INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACY AND CHEMISTRY

Available online at www.ijrpc.com

Review Article

PHARMACOVIGILANCE: AN OVERVIEW

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ABSTRACT

Pharmacovigilance is an important and integral part of clinical research. 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. Here the main focus on the aims and role of pharmacovigilance in medicines regulation and their Partners. This article describes and discusses the National programme of pharmacovigilance and centre in India. There role in collecting the reports ADRs of medicines. Further effectiveness and risk assessments of therapies are been discussed. The important role played by health care professional, pharmaceutical industries, media, and programmes carried by WHO. Finally the conclusion describes the major challenges and achievements for the future pharmacovigilance safety and toxicity is not so critical if botanicals are used in traditional forms (Harborne., 1998).

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, 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.

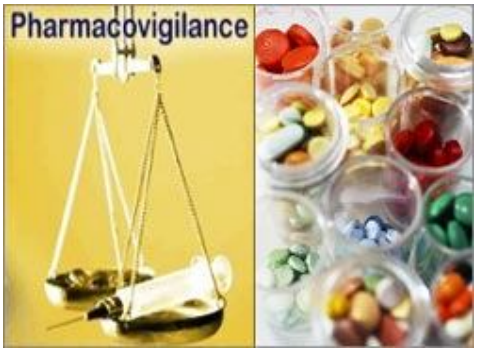
While major advancements of displine of pharmacovigilance have taken place in the western countries not much has been achieved in India. There is an immense need to understand the importance of pharmacovigilance and how it impacts the life cycle of the product. This will enable integration of good pharmacovigilance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

Pharmacovigilance is not new to India and has infact been going on from 1998[2]. When India decided to join the uppasla centre 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.

Further India is becoming a hub for clinical research activities due to its large population, high enrolment rate and low cost [3]. 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.

There by stressing the importance of developing their own adequately designed pharmacovigilance system in India. For an effective pharmacovigilance system to be functional and efficient, all the stake holders need to be alert and attentive throughout the life cycle of a medicinal product in the market .The office of the Drugs Controller General of India(DCGI) has been making sincere attempts for the implementation the National Pharmacovigilance programme (NPP) in India. To full fill the pharmacovigilance obligations for its marketed products, as per regulations, a generic company in India is mainly to carry out the following activities. Collection monitoring, and reporting of spontaneous adverse reactions, including expedited reporting of serious unexpected adverse reactions and preparations. Pharmacovigilance help to prevent adverse drug effects: Medical science has grown in leaps and bounds since the days of Hippocrates. Modern day pharmaceutical drugs are really life saves. They have increased life expectancy and improved the quality of life for millions of people. But there is the other side of the coin as well; these drugs sometimes have very adverse effects that can even be life threating.



WHAT IS PHARMACOVIGILANCE?

There is a need to monitor the effects of drugs before and after it's successfully tested and launched in the market. Pharmacovigilance involves monitoring and assessing the quality

of drugs, detection and preventing of any adverse effects of drugs. Pharmacovigilance involves evaluating information provided by health care providers, pharmaceutical companies and patients in order to understand the risks and benefits involved with a particular drug. Pharmaceutical companies spend millions of dollars and a considerably long time in developing new drugs.

They again spend a lot of money in conducting clinical trials before the drugs are approved and launched in the market. It is recognized that information technology (IT) has entered and transformed the world of health care and clinical medicine in which the work of doctors and the care of patients proceed with higher quality, efficiency and lower costs. It is also no secret that IT has merged in to clinical safety practice and sparks the creation of worldwide pharmacovigilance systems for safety signal detection.

The IT transformative force and health it adoption have fundamentally changed the conduct of clinical research, practice of medicines, and medicinal safety monitoring. In today's world, pharmacovigilance pushes new boundaries and it is no longer sufficient to simply report adverse events along with efficacy and quality requirements.

Regulators are demanding proactive surveillance programs that include comprehensive risk management plans and signal detection /analysis throughout a clinical products' life cycle.

Ø This addresses what exactly is pharmacovigilance?

Ø What do we know of its benefits and risks?

Ø What challenges are out there preventing its wide spread usage?

Ø And what does the future hold for pharmacovigilance in worldwide medicine?

