MENINGOCOCCAL VACCINE

Introduction

Bacteria called *Neisseria meningitidis* (meningococcus) is a leading cause of meningitis and fulminant septicaemia and a significant public health problem in most countries. Although meningococcal disease frequently occurs as scattered, apparently unrelated cases or in small outbreaks, in some regions this endemic situation may alternate with devastating, unpredictable epidemics.

Meningococcal disease was described as far back as 1805 when an outbreak swept Geneva, Switzerland. However, the causative agent of meningococcal meningitis was identified only in 1887. Major outbreaks were subsequently noted during the two world wars and epidemics have been reported on the African continent since 1909.

As a rule, endemic meningococcal disease occurs primarily in children and adolescents, with highest attack rates among infants aged 3 -12 months, whereas in meningococcal epidemics, rates may rise in older children and young adults.

Bacteriology

Meningococcal disease is caused by the bacterium *Neisseria meningitides* (*N. meningitidis* or meningococcus), a Gram-negative diplococcus. There are 13 known serogroups distinguished by differences in surface polysaccharides of the outer membrane capsule. Globally, serogroups A, B, C, W135 and Y most commonly cause the disease. Out of all Meningococcal serogroups A, B and C are responsible for the vast majority of morbidity and mortality.

In most parts of the world, serogroups Y and W135 are relatively uncommon causes of meningococcal infection. However, recent reports of endemic occurrence of serogroup Y meningococcal disease in the United States, and outbreaks caused by serogroup W135 strains in Saudi Arabia and sub-Saharan Africa, suggest that these serogroups may be gaining importance, at least among young adults.

Mode of transmission

N. meningitidis is transmitted by inhalation or direct contact with respiratory secretions of patients or healthy human asymptomatic carriers. The carrier rate is relatively low during childhood and high in adolescents and young adults. Transmission is relatively slow in open populations and is greater in isolated closed populations. Transmission is aggravated by smoking or presence of respiratory infections. The average incubation period is 4 days, ranging between 2 - 10 days. There is no animal or environmental reservoir for this organism.

Clinical Features

Neisseria meningitidis can cause meningitis, septicaemia or a combination of both meningitis and septicaemia. Rarely did it cause other localized infections, including pneumonia, arthritis and conjunctivitis. Meningococcal septicemia, with or without meningitis, have overall high mortality risk (about 10%) despite appropriate antibiotic therapy.

The most common symptoms of meningococcal meningitis are stiff neck, high fever, sensitivity to light, confusion, headaches and vomiting. About 10 -15% of survivors of meningococcal meningitis will suffer from significant neurological sequelae, including mental disorders, deafness, palsies and seizures. A less common but more severe form of meningococcal disease is meningococcal septicaemia which is characterized by typical haemorrhagic rash and rapid circulatory collapse. Extensive tissue necrosis, sometimes resulting in amputations of digits or limbs.

Both persons with complement factor deficiencies and functional or anatomical asplenia are at increased risk of getting meningococcal disease.

Treatment with appropriate chemoprophylaxis is an important control measure for meningococcal disease; however, it has limited effectiveness and its use should be restricted to special circumstances. These circumstances include close contacts of cases, such as households, schoolmates and institutionalized subjects. The main purpose of chemoprophylaxis is to prevent the occurrence of secondary cases by eliminating carriers with *Neisseria meningitidis*.

Patients with meningococcal infection treated in a hospital or clinic, who had received an antibiotic, which does not eliminate the carrier state (penicillins or chloramphenicol), should receive chemo-prophylaxis with an effective antibiotic (ciprofloxacin, rifampicin, or ceftriaxone) upon hospital discharge.

Epidemiology

Global Situation

Meningococcal meningitis occurs sporadically in small clusters throughout the world with seasonal variations and accounts for a variable proportion of endemic bacterial meningitis. In temperate regions the number of cases increases in winter and spring.

The largest burden of meningococcal disease occurs in an area of sub-Saharan Africa known as the meningitis belt, which stretches from Senegal in the west to Ethiopia in the east.

Serogroup A disease occurs predominantly in developing populations such as those in Africa and Asia, while serogroup B is the major cause of sporadic meningococcal disease in most developed countries.

In industrialized countries, the overall mortality from meningococcal meningitis is usually 5 - 10%; in Africa, closer to 10%. Case-fatality rates in fulminant septicaemia may exceed 15 - 20%.

Situation in Sri Lanka

No major meningococcal meningitis outbreaks have been reported from Sri Lanka, but few isolated cases mainly among children has been reported in the recent past. Around 4000 Sri Lankans visit Mecca as Hajj pilgrims annually, and it is very important to ensure that all these pilgrims are vaccinated against meningococcal meningitis before they leave

Meningococcal vaccines

Currently available meningococcal vaccines include polysaccharide vaccines and polysaccharide-protein conjugate vaccines. Although purified capsular polysaccharide antigens elicit protective antibody responses, conjugate vaccines are more immunogenic and also induce immunological memory. Both polysaccharide and conjugate vaccines are available against meningococci of serogroups A, C, W135 and Y.

