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[Intervention Review]

Pneumococcal conjugate vaccines for preventing otitis media

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ABSTRACT

Background

Acute otitis media (AOM) is a very common respiratory infection in early infancy and childhood. The marginal benefits of antibiotics for AOM in low-risk populations in general, the increasing problem of bacterial resistance to antibiotics and the huge estimated direct and indirect annual costs associated with otitis media (OM) have prompted a search for effective vaccines to prevent AOM.

Objectives

To assess the effect of pneumococcal conjugate vaccines (PCVs) in preventing AOM in children up to 12 years of age.

Search methods

We searched CENTRAL (2013, Issue 11), MEDLINE (1995 to November week 3, 2013), EMBASE (1995 to December 2013), CINAHL (2007 to December 2013), LILACS (2007 to December 2013) and Web of Science (2007 to December 2013).

Selection criteria

Randomised controlled trials (RCTs) of PCVs to prevent AOM in children aged 12 years or younger, with a follow-up of at least six months after vaccination.

Data collection and analysis

Two review authors independently assessed trial quality and extracted data.

Main results

We included 11 publications of nine RCTs (n = 48,426 children, range 74 to 37,868 per study) of 7- to 11-valent PCV (with different carrier proteins). Five trials (n = 47,108) included infants, while four trials (n = 1318) included children aged one to seven years that were either healthy (one study, n = 264) or had a previous history of upper respiratory tract infection (URTI), including AOM. We judged the methodological quality of the included studies to be moderate to high. There was considerable clinical diversity between studies in terms of study population, type of conjugate vaccine and outcome measures. We therefore refrained from pooling the results.

In three studies, the 7-valent PCV with CRM197 as carrier protein (CRM197-PCV7) administered during early infancy was associated with a relative risk reduction (RRR) of all-cause AOM ranging from -5% in high-risk children (95% confidence interval (CI) -25% to 12%) to 7% in low-risk children (95% CI 4% to 9%). Another 7-valent PCV with the outer membrane protein complex of *Neisseria meningitidis* (*N. meningitidis*) serogroup B as carrier protein, administered in infancy, did not reduce overall AOM episodes, while a precursor 11-valent PCV with *Haemophilus influenzae* (*H. influenzae*) protein D as carrier protein was associated with a RRR of all-cause AOM episodes of 34% (95% CI 21% to 44%).

A 9-valent PCV (with CRM197 carrier protein) administered in healthy toddlers was associated with a RRR of (parent-reported) OM episodes of 17% (95% CI -2% to 33%). CRM197-PCV7 followed by 23-valent pneumococcal polysaccharide vaccination administered after infancy in older children with a history of AOM showed no beneficial effect on first occurrence and later AOM episodes. In a study in older children with a previously diagnosed respiratory tract infection, performed during the influenza season, a trivalent influenza vaccine combined with placebo (TIV/placebo) led to fewer all-cause AOM episodes than vaccination with TIV and PCV7 (TIV/PCV7) when compared to hepatitis B vaccination and placebo (HBV/placebo) (RRR 71%, 95% CI 30% to 88% versus RRR 57%, 95% CI 6% to 80%, respectively) indicating that CRM197-PCV7 after infancy may even have negative effects on AOM.

Authors' conclusions

Based on current evidence of the effects of PCVs for preventing AOM, the licensed 7-valent CRM197-PCV7 has modest beneficial effects in healthy infants with a low baseline risk of AOM. Administering PCV7 in high-risk infants, after early infancy and in older children with a history of AOM, appears to have no benefit in preventing further episodes. Currently, several RCTs with different (newly licensed, multivalent) PCVs administered during early infancy are ongoing to establish their effects on AOM. Results of these studies may provide a better understanding of the role of the newly licensed, multivalent PCVs in preventing AOM. Also the impact on AOM of the carrier protein D, as used in certain pneumococcal vaccines, needs to be further established.

PLAIN LANGUAGE SUMMARY

Vaccination against a bacterium called pneumococcus for preventing middle ear infection

Review question

We reviewed the evidence about the effect of vaccination against pneumococcus (a type of bacterium) on preventing middle ear infections in children.

Background

Middle ear infection, or otitis media, is one of the most common respiratory infections in childhood. Infection with *Streptococcus pneumoniae* (pneumococcus) is a frequent cause of middle ear infection. Vaccination against pneumococcus with pneumococcal conjugate vaccines (PCVs) is primarily introduced to protect young children against severe pneumococcal infections, such as meningitis and pneumonia. We wanted to discover whether vaccination with PCV also leads to fewer middle ear infections in children.

Study characteristics

This review included evidence up to 3 December 2013. Nine trials with a total of 48,426 children were included; five trials included 47,108 infants, while four trials included 1318 children at a later age, i.e. aged one to seven years, who were either healthy (one trial, 264 children) or had previous upper respiratory tract infections, including middle ear infections. All trials had a long follow-up, varying from 6 to 40 months.

Key outcomes

When vaccinating against seven different serotypes of pneumococcus (7-valent PCV) during early infancy, the occurrence of middle ear infections either increased by 5% or decreased by 6% to 7%. One study in infants used 11 serotypes of pneumococcus together with a carrier protein from another bacterium (*Haemophilus influenzae*); this decreased the occurrence of middle ear infections by 34%.

Children with a history of middle ear infections do not seem to benefit from 7-valent PCV when immunised at an older age (after infancy).

Quality of the evidence

We judged the quality of the evidence for 7-valent PCV in early infancy to be high (further research is very unlikely to change our confidence in the estimate of effect), while we judged the quality of the evidence for multivalent (more than seven different serotypes) PCV to be moderate (further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate), as this evidence is derived from only one trial. We judged the quality of the evidence for 7-valent PCV in older children with a history of middle ear infections to be high.

Future studies on the effects of PCV in infants, with broader serotype coverage (more than seven different serotypes), are likely to provide more understanding of the role of PCV in preventing middle ear infections.