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The “influenza vaccine” – benefit, risk, costs

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Abstract More than 20 million people died during the pandemic ‘flu season 1918/1919, the largest influenza pandemic of the 20th century. Since then, influenza A virus infections have been known as a serious cause of morbidity and mortality in the whole world population. Although specific and effective antiviral therapeutics (neuraminidase inhibitors) are available, vaccinating against influenza is the first preventative measure. In Germany, influenza immunization has been yearly recommended by the current vaccination committee of the Robert Koch Institute (STIKO). Vaccinations have a special indication in elderly persons > 60 years, patients with chronic diseases and persons with higher risk of influenza infections. In general, inactivated vaccines are well tolerated by recipients. The cost effectiveness of influenza vaccination has been well established. Although the benefit of annual influenza vaccination especially for the elderly and risk groups is beyond doubt, a low acceptance of vaccine recommendations has been noticed in Germany to date.

Keywords Cost/benefit · Epidemic · Influenza · Vaccination

Introduction

The three ‘flu pandemics of the 20th century were devastating, especially in 1918/1919 the “Spanish flu”, the largest influenza pandemic. Since then, influenza has remained a serious cause of morbidity and mortality [9]. Each year, influenza is associated with 20,000 excess deaths and more than 250,000 cases of hospitalizations in Germany [2, 5].

Influenza viruses are transmitted by droplet infection; 30–50% of infections remain clinically inapparent. The infection targets the epithelial cells of the respiratory tract and leads to their destruction. After a short incubation period of 1–3 days, unspecific symptoms like fever, headache, shivering and arthralgia occur at the beginning of the disease. Most infected patients develop acute tracheobronchitis. Severe and atypical courses can be found in elderly people and in young children. Influenza pneumonia often leading to secondary bacterial infections caused by *Haemophilus influenzae* or *Staphylococcus aureus* may be associated with fatal course.

Although specific and highly effective antiviral therapeutics such as neuraminidase inhibitors are currently available, vaccinating against influenza is the first measure for prevention of influenza.

Vaccine recommendations

In Germany, inactivated split or subunit influenza vaccines are used. They contain 15 µg of viral antigens per 0.5 ml dose of two influenza A virus strains and one influenza B strain. Because of the high antigen variability (antigen shift and drift) of the influenza A viruses, the vaccine strains must be adapted annually. Recommendations of the World Health Organization (WHO) for the composition of the influenza vaccines used in the northern hemisphere are issued in February of each year and concern the virus strains to be included in the vaccine production for the forthcoming winter. For 2001/2002, the vaccines should contain the following strains of influenza A and influenza B viruses [3]:

- A/New Caledonia/20/99(H1N1)-like virus
- A/Moscow/10/99(H3N2)-like virus
- B/Sichuan/379/99-like virus.

In Germany, influenza vaccination has been yearly recommended by the current vaccination committee of the Robert Koch Institute (STIKO) [10]. Regularly

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repeated immunizations lead to sufficient immunity at the beginning influenza season. Failure of vaccination occurs in up to 30%, most of which have been vaccinated once [2, 3, 5]. Vaccination is specially indicated in elderly persons >60 years, patients with chronic diseases, persons working in hospitals or schools and persons with a high risk of infections. The latest recommendations for influenza vaccination also include patients with disseminated sclerosis, transplanted and carcinoma patients. Influenza vaccine should be avoided by persons with known allergy to eggs or to any components of the vaccine, e.g. thiomersal [8, 10], and those with an acute respiratory or other active infection.

In general, influenza vaccines are well tolerated by recipients. The vaccines contain either inactivated viruses extracted with ether and detergents to reduce side-effects (split vaccines) or their highly-purified hemagglutinin and neuraminidase antigens (subunit vaccines). Therefore, they are not able to induce the influenza. Mild respiratory diseases often observed after vaccination represent in most cases coincidental viral or bacterial infections, like due to adenoviruses, parainfluenza viruses, coronaviruses, rhinoviruses, respiratory syncytial viruses or *Mycoplasma pneumoniae*. To avoid these infections, influenza vaccination should be performed as early as possible; that means at the beginning of the autumn season, before most of respiratory infections occur.

