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Original Article

Prevalence of Influenza Vaccination in Chronic Obstructive Pulmonary Disease Patients and Impact on the Risk of Severe Exacerbations☆

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ABSTRACT

Objective: To determine the prevalence of influenza vaccination in chronic obstructive pulmonary disease (COPD) patients, and the effectiveness of the procedure.
Methods: Retrospective population-based cohort study. On 31 December 2011, influenza vaccination history was retrieved from 899 patients with confirmed COPD selected by simple random sampling from all COPD patients in Cantabria (northern Spain). Severe exacerbations (hospitalization due to COPD exacerbation) and overall mortality during 2012 were treated as dependent variables. Odds ratios (OR) were estimated by logistic regression, adjusting for age, sex, smoking status, severity of COPD, and frequency of exacerbations during the previous year. Prevented fraction among the exposed (PFe-adjusted) was determined as a measure of impact.
Results: Overall prevalence of influenza vaccination was 62.7%, but this rate fell in patients classified as more severe according to FEV1 (52.0%). Influenza vaccination showed a statistically significant protective effect against severe exacerbations in the following year: aOR: 0.54 (95% CI: 0.35–0.84); FPe-adjusted: 0.46 (95% CI: 0.16–0.65). A non-significant protective effect for overall mortality was observed: aOR: 0.76 (95% CI: 0.41–1.40). When stratified according to COPD severity (FEV1), the protective effect against risk of hospitalization was higher in more severe COPD patients: aOR: 0.23 (95% CI: 0.11–0.48); FPe-adjusted: 0.77 (95% CI: 0.52–0.89).
Conclusions: We found that influenza vaccination has a protective effect and reduces the risk of hospitalization due to exacerbations in the following year. Despite the evidence for protection, prevalence of vaccination was not optimal, especially in more severe COPD patients.

Prevalencia de vacunación antigripal en pacientes con enfermedad pulmonar obstructiva crónica e impacto en el riesgo de agudizaciones graves

Palabras clave:
Enfermedad pulmonar obstructiva crónica
Vacunación antigripal
Prevención primaria

RESUMEN

Objetivo: Determinar la prevalencia de vacunación antigripal en una muestra poblacional de pacientes EPOC y la efectividad de la vacunación.
Metodología: Estudio de cohortes retrospectivo. Se identificaron los antecedentes de vacunación antigripal (campaña 2011-2012) en 899 pacientes con EPOC confirmada obtenidos mediante muestreo aleatorio simple a partir de todos los EPOC identificados a 31 de diciembre de 2011 en Cantabria. Las agudizaciones graves (ingresos por agudización EPOC) y la mortalidad por todas las causas durante el año 2012

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fueron tratadas como variables dependientes, calculándose odds ratios ajustadas (ORa) como medida de asociación y fracciones de prevención ajustadas en los expuestos (PFe-ajustada) como medida de impacto.
Resultados: La prevalencia global de vacunación fue del 62,7%. Esta prevalencia fue menor en EPOC muy grave en base al FEV1 (52,0%). La vacunación antigripal mostró un efecto protector estadísticamente significativo sobre el riesgo de agudizaciones graves al año siguiente: ORa: 0,54 (IC 95%: 0,35-0,84); PFe-ajustada: 0,46 (IC 95%: 0,16-0,65). El riesgo de mortalidad fue menor, pero sin alcanzar significación estadística: Ora: 0,76 (IC 95%: 0,41-1,40). Al estratificar en función de la gravedad de la EPOC, el efecto protector para el riesgo de ingreso por agudización fue mayor en EPOC más graves: Ora: 0,23 (IC 95%: 0,11-0,48); PFe-ajustada: 0,77 (IC 95%: 0,52-0,89).
Conclusiones: Nuestros resultados apoyan el efecto protector de la vacunación antigripal, disminuyendo el riesgo de ingreso por agudización. A pesar de nuestros resultados protectores, la prevalencia global de vacunación antigripal fue subóptima, especialmente en los EPOC con un estadio más grave.

