Viewpoint

National Pharmacovigilance Program

Sandeep B. Bavdekar*
Sunil Karande*

Introduction

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems(1). An "adverse event" is defined as any untoward medical occurrence that may present during treatment with a drug but which does not necessarily have a causal relationship with its use(1). An "adverse drug reaction" is any noxious, unintended and undesired effect of a drug, which occurs at a dose used in humans for prophylaxis, diagnosis, therapy or modification of physiological functions(2). Spontaneous reporting of adverse events and adverse drug reactions is the commonest method utilized for generating safety data(3).

Adverse drug reactions in children constitute a significant health issue given their reported incidence of 9.5%. They also account for 2.1% of hospital admissions, with 39.3% of them being life-threatening(1,4). Safety data generated from clinical trials is incapable of identifying infrequent or late-onset adverse drug reactions(5). When a new drug is marketed, only limited information regarding its safety in children is available. Currently, several new drugs are being launched in India almost simultaneously as in the world market. Hence even minimal post-marketing safety data is unavailable(6). The types of diseases and co-morbid conditions (*e.g.*, malnutrition, anemia and infestations) in Indian children, diverse genetic composition, and concomitant use of drugs belonging to alternative medicine could result in unforeseeable adverse drug reactions(7-9). Hence, it is mandatory that our country should have an active pharmacovigilance network.

Pharmacovigilance benefits everybody: The patients are protected from unsafe drugs; doctors and pharmaceutical industry keep their reputations intact and drug regulators receive pertinent data that helps them to take regulatory decisions. Although, Indian Council of Medical Research and Drugs Controller General of India began establishing Adverse Drug Reaction centers in 1980s, these activities remained confined to a few institutions and practicing doctors have remained largely oblivious of these activities(7,10).

