

7

Adverse Events Following Immunization

Introduction

An adverse event following immunization (AEFI) or vaccine associated adverse event (VAE) is defined as an untoward, temporally associated event following immunization that might or might not be caused by the vaccine or the immunization process. These events may be recognized during clinical trials or during post marketing surveillance (eg intussusception following rotashield vaccine, febrile seizures following Proquad vaccine and GBS following meningococcal conjugate vaccines). Tolerance to vaccine associated adverse events is generally lower as these are administered to healthy children unlike other pharmaceutical products used in morbid populations. Vaccine associated adverse events are more likely to be noticed and communicated and can often significantly impact immunization programs as noticed with measles, MMR and pertussis vaccines.

Classification

AEFI may be a mere coincidence (eg sudden infant death syndrome following whole cell pertussis vaccines) or a true adverse immunization reaction. Adverse immunization reactions may be further classified as

- Adverse vaccine reaction (vaccine induced). Here the vaccine is causally related to the reaction; e.g. VAPP due to oral polio vaccine, anaphylaxis.
- Trigger reaction (vaccine potentiated). Here the reaction is triggered by the vaccine, e.g. febrile seizure following vaccination in a predisposed child.

- Programmatic errors. These are most common cause for serious adverse events and death following vaccination. Deaths following measles vaccination due to toxic shock syndrome resulting from improper reconstitution and storage of measles vaccine is the most recent example of this phenomenon.
- Injection reaction. Examples include syncope due to pain of vaccination, injection site abscesses, sciatic nerve damage due to gluteal injection and transmission of blood borne pathogens such as HIV/HBV/HCV.

It is extremely important to distinguish vaccine reactions that are causally related to the vaccine (adverse vaccine reactions) from other adverse events so that compliance to vaccines does not drop.

AEFI may also be classified as serious or non serious. A serious adverse event (SAE) is defined as that which is either (i) fatal or life threatening or (ii) results in persistent or significant disability, incapacity or (iii) results in or prolongs hospitalisation or (iv) leads to congenital anomalies/birth defects. Important adverse reactions that are not immediately life-threatening or do not result in death or hospitalization but may jeopardise the patient should also be considered as serious.

Based on causal association, AEFI may also be classified as (i) definitely (ii) probably (iii) possibly (iv) unlikely to be related to the vaccine.

Adverse Vaccine Reactions

Adverse vaccine reactions are those that are causally related to vaccines and may be classified as local, systemic or allergic. Adverse vaccine reactions have been discussed in detail in the chapter on individual vaccines. Some common and or serious reactions are discussed further.

Local Reactions

Most parenteral vaccines induce some degree of local reactions including pain, erythema and induration. Local reactions are

more with whole cell pertussis vaccines and aluminium adjuvanted (DTPw, DTaP, DT, Td, Tdap, TT, Hep B, Hep A, inactivated combination vaccines, HPV and PCV7) vaccines. Most studies show the frequency of local reactions to increase with subsequent doses and frequently administered doses (TT). Local reactions may be partly ameliorated by ice application and paracetamol.

Systemic Reactions

Fever is the most common systemic reaction and like local reactions, fever is more common with whole cell pertussis vaccines and aluminium adjuvanted vaccines. However unlike local reactions the incidence of fever and other systemic reactions usually declines with increasing age and increasing number of doses. Administration of paracetamol at the time of vaccination and later on a regular basis is helpful and indicated especially in children predisposed to febrile seizures. Fever due to vaccination does not usually last for more than 48 hours and any fever persisting beyond this time should be evaluated for other causes.

Severe Allergy

Severe allergy or anaphylaxis or anaphylaxis like reactions including generalized urticaria or hives, wheezing, swelling of the mouth and throat, difficulty breathing, hypotension, and shock occur rarely at a frequency of 1 per 10,00,000 vaccinees. These reactions are rarely due to the vaccine antigen; they are usually due to other vaccine constituents including residual animal protein (e.g egg), stabilizers (e.g. gelatin), antimicrobials (e.g. neomycin) or preservatives (e.g. thiomersol). As a precautionary measure, the vaccine should be questioned for any immediate type of hypersensitivity to any of the vaccine constituents listed on the package insert prior to vaccination. Patients with history of *serious allergy* to any of the vaccine constituents should not receive the vaccine (exception children with egg allergy can safely receive measles and MMR vaccines). Since

occurrence of anaphylaxis cannot be predicted in most vaccinees, all vaccinees should be observed for 15 minutes after vaccination and resuscitative equipment including ambu bag and mask, laryngoscopes, endotracheal tubes, IV access devices, epinephrine, hydrocortisone, antihistaminics, and inotropes should be kept standby. Management of anaphylaxis is detailed in Table 7.1.

Table 7.1: Emergency management of anaphylaxis

1	Administer epinephrine (1: 1000 solution) 0.01 ml/kg/dose (max 0.5 ml) intramuscular in anterolateral thigh.
2	Set up IV access.
3	Lay patient flat and elevate legs if tolerated. Give high flow oxygen and airway/ventilation if needed.
4	If hypotensive also, set up additional wide bore access and give IV normal saline 20 ml/kg under pressure over 1-2 minutes.
5	IM adrenaline may be repeated after 3-5 minutes if required.
6	Oral antihistaminics may be given to ameliorate skin symptoms but IV antihistaminics are not recommended. Oral or injectable corticosteroids equivalent to prednisone 1-2 mg/kg may be given but benefit is yet unproven.

Controversies in Vaccine Safety

Vaccines and Autism

Over the past decade there has been tremendous controversy on the relationship between vaccines particularly MMR and autism/autistic spectrum disorder. Review of all currently available evidence does not support any causal relationship between MMR vaccine and autism.

Safety of Thiomersol

Thiomersol (50% ethyl mercury) a preservative in inactivated vaccines particularly in multi dose vials has been linked in the past to autistic spectrum disorders and neuro-development disorders. Consequently most of the vaccine preparations available in the developed nations are thiomersol free. Systematic review of evidence however has not supported any causal association between thiomersol

and neurotoxic effects. Therefore in developing nations, where multi dose vials significantly bring down vaccine costs and cold chain space requirement, the benefits of thiomersol far outweigh any possible risks.

Vaccine Associated Adverse Event Reporting System (VAERS)

A system for reporting VAERS is crucial in any immunization program so as to pick up previously unrecognized adverse effects and generate further data on vaccine safety. A robust system for reporting VAERS exists in most developed countries including the US. However such a system is currently not available in India. Pediatricians are encouraged to report VAERS to the IAP immunization website www.iapcoi.com. Events that should be reported include all SAE irrespective of causal association, non serious adverse events that are unexpected in nature, severity, frequency or outcome, vaccine failures, and all usage in pregnancy.

Conclusion

Vaccines are largely safe. Serious outcomes are usually programmatic/human errors. It is therefore extremely important to use vaccines strictly as per recommendation and be prepared to handle any eventuality.