Meningococcal B Vaccine

Abstract:

Bexsero, a 4 component protein-based meningococcal B vaccine (4CMen B) manufactured by Novartis was authorised for use by the European Medicines[1] in January 2013. The development of 4C Men B has taken long years of research because of the similarity between the serogroup B capsule and the human antigen neural-cell adhesion molecules. It necessitated a new approach called reverse vaccinology which involves whole-genome sequencing of bacteria and the identification of proteins that provoke an immunological response. The 4CMen B vaccine has 4 antigenic components. The clinical trials have involved 8000 children. One month after the third dose, 84-100 per cent had a satisfactory immunological response[2]. The new vaccine should protect against 73% of the strains that cause the disease. The recommended immunisation for infants is 3 doses commencing at 2 months with 2 further doses at least 1 month apart. For unvaccinated older children 2 doses are recommended. Since 1999 serogroup C conjugate vaccine has been available for the prevention of meningococcal C disease and has led to a dramatic reduction in the incidence of the disease.

Although the vaccine is the culmination of 15 years of development it has already been subject to controversy. In the UK, the Joint Committee for Vaccinations and Immunisations (JCVI) has recommended not to introduce the vaccine to the immunisation schedule[3]. The basis of the decision made by the JCVI was that the vaccine would not be cost-effective. The cost-effectiveness analysis was submitted to the JCVI by the University of Bristol and London School of Hygiene and Tropical Medicine. The analysis is done by using an internationally recognised system known as quality-adjusted life years (QALY). A QALY is an assessment of how many extra years of life of a reasonable quality a person might gain as a result of a treatment. In other words the cost of introducing the vaccine would be greater that resulting from clinical impact of meningococcal infection. To be cost-effective, any new vaccine, cancer medicine or heart treatment should cost no more than £20-30,000 for every QALY it saves. The JCVI has concluded that the MenB vaccine did not meet the economic criteria at any level. In other words, introducing the vaccine would not be a good use of NHS resources.

There were also concerns raised around the vaccineâ s effectiveness, its coverage and impact on carriage and transmission of Men B bacteria. Another issue is that in some cases it is associated with post-immunisation pyrexia which could lead to anxiety among parents about the vaccination programme in general. The Committee noted that over the last 10 years the incidence of invasive meningococcal disease decreased by half and now stands at 25 cases per 100,000 children under 1 year and 2 per 100,000 across all ages combined. The JCVI also stated that the incidence of meningococcal disease will further decrease if population reduction in smoking and influenza continues, both are known risk factors. It was suggested that routine infant immunisation with Bexsero would prevent directly around 25% of cases over the lifetime of each single vaccinated birth cohort. JCVI concluded that routine infant or toddler immunisation with Bexsero was highly unlikely to be cost effective at any vaccine price and could not be recommended. Dr David Elliman, immunisation expert at the Royal College of Paediatrics and Child Health, said it must have been a very difficult decision for the JCVI to make. "Nobody doubts that meningococcal B disease can be catastrophic and that all reasonable means should be taken to prevent it. However, before introducing a new vaccine or drug, it is important to be sure that not only is it safe and effective, but bearing in mind the increasing financial pressures on the NHS, it also has to be cost-effective. We need to know how well it will protect, how long it will protect and if will stop the bacteria from spreading from person to person. David Salisbury, director of immunisation at the UK department of health stated that we have a new vaccine against Men B but we lack important evidence.

The JCVI decision not to recommend meningococcal B vaccination for the present has raised considerable debate. This is understandable because meningococcal disease has struck fear into generations of parents and doctors. It can cause death in a previously healthy child in a short few hours. The mortality rate may be as high as 10% per cent and among survivors one in five will have long term morbidity including neurological sequelae and limb loss. The initial diagnosis can be difficult to distinguish other intercurrent illnesses. In particular it may resemble the â flu in the early stages of the disease. Another problem is that the patient may not get to medical attention in time. Although the incidence may be low the only measure that we can take against a rapid onset, potentially fatal disease such as Men B is to vaccinate. Furthermore the public have great difficulty understanding risk and rates per 100,000 have a limited meaning. There is a much greater understanding when the risk is quoted as the number of new cases per week. In Ireland in 2011 there were 84 cases of meningococcus B infection and 2 deaths according to R. Cunney at HPSC.

Chris Head from the Meningitis Research Foundation[4] has expressed his disappointment at the decision. Measuring the cost burden of meningococcal disease is difficult because the sequelae are wide-ranging and variable. The Foundation supports a population based evaluation of the vaccine.

In other correspondence in the Lancet it is pointed out that cost-effectiveness studies can be unfavourable for preventative strategies such as vaccination. Cost-effectiveness models may be over-influenced by short-term benefits and do not give sufficient emphasis to future benefits[5]. Furthermore this type of analysis tends to favour mild but common diseases rather than more rare diseases with a high morbidity and mortality. Some commentators have suggested that decision makers should view the potential to prevent needless suffering and death as the primary goal of vaccination and make decisions on that basis.

No country has yet taken up the Men B vaccine as part of the national immunisation programme. The JCVI has asked for comments on their interim statement. Many other national health services will follow the deliberations with interest. Moxon and Snape[6] urge that as little time as possible is lost in reaching a decision and that hopefully the matter will not be shelved.

JFA Murphy

Editor

1. European medicines agency press release on Bexsero 2012

2. A new Men B (meningococcal B) vaccine. Meningitis wise.

3. JCVI interim position statement on use of Bexsero meningococcal B vaccine in the UK. July 2013

4. Head C. Immunisation against meningococcus B. Lancet 2013;382:935

5. Rappuoli R. Lancet 2013;382:935-6.

6. Moxon R, Snape MD. The price of prevention: what now for immunisation against meningococcus B? Lancet 2013;382:369-70

Comments: