

SHORT REPORT

Bacterial infections, immune overload, and MMR vaccine

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Combined measles, mumps, and rubella (MMR) vaccine did not increase the risk of hospitalisation with invasive bacterial infection in the three months after vaccination; rather there was a protective effect. These results provide no support for the concept of “immunological overload” induced by multiple antigen vaccinations, nor calls for single antigen vaccines.

Current calls for the provision of single measles, mumps, and rubella (MMR) vaccines have been fuelled by concerns that combined MMR vaccine might overwhelm the immune system as a result of simultaneous exposure to multiple antigens. The mild immunosuppressive effects, as evidenced by a transient reduction in tuberculin sensitivity, of measles vaccine and to a lesser extent mumps and rubella vaccines, lends some biological plausibility to such concerns. While there are theoretical arguments against the concept of “immune overload”, direct evidence of this in relation to MMR vaccine is lacking.¹ Indeed it has been postulated that as a result of this hypothetical immune interference, persistent virus infection can occur when the measles vaccine is given as part MMR, leading to chronic disease such as bowel problems or autism.²

If MMR vaccine does induce clinically significant immunosuppression, susceptibility to infection should be increased in the post-vaccination period.¹ We have tested this hypothesis using cases of invasive bacterial infection and pneumonia in children aged 12–23 months admitted to hospital between April 1991 and March 1995 in selected districts in the Thames region of southern England.

METHODS

Cases were identified from computerised discharge records using international classification of disease (ICD) 9 codes 036 (meningococcal infection), 038 (septicaemia), 320 (bacterial meningitis), 711.0 (pyogenic arthritis), 730.0 (acute osteomyelitis), and 481 (lobar (pneumococcal) pneumonia). Hospital records were linked with computerised district immunisation records by sex, date of birth, and post code. Only MMR vaccine is given in the second year of life. Cases in children with additional diagnostic codes indicating an underlying disorder predisposing to bacterial infection, such as immunosuppression,

malignancy, cystic fibrosis, congenital heart defect, or a cerebrospinal fluid shunt, were excluded.

The incidence of admission for bacterial infection in the 12 week period after MMR vaccine, and each of the three contained 30 day periods, relative to the background rate was measured using the self controlled case series analysis method.³ This method, which tests for clustering in predefined post-vaccination periods, does not require a separate control group and is more powerful and less prone to bias than a case-control study.³ Since the incidence of bacterial infection varies with age, the potential confounding effect of age was adjusted for by stratifying age into 26 two week intervals. Seasonal effects were adjusted for by stratifying the analysis by calendar month. A prevaccination low risk period of 14 days was defined to allow for a delay to vaccination after hospital admission for an infection. Readmissions within 14 days were considered to be the same episode. Separate analyses were carried out for cases of invasive disease and lobar pneumonia without an invasive code.

RESULTS

A total of 436 admissions with one or more of the bacterial infection codes and with a linked MMR vaccination record were identified; of these 25 were admissions in children with an underlying disorder and 16 were considered repeat admissions for the same episode. The remaining 395 admissions occurred in 387 children (169 in 165 females, and 226 in 222 males); 116 had a diagnosis of invasive bacterial infection and 279 had lobar pneumonia.

Table 1 shows the relative incidence (RI) of admission for a bacterial infection within 90 days of MMR vaccination and in the month before vaccination. None of the post-vaccination risk periods showed an RI significantly greater than one. RIs in those admitted with pneumonia were consistently below one, the RI in the 0–90 day period being 0.70 (0.50–0.97). The RI in the prevaccination low risk period was also significantly less than one, 0.25 (0.09–0.64) for pneumonia and invasive infection codes combined.

DISCUSSION

This study does not suggest that MMR vaccine impairs the ability to respond to the immune challenge posed by exposure

Abbreviations: MMR, measles, mumps, and rubella; RI, relative incidence

Table 1 Relative incidence, 95% CI [total cases in the risk periods]

Risk period (days)	Lobar pneumonia code	Invasive bacterial infection code	Both codes
–14 to –1	0.26 (0.09 to 0.79) [3]	0.19 (0.03 to 1.37) [1]	0.25 (0.09 to 0.64) [4]
0 to 30	0.77 (0.48 to 1.23) [23]	1.00 (0.52 to 1.94) [12]	0.81 (0.56 to 1.19) [35]
31 to 60	0.80 (0.50 to 1.28) [24]	1.17 (0.62 to 2.20) [14]	0.90 (0.62 to 1.31) [38]
61 to 90	0.52 (0.30 to 0.90) [16]	0.62 (0.27 to 1.40) [7]	0.56 (0.36 to 0.89) [23]
0 to 90	0.70 (0.50 to 0.97) [63]	0.93 (0.58 to 1.49) [33]	0.76 (0.58 to 0.99) [96]

to heterologous infectious agents. It therefore provides no support for either the concept of "immune overload" resulting from simultaneous administration of three live attenuated viruses to young children, or for the calls to provide single measles, mumps, and rubella in order to avoid such hypothetical effects. Interestingly, there was some evidence of a reduction in invasive bacterial infections in the 12 week period following MMR vaccination. Peltola and Heinonen, in a double blind, placebo controlled crossover study in twins, found a reduction in respiratory symptoms 2–3 weeks after MMR vaccine and postulated a transient protective effect against heterologous viral infections associated with interferon production.⁴ Although this is unlikely to result in direct protection against bacterial infection persisting over a 90 day period, a respiratory viral infection may predispose to subsequent invasive bacterial disease. In addition, some cases of lobar pneumonia might be primarily viral. An earlier case-control study of invasive bacterial infection in the 90 days after diphtheria/tetanus/pertussis, oral poliovirus, and MMR vaccines found a significantly reduced risk for all vaccines combined in the 0–90 day period, but the potential for confounding arising from selection bias in the controls could not be excluded.⁵ This source of bias does not affect the self controlled case series method.³ The hypothesis that there is a reduced risk of severe bacterial infection in the three months after MMR and other paediatric vaccines merits further investigation.

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