

Exposed to Varicella: Is Vaccination of Any Use Now?

Macartney K, McIntyre P. Vaccines for post-exposure prophylaxis against varicella (chickenpox) in children and adults. Cochrane Database of Systematic Reviews 2008; 3: CD001833. This version first published online: 16 July 2008.

INTRODUCTION

The efficacy of live attenuated varicella vaccine for the prevention of chickenpox is well known but most countries do not use it for routine immunization. Although the disease is often mild, complications such as secondary bacterial infection, pneumonia and encephalitis occur in about 1% of cases, usually leading to hospitalization. School absenteeism and loss of productivity occurs even in uncomplicated cases. In populations where universal immunization with varicella is not practiced routinely, the use of varicella vaccine as a post-exposure prophylaxis (PEP) is a potential strategy to prevent chickenpox related morbidity. The present review was aimed at evaluating the efficacy and safety of vaccines for use as PEP for prevention of varicella in children and adults.

SUMMARY

Three studies enrolling a total of 110 children (56 vaccinated and 54 placebo or no intervention) between the ages of 1 month to 16 years were included in this review. The vaccine was used as a PEP following household exposure of nonimmune children to siblings with varicella. Susceptibility was assumed if there was no past history of chickenpox or varicella vaccination and serological evidence of no past infection. Vaccination with live attenuated varicella vaccine was done within five days following known exposure to case of chicken pox, with comparison to placebo (2 studies; $n=68$) or no intervention (1 study; $n=42$). These studies were conducted in Japan, Israel and United States, respectively and used three different live attenuated

varicella vaccines. The primary outcome variable was clinical varicella infection in the exposed siblings.

Overall, 13 of 56 (23%) vaccine recipients developed varicella compared with 42 of 54 placebo (or no vaccine) recipients (78%). All vaccine recipients experienced either no disease or only mild disease, with the exception of one participant who had moderate to severe varicella. A meta-analysis was not performed because of the heterogeneity in quality of the studies and the different types of vaccine used. However, all three studies showed an effect individually in the prevention of moderate to severe disease. The efficacy of vaccine in preventing varicella when given within 3 days post-exposure could only be assessed in 64 healthy children from two studies. Of the 30 subjects who received vaccine within three days in these two studies, none developed moderate to severe disease compared with 33 of 34 in the control groups. Outcomes of vaccine safety could not be evaluated due to small sample size and inadequate information from the included studies. The authors concluded that varicella vaccine administered within 3 days to children following household contact with a varicella case reduces the rate of infection and severity of disease.

COMMENTARY

Are the Results Valid?

The problem addressed in this review is relevant but the utility would have been more if children at risk of complications due to varicella such as immunocompromised and cancer patients were also included. The search of literature was comprehensive and authors could identify a large number of studies. Most studies, however, did not fulfill the inclusion criteria as these were either uncontrolled or did not use varicella vaccine as PEP. The finally included studies ($n = 3$), though randomized controlled trials, were small and two of them had methodological concerns such as uncertain method of randomization and allocation concealment. Although the authors did not perform a formal meta-analysis because of the heterogeneity in

KEY MESSAGES

- Varicella vaccine used as post-exposure prophylaxis in children within 5 days of exposure significantly reduces the chance of developing clinical varicella infection.
- The effect is more pronounced if vaccine is given within 3 days of exposure and prevents nearly all cases of moderate to severe varicella.

the type of vaccine used, we believe that it was not a major issue as far as primary outcome measure of prevention of clinical varicella was concerned as the strain of vaccine was same in all three studies with the difference being only in the viral titer. However, it is true that the quality of the included studies varied and in general was low.

The primary outcome of prevention of clinical varicella infection is functionally important but the issue of prevention of complicated varicella disease (e.g. pneumonia, encephalitis, ataxia) would have been more relevant. The small sample size of the studies included, however, preclude any interpretation regarding prevention of these uncommon complications.

How precise and clinically significant is the treatment effect?

The pooled results from the review reported a 55% absolute reduction in the risk of developing clinical varicella infection in children given vaccine in comparison to placebo or no vaccination (78% vs. 23%). In other words, we need to give vaccine to 2 exposed children to prevent one clinical varicella infection (Number needed to treat NNT = 1.8). In terms of prevention of moderate to severe disease, the quantum of benefit is even greater; 3 such varicella infections will be prevented with 4 vaccinations (76% vs. 2%; NNT = 1.35). If analysis is done to include only those cases who receive vaccine within 3 days of exposure, the efficacy in preventing the moderate to severe disease becomes almost 100% (0% vs. 97%; NNT= 1.03). The range of therapeutic benefit can not be calculated from the data provided as a formal meta-analysis was not done and thus 95% CI are not available.

Implications for Practice and Policy

In the absence of universal immunization against

varicella, parents often approach pediatricians for preventing the disease in unimmunized children when one of the family member is affected. Evidence provided in this review support the use of varicella vaccine as PEP in settings where a known contact is present and secondary transmission rates are high. The findings of this review are particularly applicable to young children in the household or other close contact settings. Future studies should focus on role of varicella vaccine as PEP in people who are at high risk of complications. In view of the high cost of vaccine, the prophylactic role of antiviral agents such as acyclovir should also be directly compared with the results of vaccination. Safety issues also need to be addressed.

Note

A number of errors and contradictions were noted in reporting of the results of this systematic review. There was a discrepancy in number of subjects allocated to intervention or no intervention group in one of the study as reported in the table (21 vaccinated and 21 unvaccinated) and the study description (24 vaccinated and 19 unvaccinated). Also, there is miscalculation of percentages; 13 out of 56 vaccinees who developed varicella has been calculated as 18% in place of actual figure of 23%. Also, the figure of children who received vaccine within three days post-exposure should be 30 in place of 34 as described at relevant place.

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