

Influenza Vaccine for Egyptian Elderly Patients with Chronic Obstructive Pulmonary Disease

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Abstract

Background: Acute exacerbations of chronic obstructive pulmonary disease are a major cause of morbidity and mortality worldwide. Most acute exacerbations are triggered by community-acquired respiratory infections. Influenza vaccines are currently recommended for all persons with COPD.

Aim: To determine the effectiveness of influenza vaccination on influenza-related acute respiratory illness (ARI) and overall ARI in patients with COPD.

Methods: A case control study was conducted on 90 elderly patients with COPD (58 years and older) recruited from the outpatient geriatric clinic of Ain shams university hospital. 90 patients with COPD were classified based on their FEV1 as having mild, moderate, and severe COPD. They were classified into two groups; 45 COPD patients (cases) who received the influenza vaccine & 45 COPD patients (controls) who refused to receive the influenza vaccine. We compared the two groups as regard exacerbation rates, hospitalizations, mortality, lung function and adverse effects.

Results: Inactivated vaccine in COPD patients resulted in a significant reduction in the total number of exacerbations per vaccinated subject (1.8 ± 1.3) compared with those who did not receive the influenza vaccine (3.0 ± 1.9). The exacerbations rate were (2.1 ± 2.2), (3.2 ± 1.9), and (3.7 ± 1.2) in the patients with mild, moderate, and severe COPD, respectively in non-vaccinated group, and (1.6 ± 1.4), (2.0 ± 1.2), and (2.3 ± 1.4) in the patients with mild, moderate, and severe COPD, respectively in the vaccinated group. The hospitalization rate was Lower in vaccinated subjects (44.4%) than non-vaccinated group (75.6%) p value 0.002. Also mortality rate was lower in vaccinated subject (11.1%) than non-vaccinated group (26.7%).

Conclusions: Influenza vaccination is highly effective in the prevention of influenza-related acute respiratory illness (ARI) regardless of the severity of COPD. Influenza vaccination should be recommended to all patients with COPD.

Keywords: Influenza vaccination; COPD; Elderly

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Introduction

Chronic obstructive pulmonary disease (COPD) is currently the fourth leading cause of mortality worldwide [1]. By 2020, it is predicted that COPD will have risen to be the third leading cause of mortality [2]. The estimated annual cost of COPD is \$32.1

billion worldwide and 70% of these costs are related to acute exacerbations that require hospitalization [3,4].

In Egypt, although COPD is a rising significant health problem, data on its prevalence, morbidity, and mortality are still lacking and have to be estimated [5]. Economic evaluations in the USA

based on studies comparing vaccinated and non-vaccinated populations, have shown that influenza vaccination is a cost effective way of reducing morbidity and saving lives in people over 65 [6,7].

A recent prospective study of COPD exacerbations [8] demonstrated an in-hospital mortality rate of 8% and a 1-year mortality rate of 23%. Patients with frequent exacerbations of COPD have a more rapid decline in lung function [9] and report worse health-related quality of life than those who do not have frequent exacerbations [10].

The primary triggers of most exacerbations are community-acquired respiratory infections caused by viral and bacterial pathogens [11]. Effective treatments to manage exacerbations caused by infection are currently limited. Therefore, identifying evidence-based strategies that prevent respiratory infections that cause COPD exacerbations would have a significant impact on reducing the mortality and morbidity of this disease. The introduction and widespread use of vaccines has resulted in dramatic advances in preventing disease, disability, and death from infectious diseases. Current guidelines recommend that all patients with COPD, as well as other high-risk subgroups, receive influenza vaccination annually [12].

The influenza vaccine has been shown to be effective in reducing infection, associated illness, hospitalization and mortality in older people when the infectious and vaccine strains are closely related. A recent randomized placebo controlled trial established that the vaccination of people over the age of 60 halved the risk of influenza infection confirmed by a blood test [13]. Hence, this study is being undertaken to study the effect of influenza vaccine in a sample of Egyptian elderly with COPD.

