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EFFECTIVENESS OF FLU SHOT VACCINE

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Abstract:

Introduction: *Influenza is responsible for serious illness, especially in elderly. It has short term morbidity as well as long term morbidity and mortality during the acute infection, recovery could be long and sometimes incomplete. This could lead to persistent decrease in health and function, involving catastrophic disability, which has acute complications on the well-being and support needs of older adults and their caregivers. This means that prevention of infection and effective management when illness has occurred are of great importance.*

This sets the stage for a discussion of newer influenza vaccine products that have been developed with the aim of improving vaccine effectiveness in older adults. We will highlight the importance of influenza prevention to support healthy aging, along with the need to improve vaccine coverage rates using available vaccine products, and to spur development of better influenza vaccines for older adults in the near future.

Aim of work: *In this review, we will discuss flu shot*

Methodology: *We did a systematic search for flu shot using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). All relevant studies were retrieved and discussed. We only included full articles.*

Conclusions: *Elderly are susceptible to poor outcomes from influenza in short- and long-term. Both complications of acute illness and continued functional disability have major effects on the health and well-being of elderly and their families. So, prevention is of highly importat as to support healthy elderly. Though immune responses to vaccination could be less optimal in elderly, especially those who are weak, vaccination remains to be an important method in the prevention of severe outcomes from influenza. Many vaccines are available for older adults, including standard-dose trivalent and quadrivalent formulations of split virus and subunit vaccines, high-dose split-virus vaccine, adjuvanted subunit vaccine, and recombinant HA vaccine. Due to the relative qualities and availability of these products could change between jurisdictions, vaccinating with whatever proper and approved product is available continues to be a major recommendation; vaccination coverage continues to be less optimal in most states. As our understanding of immune changes with aging, and frailty progresses, vaccine products will perfectly be more tailored to generate optimal protection for this susceptible population*

Key words: *flu shot, indication, elderly, recent updates, primary care.*

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INTRODUCTION:

Influenza is responsible for serious illness, especially in elderly. It has short term morbidity as well as long term morbidity and mortality during the acute infection, recovery could be long and sometimes incomplete. This could lead to persistent decrease in health and function, involving catastrophic disability, which has acute complications on the well-being and support needs of older adults and their caregivers. This means that prevention of infection and effective management when illness has occurred are of great importance.

This sets the stage for a discussion of newer influenza vaccine products that have been developed with the aim of improving vaccine effectiveness in older adults. We will highlight the importance of influenza prevention to support healthy aging, along with the need to improve vaccine coverage rates using available vaccine products, and to spur development of better influenza vaccines for older adults in the near future.

In this review, we will discuss the most recent evidence regarding flu shot.

METHODOLOGY:

We did a systematic search for flu shot using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). All relevant studies were retrieved and discussed. We only included full articles.

The terms used in the search were: flu shot, indication, elderly, recent updates, primary care.

Influenza Can Have a Severe and Lasting Impact on Older Adults' Health and Well-Being

Elderly people are excessively affected by influenza and its complications. In the acute-phase, morbidity and mortality are highest [1]. Globally, it is believed that more than two hundred thousand people suffer death from influenza and its respiratory complications yearly, of whom older adults age 75+ years are at the highest risk, with more than fifty deaths per 100,000 people aged 75+ years [2]. Remarkably, elderly people with severe illness need hospital admission. As an example, in the Canadian Serious Outcomes Surveillance (SOS) Network of acute care hospitals, more than 3394 adults were admitted to hospital with laboratory-confirmed influenza over three consecutive influenza seasons. At ten percent, mortality was high in the overall cohort, and increased with age [3]. Data from other national and international surveillance networks paints a similar picture of serious outcomes being more often experienced by elderly; this data contributed to international advisory body suggestions as discussed below. In spite of the severity of outcomes linked to influenza, and recommendations for vaccination for older adults and other high-risk groups in several states, vaccine coverage remains below the seventy five percent for the over 65 years population [4]. For example, in the US [5] and Canada, vaccination rates among elderly have remained to be the same and below seventy percent. In the European Union, influenza vaccine coverage in high-risk groups has decreased since 2007; for those aged 65 + years, coverage varied widely across member states, with a median vaccination rate of around forty five percent [6].

