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Pharmacovigilance in India - The Past, Present and Future

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The concept of pharmacovigilance (PV) in India traces its roots to 1986, in which year an official Adverse Drug Reaction (ADR) monitoring system involving 12 regional centres covering a population of 50 million each, was proposed. In the year 1989, six regional centres were set up for ADR monitoring, of which only two were eventually active.[1] These early PV environments were complicated and the outdated systems meant that the amalgamation of data was unreliable and limited. After facing several roadblocks, India registered in 1997 as a member of the World Health Organisation (WHO) Programme for International Drug Monitoring, managed by the Uppsala Monitoring Centre (UMC). In November 2004, with funding support from the World Bank approved upon request of the Government of India, the Central Drugs Standard Control Organization (CDSCO)

launched the National Pharmacovigilance Programme (NPP) with the immediate objective of nurturing a reporting culture amongst healthcare professionals (HCPs). Contrary to the overwhelming expectations from the policymakers, the programme did not progress, with the absence of continuous funding being a key reason. Recognising the need to re-conceptualise the NPP with more forethought and with a long-term strategy in place, the programme was rechristened the Pharmacovigilance Programme of India (PvPI) and commenced by CDSCO, the Directorate General of Health Services (DGHS) under the Ministry of Health and Family Welfare (MOHFW) in collaboration with the All India Institute of Medical Sciences (AIIMS). From April 2011, the Indian Pharmacopoeia Commission (IPC) took over as the National Coordinating Centre (NCC) for PvPI.

The focus of PvPI is towards establishing a unique drug safety ecosystem with a broad objective to safeguard the health of the 1.31 billion people of India by ensuring that the benefit of use of medicine outweighs the risks associated with its use. PvPI collects, collates, analyses the data, recommends regulatory interventions and communicates risks to HCPs and public.[2] In a strategic move, PvPI has collaborated with a number of medical colleges and hospitals, which began to function as Adverse Drug reaction Monitoring Centres (AMCs) for collecting suspected ADR reports and forwarding them to NCC. The total number of AMCs currently functioning under the PvPI programme is 179, with 99 Causality Assessment Committees (CACs). IPC is in the process of enrolling additional centres under the PvPI such that the strength of AMCs will increase to 200 by the end of March 2016. It is remarkable that India became the first Asian country to report over 100,000 Individual Case Safety Reports (ICSRs) to VigiFlow, UMC's web-based PV system.[3] Furthermore, India is currently the 7th largest contributor to the UMC's international drug safety database (Vigibase). Adding another feather to India’s cap is the UMC’s completeness score of 0.94 out of 1 assessed for Indian ICSRs, positioning India among the top-rankers in the completeness score criterion.[4] The Regional Resource Centres for Training and Technical Support (RRCTTS) play a significant role in enhancing the awareness of PvPI among different stakeholders and motivating them to participate in it. Considering the significant role of RRCTTs, IPC is seriously contemplating to expand all its RRCTTS by undertaking requisite capacity building measures for infrastructural, technical, and logistical development based on PvPI recommendations, which will provide uniform training to all AMC(s) teams and enhance skill development for PvPI personnel while also strengthening the concerned AMC’s status. The Core Training Panel of PvPI interacts with international agencies for participation and implementation of training programmes related to pharmacovigilance.

Recent initiatives unveiled by PvPI include provision of a toll-free number, a revolutionary mobile application which simplifies the process of ADR reporting, adverse event reporting forms in six regional languages to encourage consumer reporting and a mandate to the pharmaceutical industry to submit reports in XML-E2B (Extensible Mark-up Language) format. It is worth noting that various Indian headquartered global pharmaceutical companies have established in-house PV units that operate by adopting global standards even before PvPI rolled out any mandates, in order to remain compliant with PV regulations outside India. PvPI has also set up a PV system in tuberculosis and HIV/AIDS-related health programmes with WHO support. The IPC is all set to become the first WHO Collaborating Centre for safety of medicines and vaccines in South-East Asia.[5] It is evident that, by being a progressive program of the CDSCO and without the controls for any executive jurisdiction, PvPI has made positive strides. Earlier in 2015, the Drugs Technical Advisory Board (DTAB) recommended mandating pharmaceutical companies to report adverse effects of marketed medicines.[6] Although recommendations were proactive, the legislation for mandate came in only in March 2016. The periodic communications and interactive discussions between PvPI and its stakeholders have brought progression in receiving ADR reports as many pharmaceutical companies consider reporting ADRs as an industry practice. As a result, the ADR reporting rate by the pharmaceutical industry to PvPI was 18.80 per cent in the year 2015.[7]

To broaden the involvement of the medical community in ADR reporting, IPC has started to collaborate with the IMA (Indian Medical Association), which represents over 360,000 medical practitioners. This will enable a greater role for the private practitioners and corporate hospitals since only government hospitals, institutions and colleges have been directly involved in PvPI until recently. Interestingly, ADR reporting by the corporate hospitals is mandatory for the National Accreditation Board for Hospitals & Healthcare Providers (NABH) accreditation of hospitals. To give further momentum to this initiative, both PvPI and IMA have agreed to celebrate a National Day of Patient Safety.[8] The achievements of PvPI from 2010 to date is shown in Figure 1.

