Print ISSN: 2319-2003 | Online ISSN: 2279-0780

IJBCP International Journal of Basic & Clinical Pharmacology

DOI: http://dx.doi.org/10.18203/2319-2003.ijbcp20184338

Review Article

Pharmacovigilance programme of India: revival of the renaissance

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Received: 10 September 2018
Accepted: 13 October 2018

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ABSTRACT

Adverse drug reactions (ADRs) are the fourth leading cause of morbidity in the world. In order to safeguard the health of the community, Pharmacovigilance Programme of India (PvPI) is implemented as the monitoring body by Indian Pharmacopoeia Commission (IPC). It is leading national authority. National Coordinating Centre (NCC) PvPI works as the World Health Organization (WHO) collaborating centre for pharmacovigilance. Adverse drug reactions are reported to NCC PvPI which are then directed towards WHO Uppsala Monitoring Centre (UMC) Sweden which is the global monitoring centre for worldwide data. Central Drugs Standard Control Organization (CDSCO) is the regulatory authority of India under the Ministry of Health and Family Welfare (MOHFW), Government of India. This article focusses on the various strands of pharmacovigilance at the healthcare professional and consumer level. It also discusses the pitfalls in the journey of pharmacovigilance thus helping in enhancing the quality of health safety. Even a minuscule contribution by a health care professional or a consumer can voluminously help in promotion of drug safety. Therefore, there is a need of inculcating the culture of adverse drug reaction reporting for the welfare of the vulnerable masses.

Keywords: ADRs, Adverse events, IPC, NCC, Pharmacovigilance

INTRODUCTION

Adverse drug reaction (ADR) is defined as any noxious change which is suspected to be due to a drug, occurs at doses normally used in man, requires treatment or decrease in dose or indicates caution in the future use of the same drug.[1]

ADR are the 5th most common cause of hospital death and 4th most common cause of morbidity in the world.3.7% of the patients are admitted in the hospital are due to ADR. Out of these, 1.8% are fatal.[2]

In a recent study by Patel TK et al, the incidence of ADRs that lead to hospitalization in Indian hospitals was 2.85% while that of ADRs developed in hospitalization was 6.34%.[3] The increasing burden of ADR in current scenario is responsible for increased morbidity and mortality which eventually affects patient safety. Here, pharmacovigilance plays a vital role in assessing and preventing the incidence of ADRs thus, contributing a step towards patient safety on a global scale.

PvPI is one such integral part of the safety program which analyses, facilitates corrective and preventive actions to help in minimizing the potential risks associated with the drug or blood and blood products or medical devices.

It also utilizes ADR data for signal generation and strengthening, monitoring and regulation of drugs by drug authority and manufacturers and education purpose.

REVIEW OF LITERATURE

Pharmacovigilance- memory down the lane

Pharmacovigilance was first introduced in the year 1961 with a publication of a letter which was a case report in the Lancet journal by McBride W, who first suspected the cause of phocomelia to be thalidomide, a drug used as an anti-emetic in pregnant women introduced in the market in 1957.[4] This was a milestone in the career of pharmacovigilance. Incidence of sulfanilamide in 1937 used in the treatment of streptococcal infections has been a quantum leap in the initiation of journey towards patient safety.[5] In this regard, WHO launched 'programme for international drug monitoring' in 1968 with a vision of compiling the global data on ADR. In 1998, India became a part of it which is managed by uppsala monitoring centre in Sweden. The MOHFW took initiative in starting a nationwide PvPI in year 2010 with All India Institute of Medical Sciences (AIIMS) as NCC with 22 regional adverse drug reaction monitoring centres (AMCs) across the country. The zonal centre for North is Ghaziabad; for East it is Kolkata; for South it is Chennai and for West it is Mumbai. Under the MOHFW, IPC is an autonomous body located in Ghaziabad was formed as an NCC for PvPI since 2011. Currently 250 AMCs are functioning in India with many more being added every year.[6]

Inculcating the culture of reporting of ADR

The reporting of ADR is not only limited to health care professionals (HCP) but consumer and stakeholders as well. The main function of AMCs is collection of ADR reports and uploading them in a software named Vigiflow. The ADR reports are documented in ADR reporting form called 'Suspected Adverse Drug Reaction Reporting Form' (SADR) consisting of 4 sections i.e. patient's information, suspected adverse reaction, suspected medication(s), and reporter's information submitted to the respective AMC. These spontaneous reports are the individual case safety reports (ICSR). After the collection, causality assessment is done using WHO-UMC scale.[7] For a non-health care professional, i.e. patients or consumers there exists a simple reporting form in 10 vernacular local Indian languages. It consists of 7 sections i.e. patient details, health information, reporter details, details of medicine taken, details of the side effect and intensity of the side effect. This initiative of consumer side effect reporting form was started back in 2015 due to under reporting of ADR by developing countries as compared to that of developed.[8] The contribution of PvPI to WHO-UMC is only 4.2% upto 2016 as compared to that of USA which is 49.4%.[9]

