HAEMOPHILUS INFLUENZAE TYPE B (Hib) VACCINE

Introduction

Haemophilus influenzae type b disease, primarily pneumonia and meningitis in young children, is a significant public health concern in many parts of the world where large-scale Hib immunization has not yet been implemented. Hib disease is defined as invasive when the bacterial agent is detected in body fluids or tissue that normally are sterile (blood, cerebrospinal fluid, peritonea fluid, pleural fluids or lung aspirates).

Bacteriology

Haemophilus influenzae b is a Gram-negative coccobacillus first described by Pfeiffer in 1889. It is a common commensal in the upper respiratory tract of children. In the pre-vaccination era, the majority of non-immune children were colonized by Hib in their nasopharynx at some time, occasionally for months, although the bacterial colonization rate varied considerably with age and socio-economic factors. Upper respiratory tract colonization of this agent drops dramatically in populations where Hib immunization has achieved high coverage. Only a tiny fraction of those who harbour this organism on their respiratory mucosa subsequently develops clinical disease.

Mode of transmission

Humans are the only known natural host for *Haemophilus influenzae* bacteria, which is spread by droplets released when an infected child sneezes or coughs and by direct close contact with an infected person.

Clinical Features

The disease burden is highest among those aged between 4 months and 18 months, but Hib disease is occasionally observed in infants aged less than 3 months and among those aged more than 5 years. In unvaccinated populations, Hib is the dominant cause of non-epidemic bacterial meningitis especially during the first year of life. Even with prompt and adequate antibiotic treatment, 3–20% of patients with Hib meningitis die. Where medical resources are limited, fatality rates for Hib meningitis may be much higher, and severe neurological sequelae are frequently observed in survivors in up to 30–40%.

In developing countries, pneumonia is more common than meningitis in children with Hib disease. Other important manifestations of Hib infection include septicaemia, septic arthritis, osteomyelitis, pericarditis, cellulites and epiglottitis, particularly in industrialized countries.

The classical clinical signs of meningitis (neck stiffness and photophobia) are often not detected in infants, who usually present with drowsiness, poor feeding and high fever.

There are no specific clinical features of any of the focal infections due to Hib which enable them to be differentiated from those due to other organisms.

Epidemiology

Global Situation

According to the WHO, in year 2000, Hib was estimated to have caused two to three million cases of serious disease, notably meningitis and pneumonia, and 386,000 deaths in young children globally. Another significant proportion of children with serious Hib disease end up with long term consequences such as deafness, learning disabilities, paralysis and mental retardation. Although this problem occurs worldwide the burden of Hib disease is most significant in resource-poor countries. Systematic vaccination has now virtually eliminated Hib disease in industrialized nations.

Situation in Sri Lanka

A recent (2004) disease burden study on *haemophilus influenzae b* carried out in Sri Lanka has indicated that it is an emerging public health issue.

Haemophilus influenzae type B (Hib) vaccine

Fortunately, *Haemophilus influenzae* b disease (Hib) is preventable. Vaccines are the only public health tool capable of preventing the majority of cases of serious Hib disease. There is a highly safe and effective vaccine routinely used in the industrialized world for over 15 years in their childhood immunization programmes and has documented virtual elimination of Hib disease. Despite recommendations from WHO that Hib vaccine be included in all countries' routine infant immunization programmes, in 2006, only 26% of children worldwide received Hib vaccine.

Sri Lanka has introduced Hib vaccine into its National Immunization schedule in year 2008 in the form of liquid pentavalent vaccine (DTP-HepB+Hib).

Characteristics of the Hib Vaccine

The second generation Hib vaccines currently licensed for use in infants consist of polyribosylribitol phosphate (PRP- the capsular polysaccharide of Hib) conjugated to a protein carrier. The first generation Hib vaccine was an unconjugated vaccine and not used now. These conjugate Hib vaccines are more immunogenic and effective in young infants.

The protein carriers used are either a mutant diphtheria toxin (Hb-OC Hib vaccine), or an outer membrane protein of *Neisseria meningitidis* (PRP-OMP Hib vaccine) or tetanus toxoid (PRP-T Hib vaccine). It should be noted that the protein conjugates used in Hib vaccines are not themselves immunogenic and do not give protection against diphtheria, tetanus or *N. meningitides.*

Types of Hib containing vaccine preparations

Available formulations include liquid Hib vaccine as well as lyophilized (freeze-dried) Hib vaccine, either monovalent or in combination with one or more other vaccines (multivalent), such as DTP, hepatitis B vaccine and inactivated polio vaccine. Many countries including Sri Lanka give Hib vaccine combined with DTP and HepB vaccines (DTP-HepB+Hib).