Figure 1 Roadmap of Pharmacovigilance Programme of India

To analyse the benefit-risk ratio of marketed medicines, the Benefit-Risk Assessment Cell for drugs under the Risk Management Plan (RMP) of PvPI was recently launched as a strategic milestone to strengthen PvPI's initiatives.[9] The scope of PV, which is currently restricted to data collection and analysis on ADRs, is also soon expected to include pharmacogenomics as a part of the scientific component of PvPI, with the aid of the Indian Council of Medical Research (ICMR).[10] The active functioning of the Signal Review Panel (SRP) under the PvPI program deserves appreciation as this apprises CDSCO about the signals generated and empowers CDSCO with evidence required to request drug manufacturers to make label changes. It is of relevance to remark that CDSCO's March 2016 Gazette notification refers to the updates in Schedule Y, which has brought in a legal obligation for the pharmaceutical companies to have a PV system in place with qualified personnel for collecting, processing and forwarding the reports to the licensing authority for information on ADRs emerging from the use of the drug manufactured or marketed by them. It is now necessary for pharmacists to be available in every district hospital to ensure the monitoring of ADRs, which distinctly helps in boosting PvPI's progress. India's sustained commitment to patient safety is also palpable from the approval of the Health Ministry to begin the 'Materio Vigilance Programme of India' (MvPI) in March 2015 on the lines of similar programmes for Biovigilance and Haemovigilance, which were launched earlier in 2012.

India is likely to be among the top three pharmaceutical markets by incremental growth and the sixth largest market globally in 2020, and has been steadily evolving into one of the world's most important pharmaceutical centres for clinical trials and research & development. It is worth mentioning that the PV outsourcing industry in India has grown by leaps and bounds in the past decade, with the number of PV professionals in the country amounting to almost 20000 people. The talent pool in India has attracted global pharmaceutical companies, encouraging them to establish huge PV hubs to run their mainstream global PV activities, ranging from basic case processing activities to complex functions such as signal detection and analysis. The spectrum of PV capabilities available in India has expanded as expected and there is a need for interlinking the thinking of various stakeholders, who could devise an integrated multi-disciplinary approach in PV. The symbiosis of global talents available in the Indian pharmaceutical industry, professional bodies, academia and all other healthcare sectors, with the CDSCO/PvPI, under a common cause will be fruitful and could pave the way towards harmonisation and capacity building in the discipline. Some professional associations such as the Indian Society for Clinical Research (ISCR) have been vocal and proactive in offering their support to the PvPI through their PV Council. The two way communication between PvPI and statutory councils, professional societies, groups with mandates and industry associations has helped in sorting out various teething problems in integrating the flow of ADRs from various sources. The research and development initiatives by ICMR, Council of

Scientific & Industrial Research (CSIR), Central Drug Research Institute (CDRI), The Society of Pharmacovigilance, India (SoPI), etc, have facilitated the support for the growth of PvPI. The imminent plan at the global level for the PvPI is to reinforce the collaboration with the WHO, UMC and harmonisation with the South Asian Association for Regional Cooperation nations (SAARC).[11]

To advance PV practices in India, it is now essential that the country undergoes a major transformation in its healthcare sector, putting patient safety at the forefront. India is keen to adopt the Internet of Things (IoT), with cloud-based apps that will bring efficiency and transparency in real-time with the active support of electronics, software and communication networks. India will need to develop specific national current reporting rate graphics and there is a pressing need for a country specific database for the public and a restructured online platform for doctors, to provide better awareness of drugs and their adverse effects. For PV as a practice to be inculcated, India needs to formulate standard guidelines, similar to European Medicines Agency's Good Pharmacovigilance Practices (GVP), to ensure patient safety. With the intention of streamlining PV practices without compromising on patient safety, the European Medicines Agency's (EMA) RMPs, signal detection, concepts of Qualified Person for Pharmacovigilance (QPPV), the Marketing Authorisation Holder (MAH) paying the EMA for review of the submitted reports could be adopted. The EMA's Medical Literature Monitoring Service (MLM) has become a hot topic of discussion in countries where PV responsibilities are emerging, since it is evident that literature cases contribute to a great extent to the volume of spontaneous cases. Adopting a system similar to the MLM could be an effective way of identifying ADRs in countries like India where pharmacovigilance is emerging, but the market is subjugated by drug manufacturers or distributors who may not have enough resources to perform literature searches. I hope that this article has given the reader an insight into where I think PV in India has come from and where it needs to go to be on par with global standards of drug safety.

References

(1) *www.ipc.gov.in/PvPI/20.%20Pharmacovigilance%20programme%20for%20India.pdf*

(2) *http://ipc.nic.in/writereaddata/linkimages/PDF%20PV%20Toolkit-1898248681.pdf*

(3) *http://ipc.nic.in/writereaddata/mainlinkFile/File398.pdf*

(4) *Kalaiselvan V, Kumar R, Thota P, Tripathi A, and Singh GN. Status of documentation grading and completeness score for Indian individual case safety reports. IndJPharmacol2015; 47(3): 325–327.*

(5) *http://pib.nic.in/newsite/PrintRelease.aspx?relid=130201*

(6) *http://www.cdsco.nic.in/writereaddata/newMinutes%20of%2068th%20DTAB%20meeting.pdf*

(7) *http://www.pharmabiz.com/NewsDetails.aspx?aid=93772&sid=1*

(8) *www.pharmabiz.com/PrintArticle.aspx?aid=93462&sid=1*

(9) *http://pharmabiz.com/ArticleDetails.aspx?aid=93612&sid=1*

(10) *http://pharmabiz.com/ArticleDetails.aspx?aid=92820&sid=1*

(11) *www.pharmabiz.com/NewsDetails.aspx?aid=92775&sid=1*