

Patterns of Adverse Events Following Childhood Vaccination

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ABSTRACT

This cross-sectional was conducted to verify the safety profile of vaccines commonly included in Universal Immunization Program of India (UIPI). Out of 158 vaccinated children, 137 children had 187 adverse events following immunization (AEFI). They were most commonly seen with pentavalent and oral polio vaccines. Common adverse effects were mild fever (58.8%), pain at injection site (18.7%), and ulceration followed by scarring (11.8%). Walking difficulty in 10 children following DPT booster injection and two cases of diarrhoea (4.4%) following measles vaccination were also noted. Causality assessment was "probable" in all the cases. None of the AEFI was serious or severe. In conclusion, vaccines covered under UIPI are found to be safe.

Key words: Immunization, Pharmaco-vigilance, Vaccine, Adverse effects, Safety profile

Abbreviations: **AEFI** - Adverse events following immunization, **BCG** - Bacillus Calmette-Guerin, **DPT** - Diphtheria Tetanus Pertussis, **OPV** - Oral Polio Vaccine, **PVV** - Pentavalent vaccine (Contains a combination of diphtheria, pertussis, tetanus, Hemophilus influenza type B and hepatitis B vaccines), **UIPI** - Universal Immunization Program of India, **WHO** - World Health Organization

Introduction

Immunization is a cost-effective public health intervention that is adopted all over the world to reduce morbidity and mortality of communicable diseases. [1] Approximately, 2 to 3 million deaths due to diphtheria, tetanus, pertussis and measles are averted every year owing to the success of vaccination programs. [2] However, like any other medication, vaccines too can cause side effects. Any AEFI assumes great significance because they occur in healthy children. AEFI is least tolerated and when publicized in mass media it undermines the confidence of general public in vaccination programme, thereby leading to poor vaccine coverage and increased incidence of vaccine-preventable diseases.[3,4]. Strict periodic supervision of vaccine safety is, therefore, essential. The aim of this study was to re-affirm the safety profile of vaccines commonly included in Universal Immunization Program of India (UIPI) and to evaluate causality, seriousness and severity of AEFI.

Methods

This cross-sectional study was conducted at the Department

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of Pharmacology, PGIMS, Rohtak - a regional pharmacovigilance centre - between July 2015 and August 2015. Ethical approval was obtained from Institutional Ethics Committee.

All children vaccinated under UIPI were included in the study. UIPI vaccines include PVV, DPT, OPV, Measles, Hepatitis-B, Bacillus Calmette-Guerin (BCG) vaccine and booster Tetanus toxoid. Vaccines not included under UIPI were excluded from the study. As per WHO, AEFI is defined as a clinical event which follows immunization and which need not necessarily have a causal relationship with the usage of vaccine. AEFI included any unfavourable or unintended symptom, sign, abnormal laboratory finding or disease that occurred following vaccination. [2]

Demographic data were recorded in a predefined *pro forma*. Children were closely observed for at least 30 minutes after vaccination to recognize immediate adverse events. Care takers were given a diary card to record local (injection site) and systemic AEFI over the subsequent 7 days (i.e. Day 0 to Day 6). Physical or telephonic follow-up was done at the end of 7 days. Fever was measured by axillary body temperature and was categorized as no fever (<38°C), mild fever (38-38.9°C), moderate fever (39-39.9°C), and severe fever (≥40°C).

Adverse event monitoring was carried out by spontaneous reporting of solicited AEFI using structured format as per Centre Drugs Standard Control Organization's AEFI reporting form. The collected AEFI reports were evaluated for causality,

severity and seriousness of reaction. The causality between vaccine and AEFI was assessed using the WHO-Uppsala Monitoring Centre criteria.[5] They include chronological relationship between drug administration and development of adverse event, response to withdrawal and re-introduction of the drug and details of any other concomitant medication. Accordingly, causal relationship is classified into four categories: certain, probable, possible, and unlikely.

Severity of AEFI was assessed using modified Hartwig-Seigal scale, which assesses factors such as requirement for change in treatment, duration of hospital stay and resultant disability. Accordingly, severity of AEFI is graded by 7 levels. [6] Level 1 and 2 are defined as mild. Levels 3, 4a, 4b as moderate and level 5 and above as serious event.

Seriousness of the AEFIs was assessed using WHO criteria which categorizes an adverse event as serious if it causes death, threatens life, requires hospitalization, causes disability, results in congenital anomalies, or requires intervention to prevent permanent impairment/damage.[7]

Collected data were uploaded in vigiflow software and sent to the National Coordinating Centre, Ghaziabad from where they are sent to Uppsala Monitoring Centre, Sweden for analysis. The data were descriptive in nature and the results are expressed in percentage.

Results

Out of 158 children enrolled in the study, 80 (50.60%) were boys and 78 (49.40%) were girls. Majority of them belonged to the age-group of 0-6 months. A total of 187 adverse events were reported in 137 children. Mild fever (58.8%), local pain (18.7%) and injection-site ulceration or scarring (11.8%) were the common AEFI. High frequency of AEFI was observed with three doses of PVV and OPV vaccines. Ten cases of difficulty in walking were observed when DPT booster vaccine was administered alone or along with measles and OPV vaccines. With measles vaccination two cases of diarrhea were observed, one with measles vaccine alone and one when it was administered along with the third dose of PVV and OPV vaccines. These cases were not severe and were easily managed with oral rehydrating solution. Causality assessment revealed that all AEFI belonged to 'probable' category. None of the AEFI was serious or severe. Severity of AEFI was moderate for PVV, DPT booster, and measles vaccine while it was mild for BCG vaccine and tetanus toxoid.

Discussion

Several vaccines are often combined, as in PVV, to enhance patient compliance, to minimize handling errors and to make them cost-effective. Causal attribution of adverse effects to individual components of such combined vaccines

is often difficult. Frequency of fever, local pain, redness, and swelling following PVV in the present study is similar to that of Eregowda et al.[8] Minor local reactions are nothing unexpected after DPT vaccination.[9] Regalado et.al have also reported high frequency of fever and pain after DPT vaccination.[10] Similar to our finding Ipp et.al have also observed decreased movement of lower extremity or walking difficulty in 49.9% of cases after DPT vaccination at 18 months of age.[11] The most common adverse event after injection of tetanus toxoid is mild local reaction. The frequency and severity of AEFI is influenced by the number of prior doses and the level of preexisting antitoxin.[12] Local adverse effects, such as ulceration and scarring, are common after BCG vaccination. Among the 46 children who received measles vaccine, 2 (4.4%) developed diarrhea. In a study conducted by Bhargava et.al 3.2% cases of diarrhea were observed after measles vaccine. [13] Thus the present study re-confirms the safety profile of vaccines reported in previous studies. Limitation of the study was that it excluded those vaccines which are not covered under UIPI. Further the sample size is too small to pick up rare adverse events.

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Ethics: The study was approved by Institutional Ethics Committee

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