Pharmacovigilance Programme of India: Recent developments and future perspectives

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Abstract: Promoting safe use of medicines is a priority of Indian Pharmacopoeia Commission that functions as the National Coordination Center (NCC) for Pharmacovigilance Programme of India (PvPI). One hundred and seventy-nine adverse drug reactions (ADRs) monitoring centers currently report ADRs to NCC. Current India contribution to global safety database reaches 3% and the completeness score is 0.93 out of 1. NCC is taking several measures to enhance patient safety including capacity building for monitoring, surveillance, collaboration with national health programs and other organizations to increase ADR reporting and to ensure that PvPI is a vital knowledge database for Indian regulators. The Central Drugs Standard Control Organization has notified important safety label changes on drugs such as carbamazepine and piperacillin + tazobactam in the year 2015, other drugs are under monitoring for regulatory interventions.

Key words: Adverse drug reaction reporting, patient safety, Pharmacovigilance Programme of India

The burden of adverse drug reactions (ADRs) in the global scenario is high and accounts for considerable morbidity, mortality, and extra-cost to the patients.[1–3] In England, 0.9% of the total hospital admissions were due to ADRs during the year 1999–2008.[4] ADRs are common in Australian healthcare system also and they contribute to 1% of hospital admissions.[5] In the United States of America, ADRs contribute 3.4%–7% of hospital admissions.[6] The percentage of hospital admissions due to ADRs in certain countries is 10% or more.[7,8] India, with a current population of 1.27 billion, is the fourth largest producers of pharmaceuticals in the world with more than 6000 licensed manufacturers and over 60,000 branded formulations in the market.[9] Studies revealed that ADRs are leading to hospitalization and constitute a significant economic burden on patients in India.[10–12] A study showed that hospital admissions due to ADRs accounted for 0.7% of total admissions and deaths due to ADRs accounted for 1.8% of total admissions in a territory referral center in South India.[13]

Therefore, medicines safety monitoring is an essential element of healthcare and for high-quality medical care. Since safety monitoring of medicines as an integral part of clinical practice, the Ministry of Health and Family Welfare (MoHFW), Government of India launched the nationwide Pharmacovigilance Programme of India (PvPI) in the year 2010 to inspire confidence and trust among patients and healthcare professionals with respect to medicines safety. Indian Pharmacopoeia Commission (IPC) under the MoHFW has been functioning as the National Coordination Centre (NCC) for PvPI since April 2011.[14] There has been rapid progress in reporting of ADRs by the healthcare professionals in the past 5 years.

Establishing the Culture of Adverse Drug Reaction Reporting

Currently, 179 Medical Council of India approved teaching hospitals and corporate hospitals have been identified as ADRs Monitoring Centers (AMCs) across the country. These centers are covered in four zonal offices of Central Drugs Standard Control Organization (CDSCO) for administrative and logistic purpose. These AMCs are connected with international networking (reporting through VigiFlow; WHO-Uppsala Monitoring Centre [UMC] software). These AMCs report ADRs to NCC

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through VigiFlow, the software owned by WHO-Uppsala Monitoring Centre (Sweden). The reluctance in reporting is now changing as the PvPI has launched a complete roadmap for a proactive pharmacovigilance system which increases the awareness about the benefits of ADRs reporting. Over 5 years, the NCC has played a significant role in creating awareness among healthcare professionals about reporting ADRs that saw more than 1,49,000 ADRs reported till December 2015 [Figure 1]. Currently, the contribution of India to the WHO global Individual Case Safety Reports (ICSRs) database is 3%. The healthcare professionals are encouraged to report through feedback and Newsletters.

Completeness Score for Indian Individual Case Safety Reports

UMC communicates the result of the documentation grading for the ICSRs to the national centers. The report completeness score is a score from 0 to 1 on an ICSR, calculated from the information provided in a structured format. The score depends on the required information of the field in the ADR report such as type of report, primary source, gender, and time to onset, age at onset, outcome, indication, and free text. Average completeness score for Indian ICSRs for the period of 2011–2015 is illustrated in Figure 2.

Integration of Pharmacovigilance Programme of India and Revised National Tuberculosis Control Program

The monitoring of safety of medicines used in national health programs has been identified as a matter of concern. The safety issues are apparent in the use of medicines for the treatment of malaria, tuberculosis (TB), HIV, etc. Since inception, the Revised National Tuberculosis Programme (RNTCP), one of the largest public health programs in India, has evaluated over 70 million persons of TB and initiated treatment for over 17 million TB patients. A diagnosed TB patient on treatment under RNTCP takes more than one anti-tubercular drug simultaneously with regimens lasting from 6 months to 2 years or more. This increases the likelihood of ADRs, some of which may be severe. The overall burden of adversity directly attributable to anti-TB medicines, that is, mortality, morbidity, and reduced quality of life, is poorly documented in published literature and by the national program.