To improve the communication of drug safety information and to protect the health of large number of populations of approx. 1.27 billion where 77.58% population uses mobile phones, PvPI launched a mobile app in 2015 for instant ADR reporting.[10] This application is poised to meet the expectations of clinicians by saving their valuable time. In order to enhance the quality of reporting of ADR and to widen the scope, PvPI has also developed a toll-free helpline number 1800-180-3024 to provide continuous assistance. There is even a consumer id pvpi.compat@gmail.com for direct consumer reporting thus easing the process.

Multiple events are conducted by PvPI in order to widen the horizon of the programme. In May 2017, PvPI decided to introduce pharmacovigilance system in drug supply chain helping in maintaining quality assurance. First intensive drug monitoring programme was launched in 2017 to monitor sodium glucose co-transporter-2 (SGLT2) inhibitors, pioglitazone and sofosbuvir in India.[11]

Active pharmacovigilance, a proactive form of safety surveillance was started for bedaquiline (a novel drug used in the treatment of multi drug resistance tuberculosis) 6 AMCs have been working on for active surveillance on bedaquiline.[12]

Pharmaceutical industries too have a crucial role in the process of pharmacovigilance. The stakeholders also play a vital role in safeguarding the patient safety by submitting periodic safety update report (PSUR) every 6 monthly for first two years and thereafter annually for 2 years.[13]

PvPI also conducts various workshops for pharmacy institutions, regional trainings on PV system, establishment and capacity building at pharma industries, skill development programme on pharmacovigilance.[14]

Drug safety alerts are also a part of PvPI where HCP, consumers or patients can closely monitor the possibility of adverse events while the warning drug has been prescribed.[10]

The functioning of NCC PvPI takes place in the following ways: ADR from health care professionals and patients are reported to AMC or CDSCO zonal/sub zonal offices which are then communicated to NCC PvPI. Here it is reviewed by different panels and then eventually sent to WHO UMC.

Other initiatives

Reporting of ADR is not only limited to drugs but also herbal medicines, medical devices, biologicals, blood and blood products and vaccines. There are different programmes for the reporting of these substances.

Materiovigilance programme of India (MvPI)[14]

MvPI was launched by Drug Controller General of India (DCGI) on 6th July 2015 at IPC, Ghaziabad. There was a incidence of loss of lives after a 8-minute power cut in dialysis unit in premier hospital in Puducherry, India.[15] There are several other incidents of coronary stent stenosis causing acute myocardial infarction after few weeks of stent angioplasty.[16] There are also incidents of infections

associated with orthopaedic implants.[17] After such several horrific cases of malfunctioning medical devices, there was a need of materiovigilance programme to come into existence. Medical device reporting form of India includes 5 sections i.e. patient details, event details, medical device details, regulatory and reporter details. These efforts were taken to ensure the safety of medical devices thereby improving the quality of health and health products.

Various adverse events related to medical devices are collated to Sree Chitra Tirunal Institute of Medical science and Technology (SCTIMST) which is the national collaborating centre and National Health System Resource Centre (NHSRC) is the technical support and resource centre. The duly filled forms are eventually communicated to IPC which is the national coordinating centre.

Hemovigilance programme of India (HvPI)[18]

It was launched in 2012 under PvPI in collaboration with National Institute of Biologicals, Noida, UP under MOHFW in order to track the ADR related to blood and blood products thus contributing to improvement of patient safety. Blood donor adverse reaction reporting has 6 sections i.e. donor information, details of blood collected, type of complications, outcomes, immutability (causality) followed by reporter details. The other is Transfusion Reaction Reporting Form (TRRF) for Blood and Blood Components' to be filled by HCP. This has patient information, transfusion product details, nature of adverse reactions, outcome, reporter details and causality assessment. There were total 2296 reports in database submitted via Hemo-Vigi software by centres under HvPI.

IPC is the NCC for HvPI. national institute of biologicals is the coordinating centre for HvPI to collect and analyse data regarding biologicals. There is a core group and advisory committee constituted for the processing. There are also various panels like the signal review, core training and quality review which are linked to the medical colleges which act as the technical associates.

Adverse event following immunization (AEFI)[19]

AEFI is any untoward medical occurrence which follows immunization, and which does not necessarily have a causal relationship with the usage of vaccine. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease. PvPI coordinated with AEFI Secretariat (universal immunization programme) since 28th Feb 2013 to monitor the safety of vaccines. The reporting of AEFI not only helps in ensuring that the vaccine products are safe but also help in strengthening the vaccine safety monitoring globally. AEFI cases submitted to PvPI are coordinated with the national level AEFI for reporting and investigation. It consists of 3 long sections- first information report form; preliminary investigation report form and detailed investigation report form to do causality assessment. 21 reports of intussusception as adverse event associated with rota vaccine were found in the database. Recommendation of prescribing information change was advised by PvPI to CDSCO. Similarly, 18 reports of lymphadenopathy associated with BCG vaccine and 3 reports of Erythema Multiforme with anti-rabies vaccine were found.