For the influenza vaccine, a low risk of side effects has been reported [2, 3, 8]. Most local reactions are soreness, pain and tenderness at the injection side and systemic reactions like fever and muscle pain. These symptoms can occur for a period of 1–2 days. Severe side effects, e.g., allergic reactions to egg protein or thiomersal, have been also rarely observed. The risk of Guillain-Barré syndrome (GBS) associated with influenza vaccines has not been clearly elucidated. Lasky et al. [8] calculated an excess of 1–2 cases per million vaccine recipients. This risk estimated is lower than the risk of severe influenza infection.

Cost effectiveness

The cost effectiveness of immunization against influenza using inactivated vaccines is well established. Vaccination reduces the morbidity of influenza, the number of hospitalized cases as well as the mortality [1, 9]. Benefits of annual influenza vaccinations have been proved especially for the elderly patients and risk groups [11]. Nichol et al. [7] found an average of 117 US dollars in direct medical costs saved for each elderly person vaccinated against influenza. In Germany, direct and indirect medical costs of diseases caused by influenza viruses have been estimated to be 1–2.5 thousand million Euro [4, 11]. These costs have been confirmed by studies carried out in other European countries and the United States of America [7, 12].

Acceptance

Considering these data, the acceptance of vaccination against influenza is surprisingly low. Only 10% of all the German population and about 15–30% of the risk groups have been vaccinated yearly [8]. Statistical analysis of the AGI (Arbeitsgemeinschaft Influenza, Marburg, Germany) showed that the lowest acceptance of influenza vaccination can be found among medical staff [2], although knowing the generally higher risk of influenza infections in hospitals. Nevertheless, an increase from a few million doses of the influenza vaccine at the beginning of nineties up to 15 million doses in 2000 has been reported.

The number of persons vaccinated in our Travel Vaccine Center showed comparable results (Fig. 1). In contrast to the mostly wanted travel-related vaccinations against yellow fever, hepatitis A or Japanese encephalitis, the influenza vaccines were only used in 0.7–1.4% of all vaccinations performed from 1995 to 2000. However, we could also observe an increase from 19 doses in 1995

Fig. 1 Annual numbers of influenza vaccinations from 1995 to 2000 at the Travel Medicine Center, University Hospital, Frankfurt am Main, Germany

up to more than 100 doses in 1999 and 2000. The majority of vaccinees belonged to high-risk groups (e.g., immunocompromised patients), the medical staff and long-term travelers. Most persons were vaccinated during the months of October and January.

Summing up, the medical and economic benefit of influenza vaccination has been evidenced. Its effectiveness depends on the vaccine virus "matching" and the health conditions of the vaccinees. The low acceptance of the vaccination remains to be improved [2, 3, 8, 10].

Conclusion

An increasing mortality rate caused by influenza virus infections has been noticed in each winter season. Influenza A virus is the most important subtype of the virus family *Orthomyxoviridae* and is characterized by antigenic shift and drift. The virus variation needs vaccine modification every year. Recommendations for the composition of the influenza vaccines used in the northern hemisphere are given by the WHO in February of each year. On the basis of the latest epidemiological data, the virus strains to be included in the vaccine production for the forthcoming winter are selected. Although an increase of vaccinations up to 15 million influenza vaccine doses in 2000 has been recorded, the acceptance of immunization against influenza is low. Only 10% of the whole German population and 15–30% of the risk groups have been yearly vaccinated. Medical staff shows the lowest acceptance for vaccinating.

Medical and economic benefits of the influenza vaccine are beyond doubt. Its effectiveness depends on

vaccine virus "matching" and the health conditions of the vaccinees. To achieve a protecting immunity in the vaccinees, early vaccinations before the beginning of influenza season are advantageous.

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