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REVIEW ARTICLE

CURRENT SCENARIO OF PHARMACOVIGILANCE IN INDIA

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ABSTRACT

Even though Pharmacovigilance is still in its infancy in India, it is not new to India and still there exists very limited knowledge about the discipline. While major advancements of the discipline of pharmacovigilance have taken place in the Western countries, not much has been achieved in India. However, with more and more clinical trials and other clinical research activities being conducted 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 processes and procedures to help ensure regulatory compliance and enhance clinical trial safety and postmarketing surveillance.

Key Words: Pharmacovigilance, Post Marketing Surveillance, Adverse Drug Reactions, National Pharmacovigilance Program.

INTRODUCTION:

WHO defines Pharmacovigilance as the Science and activities relating to the detection, assessment, understanding and prevention of adverse drug reactions.[1] Generally speaking, Pharmacovigilance is the science of collecting, monitoring, researching, assessing and evaluating information from healthcare providers and patients on the adverse effects of medications, biological products, herbalism and traditional medications with a view to identifying new information about hazards associated with medicines preventing harm to patients.[2,3] It is the process of identifying and responding to the issues of drug safety through effects usually adverse.

The way drugs are being monitored has changed, both internationally as well as on the national level. Both clinical trials safety and postmarketing pharmacovigilance are critical throughout the product life cycle.[4]

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. With a number of recent high-profile drug withdrawals, the pharmaceutical industry and regulatory agencies have raised the bar. Early detection of signals from both clinical trials and postmarketing surveillance studies have now been adapted by major pharmaceutical companies in order to identify the risks associated with the medicinal product and effectively managing the risks by applying robust risk management plans throughout the life cycle of the product. The Adverse Drug Reaction reporting programs encourage ADR surveillance, promote the reporting of ADRs and stimulate the education of health professionals regarding potential ADRs.[5] Spontaneous reporting program, a common method of drug surveillance is capable of recognizing ADRs in the daily medical practice, even though underreporting and absence of information on number of people actually exposed to the drug are its disadvantages. Unfortunately, in spite of presence of five well organized centres for drug monitoring in the country, the numbers of reports sent annually are dismal.

Need For Pharmacovigilance:[6]

To be eternally vigilant to ensure that medicines which are developed for the treatment of diseases, actually do not do more harm than good, is one of the pre-requisite for the progress of medicine.

The science and systems used for systemically identifying and correlating drugs and side effects and taking corrective actions fall under the discipline of pharmacovigilance.

Major aims of Pharmacovigilance:[7]

1. improve public health and safety in relation to the use of medicines and all medical and paramedical interventions;

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2. improve public health and safety in relation to the use of medicines;
3. contribute to the assessment of benefit, harm, effectiveness and risk of medicines, encouraging their safe, rational and more effective (including cost-effectiveness) use;
4. promote understanding, education and clinical training in pharmacovigilance and its effective communication to the public;
5. detect problems related to the use of medicines and communicate the findings in a timely manner.

The ultimate goals of pharmacovigilance:

- The rational and safe use of medical drugs.
- The assessment and communication of the risks and benefits of drugs on the market.
- Educating and informing of patients.

National Pharmacovigilance Program:

Even though pharmacovigilance is still in its infancy, it is not new to India. It was not until 1986 that a formal adverse drug reaction (ADR) monitoring system consisting of 12 regional centers, each covering a population of 50 million, was proposed for India. However, nothing much happened until a decade later when in 1998, India joined the WHO Adverse Drug Reaction Monitoring Programme based in Uppsala, Sweden.[8]

The program has three-tier structure- 2 zonal centers 5 regional centers and various peripheral centers. Pharmacovigilance centers pursue four objectives: to detect ADRs, to evaluate them, to study them, and to inform prescribing physicians.

The Central Drugs Standard Control Organization (CDSCO) launched the National Pharmacovigilance Program in November 2004 under the aegis of Directorate General of Health Services, Union Ministry of Health and Family Welfare. The basic purpose of this program is to collate, analyze and archive adverse drug reaction data for making regulatory decisions regarding drugs marketed in India.
The National Pharmacovigilance Programme will have the following goals:
1. To foster a culture of notification.
2. To engage several healthcare professionals and NGOs in the drug monitoring and information dissemination processes.
3. To achieve such operational efficiencies that would make Indian National Pharmacovigilance Programme a benchmark for global drug monitoring endeavours.
The programme shall be coordinated by the National Pharmacovigilance Centre at CDSCO, New Delhi. The National Centre will operate under the supervision of the National Pharmacovigilance Advisory Committee to recommend procedures and guidelines for regulatory interventions.

Specific objectives of the Programme:

- To create an ADR database for the Indian population.
- To create awareness of ADR monitoring among people.
- To ensure optimum safety of drug products in Indian market.
- To create infrastructure for ongoing regulatory review of PSURs (periodic safety update reports)

Various Activities of National Pharmacovigilance Program:

The national pharmacovigilance center at CDSCO will undertake the following activities:
1) Shall monitor the adverse drug reactions of medicines in order to identify previously unexpected adverse drug reactions. This information will then be keyed into the ADR database for use in aggregate analysis. These reports shall also be submitted to the WHO International Drug Monitoring Programme for international collaboration on drug safety.
2) Shall review Periodic Safety Update Reports (PSURs) submitted by pharmaceutical companies.
3) Shall maintain contacts with international regulatory bodies working in pharmacovigilance and exchange information on drug safety.
4) Shall assess the regulatory information relating to safety in order to determine what action, if necessary, needs to be taken to improve safe use.
Based on the available data, the Advisory Committee shall make recommendations on product label amendments, product withdrawals and suspension.