- **Hib with diphtheria, tetanus, whole cell pertusis and hepatitis B (DTwP-Hep B-Hib) vaccine**
  Liquid preparation of this presentation is currently used in the National Im munization programme.
  Refer to the chapter on pertussis for details

- **Monovalent Hib vaccine**
  Each 0.5 ml dose contains 10 micrograms of purified capsular polysaccha ride of Hib covalently bound to approximately 30 micrograms of tetanus toxoid.

- **Hib with diphtheria, tetanus and whole cell pertusis (DTwP-Hib) vaccine**
  Refer to the chapter on pertussis for details

- **Hib with diphtheria, tetanus, acellular pertusis, hepatitis B and inactivated polio (DTaP-HepB-IPV-Hib) vaccine**
  Refer to the chapter on pertussis for details

Indications

To prevent *haemophilus influenzae* type b infection in infants and children upto 5 years.

Efficacy

The conjugate Hib vaccines currently licensed for immunization of infants induce protective circulating antibodies and immunological memory in all age groups. Hib vaccination also reduces nasopharyngeal colonization with the organism, leading to substantially greater reduction in disease incidence than can be directly attributed to the effects of the vaccine. This indirect effect has been amply demonstrated in several post-introduction effectiveness studies in which near-elimination of the disease occurred in both industrialized and developing countries, even when vaccine coverage was suboptimal. The duration of protection following completion of primary Hib immunization is poorly defined, and it is

likely to vary according to factors such as age at vaccination, ethnicity, immune competency and natural boosting. However, in most cases primary immunization is protective during the years of highest susceptibility to invasive Hib disease.

Immunization Schedule

National immunization schedules may slightly differ depending upon local epidemiological and programmatic considerations. In general, a 3-dose primary series of Hib vaccine is given at the same time as the primary series of diphtheria–tetanus–pertussis (DTP). The first dose may be given to infants as young as 8 weeks of age, and the second and third doses may be given at 6–8 week intervals usually along with DTP. The vaccine is not generally offered to children aged more than 24 months owing to the limited burden of Hib disease among children older than that age.

For children aged more than 12-24 months who have not received their primary immunization series, a single dose of the vaccine is sufficient.

Sri Lankan National Immunization policy is to give Hib vaccination in the form of pentavalent (DTP-HepB+Hib) vaccine to all infants on completion of 2 months, 4 months and 6 months.

Dosage & Administration

All conjugate Hib containing vaccines are given intramuscularly: in infants, they are administered into the anterolateral aspect of the mid thigh or in older children into the deltoid muscle. The standard dose is 0.5 ml.

Liquid Hib vaccines are used directly from the vial, whereas freeze-dried vaccines must be reconstituted before administration, either with diluent or with another vaccine that has been specifically identified and indicated for this purpose by the manufacturer, such as DTP.

Storage

All Hib-containing vaccines should be stored at between +2 °C and +8 °C. Liquid Hib vaccine should never be frozen, stored or transported in contact with ice or ice packs.

Lyophilized vaccine may be frozen until reconstitution, but since the most commonly used diluents used for reconstitution cannot be frozen, it is recommended that lyophilized Hib vaccine should also be stored at temperatures between +2 °C and +8 °C .

Cautions and contraindications

The following conditions are considered as either contraindications or cautions for the use of Hib vaccine.

- Presence of one of the general contraindications for any vaccine.
- People who are known hypersensitivity to any component of the vaccine.

Adverse Events

Usually Hib vaccine has not been associated with any serious adverse effects. However, redness, swelling and pain at the site of injection may occur in those who have been vaccinated. Such reactions usually start within 1 day after immunization and resolve within 1–3 days.

Usage of vaccine in specific circumstances

Although immunization against Hib disease is not routinely recommended for individuals aged more than 24 months, older children and adults who are at an increased risk for invasive Hib infection should be vaccinated where resources are available. Such high-risk individuals include:

- those with HIV infection or immunoglobulin deficiency,
- recipients of stem cell transplants,
- patients undergoing chemotherapy for malignant neoplasms,
- those with asplenia (due to sickle-cell disease or splenectomy).

Sources

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