The cornerstones of pharmacovigilance apply equally to TB as to any other disease amenable to medication. Events linked to medications, particularly novel medicines or new combinations thereof, need to be recognized in a timely fashion if the events are to provide benefit to the individual patient and the public. Appropriate measures need to be put in place to ensure that harm is reduced and symptoms relieved. Healthcare workers need to be informed and trained about the methodology and routes for reporting ADRs. Keeping this in view and to improve patient care and safety in relation to the use of anti-tubercular drugs, RNTCP formally entered into collaboration with the PvPI on October 11, 2013. As a consequence, RNTCP staffs have attended IPC-WHO national workshops on pharmacovigilance held in the country. These programs are keen to customize trainings for RNTCP and take these activities further.

Integration of Pharmacovigilance Programme of India and National AIDS Control Organization

India has the third largest number of people living with HIV in the world, 2.1 million at the end of 2013 and accounts for about 4 out of 10 people living with HIV in the region, in India, the numbers of new HIV infections declined by 19%, yet it still accounted for 38% of all new HIV infections in the region. India recorded a 38% decline in AIDS-related deaths between 2005 and 2013. During this period, there was a major scale-up of access to HIV treatment. At the end of 2013, more than 700,000 people were on antiretroviral therapy (ART), the second largest number of people on treatment in any single country. During last 5 years, there were 11 ART fixed drug combination were approved for manufacturing in India. To ensure the safety of antiretroviral (ART) medicines used in the program, IPC, NCC-PvPI, and National AIDS Control Organization formally agreed to collaborate on September 15, 2014, for setting up systems and processes for reporting, analysis, and monitoring of ADRs due to ART medicines used in NACP.

Collaboration with Adverse Events Following Immunization

NCC-PvPI is assisting with adverse events following immunization (AEFI) at Immunization Technical Support
Collaborations with Central Drugs Standard Control Organization

ADR monitoring and reporting to national regulatory authority are put in place in many countries. In India, PvPI is closely working with CDSCO, drug regulatory authority of India. CDSCO understands that pharmacovigilance plays a specialized and pivotal role in ensuring ongoing safety of medicinal products in India and it seeks inputs from NCC before taking any kind of regulatory decisions. NCC-PvPI is working in close coordination with CDSCO zonal offices also for technical, administrative, and logistics matters related to PvPI. The role of NCC in collaboration with other national and international organizations to promote patients safety is illustrated in Figure 3.

**Education and Training on Pharmacovigilance at Regional Training Centers**

A primary objective of NCC-PvPI is to promote the safest use of medicines through contributing to appropriate education in pharmacovigilance and training activities across the country. The NCC identified nine Regional Training Centers (RTCs) such as JSS Medical College, Mysore; Seth GS Medical College and KEM Hospital, Mumbai; Postgraduate Institute of Medical Education and Research, Chandigarh; Institute of Post Graduate Medical Education and Research, Kolkata; All India Institute of Medical Sciences, Bhopal; B. J. Medical College, Ahmedabad; Silchar Medical College and Hospital; All India Institute of Medical Sciences, Rishikesh; and Nizam’s Institute of Medical Sciences, Hyderabad. These centers provide continual training to the personnel at AMC of their respective regions.

**Figure 3: Coordination of Indian Pharmacopoeia Commission with other organizations**

- PVPI launched under MoHFW, Govt of India and provide financial support to run the programme effectively.
- To monitor safety of medicines used in these programs
- To promote and establish Cohort Event Monitoring and Target Spontaneous Reporting in India.
- To organise training programs for stakeholders.
- Monitoring and reporting ADRs.
- To track adverse reactions and incidences associated with blood and blood products.
- To participate in International Drug Monitoring Programme and contributing in global safety database.
- To ensure the safety of vaccines.
- Take appropriate regulatory decision and actions on the basis of recommendations made by NCC.
- Propagate medicine safety related decisions to stakeholders.
- Provide administrative support to run PVPI.
Communications

NCC is committed to communicate the findings of PvPI to stakeholders and public with respect to importance of ADRs and reporting them, information about benefit-harm and effectiveness-risk, rational use of medicines, etc. A variety of methods for PvPI communication is used by NCC as follows.

Website

The websites of CDSCO (www.cdsco.nic.in) and NCC (www.ipc.gov.in) are important tools for communication to the stakeholders and public seeking specific information. PvPI documents on these websites can be searched by navigating from the home page. Examples of documents on these websites include list of AMCs, how, what, and where to report ADRs, newsletters, training module, guidance document, etc.

Media

Since medicines safety communications with healthcare professionals, patients, and the general public must be focused on joint responsibility for safe and rational therapy, NCC communicates the findings in national newspapers, electronic media, etc., on regular basis.

