The effect of influenza vaccination on the incidence of chronic obstructive pulmonary disease exacerbations in the immediate postvaccination period

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ABSTRACT

Background Influenza vaccination is an important strategy in the prevention of exacerbations in patients with chronic obstructive pulmonary disease (COPD). Despite the proven benefits, there are patients who are reluctant to have this intervention for fear of triggering an exacerbation. There are very few studies looking at the effect of the vaccination on exacerbation rates of COPD in primary care.

Methods Medical records were obtained from six primary care practices in the Derbyshire area (UK), and 293 pairs of patients were selected. All patients had a diagnosis of COPD based on post bronchodilator spirometry. Patients were matched according to age, sex, severity of COPD and comorbidities. The first group of patients received the influenza vaccination while the other group served as a control (either never received the vaccination or received it at a later date). The incidence of COPD exacerbations of both groups was recorded.

Results There were 21 exacerbations in the control group compared to 11 in the vaccinated group. The difference in exacerbation rates between groups was not statistically significant (McNemar’s p = 0.11). In the 2 weeks after receiving the influenza vaccination, the risk of experiencing an exacerbation in this group of patients was 0.52 in the vaccinated group compared to the non-vaccinated group (OR 0.52, CI 0.29 to 1.14).

Conclusion Patients with COPD should be reassured that the influenza vaccination is safe and does not cause an increase in exacerbations. They should be encouraged to take up the vaccination annually before the onset of winter.

Chronic obstructive pulmonary disease (COPD) is a common respiratory disease that has an estimated prevalence of 90 000 in the UK, and is associated with significant morbidity and mortality. It is the third most common cause of respiratory death after lung cancer and pneumonia, and acute exacerbations of COPD cost the NHS over 1 million bed days per year annually in the UK.

Prevention of acute exacerbations of COPD is one of the key objectives of managing chronic stable COPD as defined by GOLD (Global initiative for Obstructive Lung Disease). Evidence suggests that influenza vaccine reduces mortality and hospital admissions in patients with COPD in the winter. The GOLD guidelines therefore recommend that at any stage of severity of COPD, annual influenza vaccine should be administered. In the UK, the Department of Health and the National Institute for Clinical Excellence (NICE) support this strategy. NICE recommends that all patients with chronic respiratory disease (including asthma that requires continuous or repeated use of inhaled or systemic steroids or with previous exacerbations requiring hospital admission) should receive influenza vaccination. Although specific antiviral drugs such as zanamivir and oseltamivir are used to prevent influenza infections, they are generally used in specific groups of patients such as patients for whom influenza vaccination is contraindicated and is not suitable for seasonal use. NICE have therefore not recommended the use of such drugs for routine prophylaxis of influenza infections. The European Centre for Disease Prevention also supports this strategy and recommends immunisation with seasonal influenza vaccine in people with chronic respiratory diseases.

A recent Cochrane review of 11 randomised controlled trials concluded that administration of inactivated influenza vaccine is effective in decreasing “flare ups” of COPD. In our clinical practice, however, some patients with COPD do not agree to be vaccinated against influenza, and fear of inducing an exacerbation after receiving the influenza vaccination is a common reason cited by patients for declining to be vaccinated. In patients with asthma, the possibility that influenza vaccination might induce an exacerbation has been studied, but there is little in the literature to help clinicians answer the question for COPD patients.

In an attempt to assess whether patients with COPD had an increased frequency of acute exacerbation immediately after influenza vaccination, we compared the rate of exacerbation in the 2 weeks following vaccination in patients with the rate of exacerbation in the same 2-week period in matched controls who either never received the vaccination or had not (yet) been vaccinated that year.

METHODS

This is a retrospective study using the clinical records of matched pairs of patients with COPD living in the North Derbyshire area of England. The names of patients with COPD were obtained from the COPD Registers of six general practices in the North Derbyshire area. The accuracy of COPD diagnosis in each case was assessed using the spirometry records in the patient notes. Patients with no airflow obstruction on spirometry or who had reversibility of 15% or more post bronchodilator were excluded from the study. The severity of COPD was categorised using the post- bronchodilator FEV1 by the GOLD classification.
The records of 293 patients vaccinated in October–December 2005 were checked for evidence of a COPD exacerbation in the 2 weeks post vaccination (“vaccinated” group). Each of these patients was matched with a control COPD patient who received vaccination at least 2 weeks later, or who was not vaccinated at all (“control” group n=293). Matching was by age (±5 years), GOLD severity of COPD (table 1), sex and number of major comorbidities (namely ischaemic heart disease, cerebrovascular disease, other chronic respiratory disease, diabetes mellitus, any disseminated malignancy). The age range of the patients was 37–89 years with a median of 68 years. The vast majority of patients fell within moderate to severe range of COPD (GOLD stage II and III) (91.1%) (table 2). The records of both members of each matched pair were analysed in the 14-day period post vaccination of the vaccinated member of pair. An exacerbation was defined as (1) a worsening of respiratory symptoms necessitating a face-to-face consultation with a health professional and resulting in the patient starting oral steroids and/or antibiotics, (2) a hospital admission for an acute respiratory complaint, or (3) a telephone consultation with a health professional resulting in the patient starting oral medication. The study was designed with 80% power to detect a doubling of postvaccination COPD exacerbations in this patient group.

