

Is there a Role for Pharmacist in Safety Monitoring of Vaccines?

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ABSTRACT

India has approximately 7.4 million unimmunized children and responsible for more than five lakhs deaths annually. News about Adverse Events Following Immunizations (AEFIs) is one of the important barriers in India to lag behind in vaccination coverage along with lack of awareness and cultural diversity of parents. The expectation from vaccines are very high unlike drugs and any reports on adverse vaccine events may damage the public confidence in vaccination program. As an important member in the health care team, pharmacists can help the regulators in responding to the any news on AEFIs by investigating and reporting each and every adverse events which they observe following any vaccine administration. The causality assessment helps to categorizes the adverse events, in turn helps for the effective AEFI communication to the public in the right time.

Key words: Pharmacist, Safety monitoring, Vaccine pharmacovigilance, Causality Assessment

BACKGROUND

Vaccines are biological substances that produce or enhance immunity to particular vaccines preventable diseases (VPD). Immunization is one of the most cost effective public health interventions for protecting the individual and the public from VPDs, disabilities and death each year.^{1,2} Safe and effective vaccines, which protect from many VPDs are existing and many promising vaccines are in pipeline. The impact of vaccination on the health of the people globally is hard to exaggerate.² With the exception of safe water, nothing else, not even antibiotics, has had such a major effect on the reduction of mortality (deaths) and morbidity (illness and disability) and on population growth.³ Immunization currently prevents 2-3 million deaths every year globally. But an estimated 21.8 million infants worldwide are still missing out on basic vaccines.^{4,5}

India has more than 26 million births and accounts for over 20% of the child mortality worldwide. Nine million routine immunization sessions are organized each year to

target these infants and pregnant women.⁶ Though there is slight improvement in the recent years, the country still have 7.4 million unimmunized children and responsible for more than five lakhs deaths annually.^{5,6} Lack of awareness and cultural diversity of parents and AEFIs are some of the important barriers for India to lag behind.⁵

Vaccines are very special in a developing country like India as it promotes health, which has an expansive reach, it has a rapid impact and also it saves treatment cost and lives.⁷ Unlike medicines, the expectations from vaccinations are much higher and problems arising from the vaccine or vaccination are less acceptable to the general public. However, the incidence of vaccine-preventable diseases continues to decline, some people have become increasingly concerned about the risks associated with the vaccines, and less fearful of the diseases they are designed to prevent. Vaccines are usually administered to healthy people, including entire birth cohorts of infants and in vast num-

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bers.³ However, like medicinal products, vaccines are not free from adverse events while it help people stay healthy.¹ The settings in which they are administered vary from sophisticated tertiary care hospitals to primary health care centers in remote corners.³ So the safe and quality use of vaccine is of utmost importance. Failure to deal rapidly and effectively with allegations of vaccine-related adverse events can decrease the public confidence in vaccines and ultimately reduce immunization coverage and increase disease incidence.⁷

NATIONAL IMMUNIZATION PROGRAMS (NIP)

With the goal of strengthening the immunization programs, all countries in the globe delivers selected vaccines to the targeted beneficiaries, with special focus on infants and children, pregnant women and who are at a high risk of diseases preventable by vaccines.^{2,7} The number of antigens in the immunization programmes varies from country to country; however, there are a few selected antigens against diphtheria, pertussis, tetanus, poliomyelitis, measles, hepatitis B which are part of immunization programmes in most of the countries in the world.⁸

National Immunization program was launched after India was declared as smallpox free country and was called as Expanded Program of India (EPI) in 1978 by introducing Bacillus Calmette Guerin (BCG), Oral Polio Vaccine (OPV), Diphtheria Pertussis Tetanus (DPT) and Typhoid-paratyphoid vaccines. In spite of all positive changes, there are some ongoing challenges and shortcoming in the programme. Though there are at least 27 causative agents against which vaccines are available⁸, NIP of India has only nine vaccines [BCG, Hepatitis B (HepB), OPV, Pentavac (DPT+HepB+ Hemophilus Influenza), Inactivated Polio Vaccine (IPV), DPT, Tetanus Toxoid (TT), Measles- Rubella (MR), Japanese Encephalitis (JE) & Rotavirus vaccine (in selected regions)]. The coverage with vaccines in NIP is suboptimal and only 3/5th children receive all due vaccines and only 3/4th receive all three doses of DPT vaccine. There are inter- and intra-state variations in the coverage.^{5,8} Vaccines used in NIPs are considered safe and effective when used correctly.⁵ Immunization quality and safety surveillance has become as important as the efficacy of the national VPD programmes.^{3,5}

