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Immunisation of the immunocompromised child

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Summary Immunocompromised children have a higher risk of developing infections and associated higher rates of mortality and morbidity. Although this group could benefit the most from vaccine administration, specific considerations regarding immunisations are required.

This review is a summary of the vaccines that are relevant to the immunocompromised host, covering both live and non-live vaccines. The burden of disease, safety, immunogenicity/effectiveness and specific recommendations for each vaccine are described as well as specific guidelines from different organisations.

Introduction

Children who are at increased risk of infections, either due to an impaired immune system or underlying chronic illness, require specific consideration when it comes to immunisation. These individuals potentially stand to benefit most from vaccine administration, but often have sub-optimal responses or may be more likely to suffer adverse effects, particularly from live vaccines. As new vaccines become available and the epidemiology of vaccine-preventable diseases evolves, it is increasingly important for all those caring for children to be up to date with the recent changes to these guidelines, improving the traditional low uptake of additional immunisations in high risk groups.[1]

Accordingly this review will focus on new developments in the field of active immunisation in immunocompromised and 'at-risk' children, including those with primary immunodeficiencies and those on high dose immunosuppressive therapy (Table 1).

Specific vaccines with relevance to the immunocompromised host

Live vaccines

Guidelines regarding the use live vaccines in the immunocompromised host are evolving. Long considered an absolute contra-indication, a more nuanced approach has emerged.

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Table 1 Secondary immunodeficiency due to high dose immunosuppressive medication, as defined below.

1. Glucocorticoids
   - High dose glucocorticoids pulse therapy (≥2 mg/kg/day or ≥20 mg per day for 2 weeks)
2. Non-biological immunosuppressants (also known as DMARDS)
   - Methotrexate: >15 mg/m^2/week
   - Cyclosporine: > 2.5 mg/kg/day
   - Azathioprine: 1—3 mg/kg/day
   - Cyclophosphamide: 0.5—2.0 mg/kg/day
   - Leflunomide: 0.25—0.5 mg/kg/day
   - 6-mercaptopurine: 1.5 mg/kg/day
3. Biological agents (any dose considered immunosuppressive):
   - Infliximab (Anti-TNF α)
   - Rituximab (Anti B cell activity)
   - Abatacept (reduced T cell activation)
   - Tocilizumab (Anti IL-6)
   - Eculizumab (reduced complement activation)

Adapted from: Heijstek M et al. Ann Rheum Dis 2011.

This reflects the need to balance the degree of immunosuppression, the risk of natural exposure and the availability of non-live alternatives. Such decisions should therefore be made on a case by case basis, considering the current health status as well as the type of immunodeficiency.

Rotavirus

The rotavirus vaccine is an oral live vaccine available in two different versions; a monovalent vaccine licensed as a two dose schedule and a pentavalent version with a three doses schedule.[2,3]

Burden of disease

Despite evidence of herd-immunity in populations with high immunisation rates, it remains likely that immunocompromised children in such countries will be exposed to this virus, albeit potentially at an older age than in a non-immunised population.[4,5]

Although there are relatively few data on the clinical outcome in immunocompromised children with rotavirus infection, an observational study in 28 paediatric oncology patients receiving intensive chemotherapy showed the mean length of hospital stay in children with confirmed rotavirus infection was 12.6 days (± 2.3 days), significantly longer than matched children without rotavirus infection (5.0 days ± 1.5 days.) These children also required higher rates of parental nutrition or tube feeding ($p < 0.001$)[6] than non-infected patients. Reports of rotavirus infection in paediatric liver transplant recipients also emphasise the severity of illness in solid organ transplant recipients.[7,8]

Safety

There have been three case reports of infants with Severe Combined Immunodeficiency (SCID) developing "vaccine associated disease" following rotavirus immunization.[9] The main symptoms cited were severe diarrhoea and dehydration after immunisation. In all of the cases, nucleic acid isolated from stools using RT-PCR analysis showed amplification of the rotavirus vaccine strains, with prolonged shedding when compared with healthy children.[9]

By contrast, a double blind study of 100 human immunodeficiency virus (HIV)-infected mildly or a-symptomatic infants, who were randomised 1:1 to receive human rotavirus RIX4414 strain vaccine or placebo, showed that the vaccine was well tolerated, with symptoms occurring at a similar frequency in both groups.[10] The peak and duration of vaccine virus shedding was similar to that reported in healthy infants, although there was one case with prolonged shedding that resolved between day 56 and 70.[10]

Immunogenicity/effectiveness

Although no data are available on the efficacy of rotavirus immunisation in immunocompromised children, the above study showed that the vaccine was immunogenic in HIV-infected infants, with 57% of vaccine recipients achieving the threshold of 20 U/mL serum antirotavirus IgA compared with 18% in controls.[10]

Recommendations

This vaccine should be avoided in infants with SCID, but is recommended for infants with HIV infection.[11] Although of uncertain efficacy and safety in infants with other immunocompromising conditions, the majority of the children are likely to benefit, by potentially avoiding the severe outcome associated with a natural rotavirus infection is this population.[2,6,7]

Varicella

Two monovalent varicella vaccines are available, both of which are contain the live attenuated 'OKA' strain. The vaccines are licensed from 12 months of age and two doses are normally administrated at least four to eight weeks apart.[3] The vaccine strain is susceptible to aciclovir and, unique amongst immunisations, establishes a latent infection in the recipient.

Burden of disease

In countries without routine immunisation exposure is almost inevitable. The risk of devastating varicella infections in immunocompromised children is well documented, with hospitalisation rates in HIV positive children on highly active antiretroviral treatment (HAART) 16 times higher than the general population in the UK (and 150 times higher if not on treatment).[12] For children on anti-tumor necrosis factor (TNF) immunosuppressive treatment the hospitalisation rate due to shingles and varicella was 32 and 26 cases per 100,000 patients respectively, considerably higher than rates of 3.4 and 1.9 (respectively) in the general paediatric population.[13]

Accordingly varicella seronegative immunocompromised children frequently receive administration of immunoglobulin or aciclovir prophylaxis following natural exposure, adding to the burden of their underlying disease.[14]

Safety

A cohort of 97 HIV positive children who were varicella-zoster virus (VZV) naïve and had a CD4+ percentage of ≥15% and a CD4+ T cell count ≥200 cells/μL were immunised with two doses of live varicella vaccine three