It is becoming more apparent that longer-term complications are as well common. After an acute care hospitalization, a significant proportion of elderly will not go back to their baseline of health and functional status [7]. In the SOS Network, it is estimated that around nineteen percent of elderly aged 65 + years admitted with respiratory illness, involving laboratory-confirmed influenza, suffered catastrophic disability. Even elderly who are not hospitalized can suffer persistent decrease in function and prolonged recovery from influenza or influenza-like illness.

Frailty is an important concept when it comes to elderly and influenza and can be estimated and defined in several ways. Generally, frailty embodies vulnerability to adverse effects [8]. Frailty is linked to a reduced vaccine effectiveness, and so important to consider in studies of vaccine protection [9]. Frailty can predict outcomes from influenza illness; frail elderly is more vulnerable to suffer adverse outcomes and less likely to return to their prior baseline function.

It is important to differentiate between vaccine efficacy and vaccine effectiveness. Vaccine efficacy estimations are derived from research study settings, often randomized controlled studies, under perfect conditions. While, vaccine effectiveness indicates the benefit seen with a specific vaccine in real settings [10]. Surprisingly, both can be abbreviated as 'VE', therefore it is important to know to which a particular study is referring. It is also vital to define the outcomes measured in vaccine-effectiveness studies clearly. Several studies, from outpatient sentinel surveillance networks, report vaccine effectiveness (VE) for the prevention of medically attended influenza [11].

Vaccine effectiveness estimates could be different between different studies that report on the prevention of medically attended influenza and those that examine prevention of severe outcomes. A report from the European I-MOVE network study in the 2016/2017 influenza season found an adjusted VE against medically attended influenza in primary care of 38.0% for all age groups; among adults, the VE was lower in those ≥ 65 years of age.

Vaccine Effectiveness of Flu Vaccine Traditional Products

Classic influenza vaccines are either split-virus or subunit vaccines that have distinctive antigens that are selected to match predicted circulating strains each season. The hemagglutination inhibition (HAI) assay is the gold-standard assay of antibody titers against HA and is used as a surrogate of vaccine efficacy for the prevention of influenza infection. Trivalent vaccines have 3 strain antigens (2 influenza A strains, A/H1 and A/H3) and one B lineage (either Victoria or Yamagata).

While antibody responses have a major role in the prevention of influenza infection, cell-mediated immune responses play a role in both the prevention of infection and of serious complications of influenza, especially when antibody levels are low (as in the case of an influenza pandemic), or fail to prevent infection (as is often the case in older adults) [12]. In comparison to the usual surface protein vaccine targets (HA and NA), internal virus proteins evolve more slowly and are more often preserved across influenza, strains, types and subtypes, making them attractive potential vaccine targets. Cell-mediated immunity, notably cytotoxic T lymphocyte (CTL) responses to internal viral proteins, including M1 and NP, is becoming more recognized as important in protecting against severe outcomes of influenza; CTLs are needed to clear influenza from the lungs.

Irrespective of the specific details of differences in VE across seasons and age groups, it is obvious that elderly are disproportionately affected by influenza and its complications.

Influenza and the Aging Immune System

Functional integrity of the immune system is influenced by aging, presenting as reductions in humoral immunity, decrease in specific characteristics of cell-mediated immunity, and dysregulation of cytokine responses needed to activate both innate and adaptive immune mechanisms. Anti-inflammatory responses protect against damaging of the tissues effects of chronic inflammation linked to several chronic diseases, referred to as 'inflammaging'. But, in the setting of acute infection like influenza, regulation of these inflammatory processes is requied to turn on cell-mediated immune mechanisms and protect against tissue damage.