Newsletter

PvPI Newsletter is unique among healthcare professionals because it focuses on the ADRs-related informations. Three issues per year guides how to take a leading role in monitoring, reporting, and preventing ADRs. It is available in a convenient electronic format and printed version is circulated to AMCs, corporate hospitals, academic institutions, health departments, etc.

Scientific Journals

NCC publishes original and review articles on PvPI in national and international journals.[14‑25]

Helpline Facility to Provide Assistance in Adverse Drug Reaction Reporting

To enhance the participation of patients, healthcare professionals, and the pharmaceutical industry in enhancing medicines safety by reporting suspected ADRs to the PvPI, NCC recently launched a helpline number (toll free), i.e., 1800 180 3024 facility for reporting adverse events. This facility was dedicated to the nation on October 11, 2013. This may be one of the innovative methods to create awareness and to reach every corner of the country for the pharmacovigilance activity. This facility will be useful for the healthcare professionals those who are working in tertiary healthcare system to report ADRs. Adverse events-related information which received at NCC will be communicated to nearest AMCs for validating the reports. Since sending timely feedback or acknowledgement will build public confidence recently this facility has been upgraded by sending short message service feedback/acknowledgment to the ADRs reporters.

Android Mobile Application for Adverse Drug Reaction Reporting

In developing countries such as India, under-reporting of ADR remains serious concern. In India, IT is becoming a great facilitator for promoting public health. India is cementing its place IT sector through mobile connections to reach every individual in a population of 1.27 billion where approximately 77.58% population is already using mobile phones. Hence, it is more rationale to introduce the concept of PvPI to stakeholders through mobile phones. NCC-PvPI in technical collaboration with NSCB Medical College, Jabalpur, developed a mobile application for the healthcare professionals to promote easy and instant reporting of ADR. This facility was launched by Secretary Health, MoHFW, Government of India, on May 22, 2015.

Utilization of Periodic Safety Update Reports Reporting

Periodic safety update reports (PSURs) are a tool to monitor the safety of ongoing medicines in the market. In India, marketing authorization holders (MAHs) are required to prepare PSURs and to submit them to CDSCO twice in a year for 2 years and annually for another 2 years. Since PSURs are not directly linked with PvPI, NCC has taken the initiatives in collaboration with CDSCO to utilize the data for PvPI. The first interactive session on “Review of Periodic Safety Update Report/Post Marketing Surveillance Data and Pharmacovigilance Planning of Marketed Products” was held on December 18 and 19, 2013 at New Delhi. Representatives from MAHs, CDSCO, and NCC-PvPI were participated and discussed the issues and roadmap for better coordination and participation of MAHs in PvPI.

Availability of Medicine Side Effect Reporting Form for Consumers in Different Vernacular Languages

Patients or consumers are the end users of pharmaceutical products, to ensure the safe use of them is the ultimate goal of pharmacovigilance activities. In an increasing number of countries, patients are now allowed to report ADRs to the spontaneous reporting system.[18‑20,26‑27] Option of ADRs reporting by patients to PvPI was started at NCC-PvPI on August 1, 2014. Patient or his/her representative (relative) are encouraged to report ADRs either directly to the NCC-PvPI through toll free helpline number: 1800-180-3024 or E-mail id: pvpi.compat@gmail.com or to their nearest AMC under PvPI by submitting “Medicines Side Effect Reporting form for Consumers” (blue form) which can be downloaded from the official website of IPC www.ipc.gov.in[28] and by the end of 2015, this form is available in ten vernacular languages such as Hindi, Kannada, Malayalam, Assamese, Bengali, Odiya, Tamil, Telugu, Gujarati, and Marathi.

Future Perspectives

NCC has mandated the RTCs to organize advance level training for the personnel’s of all AMCs under their respective regions and one CME in pharmacovigilance at an AMC under their region to increase the awareness of healthcare professionals about the ADR reporting. In near future, all Medical Council of India approved institutions will be enrolled under the PvPI. As IPC was recognized as the WHO Collaborating Center for medicines and vaccine safety in the South East Asia region during 38th Annual Meeting of National Pharmacovigilance Centers participating in the WHO program for international
drug monitoring, plan to initiate, and coordinate with countries in South East Asia region for potential signals from the built safety database. NCC is in a process of developing and promoting an effective channel for ADRs reporting such as online reporting system.

**Conclusion**

ADRs reporting through PvPI improved with the measures such as education, training, and provision of technical assistance. The PvPI is a vital knowledge databases for Indian drug regulation. The CDSCO has notified important safety label changes for carbamazepine and piperacillin + tazobactam in the year 2015. The PvPI plans to expand its scope of activities to widen its reach to other healthcare professionals and to strengthen measures for capacity building.

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**Conflicts of Interest**

There are no conflicts of interest.

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