Subjects

A case control study was conducted on 90 patients with COPD recruited from the geriatric outpatient clinic of Ain Shams University Hospital during the period of September and October 2012 and followed till August 2013 through telephone calls. Subjects were eligible for this trial were elderly (age >60), had a clinical diagnosis of COPD while those who had a history of allergy to eggs or were immune compromised or receiving any immunosuppressive drug except corticosteroids, or had associated malignancy or any disease that would be likely to shorten their survival to <1 year were excluded. COPD was defined and classified according to the British Thoracic Society Criteria [14]; FEV₁/FVC ratio less than 70% and a post-bronchodilator increase in FEV₁ of less than 12% and 200 ml from the initial value. FEV₁ predicted above 60% diagnose mild COPD, moderate (40–59.9%) and severe (less than 40%). Ninety patients with COPD were classified based on their FEV₁ as having mild, moderate, and severe COPD. They were classified into two groups; Group A (case group): This group included 45 COPD patients who agree to receive the vaccine the influenza vaccine & Group B (control group) which included 45 COPD patients who refused to receive the influenza vaccine. We compared the two groups as regard exacerbation rates, hospitalizations, mortality, lung function and adverse effects. At the vaccination session, each patient received an IM injection of influenza vaccine in the deltoid muscle. The vaccine is inactivated and complies with the WHO recommended strains.

Demographic data, comorbid diseases, and history of cigarette smoking were collected for all patients studied. Baseline evaluation of clinical symptoms and lung functions were performed. On first visit, patients were informed about possible symptoms of acute respiratory illness (ARI). Patients were told to notify the doctor immediately if they had these symptoms. Patients were followed as regards, the number of acute exacerbations of COPD (defined as an increase in breathlessness and/or the volume and/or purulence of sputum), the number of hospital admissions, Mortality in the year following vaccination which may include mortality from respiratory disease, all causes, and causes other than respiratory disease; adverse effects and they had a second visit at the end of the study period to check for any change in lung function from baseline. The study was approved by the ethical committee of the Faculty of Medicine, Ain Shams University. Written/oral informed consents were obtained from every participant.

Statistical methods: The collected data was coded, tabulated, revised and statistically analyzed using SPSS program (version 16). Quantitative variables were presented in the form of means and standard deviations. Qualitative variables were presented in the form of frequency tables (number and percent).

Results

Ninety participants recruited for this study all diagnosed as having COPD. The mean age of the participants was 64.65 ± 6.23 years. General characteristics of participants are presented in **Table 1**.

Table 2 shows a significant reduction in the total number of exacerbations per vaccinated subject (1.8 ± 1.3) compared with non-vaccinated group (3.0 ± 1.9). The hospitalization rate was significantly lower in vaccinated subjects (44.4%) than the non-vaccinated group (75.6%) p value 0.002. Also mortality rate was lower in vaccinated subject (11.1%) than non-vaccinated group (26.7%)

Table 3 shows that there was no significant difference among mild, moderate and severe COPD regards exacerbation rate, hospitalization and mortality rate in both groups.

Discussion

In the present study we evaluated the effectiveness of influenza vaccination on influenza-related acute respiratory illness (ARI) and overall ARI in patients with COPD. A case control study was conducted on 90 elderly patients with COPD (58 years and older) recruited from the outpatient geriatric clinic of Ain Shams university hospital. 90 patients with COPD were classified based on their FEV₁ as having mild, moderate, and severe COPD. They were classified into two groups; 45 COPD patients (cases) who received the influenza vaccine and 45 COPD patients (controls) who did not like to receive the influenza vaccine. We compared the two groups as regard exacerbation rates, hospitalizations, mortality, lung function and adverse effects. Research evidence supports a policy of influenza vaccination for all older people. The vaccination of all older people has also been recommended in research reviews undertaken by the US and the Canadian Preventive Task Forces [15,16].

Table 1 The participants' characteristics.

Gender	Male	81 (90.0%)
	Female	9 (10%)
Age		64.65 ± 6.23
Vaccination		45 (50.0%)
Smoking	Current	42 (46.7%)
	Ex-smoker	36 (40.0%)
	Non Smoker	12 (13.3%)
Dm		34 (37.8%)
Htn		39 (43.3%)
Chf		17 (18.9%)
Cld		4 (4.4%)
Fev1		56.31± 16.77
Copd Severity	Mild	38 (42.3%)
	Moderate	31 (34.4%)
	Severe	21 (23.3%)

Table 2 Comparison between both groups.