PvPI has also extended its roots to private general practitioners through training of Medical representatives (MR) on pharmacovigilance as MRs have a role in communication with HCP.[19]

Various national health programmes have also been included in PvPI thus raising the bar in nationwide drug safety. PvPI also conducts various training workshops and skill development programmes for HCPs so that they understand the systems and procedures involved in ADR reporting. This contributes to the improvement in the field of pharmacovigilance thus promoting safety.[9]

Hurdles in pharmacovigilance in India

In a study conducted by Tandon et al, it was found that underreporting of ADR is a major hurdle in the sector of pharmacovigilance. Lack of knowledge and awareness about PvPI, lack of time, workload and lack of training were among the many factors responsible for the underreporting.[20] However, sometimes ADRs are not easily diagnosed by physicians which eventually leads to increase in morbidity and mortality thus affecting a wide stratum of public health. Emphasis should be made on making pharmacovigilance mandatory for the physicians inspite of the wide patient load and should start the culture of pharmacovigilance inspections. Thus, healthcare settings should be targeted to change the concept of considering ADR reporting as a common accepted daily routine practice.[21]

Pharmacovigilance should be included in curriculum on a large basis in undergraduate and postgraduate pharmacology. The amount of time dedicated to pharmacovigilance teaching in undergraduate and postgraduate courses is low. Factors discouraging reporting of ADR also included uncertainty about causality assessment between ADR and drug, forgetfulness, diffidence and lack of time.[20]

Stretch of pharmacovigilance

In near future, all medical institutions, hospitals, colleges both government and private will participate in PvPI and report ADRs to IPC so that all data generated will be collated and analysed at one place. The gathering and communication of ADR reporting is an important goal of pharmacovigilance.[21] DCGI should act quickly to improve pharmacovigilance and to inculcate good pharmacovigilance practices into the modules and procedures in order to ensure regulatory compliance and clinical trial safety and post marketing surveillance.[21] It will not only benefit HCPs but also patients, stakeholders

and regulatory authorities. ADR reporting data can be utilized for promoting rational use of drugs, changing or updating package information by pharmaceutical industries and for research and development.[9] Post marketing pharmacovigilance is currently a challenging process for both industry and regulatory agencies.

Detection of ADRs can be strengthened by intensive monitoring approach.[22] Various approaches have been recommended for the same. These included forming ADR reporting network within hospital, increasing patient awareness and educating them and making ADR reporting compulsory for nursing staff.[21,23] IPC have also appointed PV associates at all AMCs who is responsible for smooth and effective functioning of AMC. The associate is responsible for collection, follow up, reporting, analysing and entry of ADR into the Vigiflow database. He/she is accountable to send monthly ADR status reports to NCC. In case of AEFI, PV associate has to inform the AEFI on the basis of the seriousness criteria and to report to District Immunization Officer (DIO). PvPI have also expanded their network by making sure that each institution has a PV Committee each consisting of experts from medicine, surgery, pharmacology, pharmacy, toxicology. PvPI Vision 2020 is a document which will help to implement PvPI in a well-defined manner.[14]

Effective communication is a must in order to strengthen the process of pharmacovigilance and other aspects.

DISCUSSION

ADR are considered to be one of the important and easily preventable causes of morbidity and mortality. Pharmacovigilance forms a vital role in detecting, assessing and preventing them. Therefore, it is our moral responsibility to contribute for the same. HCP and consumers should be encouraged by making policies so that they shell out in safeguarding public health. Clinicians, inspite of their heavy working hours should be made to spare some of their time in reporting and give a hand in making India a pharmacovigilant nation. India is amongst the largest pharmaceuticals in the world but because of the challenges like underreporting, lack of knowledge and time, possesses a major threat to a cause which can be prevented by risk mitigation measures.[20] Pharmacovigilance has emerged out to be a dawn in the new era by making the process of reporting easy for the potential benefit of the community. Spontaneous reporting through ADR reporting forms, consumer reporting forms, mobile app, toll free helpline number; pharmacovigilance has indeed become a significant tool in growing hub of technology. The members of PvPI are trying their best to reach the masses.[11] It is one such magnificent drive for combating one of the major causes of death in the world.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Gadhade JB, Hiray RS, Aherkar RY, Shah KU. Pharmacovigilance programme of India: revival of the renaissance. Int J Basic Clin Pharmacol 2018;7:2281-5.