The programme recommends mandatory reporting of:

- 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).
- ALL suspected drug interactions.
- Reactions to any other drugs which are suspected of significantly affecting a patient's management, including reactions suspected of causing.

The activities with which various centers are endorsed with include but are not limited to:
Zonal centers coordinate the nationwide program and provides for the facilities like a PC with internet facility, access to fax, telecom, etc. [AIIMS for North and East and KEM-Mumbai for South and West]. Other activities include:

- collate the data (approx. 1000-1200 forms) received from RPCs.
- verify / validate the causality analysis.
- prepare MIS reports for NPC in a specified format.
- pass on the final data to WHO Uppsala Centre for their global data pool.
- publish a periodic newsletter.

Regional Centers will undertake the following activities:

- collate and scrutinize the data received.
- perform the causality analysis of all 120 to 150 forms received every month.
- submit a monthly report – prepared in a specific form to be forwarded to National Pharmacovigilance Centre (NPC) every month.
- report any alarming or critical ADRs to NPC along with supporting evidence.

Peripheral centers (ideally medical institutions in each state and Union territory) to record at least 30 events each month (statistically speaking 30 events in about 1500 patients who visit each month would be quite easy to record). Completed event forms shall be forwarded to the concerned regional centers at the end of each month.

Major Challenges to the National Pharmacovigilance Program:

In spite of all these efforts, it would be dishonest on our part to say that all is well. The "spontaneous" part in reporting by the prescribers is somewhat lacking. This is one of the important objectives of the NPP and hence also of our Center. There could be many reasons for this but primarily it seems to be an apathy and lack of awareness among prescribers. We have observed that the ADRs are reported spontaneously usually after a reminder or following a scientific meeting or other awareness programs. However, they decrease over a period of time. This means that generating spontaneous reports requires a sustained effort. Currently, we have been achieving this goal only partially; a learning for us because it obviously means that more efforts are necessary in this direction.

The services provided to the center by the NPP, whether financial, academic, or other have been very useful. But if we are to evolve further, rather than just stagnate at collecting reports and submitting them to higher centers, we could look "upwards" for more. That could be in the form of scientific support, academic resources and training to the people involved. Additional infrastructure (personnel, a dedicated telephone line and internet connection) can also improve the scope and functioning of the center. It will certainly make us feel nice if we came to know that we are also a part of the global database.[8, 9]

In addition, India-based drug companies have increased their capacity to develop and launch new drugs through their own research efforts and this have heightened the importance of developing adequate internal pharmacovigilance standards to detect adverse drug events. Traditionally, pharmacovigilance was never done in India in Pharmaceutical companies, be it Indian or MNCs, so there is an immense shortage of knowledgeable people who will be able to advice the Drug Controller General of India on this matter, as pharmacovigilance is a very complex subject, interwined with regulations and complex systems. India is the fourth largest producer of pharmaceuticals in the world and is also emerging as a clinical trials hub. Many new drugs are being introduced in the country, so there is an immense need to improve the pharmacovigilance system to protect the Indian population from potential harm that may be caused by some of the new drugs.[10] the problem areas which have identified in India includes:

1. Lack of organization and funding of pharmacovigilance systems
2. Extreme shortage of qualified trained people to handle pharmacovigilance within the DCGI.
3. Information obtained to date in the zonal centers from various peripheral centers is often poor and not well analyzed because of insufficient research on ADR in India.
4. Understanding, knowledge and motivation by healthcare professionals is almost negligible.

Recommendations for the Future:

Experience has shown that for a country to be able to rely on its own pharmacovigilance programme a number of elements need to be in place. These are as follows:
1. A dedicated pharmacovigilance centre, independently funded (usually by the state), and staffed by a person or persons with expert knowledge of drug safety and of the evaluation of reports of adverse events;
2. Links, electronic and personal, between the pharmacovigilance centre and WHO, specifically with the Uppsala Monitoring Centre;
3. Close operational ties with the national MRA that fulfil the mutual needs of the MRA and the pharmacovigilance centre for the evaluation and continuous monitoring of the safety of medicines;
4. Access to comprehensive and unbiased drug information relevant to the medicines available in the country.

5. Involve professional organizations of healthcare providers to educate their members about the program and there by sustain their participation.
6. Making pharmacovigilance reporting mandatory and introducing pharmacovigilance inspections.
7. Employing trained scientific and medical assessors for pharmacovigilance to strengthen the DCGI office.
8. In addition to the CDSCO website, use newsletters and pamphlets to inform healthcare providers about the program's activities.
9. Recognize the contribution of notifiers and centers with consistent high quality performance through citation on the website and in the newsletter to help motivate everyone to report adverse events.
10. Creating a clinical trial and postmarketing database for serious ADRs and ADRs for signal detection and access to all relevant data from various stakeholders.
11. Education and training of medical students, pharmacists and nurses in the area of pharmacovigilance and building a network of pharmacovigilance and pharmacopeidemiologists in India.

CONCLUSIONS:

Though pharmacovigilance is still in its infancy in India, this is likely to expand in the times to come. This is because, as the newer and newer drugs hit the market, the need for pharmacovigilance grows more than ever before. India is now considered to be a hub for clinical research. The DCGI has shown its commitment to ensure safe use of drugs by establishing the National Pharmacovigilance Program. Pharmacovigilance is a complex process and robust systems are essential to undertake the activity. The foundation for building a robust pharmacovigilance system has already been done to some extent by the DCGI staff. However, the system needs to be refined with the help of pharmacovigilance experts in collaboration with information technology. Pharmaceutical companies will need to show both regulators and consumers that they are doing everything possible to assure drug safety, while finding more effective approaches to manage drug safety data. This will require the ability to pull and analyze data from adverse event reporting systems in conjunction with other internal company data or external data sources to respond to any ad hoc safety queries or issues from the regulators.

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