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DECREASED RESPONSE AFTER CONJUGATED MENINGOCOCCAL SEROGROUP C VACCINATION IN CHILDREN WITH DOWN SYNDROME

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Published in The Pediatric Infectious Disease Journal

INTRODUCTION

Meningococcal serogroup C conjugate (MenC) vaccine is part of the Dutch immunization program since 2002. In the MenC vaccine, the polysaccharide antigen is linked to the protein carrier tetanus toxoid with the aim to achieve an adequate immune response at an early age, which would not be possible with a pure polysaccharide vaccine. The immune response to a conjugate vaccine is characterized by T-cell-dependent isotype-switching to IgG-antibodies, especially IgG_1, and induction of immunological memory.

METHODS

In a catch-up campaign, all children (1-18 years) were offered a single dose of MenC in the Netherlands in 2002. Blood samples of 19 Down syndrome (DS) children (mean age 10.6, range 5.3-17.4 years) were taken during regular hospital visits 3 months (n=7; mean 13 weeks, range 39-107 days), or around 1 year (n=12; mean 50 weeks, range 275-447 days), after this single dose of MenC vaccination. MenC polysaccharide (PS) specific IgG, IgM and IgA levels were measured using an antibody-capture enzyme-linked immunosorbent assay.[1] Results were compared with reference values of healthy adults from the same laboratory, 1 month (n=12) and 1 year (n=11) after single MenC vaccination.

RESULTS

At 3 months post-vaccination, geometric mean MenC/PS specific IgG, IgA and IgM serum levels were 5.5 (range 1.4-41), 0.71 (0.03-11) and 0.61 (0.10-7.5) µg/mL, compared to 26 (5.6-59), 5.6 (2.1-11) and 5.2 (1.7-35) µg/mL in healthy controls (p= 0.014, 0.028, 0.12 assessed by Mann-Whitney test respectively). One year after vaccination, geometric mean MenC/PS specific IgG, IgA, and IgM levels were 2.7 (0.78-15), 0.19 (0.02-1.2) and 0.28 (0.15-0.76) µg/mL, whereas reference values were 4.5 (0.68-19), 0.79 (0.13-3.8), and 0.71 (0.16-5.1) µg/mL (p= 0.204, 0.019, <0.001 assessed by Mann-Whitney test respectively). The 19 DS children did reach protective, but lower levels after a single MenC vaccination in comparison to healthy adults, despite the fact that 9 of them showed hypergammaglobulinemia according to age-matched reference values.[2]

CONCLUSIONS

Assaying specific antibody production against well-defined antigens can be used as a model to assess T-cell-dependent (anti-protein) and T-cell-independent (anti-polysaccharide) antibody responses; conjugated protein-polysaccharide vaccines like MenC show aspects of both types of responses. Impaired specific antibody responses to unconjugated pneumococcal polysaccharide have been described in DS, suggesting a B-lymphocyte problem.[3] Impaired responses to influenza, hepatitis B and tetanus (protein-prototype) have been described as well, suggesting an additional T-lymphocyte or T-B-interaction problem.[3] Not unexpectedly therefore, our data show that protein conjugation does not fully overcome the impaired antibody production to this polysaccharide antigen in DS.

Of course, decreased antibody production upon vaccination may have clinical implications as well. DS children have frequent respiratory infections, but an increased frequency of meningococcal disease has not been described in recent surveys, either in the pre-[4] or post-MenC[5] era, but specific attention was not given to this subject. So, it is as yet unclear whether children with Down syndrome are at greater risk of meningococcal disease, or whether they would benefit from an additional dose of conjugated meningococcal vaccination. Further studies are needed to elucidate this.

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