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COCHRANE CORNER

Role of vaccines in preventing influenza in healthy children

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The role of an influenza vaccine is to minimise illness and death. Vaccines provide good protection against influenza strains and significantly reduce time off work. However, the recommendation for use depends on the efficacy, effectiveness and safety of the vaccines. We highlight a Cochrane review that sought to determine the efficacy, effectiveness and safety of seasonal influenza vaccines in healthy children, and provide implications for practice for vaccination of children. The findings suggest that influenza vaccines play a key role in reducing serious morbidity and mortality among children. There were few data available to provide firm conclusions on adverse events. Vaccinating against influenza not only reduces its incidence among children, but also extends these benefits to the unvaccinated population, such as the elderly. In light of the many direct and indirect benefits of vaccinating children aged 2 - 16 years, there is a need to provide access to influenza vaccines to all eligible South African children.

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In 2018, Jefferson *et al.*[1] updated a Cochrane review first published in 2008, in which they assessed the effects of influenza vaccines in healthy children. Vaccination against influenza remains the best way to protect individuals from developing influenza, which is often common in countries with a temperate climate. Children, particularly those <5 years of age, although at high risk of serious complications of influenza, are yet to be a group for whom influenza vaccination is strongly recommended.[2] In South Africa (SA), from 2013 to 2015, the estimated mean annual number of influenza-associated illness episodes was 10 737 847, of which 10 598 138 (98.7%) were mild, 128 173 (1.2%) were severe but non-fatal, and 11 536 (0.1%) resulted in death. Influenza-associated death rates of individuals in the population were high among children aged <1 year (80.3/100 000) and persons ≥65 years (137.9/100 000).[3,4]

The economic burden of influenza is equally substantial. Currently, SA spends an estimated USD270.5 million each year to treat influenza-associated illness.[3] Economic loss due to absenteeism caused by influenza amounted to >USD200 million each year across all sectors.[5] Even though SA is one of the first 4 countries in Africa to have introduced the influenza vaccine to target risk groups, children <5 years of age are not prioritised for seasonal influenza vaccination by the National Department of Health.[2]

Objectives

Jefferson *et al.*[1] sought to determine the efficacy, effectiveness and safety of seasonal influenza vaccines in healthy children between 2 and 16 years of age. Efficacy of the influenza vaccine was defined as a reduction in the number of laboratory-confirmed cases, while effectiveness was a reduction in influenza-like illness (ILI) symptomatic cases.

Methods

Two types of vaccines, i.e. live attenuated influenza vaccines (LAIVs) or inactivated influenza vaccines (IIVs), were compared with a placebo or no vaccine. The authors of the review included 41 randomised controlled trials (RCTs) with >200 000 children in studies conducted over single influenza seasons. The review also retained 21 cohort and 12 case control studies previously included in the last review. The studies from 1974 to 2016 were mainly from the USA, Western Europe, Russia and Bangladesh. Electronic databases, such as the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) and ClinicalTrials.gov, were comprehensively searched for published or unpublished studies. All the included studies were independently screened and assessed for risk of bias. Risk ratio (RR) and odds ratio (OR) were used to measure the benefits of the vaccines between the vaccinated group and comparison group. Data synthesis for LAIV and IIV was analysed separately and by grouping studies together, based on their study designs. Pooled estimates were assessed for heterogeneity by performing a sensitivity analysis.

Results

The overall efficacy of LAIVs in reducing laboratory-confirmed influenza among healthy children aged 3 - 16 years was 78%, while effectiveness in reducing ILI was only 31%. In children aged 2 - 16 years, efficacy of inactivated influenza vaccines was 64% in reducing influenza and effectiveness was 28% in reducing ILI. Based on the risk difference of the disease reduction, 7 children vaccinated with LAIVs or 5 children vaccinated with IIVs are needed to prevent 1 case of laboratory-confirmed influenza. Similarly, 20 children vaccinated

with LAIVs or 12 children vaccinated with IIVs are needed to avoid 1 case of ILI. There were few data available to provide firm conclusions on adverse events, hospitalisation and school and work absenteeism.

Conclusions

LAIV and IIV are effective in reducing influenza and ILI in children aged 2 - 16 years. However, reduction estimates for both types of vaccines varied considerably among study populations, making it difficult to predict the precise size effects of the vaccine in other settings and for different seasons.

Implications for practice

Although the synthesised evidence was drawn from many studies conducted in populations outside Africa, the findings are very relevant to the SA context. LAIVs and IIVs provide significant protection against influenza in children aged 2 - 16 years. The WHO recommends IIVs in children >6 months old and LAIVs in individuals aged 2 - 49 years.[6] Vaccination against influenza does not only reduce its incidence among younger individuals, but also extends these benefits to the unvaccinated population.[7]

Children have a high attack rate and play a significant role in influenza transmission in the household, schools and community owing to their prolonged virus shedding and tendency to mix more often with contacts of individuals. By targeting children, one could possibly reduce transmission to the elderly, who are at increased risk of severe outcomes due to influenza. As children respond better to vaccines than adults owing to their excellent immunological function, they are more likely to establish secondary effects over time, which are useful to stop the spread of the disease. Children's protective benefits imply that the elderly are not directly exposed to influenza, thereby effectively enjoying protection offered by a vaccinated child. Furthermore, the working population enjoys this protection rendered by vaccinated children, as the latter are no longer vectors of transmission. The vaccination of children is an important strategy in preventing work absenteeism, which costs the SA government >ZAR3 billion yearly.[3]

For adults, indirect benefits may be obtained by vaccinating only 20 - 25% of children with a trivalent-LAIV, which subsequently results in secondary protection of 8 - 18% against medically attended acute respiratory illness.[8,9] Loeb *et al.*[7] suggest that if 61% of children and adolescents aged 3 - 15 years are immunised with the trivalent influenza vaccine, it will create a situation where the virus no longer circulates among unvaccinated persons. This corresponds to a study by Reichert *et al.*,[10] who vaccinated >80% of schoolchildren between 1962 and 1987, resulting in a significant reduction in mortality in the elderly and adults.

In light of the many direct and indirect benefits of vaccinating children aged 2 - 16 years, there is a need to provide access to influenza vaccines to all eligible SA children.

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Conflicts of interest. None.

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