RESULTS

There were 21 exacerbations in the control group compared to 11 in the vaccinated group (table 3). The difference in exacerbation rates between groups was not statistically significant (McNemar’s p=0.11). In the 2 weeks after receiving the influenza vaccination, the risk of experiencing an exacerbation in this group of patients was 0.52 in the vaccinated group compared to the non-vaccinated group (OR 0.52, CI 0.29 to 1.14).

DISCUSSION

In the Cochrane review by Poole et al, out of the 11 trials analysed, only 6 were specific to patients with COPD. In addition, these trials analysed hospital inpatients and outpatients, and none had looked at the outcome of patients vaccinated in primary care. Reasons for non-compliance such as trust or mistrust in modern medicine, prior experience of vaccination and perceived risk from influenza have been identified particularly in the older population. This study is aimed at dispelling some of these myths surrounding the influenza vaccination and also analysing the immediate rather than late effects of the vaccination.

| Table 1 Demographics of the patients included in the study |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| Age range       | 37–89 years     | Gender          | Male-to-female ratio |
| Median age      | 68              | Male            | 1.84:1           |
| Male            | 10 (1.7%)       | Female          | 6 (1.0%)         |
| Female          | 6 (1.0%)        | GOLD stage I    | 16 (2.7%)        |
| GOLD stage II   | 358 (61.1%)     | GOLD stage III  | 176 (30.0%)      |
| GOLD stage IV   | 36 (6.1%)       | GOLD stage IV   | 36 (6.1%)        |
| GOLD stage V    | 1 (0.1%)        |                  |                  |

By analysing the same 2-week period for each postvaccine and control pair, we controlled for environmental factors such as weather conditions and prevalence of respiratory viral pathogens in the community at that time. Our findings suggest that influenza vaccination does not cause an increase in the likelihood of an acute exacerbation in COPD patients in the immediate 2 weeks following the vaccination period. We found a trend towards reduced exacerbations immediately postvaccination, although this did not reach statistical significance.

The study has several limitations. First, it is retrospective. Second, it is likely that patients receiving vaccination will have been judged to be in a stable condition at the time of vaccination by the health worker who gave it, whereas the controls will not have been seen at the start of the study period. This would bias the study to favour the vaccinated partner in the pair. The third problem was that we were unable to determine the smoking status of the patients used in the study due to insufficient data in the case notes. Fourth, we have not matched for covariates such as socioeconomic status; it is reasonable to assume that patients from different socioeconomic backgrounds may have different views and willingness to receive the influenza vaccination. However, as the practices from where the patients came were within close proximity to each other, this may not be a significant issue. Finally, the majority of our patients were classified as moderate, and fears regarding vaccination causing exacerbation are more pertinent in patients with severe disease. These problems could be overcome by designing a prospective study using similar methodology.

CONCLUSION

Despite these limitations, this analysis supports the view that we should reassure patients with COPD that the influenza vaccination is unlikely to cause them to experience a disease flare

| Table 2 Distribution of patients according to COPD severity |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| GOLD stage I, n (%) | GOLD stage II, n (%) | GOLD stage III, n (%) | GOLD stage IV, n (%) |
| Male            | 10 (1.7%)       | 228 (38.9%)     | 112 (19.1%)     | 30 (5.1)        |
| Female          | 6 (1.0%)        | 130 (22.2%)     | 64 (10.9%)      | 6 (1.0%)        |

What is already known on this subject

Administration of the influenza vaccination to specific patient groups, including those with chronic lung disease, is globally recommended by various health organisations worldwide. Advising patients to receive the vaccination before the onset of winter has been generally accepted as standard practice in managing patients with chronic lung disease in the UK.

What this study adds

This study specifically looks at the short-term effect of the vaccination on the incidence of acute exacerbations of COPD. This study will help clinicians reassure patients with COPD about the safety and impact of influenza vaccination on their underlying respiratory disease.
up in the immediate postvaccination period. Further research on this subject would be helpful to allay patient fears, to help clinicians advise patients and to increase vaccine coverage in the population of COPD patients.

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