IMPORTANCE OF SAFETY MONITORING OF VACCINES

By definition, Adverse Events Following Immunization is “any untoward medical occurrence which

follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease”.¹ In addition to the vaccines themselves, the process of immunization is a potential source of an adverse reaction.¹ Vaccines has variety of components including antigens, stabilizers, adjuvants, antibiotics, preservatives and residual by products from the production process which all has the potential to cause AEFIs.⁷

As per the position paper of Indian Academy of Pediatrics published in 2013, AEFI is a critical component of immunization program. The risk of AEFI with vaccination is always weighed against the risk of not immunizing a child. It is only when the benefit outweigh the risk, a vaccine is considered safe. However, even at a relatively low rate, because of the high absolute number of beneficiaries, there is risk of a few serious adverse events in the vaccinated children.⁹

Monitoring for adverse effects of vaccine is a major safety component in pre licensure clinical trials and which identifies common and acute side effects. Post marketing surveillance (PMS) of vaccines are critical due to many reasons like pre pre-licensure clinical trial fails to realize the rare, unexpected and delayed onset events, which includes only healthy study population and enroll only less than 10,000 subjects.

In clinical practice, vaccines will be administered in combination to a large group who were not included during the clinical trials.¹⁰ Thus PMS helps to identify the potential signals. PMS is also needed for established vaccines to monitor the rate of known reactions to observe whether the rate exceeds the expected rate. Unlike adverse drug reaction (ADR) monitoring, AEFI assessment helps to understand the not only the vaccine side effects but also the program errors, quality defects while manufacturing and coincidental events which helps to answer the public concerns on the safety of vaccines immediately. The different type of AEFIs are described in the below mentioned Table 1.

Spontaneous reporting system is one of the best method practicing at many countries worldwide for reporting AEFIs.^{7,10,11} Underreporting is a known limitation of spontaneous reporting all over the world. Lack of knowledge in AEFIs and its reporting may lead to inconsistent adverse events data collection which may lead to inaccurate calculation of incidence of AEFIs, by delaying or missing important vaccine safety concerns.¹¹ Each report may contain AEFI core variables like identity of the subject, details of case, vaccine and the event, reporter information and comments if any for the better causality assessment.¹²

Table 1: World Health Organization (WHO) cause specific definition/ type of AEFIs

Type	Description	Example
Vaccine product related reaction	An AEFI that is caused or precipitated by a vaccine due to one or more of the inherent properties of the vaccine product.	Extensive limb swelling following DTP vaccination.
Vaccine quality defect related reaction	An AEFI that is caused or precipitated by a vaccine that is due to one or more quality defects of the vaccine product including its administration device as provided by the manufacturer	Failure by the manufacturer to completely inactivate a lot of inactivated polio vaccine leads to cases of paralytic polio
Immunization error related reaction	An AEFI that is caused by Inappropriate vaccine handling, prescribing or administration	Transmission of infection by contaminated multidose vial
Immunization anxiety related reaction	An AEFI arising from anxiety about the immunization	Vasovagal syncope in an adolescent following vaccination
Coincidental events	An AEFI that is caused by something other than the vaccine product, immunization error or immunization anxiety	A fever after vaccination (temporal association) and malarial parasite isolated from blood.

Table 2: Causality Assessment Classification

A. Consistent causal association to immunization
A1. Vaccine product related reaction
A2. Vaccine quality related reaction
A3. Immunization error related reaction
A4. Immunization anxiety related reaction
B. Indeterminate
B1. Temporal relationship is consistent but there is insufficient definitive evidence for vaccine causing event
B2. Reviewing factors result in conflicting trends of consistency with causal association to immunization
C. Inconsistent causal association to immunization
Coincidental
Unclassifiable

*B1 : Potential signal and may be considered for investigation

Typically, monitoring of licensed vaccines is done through spontaneous reporting systems whereby adverse events that follow immunization are reported to health authorities. Detection of an adverse event following immunization does not necessarily mean the vaccine caused the event. Determination of a cause and effect relationship requires further investigation^{2,10} and WHO has come out with a new classification for the causality assessment of AEFIs. The new WHO's classification of causality assessment¹⁰ is present in the below mentioned Table 2.