	Vaccinated	Non	P value
	N= 45	vaccinated	
		N= 45	
Age	64.22 ± 6.54	65.08± 5.97	0.51
FEV1	58.28± 17.41	54.33 ± 16.91	0.26
Hospitalization	20 (44.4%)	34 (75.6%)	0.002*
No of hospitalization	1.0 ± 1.4	1.82 ± 1.57	0.008*
Maximal duration	4.37 ± 6.95	10.05 ± 10.08	0.002*
Mortality	5 (11.1%)	12 (26.7%)	0.052
No of exacerbations	1.8 ± 1.3	3.0±1.9	0.003*
Adverse effects	5 (11.1%)	4 (8.9%)	0.5
Smoking	Current Smoker	21 (46.7%)	21(46.7%)
	Ex-smoker	21(46.7%)	15(33.3%)
	Non smoker	3(6.7%)	9 (20%)
Gender	Male	42(93.3%)	39(86.7%)
	Female	3(6.7%)	6 (13.3%)
Severity	Mild	23 (51.1%)	15 (33.3%)
	Moderate	12 (26.7%)	19 (42.2%)
	Severe	10(22.2%)	11(24.4%)

In susceptible persons, usually smokers, exposure to inhaled noxious particles and gases results in inflammation in the bronchial mucosa, lung parenchyma, and pulmonary vasculature [17]. Other processes believed to be of importance are an imbalance of proteinases and anti-proteinases and oxidative stress. Many cells and mediators are involved in the pathogenesis of inflammation in COPD. Respiratory viruses are considered to be amongst the most important triggers of exacerbations. Between

15% and up to 64% of COPD exacerbations have been found to be associated with symptomatic colds precipitated by viruses [18,19]. Protection by influenza vaccination is only effective in 70% of patients and only lasts for one year[20].

In the current study there was a significant reduction in the total number of exacerbations per vaccinated subject (1.8 ± 1.3) compared with those who did not receive the vaccine (3.0 ± 1.9). This agrees with Poole and colleagues [21] who concluded that administration of an inactivated influenza vaccination has a clinically important and significant effect in reducing exacerbations, caused by influenza, occurring three or more weeks after vaccination, and probably an effect on the total number of exacerbations in COPD patients.

Our results showed that the hospitalization rate was significantly lower in vaccinated subjects (44.4%) than the control group (75.6%) p value 0.002. Also mortality rate was lower in vaccinated subject (11.1%) than the control group (26.7%). This agrees with Nichol et al. [22] who found that in subjects with chronic lung diseases, vaccination resulted in a 52% reduction in hospitalizations and a 70% decrease in death rates during influenza seasons.

A meta-analysis of published effects of influenza vaccination by Gross and colleagues [23] showed a 56% reduction in respiratory illnesses, a 50% reduction in hospitalizations, a 68% reduction in all cause deaths, and a 53% reduction in pneumonia in vaccinated subjects. In the current study there was no a significant statistical difference between vaccinated and non-vaccinated groups regards the adverse effect of vaccine, this agrees with Gorse [24] who found that the proportion of patients with adverse effects at least possibly related to immunization was said to not differ between groups. We also not found an increase in early exacerbation after vaccination and this constant with Poole et al. [21] they also concluded that there was no evidence of an increase in early exacerbations. Yet, in the experience of many clinicians, transient increases in symptoms may occur in the weeks after vaccination.

Conclusions

Influenza vaccination is highly effective in the prevention of influenza-related ARI regardless of the severity of COPD. Influenza vaccination should be recommended to all patients with COPD.

Author Contribution

Hend M.Taha: Study design, analysis and interpretation of data and drafted the article. Gave final approval of the version to be published.

AmiraH.Mahmoud: Acquisition, analysis and interpretation of data. Gave final approval of the version to be published.

WalaaW.Aly: Acquisition and analysis of data. Gave final approval of the version to be published

Table 3 Comparison between both groups (each divided into 3 subgroups according to COPD severity).

	Vaccinated			p	Non vaccinated			p
	Mid	Moderate	Severe		Mild	Moderate	Severe	
	23	12	10		15	19	11	
Age	62.7±7.8	65.4±5.4	66.2±3.3	0.23	64.2±5.9	64.1±5.8	67.9±5.7	0.19
Hospitalization	10(43.50%)	5 (41.7%)	5(50.0%)	0.91	9(60%)	15(78.9)%	10(90.9%)	0.17
No of Hospitalization	0.82±1.07	1.5±2.2	0.80±0.91	0.38	1.4±1.7	2.05±1.5	2.09±1.3	0.49
Maximal duration	5.2±8.6	3.0±4.4	4.1±4.4	0.66	11.2±15.8	9.1±6.0	10.18±5.7	0.84
Mortality	1(4.3%)	3 (25%)	1(10%)	0.18	4(26.7%)	6(31.6%)	2(18.2%)	0.72
No of exacerbations	1.6±1.4	2.0±1.2	2.3±1.4	0.44	2.1±2.2	3.2±1.9	3.7±1.2	0.09
Adverse effects	1(4.3%)	3 (25%)	1(10%)	0.18	1(6.7%)	2(10.5%)	1(9.1%)	0.92