Given these modifications in all aspects of the immune system, traditional measures of vaccine response such as antibody titers do not correlate well with strain-specific vaccine efficacy. These are obvious challenges for predicting responses to vaccination. Antibody responses are usually used to screen new vaccines however their limitations as sole predictors of vaccine efficacy are increasingly recognized. For example, vaccinated older adults who develop laboratory confirmed influenza illness due to A/H3N2 infection can likewise A/H3N2-specific antibody titers following vaccination compared with those who do not develop laboratory confirmed influenza [13],

There are many options that have been explored to date for improved influenza vaccines involving *increasing the dose* of antigen to better stimulate weaker adaptive responses, adding chemical agents (*adjuvants*) that promote the innate inflammatory response and improve the ability of dendritic cells to present antigen to T cells, so bringing more exposure to adaptive immune cells in the reactive milieu which ensues, and using re*combinant an*tigens.

Overview of Currently Available Influenza Vaccine Products Specifically Targeted to Older Adults

3.1 High-Dose Influenza Vaccine

To improve the antibody response in elderly, high-dose antigen vaccines have been created to increase vaccine efficacy/effectiveness. The recent high-dose formulation is a split-virus influenza vaccine (includes M1 and NP) containing 4 times the dose of each of the three influenza antigens in comparison with standard-dose trivalent vaccines. Several studies showed that this strategy provokes a more robust immune response in elderly.

Significantly, this benefit was shown even in those older than seventy-five years of age and among participants with laboratory confirmed influenza A(H3N2) [14]. These results are furthermore supported by a meta-analysis of seven trials, which concluded a significant reduction in the risk of

developing laboratory-confirmed influenza among older persons receiving high-dose vaccine versus those having received standard dose. A study analysis of the CMS database for the 2012/2013 influenza season among about two million Medicare beneficiaries reported high-dose TIV concluded an overall relative effectiveness of twenty two percent for the prevention of laboratory-confirmed influenza. Benefit of the high-dose TIV in comparison to standard TIV appears to be greatest against influenza A(H3N2). In a comparative effectiveness study among US Medicare beneficiaries, overall relative effectiveness of high-dose TIV was 24% for the prevention of 30-day mortality following an emergency room visit or hospitalization with an administrative code for influenza over 2 influenza seasons.

A cluster-randomized trial of US nursing home residents showed a reduction in risk of hospital admission for respiratory illness during a single influenza season among facilities that used high-dose vaccine versus those that administered standard dose. In spite of its higher product cost, high-dose vaccine has been found to be cost effective due to a reduction in overall influenza-related medical encounters, especially hospitalizations. Together, these data conclude that high-dose influenza vaccine decrease laboratory-confirmed influenza and influenza-related hospitalizations even among nursing home residents, who are more vulnerable to be frail, and is cost effective when compared with standard-dose influenza vaccine.

CONCLUSIONS:

Elderly are susceptible to poor outcomes from influenza in short- and long-term. Both complications of acute illness and continued functional disability have major effects on the health and well-being of elderly and their families. So, prevention is of highly importat as to support healthy elderly. Though immune responses to vaccination could be less optimal in elderly, especially those who are weak, vaccination remains to be an important method in the prevention of severe outcomes from influenza. Many vaccines are available for older adults, including standard-dose trivalent and quadrivalent formulations of split virus and subunit vaccines, high-dose split-virus vaccine, adjuvanted subunit vaccine, and recombinant HA vaccine. Due to the relative qualities and availability of these products could change between jurisdictions, vaccinating with whatever proper and approved product is available continues to be a major recommendation; vaccination coverage continues to be less optimal in most states. As our understanding of immune changes with aging, and frailty progresses, vaccine products will perfectly be more tailored to generate optimal protection for this susceptible population

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