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[Intervention Review]

Vaccines for preventing influenza in healthy children

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ABSTRACT

Background

The consequences of influenza in children and adults are mainly absenteeism from school and work. However, the risk of complications is greatest in children and people over 65 years of age.

Objectives

To appraise all comparative studies evaluating the effects of influenza vaccines in healthy children, assess vaccine efficacy (prevention of confirmed influenza) and effectiveness (prevention of influenza-like illness (ILI)) and document adverse events associated with influenza vaccines.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2011, Issue 3) which includes the Acute Respiratory Infections Group's Specialised Register, OLD MEDLINE (1950 to 1965), MEDLINE (1966 to November 2011), EMBASE (1974 to November 2011), Biological Abstracts (1969 to September 2007), and Science Citation Index (1974 to September 2007).

Selection criteria

Randomised controlled trials (RCTs), cohort and case-control studies of any influenza vaccine in healthy children under 16 years of age.

Data collection and analysis

Four review authors independently assessed trial quality and extracted data.

Main results

We included 75 studies with about 300,000 observations. We included 17 RCTs, 19 cohort studies and 11 case-control studies in the analysis of vaccine efficacy and effectiveness. Evidence from RCTs shows that six children under the age of six need to be vaccinated with live attenuated vaccine to prevent one case of influenza (infection and symptoms). We could find no usable data for those aged two years or younger.

Inactivated vaccines in children aged six years or older are not significantly more efficacious than placebo. Twenty-eight children over the age of six need to be vaccinated to prevent one case of influenza (infection and symptoms). Eight need to be vaccinated to prevent one case of influenza-like-illness (ILI). We could find no evidence of effect on secondary cases, lower respiratory tract disease, drug prescriptions, otitis media and its consequences and socioeconomic impact. We found weak single-study evidence of effect on school absenteeism by children and caring parents from work. Variability in study design and presentation of data was such that a meta-analysis of safety outcome

data was not feasible. Extensive evidence of reporting bias of safety outcomes from trials of live attenuated influenza vaccines (LAIVs) impeded meaningful analysis. One specific brand of monovalent pandemic vaccine is associated with cataplexy and narcolepsy in children and there is sparse evidence of serious harms (such as febrile convulsions) in specific situations.

Authors' conclusions

Influenza vaccines are efficacious in preventing cases of influenza in children older than two years of age, but little evidence is available for children younger than two years of age. There was a difference between vaccine efficacy and effectiveness, partly due to differing datasets, settings and viral circulation patterns. No safety comparisons could be carried out, emphasising the need for standardisation of methods and presentation of vaccine safety data in future studies. In specific cases, influenza vaccines were associated with serious harms such as narcolepsy and febrile convulsions. It was surprising to find only one study of inactivated vaccine in children under two years, given current recommendations to vaccinate healthy children from six months of age in the USA, Canada, parts of Europe and Australia. If immunisation in children is to be recommended as a public health policy, large-scale studies assessing important outcomes, and directly comparing vaccine types are urgently required. The degree of scrutiny needed to identify all global cases of potential harms is beyond the resources of this review.

This review includes trials funded by industry. An earlier systematic review of 274 influenza vaccine studies published up to 2007 found industry-funded studies were published in more prestigious journals and cited more than other studies independently from methodological quality and size. Studies funded from public sources were significantly less likely to report conclusions favourable to the vaccines. The review showed that reliable evidence on influenza vaccines is thin but there is evidence of widespread manipulation of conclusions and spurious notoriety of the studies. The content and conclusions of this review should be interpreted in the light of this finding.

PLAIN LANGUAGE SUMMARY

Vaccines for preventing influenza in healthy children

Children (< 16 years old) and the elderly (above 65 years old) are the two age groups that appear to have the most complications following an influenza infection. Influenza has a viral origin and often results in an acute respiratory illness affecting the lower or upper parts of the respiratory tract, or both. Viruses are mainly of two subtypes (A or B) and spread periodically during the autumn-winter months. However, many other viruses can also cause respiratory tract illnesses.

Diffusion and severity of the disease could be very different during different epidemics. Efforts to contain epidemic diffusion rely mainly on widespread vaccination. Recent policy from several internationally-recognised institutions, recommend immunisation of healthy children between 6 and 23 months of age (together with their contacts) as a public health measure.

The review authors found that in children aged from two years, nasal spray vaccines made from weakened influenza viruses were better at preventing illness caused by the influenza virus than injected vaccines made from the killed virus. Neither type was particularly good at preventing 'flu-like illness' caused by other types of viruses. In children under the age of two, the efficacy of inactivated vaccine was similar to placebo. It was not possible to analyse the safety of vaccines from the studies due to the lack of standardisation in the information given, but very little information was found on the safety of inactivated vaccines, the most commonly used vaccine in young children.