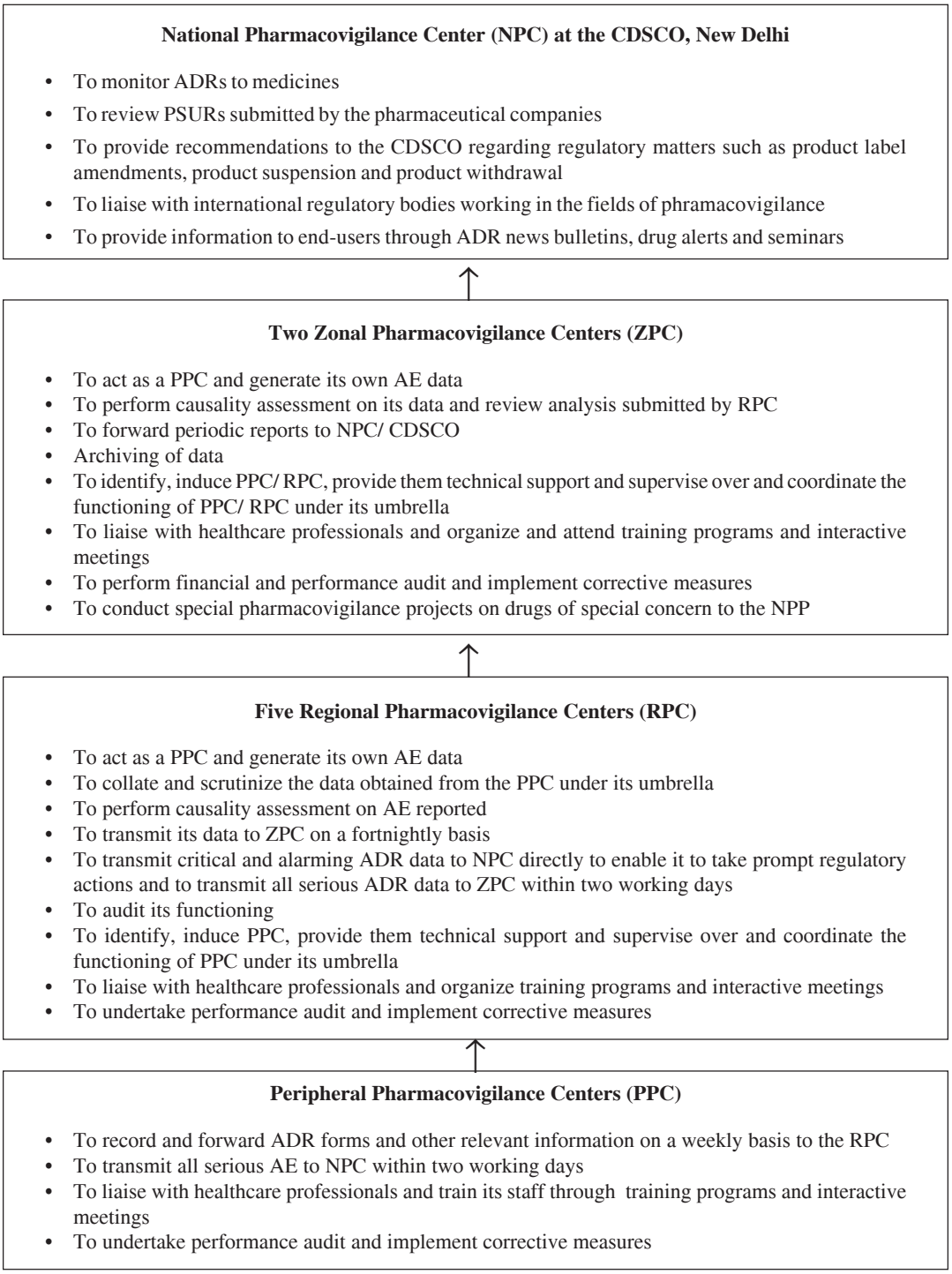
National Pharmacovigilance Program

To improve the current state of functioning of pharmacovigilance activities, the central drug regulatory agency. The Central Drugs Standard Control Organization launched the National Pharmacovigilance Program in November 2004 under the aegis of Directorate General of Health Services, Union Ministry of

*From the *Department of Pediatrics, Seth GS Medical College and KEM Hospital, Parel, Mumbai 400012 and **Department of Pediatrics, Lokmanya Tilak Municipal Medical College and General Hospital , Sion, Mumbai 400 022, India.*

Correspondence to: Dr. Sandeep B. Bavdekar, 9, A2 Worli Seaside, CHS, Pujari Nagar, KAG Khan Road, Worli, Mumbai 400 018, India. E-mail: drsbavdekar@vsnl.com

Fig. 1. National Pharmacovigilance Program: Selected Functions Carried Out at Various Levels.



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 program has a three-tier structure consisting of peripheral, regional and zonal Pharmacovigilance Centers in addition to the National Pharmacovigilance Advisory Committee and the National Pharmacovigilance Center based at the Central Drugs Standard Control Organization, New Delhi at its apex (*Fig. 1*). All centers can report alarming or critical adverse drug reactions to the National Pharmacovigilance Center directly so that regulatory decisions can be taken promptly.

Under the program, Peripheral Pharmacovigilance Centers will be established in teaching and non-teaching hospitals, clinics and pharmacies in each state and union territory. Each Peripheral Pharmacovigilance Center will record adverse events and forward the adverse drug reaction forms and relevant information to its respective Regional Pharmacovigilance Center on a weekly basis. The Regional Pharmacovigilance Centers would cover five regions of the country: North, East, Central, West, and South and will be responsible for recording adverse drug reaction data locally and scrutinizing data received from the Peripheral Pharmacovigilance Centers situated in their respective regions. Each Regional Pharmacovigilance Center will subject its data to causality assessment and also report to its Zonal Pharmacovigilance Center. Two Zonal Pharmacovigilance Centers have been established: at KEM Hospital, Mumbai and at All India Institute of Medical Sciences, New Delhi. In addition to generating its own adverse drug reaction data and performing causality assessment, each Zonal Pharmacovigilance Center would also prepare reports for the National Pharmacovigilance Center and conduct special pharmacovigilance projects on any drug of special concern to the National Pharmacovigilance Programme. The National Pharmacovigilance Center would recommend the Central Drugs Standard Control Organization regarding regulatory actions (including amendments to label and suspension or withdrawal of the product) based on the adverse drug reaction data generated in the country and Periodic Safety Update Reports submitted by pharmaceutical companies. It would disseminate relevant information through adverse drug reaction news bulletins, drug alerts and seminars. As a part of international collaboration, the National Pharmacovigilance Center will network with national pharmacovigilance bodies from other countries and also provide data for the World Health Organization International Drug Monitoring program.

