VACCINES AGAINST GROUP B MENINGOCOCCAL DISEASE - PROBLEMS AND PERSPEETIVES

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Introduction

During the last three decades serogroup B *Eeisseria meningitidis* has emerged as a cause of epidemics in several European countries, the Americas, and South Africa. Whereas polysaccharide vaccines of serogroup A, C, Y and W135 offer good protection against meningococcal disease in adults and in children over 2 years, the serogroup B polysaccharide (B-ps) is poorly immunogenic. Therefore, alternative vaccine approaches, based on noncapsular surface antigens such as outer membrane proteins (OMPs), detoxified lipopolysaccharides (LPS) or chemically modified B-ps, have been suggested. Several outer membrane antigens have been identified as potential vaccine candidates. Particular interest has been focused on the porins (PorA and PorB) since antibodies against these components are strongly bactericidal or opsonic. However, there is a large amount of antigenic diversity among the group B strains. Aproximately 20 different serotypes have been defined, based upon immunological differecences in the class 2/3 protein (PorB). Further antigenic diversity is seen among the class 1 protein (PorA), which contain the subtype- specific antigens. LPS depleted outer membrane vesicles (OMVs) are excellent immunogens, produced by relatively simple technology, and have been shown to be safe in humans. The OMVs induce functional antibodies to multiple membrane antigens. Two OMV based vaccines, based on different group B strains have been tested for protective efficacy in large clincal trials and shown to give protection although the observed efficacy seemed to vary by age groups and epidemiological situation.

The serum bactericidal activities (SBA) of the Norwegian (B:15:P1.7,16) and the Cuban (B:4:P1.15,19) OMV vaccines have been compared in different populations and against different meningococcal strains. Both vaccines induced high levels of functional antibodies, which, in most of the vaccinees were mainly serosubtype (PorA) specific. The immune response to homologous meningococcal strains was independent of the age of the vaccinees; after vaccination with the Norwegian vaccine about 100 % of the vaccinees responded in SBA against the vaccine strain, also in infants less than 1 year. Compared to two doses, a third dose of vaccine induced more cross-reactive antibodies and the level of cross-reactive bactericidal antibodies increased by age of the vaccinees. At present, none of the existing vaccines can be considered as general group B vaccines. One alternative is to include several PorA and PorB proteins in one vaccine. Attempts have been made to adress this for the PorA protein by constructing vaccine strains capable of expressing more than one subtype epitope of this protein. Recently, a hexavalent vaccine based on PorA from dominant serogroup B isolates from the UK and the Netherlands has been developed. However, the bactericidal responses of these genetieally constructed vaccines seems to be inferior to that observed with the normal OMVs. As long as no broadly cross-reactive antigens, inducing protective antibodies, have been identified, an alternative approach is to produce new vaccines based on the actual epidemic, or to combine OMVs from several epidemiological relevant strains. There will then be a need for continous detailed epidemiological surveillance in order to predict the optimal vaccine composition for any given time and place. Our studies offers evidence for the successful eontrol of serogroup B meningococcal disease among infants, children and adult through the development of multivalent, OMV based vaccines. Such experimental vaccines are now produced and tested in our laboratory.