It is now generally accepted that part of the process of evaluating drug safety needs to happen in the post marketing phases through judgment as to whether and how this might happen lies with the regulators. The stronger the national systems of pharmacovigilance and adverse drug reaction (ADR) reporting, the more likely reasonable regulatory decisions will be made for the early release of new drugs with the promise of therapeutic advances. Care full safety monitoring is not restricted, however to new drugs or to significant therapeutic advances. It has a critical role to play in the introduction of generic medicines, and in review of the safety profile of older medicines already available as well, where new safety issues may have arises. While spontaneous reporting remains a corner stone of pharmacovigilance in the regulatory environment, and is indispensable for signal detection, the need for more active surveillance has also become increasingly clear. Without information on utilization and on the extent of consumption, spontaneous reports are unable to determine the frequency of an ADR attribution to a product or its safety in relation to a comparator.

More systematic and robust epidemiological methods that take in to account the limitations of spontaneous reporting or post marketing studies are required to address these key safety questions. They need to be incorporated in to post marketing surveillance programs. This includes the use of pharmaco epidemiologic studies.

These activities are under taken with the goal of identifying adverse events and understanding, to the extent possible, their nature, frequency, and potential risk factor. Pharmacovigilance in principle involves the identification and evaluation of safety signals. Safety signal refer to a concern about an excess of adverse events compared to what would be expected to be associated with products use.

Signals can arise from post marketing data and other sources, such as pre clinical data and events associated with other products in the same pharmacological class[4] . Pharmacovigilance is particularly concerned with adverse drug reactions. Many other issues are also relevant to pharmacovigilance science are substandard medicines, medication errors, lack of efficacy reports, use of medicines for indications that are not approved and for which there is inadequate scientific basis, case reports of acute and chronic poisoning, assessment of drug related mortality, abuse and misuse of medicines, adverse interactions of medicines with chemicals, other medicines and food.

AIMS OF PHARMACOVIGILANCE

Ø Improve patient care and safety in relation to the use of medicines and all medical and Para medical interventions[5].

Ø 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.

Ø Pharmacovigilance keeps track of any drastic effects of drugs.

Ø Improve public health and safety in relation to the use of medicines.

Ø Contribute to the assessment of benefit, harm, effectiveness and risk of medicines, encouraging their safe, rational and more effective (including cost-effective) use.

Ø 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.

For good reason, therefore, it is essential that new and medically still evolving treatments are monitored for their effectiveness and safety under real-life conditions post 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

"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:

Ø Clinical trials;

Ø The safety of complementary and traditional medicines, vaccines and biological medicines;

Ø 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.

NATIONAL PROGRAMME OF PHARMACOVIGILANCE

Before a product is marketed, experience of its safety and efficacy is limited to its use in clinical trials, which are not reflective of practice conditions as they are limited by the patient numbers and duration of trial as well as by the highly controlled conditions in which Clinical Trials are conducted. The conditions under which patients are studied during the pre-marketing phase do not necessarily reflect the way the medicine will be used in the hospital or in general practice once it is marketed.

Information about rare but serious adverse drug reactions, chronic toxicity, use in special groups (e.g. pregnant women, children, elderly) and drug interactions is often incomplete or not available. Certain adverse drug reactions may not be detected until a very large number of people have received the medicine.

Pharmacovigilance is therefore one of the important post-marketing tools in ensuring the safety of pharmaceutical and related health products.

- Assessing the risks and benefits of medicines in order to determine what action, if any, is necessary to improve their safe use
- Providing information to users to optimise safe and effective use of medicines
- Monitoring the impact of any action taken

RESOURCES FOR PHARMACOVIGILANCE CENTRES

The following books shall be provided to various centres as identified by the NPAC: Current editions of:

Ø Meyler's Side Effects
Ø AHFS Drug Information hand book
Ø Martindale/online
Ø Davies Text Book of ADR
Ø Physician's Desk reference
Ø British National Formulary

THE NATIONAL PHARMACOVIGILANCE CENTRES

At present, post-marketing surveillance of medicines is mainly co-ordinated by national pharmacovigilance centres. In collaboration withthe Uppsala Monitoring Centre (UMC) the National Centres have achieved a great deal in:

Ø Collecting and analysing case reports of ADRs
Ø Distinguishing signals from background 'noise'
Ø Making regulatory decisions based on strengthened signals
Ø Alerting prescribers, manufacturers and the public to new risks of adverse reactions.
Ø The number of National Centres participating in the WHO International Drug Monitoring Programme has increased from 10 in 1968 when the Programme started to 67 in 2002. The centres vary considerably in size, resources, support structure, and scope of activities. Collecting spontaneous reports of suspected ADRs remains their core activity.

National pharmacovigilance centres are responsible for:

Ø Promoting the reporting of adverse reactions;
Ø Collecting case reports of adverse reactions;
Ø Clinically evaluating case reports;
Ø Collating, analyzing and evaluating patterns of adverse reactions;
Ø Distinguishing signals of adverse reactions from "noise";
Ø Recommending or taking regulatory action in response to ?ndings supported by good evidence;
Ø Initiating studies to investigate signi?cant suspect reactions;
Ø Alerting prescribers, manufacturers and the public to new risks of adverse reactions; and
Ø Sharing their reports with the WHO Programme for International Drug Monitoring.

National centres have played a signi?cant role in increasing public awareness of issues relevant to the safety of medicines. As a result, in some countries, pharmacovigilance is increasingly being seen as much more than a regulatory activity as it also has a major part to play in clinical practice and the development of public health policy. This development is partly attributable to the fact that many national and regional centres are housed within hospitals, medical schools or poison and medicine information centres and is in collaboration with a Medicines Regulatory Authority (MRA). The scope of activities of national centres has expanded to include communication of information about the bene?ts, harm and effectiveness of medicines to practitioners, patients and the public.

The Central Drugs Standard Control Organization (CDSCO) is initiating a country-wide pharmacovigilance programme under the aegis of DGHS, Ministry of Health & Family Welfare, and Government of India. The programme shall be coordinated by the National Pharmacovigilance Centre at CDSCO. The National Centre will operate under the supervision of the National Pharmacovigilance Advisory Committee to recommend procedures and guidelines for regulatory interventions.

What to report

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

The programme particularly solicits reports of:

Ø All adverse events suspected to have been caused by new drugs and 'Drugs of current interest' (List to be published by CDSCO from time to time)
Ø All suspected drug interactions

Ø Reactions to any other drugs which are suspected of significantly affecting a patient's management,
Ø including reactions suspected of causing:
Ø Death
Ø Life-threatening (real risk of dying)
Ø Hospitalisation (initial or prolonged)
Ø Disability (significant, persistent or permanent)
Ø Congenital anomaly
Ø Required intervention to prevent permanent impairment or damage

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

Where to report?
After completion the form shall be returned/forwarded to the same pharmacovigilance Centre from where it was received. Reporting can be done to any one of the country vide pharmacovigilance Centres nearest to the reporter. (Complete list of pharmacovigilance Centres is available at www.cdsco.nic.in) In case of doubt the form may be sent to the national pharmacovigilanc **Centre at:** Central Drugs Standard Control Organisation, New Delhi.

What happens to the information submitted?
The information in the form shall be handled in strict confidence. Peripheral Pharmacovigilance Centres shall forward the form to the respective Regional Pharmacovigilance Centres who will carry out the causality analysis. This information shall be forwarded to the Zonal Pharmacovigilance Centres. The data will be statistically analysed and forwarded to the global Pharmacovigilance Database managed by WHO Uppsala Monitoring Centre in Sweden. The final report based on the analysed data will be periodically reviewed by the National Pharmacovigilance Advisory Committee constituted by the Ministry of Health and Family Welfare. The Committee is entrusted with the responsibility to review data and suggest any regulatory interventions that may be required with respect to the drug/drugs or class of drugs.

CONCLUSION

Pharmacovigilance remains a dynamic clinical and scientific discipline. It continues to play a crucial role in meeting the challenges posed by the ever increasing range and potency of medicines, all of vitamins unpredictable potential for harm. When adverse effects and toxicity do appear especially when previously unknown it is essential that these are reported, analysed and their significance communicated effectively to an audience that has the knowledge to interpret the information. Which carry an inevitable and some-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:
Ø Serve public health, and to foster a sense of trust among patients in the medicines they use that would extend to confidence in the health service in general;
Ø Ensure that risks in drug use are anticipated and managed;
Ø Provide regulators with the necessary information to amend the recommendations on the use of the medicines;
Ø Improve communication between the health professionals and the public;
Ø Educate health professionals to understand the effectiveness/risk of medicines that they prescribe. This is the important role of pharmacovigilance.

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