Introduction

Several systematic reviews and meta-analyses have been published recently, supporting the safety and benefits of influenza vaccination in the general adult population. In this population, vaccination is expected to have a modest effect on influenza-like symptoms and time off work.[1,2]

In specific risk subgroups, such as patients with chronic obstructive pulmonary disease (COPD), the general consensus is in favor of influenza vaccination, but the number of published studies is smaller.[3]

Moreover, in developed countries, rates of vaccination among COPD patients vary widely, and the prevalence of vaccination is largely described as suboptimal.[4,5] COPD prevalence also varies among different series, depending on the country and region of the study, according to international consensus guidelines.[6]

For this reason, most COPD studies and reviews[7–13] conclude that more work is needed to determine the effectiveness of influenza vaccination in different geographical regions and patient subgroups.

This heterogeneity in vaccination prevalence appears to be greater in Spain, where the latest studies report a prevalence of between 52.2%[13] and 87.2%.[14,15] Similarly, COPD prevalence appears to vary in Spain, depending on the region under study.[16]

The main objective of our study was to determine influenza vaccination rates in a population sample of COPD patients in Cantabria, and the effectiveness of the vaccine in reducing the risk of severe exacerbations.

Methodology

Study Design and Population

This was a retrospective cohort study. The flow chart for selecting study patients is shown in Fig. 1.

We examined an overall population of 362 372 healthcare users aged 35 years or older, registered in the public health system of Cantabria as of December 31, 2011, and selected those with an International Classification of Primary Care (ICPC)[17] consistent with COPD (codes R91 and R95). A total of 9334 cases were identified. Of these, a simple randomized sampling procedure was used to select 2000 cases.

Data were collected from the individualized review of health center clinical records, using the OMP-AP database and the Corporate Visor (eVISOR), which provides access to emergency department reports, discharge reports and outpatient clinic records in hospitals in Cantabria.

The personal clinical records of 11 cases could not be accessed, for reasons unknown, despite consulting the CIVITAS population data system which records registrations and deregistrations (deaths, relocation, loss of health cover, etc.).

An active search was performed in the clinical records of the 1989 accessible patients, and of these, COPD was ruled out in 70 who had a reversible obstructive pattern on least 1 post-bronchodilator spirometry. The spirometries of another 127 patients showed a non-obstructive pattern, so COPD was also ruled out in these patients.

No spirometry records were available for 315 patients, so in these cases diagnosis could be neither confirmed nor ruled out. At least 1 spirometry showing an obstructive pattern was available for 577 patients, but either no post-bronchodilator challenge was performed, or no record of post-bronchodilator challenge was available, so diagnosis was also inconclusive in these patients.

COPD could be confirmed in 45.3% (n=900) of the patients included in the original sample, according to confirmed spirometric data (FEV1/FVC<70% post-bronchodilation). We decided to use an analysis strategy that would prioritize internal validity, limiting the analysis to that population.

Variables

Sociodemographic characteristics were collected for each patient, including sex, age, smoking habit, alcohol consumption, comorbidities, years since COPD diagnosis, treatments, and history of 23-valent pneumococcal and influenza vaccination (seasons 2011–2012 and 2012–2013), and number and severity of COPD exacerbations.

"COPD exacerbation" was defined as any episode involving an increase in the patient's baseline COPD symptoms (cough, expectoration, and/or dyspnea), requiring the prescription of an antibiotic and/or systemic corticosteroid (moderate exacerbation), or hospitalization for more than 24 h (severe exacerbation).[18–20]

The total frequency of exacerbations (moderate and severe) was quantified in the previous year (2011) and the following year (2012). "Exacerbator phenotype" was defined as a patient who presented at least 2 exacerbations in 1 year, according to the definition of the main national and international guidelines.[6,13,18,20] A "non-exacerbator phenotype" was one who had $\leq$1 exacerbation in 1 year.

Each exacerbation had to be separated by a period of at least 4 weeks since the end of treatment for the previous exacerbations, to differentiate a new event from a previous treatment failure.

All-cause mortality in 2012 was calculated.

Study patients were classified in 2 cohorts, according to whether they had received or not received influenza vaccination in the 2011–2012 campaign (between 18 October and 30 November). Information for this variable was obtained in 899 of the 900 patients.