References

- 1 Pauwels RA, Buist AS, Calverley PM, et al. (2001) Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) workshop summary. *Am J Respir Crit Care Med* 163: 1256-1276.
- 2 Lopez AD, Murray CC (1998) The global burden of disease. *Nat Med* 4: 1241-1243.
- 3 Sullivan SD, Ramsey SD, Lee TA (2000) The economic burden of COPD. *Chest* 117: 5S-9S.
- 4 Ruckdeschel EA, Kirkham C, Lesse AJ (2008) Mining the *Moraxella catarrhalis* genome: Identification of potential vaccine antigens expressed during human infection. *Infect Immun* 76:1599-1607.
- 5 Egyptian Society of Chest Diseases and Tuberculosis (ESCT) (2003) The Egyptian guidelines for the management of chronic obstructive pulmonary disease. *Egypt J Chest Dis Tub* 52: 1-28.
- 6 Mullooly JP, Bennett MD, Hornbrook MC, Barker WH, Williams WW, et al. (1994) Influenza vaccination programs for elderly persons: Cost-effectiveness in a Health Maintenance Organization. *Ann Intern Med* 121: 947-952.
- 7 Nichol KL, Margolis KL, Wuorenma J, Sternberg von T (1994) The efficacy and cost effectiveness of vaccination against influenza among elderly persons living in the community. *N Engl J Med* 22: 778-784.
- 8 Groenewegen KH, Schols AMWJ, Wouters EFM (2003) Mortality and mortality related factors after hospitalization for acute exacerbation of COPD. *Chest* 124: 459-467.
- 9 Cote CG, Dordelly LJ, Celli BR (2007) Impact of COPD exacerbations on patient-centered outcomes. *Chest* 131: 696-670.
- 10 Decramer M, Nici L, Nardini S (2008) Targeting the COPD exacerbation. *Respir Med* 102: S3-S15.
- 11 Furumoto A, Ohkusa Y, Chen M (2008) Additive effect of pneumococcal vaccine and influenza vaccine on acute exacerbation in patients with chronic lung disease. *Vaccine* 26: 4284-4289.
- 12 Global Initiative for Chronic Obstructive Lung Disease (2008) Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease.
- 13 Govaert TME, Thijs CT, Masurel N, Sprenger MJ, DinantGJ, et al. (1994) The efficacy of influenza vaccination in elderly individuals. A randomized double-blind placebo-controlled trial. *JAMA* 272:1661-1665.
- 14 British Thoracic Society (1997) Guidelines for the managements of Chronic Obstructive Pulmonary Disease. *Thorax* 52: s1-s128.
- 15 U. S. Preventive Services Task Force Guide to clinical preventive services (1996). Williams & Wilkins. Baltimore.
- 16 The Canadian Task Force on the Periodic Health Examination Clinical preventive health care (1994) Ottawa.
- 17 National Heart, Lung and Blood Institute Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease (2006) NHLBI/WHO workshop report.
- 18 Seemungal TA, Harper-Owen R, Bhowmik A (2001) Respiratory viruses, symptoms and inflammatory markers in acute exacerbations and stable chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 164: 1618-1623.
- 19 Wedzicha JA (2004) Role of viruses in exacerbations of chronic obstructive pulmonary disease. *Proc Am Thorac Soc* 1: 115-20.
- 20 World Health Organization Influenza vaccines: Position paper (2005) *Wkly Epidemiol Rec* 80: 279-87.
- 21 Poole PJ, Chacko E, Wood-Baker RWB (2006) Influenza vaccine for patients with chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 1: CD002733.
- 22 Nichol KL, Baken L, Nelson A (1999) Relation between influenza vaccination and out-patient visits, hospitalization, and mortality in elderly persons with chronic lung disease. *Annals Internal Med* 130:397-403.
- 23 Gross PA, Hermogenes AW, Sacks HS (1995) The efficacy of influenza vaccine in elderly patients. *Ann Intern Med* 123: 518-523.
- 24 Gorse GJ, O'Connor TZ, Young SL, Mendelman PM, Bradley SF (2003) Efficacy trial of live, coldadapted and inactivated influenza virus vaccines in older adults with chronic obstructive pulmonary disease : A VA cooperative study. *Vaccine* 21: 2133-2144.