Majority of the health care providers (HCPs) reports only serious events and not the minor or moderate events, which can be a signal. There is an evolving AEFI surveillance system in India for the vaccines delivered through 'universal immunization program' (UIP) of government sector, but the reporting remained suboptimal for long in the country, and there is almost no participation from private sector. The AEFI reporting from private sector will provide vital information on the safety of new and underutilized vaccines, not part of

the UIP in India. All the HCPs involved in vaccination, especially in private sector have a crucial role to play with reporting of AEFI with newer/underutilized vaccines.⁹ Ministry of health and family Welfare released a standard operating procedure for the investigation of AEFIs in 2010. It gives a clear description about different types of AEFIs, different AEFI investigation committees and the AEFI reporting forms.¹³

The surveillance of adverse events following immunization is a critical monitoring function of national regulatory authorities (NRA) and immunization programmes. Surveillance and the causality assessment of the reported AEFIs allows NRA to detect different type o events such as vaccine product related reactions, immunization quality defect related reactions, immunization anxiety related reactions, Immunization error related reactions, coincidental events etc. This is of utmost importance, especially during vaccination campaigns, when a large number of doses are administered in a short time and in routine immunization sessions.^{7,13} The back ground rates of the adverse effects

of each country is published by WHO. Understanding this background rates will be a helpful parameter for the AEFI surveillance system to detect the changes in the frequency of the adverse effects. An increase in the frequency of AEFI is an alert to consider the quality of vaccine or consider a special risk among the local population.¹³

Ensuring the quality and safety of vaccine is one of the highest priority objective of WHO. World Health Organization closely work with the regulatory authorities of the different country to ensure that the global standard are made and easily available for the safe and quality use of biological agents including vaccines. The WHO strategy for the appropriate and safe use of vaccines has different objectives (1)formulating national policies and plans for the safe and appropriate use of injections, (2) ensuring quality and safety of injection equipment, (3) facilitating equitable access to injection equipment and (4) achieving appropriate, rational and cost effective use of injections. Ensuring the safety of immunization related injections interests with that of injection safety. Further information on this area can be found below.¹⁴

ROLE OF PHARMACIST

As per the American Society of Health-system Pharmacists (ASHP) Guidelines, pharmacists have a major role in disease prevention by advocating and administering vaccines. These activities are in consistent with the preventive aspects of the pharmaceutical care and is a part of the pharmacy practice since many decades. Many countries grant legal authority of pharmacists to administer vaccine after they achieve competency in all aspects of vaccine administration.¹⁵ But in India, pharmacists play major role in the storage and transportation of vaccines than administration.

Public awareness of vaccine safety has grown through increased access to information through the internet, television and other media. In order to maintain and improve public confidence in national immunization programmes, all HCPs should be aware of AEFI and be prepared to respond to public concerns. Timely response to public concerns about the safety of vaccines, as well as prompt communication, will protect the public and preserve the integrity of the immunization programme.⁵As the Pharmacists are the easily accessible HCPs in the community, they can take the initiative of reporting these events to the NRAs. The pharmacists can maintain a link between the patient and his/her other health care professionals in primary health care setting and can take up the responsibility to report the

AEFIs.¹⁶ Consumer reporting of AEFIs also in place in some of the developed countries.¹⁷ Parents of babies may be the right resources to identify different AEFIs and the professional interaction of pharmacists with the consumers may help to improve the rate of AEFI reporting.

In a systemic evaluation of 1,10,000 individual case safety reports(ICSR) received at National collaborating centre- Pharmacovigilance program of India (NCC-PvPI), 15.13% were reported by the Pharmacist and the study described that the ADR reporting by the Pharmacists are slowly increasing from 2011.¹⁶ Similar efforts has to be taken by the pharmacists to report AEFIs.

IS THERE ANY BARRIERS IN REPORTING AEFIS?

Major barriers found among the HCPs in reporting AEFIs were time constraints and non satisfactory reporting process, ignorance of reportable events, lack of awareness of the reporting forms, guilt about causing harm and being responsible for the event and insecurity regarding the causal association of the event with the vaccine .¹¹All these barriers can overcome by increasing awareness about the importance and the process of AEFI reporting among the HCPs, encouraging the staff to report AEFIs even in situations of uncertainty, emphasizing that the investigation is o fine the problems with the system and not to blame the individual and by giving positive feedback on reporting the AEFIs.¹⁸

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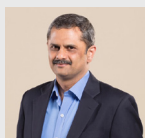
PICTORIAL ABSTRACT



SUMMARY

- Pharmacist being the most approachable health care member, can educate the parents on the possibility of the AEFI after each vaccination and the importance of its reporting.
- Pharmacists can take initiative to collect and assess the complete information about each reported AEFI and communicate to the NRA.
- Pharmacist can be a member in the causality assessment team which assess the causal relation between the event and vaccine.

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