Noteworthy Features of NPP

- Its immediate objective is to foster a culture of notification not only amongst doctors but also amongst other healthcare providers, *viz*., pharmacists and nurses.
- Although the drug regulators would be more interested in receiving information on adverse drug reactions of newly marketed drugs, the program allows reporting of common or non-serious adverse drug reactions of even well established drugs. This has been done to encourage every healthcare provider to start reporting adverse events.
- The reporting forms maintain patient confidentiality. Identification of notifier, however, is obligatory to allow for verification of information and discourage submission of spurious data.
- Now even practicing doctors and pharmacists can establish Peripheral Pharmacovigilance Centers and get

involved in pharmacovigilance. Earlier only pharmacologists were involved.

Considerations for the Future

The program represents a significant commitment to help generate adverse drug reaction data. Various stakeholders can help the program achieve its objectives comprehensively:

For Program Managers

- Involve professional organizations of healthcare providers (*e.g.,* Indian Academy of Pediatrics, National Neonatology Forum, Indian Medical Association, Association of Physicians of India, Trained Nurses Association of India, Indian Pharmaceutical Association, Indian Hospital Pharmacists' Association) to educate their members about the program and there by sustain their participation.
- *Use of other modes of communication:* In addition to the Central Drugs Standard Control Organization website, use newsletters and pamphlets to inform healthcare providers about the program's activities.
- *Address clinicians' concerns:* Doctors may be hesitant to report adverse events on medico-legal grounds and fear of public outcry. They will feel secure if steps are taken to inform the public that an unexpected adverse event occurring during therapy need not necessarily be drug-related, even though it may have to be reported as an adverse event.
- *Focus on drug safety issues in children:* At present, the National Pharmacovigilance Advisory Committee does not have a pediatrician as its member. It should co-opt at least one expert Indian Academy of Pediatrics-recommended pediatrician on its panel.
- Collect adverse drug reaction data involving drugs of alternative medicine and their interactions with drugs of modern medicine.
- Consider including reports of "lack of efficacy" and poisoning.
- Establish a link with public healthcare authorities to obtain data regarding adverse events following immunization.
- Make the Central Drugs Standard Control Organization website more informative by providing the latest data about the adverse events/ adverse drug reactions reported, their causal relationship and performance reports. The program newsletters should be available at the website.
- 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.
- Allow healthcare providers working in rural areas and at primary health centers to avail Internet and facsimile facilities to report adverse events: This would encourage reporting from remote areas, help expand the program's coverage and cut the red tape.

For Pharmacovigilance Centers

- Each center should set up an institutional pharmacovigilance committee to sustain this program. It should present its adverse drug reaction data at institutional meetings and disseminate information regarding unusual adverse drug reactions through institutional newsletter or website to help engage its healthcare providers.
- *Act locally:* Each center should establish rapport with all the doctors and pharmacists in its locality and satisfy their "felt needs" about drug information, new

Key Messages

- The National Pharmacovigilance Program has been launched to improve the current state of functioning of pharmacovigilance activities. Its basic purpose is to analyze adverse drug reaction data for making regulatory decisions regarding drugs marketed in India.
- Not only doctors but other healthcare providers, *viz.*, pharmacists and nurses can now actively participate in the program. They should start reporting adverse events to help ensure that children in our country receive safe drugs.

formulations and management of adverse events, when encountered.

- *Local networking:* Without waiting for the linkages at central level to percolate downward, each center should network with local branches of professional organizations to reach their members.
- *Extend more than common courtesies:* Provide information about similar reports, feedback of the causality assessment and enlist the notifier as a partner when the adverse drug reaction is presented or published.
- *Managerial interventions:* Individual centers could implement periodic reporting and "zero reporting" to inculcate a "reporting culture".

For Indian Academy of Pediatrics

- The Academy has shown its commitment to ensure safe use of drugs in children by establishing a pharmacology cell, having its own adverse drug reaction reporting form and publishing an Indian Academy of Pediatrics drug formulary. Being an important stakeholder, the Indian Academy of Pediatrics should also take the initiative in collaborating with the program managers by sensitizing, informing and educating its members about the National Pharmacovigilance Program by regularly allotting time for discussion on pharmacovigilance at the various academic events organized by its branches all over the country.
- Its official journal, Indian Pediatrics, should have a regular column related to drug safety in children and encourage publication of pediatric adverse drug reaction data.

Pediatricians should appreciate that now there is a system and a tool in place to collect and analyze adverse drug reaction data. They should start reporting adverse events and actively participate in the National Pharmacovigilance Program to help ensure that children in our country receive safe drugs.

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