycle clinical trials safety and post marketing pharmacovigilance plays a critical role. The word pharmacovigilance springs from two words one Parmakon may be a Greek word which suggests “drug” and another vigilare may be a Latin word which suggests to stay awake or to stay watch.” Pharmacovigilance is

"defined because the pharmacological science concerning the detection, understanding, assessment and prevention of adverse effects, particularly future and short term adverse effects of medicines".

According to WHO Pharmacovigilance (PV) is that the pharmacological science relating to the detection, evaluation, understanding and prevention of adverse effects, especially long term and short term side effects of medicines.

Aim of Pharmacovigilance

Improve patient care and safety in relation to the use of medicines and all medical and Para medical interventions.

- Research the efficacy of drug and by monitoring the adverse effects of drugs right from the lab to the pharmacy and then on for many years
- Pharmacovigilance keeps track of any drastic effects of drugs.
- Improve public health and safety in relation to the use of medicines.
- Contribute to the assessment of benefit, harm, effectiveness and risk of medicines, encouraging their safe, rational and more effective (including cost-effective) use.
- Promote understanding, education and clinical training in pharmacovigilance and its effective communication to the public.

The processes involved in the clinical development of medicines. Once put onto the market, a medicine leaves the secure and protected scientific environment of clinical trials and is legally set free for consumption by the general population. At this point, most medicines will only have been tested for short-term safety and efficacy on a limited number of carefully selected individuals. In some cases as few as 500 subjects, and rarely more than 5000, will have received the product prior to its release.

More information is generally needed about use in specific population groups, notably children, pregnant women and the elderly, and about the efficacy and safety of chronic use, especially in combination with other medicines.[6] Experience has shown that many adverse effects, interactions (i.e. with foods or other medicines) and risk factors come to light only during the years after the release of a medicine.

Table: Classicial example of serious and unexpected adverse reaction

MEDICINE	**ADVERSE REACTION**
Reserpine	Depression
Aminophenazone (amidopyrine)	Agranulocytosis
Practolol	Sclerosing peritonitis
Fluothane	Hepatocellular hepatatis
Chloramphenicol	Aplastic anaemia
Oral contraceptives	Thromboembolism
Statins	Rhabdomyolysis

Need of Pharmacovigilance

Reason 1: Humanitarian concern - Insufficient evidence of safety from clinical trials Animal experiments Phase 1-3 studies prior to marketing authorization

Reason 2: Medicines are supposed to save lives Dying from a disease is sometimes unavoidable; dying from a medicine is unacceptable.

Reason 3: ADR-related cost to the country exceeds the cost of the medications themselves.

Reason 4: Promoting rational use of medicines and adherence.

Reason 5: Ensuring public confidence

Reason 6: Ethics, to know of something that is harmful to another person who does not know, and not telling, is unethical.

"Role of pharmacovigilance" in medicines regulation"

Robust regulatory arrangements provide the foundation for a national method of medicine safety, and for public confidence in medicines. To be effective the remit of drug regulatory authorities needs to go further than the approval of new medicines, to encompass a wider range of issues relating to the safety of medicines, namely:

- Clinical trials
- The safety of complementary and traditional medicines, vaccines and biological medicines
- The development of lines of communication between all parties which have an interest in medicine safety, ensuring that they are able to function efficiently and ethically, particularly at times of crisis.

In order to achieve their respective objectives pharmacovigilance programmes and drug regulatory authorities must be mutually supporting. On the one hand, pharmacovigilance programmes need to maintain strong links with the drug regulatory authorities to ensure that the latter are well briefed on safety issues in everyday clinical practice, whether these issues are relevant to future regulatory action or to concerns that emerge in the public domain. On the other, regulators need to understand the specialized and pivotal role that pharmacovigilance plays in ensuring the ongoing safety of medicinal products.

Conclusion

Pharmacovigilance looks at all available information to assess the safety profile of a drug. Pharmacovigilance should also take the benefit of the drug in account. Pharmacovigilance required for systematically identifying and correlating drugs and side effects and taking corrective actions.

References

1. Pipasha, B. , Arun , K.B.„Setting standards for proactive pharmacovigilance in India : 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. Zhengwu Lu.„ information technology in pharmacovigilance : Benefits , challenges , and future directions from industry perspectives" , Drug, Health Care and patient safety, 2009; 1: 35-45.
5. WHO, Pharmacovigilance: ensuring the safe use of medicines, Geneva: WHO 2004.
6. WHO, Pharmacovigilance: ensuring the safe use of medicines, Geneva: WHO 2004.
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, Safety of medicines in public health programmes : pharmacovigilance an essential tool, WHO, 2006.
10. Yves snoeckx, m.pharm. : Pharmacovigilance for pharmacist, Johnson &Johnson 2006
11. Barton, C., Silvey, J. „the internet and drug safety: What are the implications for pharmacovigilance", Drug Safety 1999; 20(2): 95-107.
12. Don chin, Y., Seagull, FJ. „The hostile environment of the intensive care unit", curro pin critcare 2002; 8: 316-320.
13. Department of CDSCO, Ministry of Health and Family Welfare, Government of India: Protocol for National pharmacovigilance program, November 2004.
14. Edwards, A. ,Elwyn,G. „How should effectiveness of risk communication to aid patients decision be judged", A review literature. Medical Decision Makang 1999; 19(4): 128-434.
15. Edwards, IR. „The accelerating need for pharmacovigilance", Journal of the Royal college of Physicians, 200; 34: 48-51