Serogroup B vaccines are based on protein extracted from selected outbreak strains. Strain-specific serogroup B vaccines have been used successfully in some countries to limit outbreaks, but they are not widely available.

Characteristics of Meningococcal vaccines

There are 2 different types of meningococcal vaccine available: the meningococcal conjugate vaccines and meningococcal polysaccharide vaccines . The difference between these 2 types of vaccines lie in the different way that each vaccine stimulates an immune response.

Meningococcal polysaccharide vaccines

Internationally marketed meningococcal polysaccharide vaccines are based on purified, heat-stable, lyophilized capsular polysaccharides from meningococci of the respective serogroup. They are available in bivalent (A,C), trivalent (A, C, W135), and quadrivalent (A, C, W135,Y) formulations. The vaccines contain 50 μg of each of the individual polysaccharides. No adjuvants are included.

Meningococcal conjugate vaccines

Licensed meningococcal conjugate vaccines are currently available in monovalent (A or C) or quadrivalent (A, C, W135, Y) and also include a combination vaccine based on *Haemophilus influenza* type b and *Neisseria meningitidis* serogroup C vaccines (HibMenC). The protein conjugate of these vaccines consists of either diphtheria toxoid or a non-toxic mutant of diphtheria toxin (CRM 197), or tetanus toxoid.

Indications

Vaccination with meningococcal vaccines is recommended in the following situations;

- Patients with terminal complement component deficiencies
- Patients with functional or anatomic asplenia.
- control of meningococcal outbreaks
- laboratory personnel who are exposed routinely to *N. meningitidis*
- people who intend travelling to meningococcal endemic regions
- pilgrims attending the annual Hajj in Saudi Arabia

Efficacy

Meningococcal polysaccharide vaccines

The antibody responses to each of the four polysaccharides in the polysaccharide vaccine are serogroup-specific and independent. Vaccine efficacy within the year of immunization is between 87% and 94%. Lower efficacy (0- 67%) has generally been observed in young children. Vaccine efficacy was strongly related to age at immunization: 83% for ages 15 to 20 years, 75% for ages 10 to 14years, and 41% for ages 2 to 9 years.

Meningococcal conjugate vaccines

Vaccine effectiveness after one year ranged from 87% - 98%. There was no significant difference in effectiveness between age groups. However, after 4 years of follow-up, the vaccine effectiveness among children declined significantly to 66%.

Dosage & Administration

Meningococcal polysaccharide vaccines

Single dose of 0.5 ml is recommended for both children more than 2 years of age and adults. Reconstituted vaccine administered by subcutaneous injection. Meningococcal polysaccharide vaccine can be administered concurrently with other

vaccines. Protective level of antibody is usually achieved within 7 – 10 days of vaccination. Protection lasts for 3 – 5 years.

Meningococcal conjugate vaccines

Meningococcal conjugate vaccines are licensed for children aged more than 2 months, adolescents and adults. The dose is 0.5 ml given by IM injection.

Infants aged 2–11 months are given 2 doses (0.5 ml per dose) with at least 2 months apart, followed by a booster dose about one year later.

The possible need for boosters is not yet established for individuals >1 year of age, who normally receive one dose only.

Storage

Both polysaccharide and conjugate meningococcal vaccines should be stored at +2°C to +8°C. Do not freeze.

Cautions and contraindications

The following conditions are considered as contraindications for the use of both polysaccharide and conjugate meningococcal vaccines.

- Presence of one of the general contraindications for any vaccine.
- History of an allergy to any of the vaccine components.
- Anyone who has experienced anaphylaxis to a previous dose of meningococcal vaccine.

Both conjugate and polysaccharide meningococcal vaccines are efficacious and safe when used in pregnant women.

Adverse Events

Meningococcal polysaccharide vaccines

Adverse reactions to polysaccharide meningococcal vaccines are usually mild; the most frequent reaction is 1–2 days of pain and redness at the site of injection. Transient fever is reported in <5% of recipients. Very rarely systemic allergic reactions (e.g.urticaria, wheezing, rash) and anaphylaxis have been reported.

Meningococcal conjugate vaccines

All meningococcal conjugate vaccines have an excellent safety records. None has been associated with any serious adverse effects, either during clinical trials or in post-marketing surveillance. Redness, swelling and pain at the site of injection may occur. Such reactions usually start within the first day after immunization and last 1 to 3 days. Less commonly, children may develop fever or be irritable for a short period.

Travellers

Travellers from low-endemic regions visiting countries which are highly endemic or epidemic for meningococcal disease should consider meningococcal vaccination. For travellers to the African meningitis belt, the risk of acquiring infection is greatest in the dry season and for those with prolonged contact with the local population.

Proof of quadrivalent (A,C,W135,Y) vaccination against meningococcal disease is required for all persons more than 2 years travelling to Mecca during the annual Hajj and the Umrah pilgrimages. The vaccine should be given at least 10 days before arrival at Mecca. Vaccination is valid for three years.

In Sri Lanka currently travellers can get meningococcal vaccination with quadrivalent (A,C,W135,Y) polysaccharide vaccine either from Port Health Office at Medical Research Institute or from the private sector.

Sources

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