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Hospital Admissions in Patients with COPD during the 2009 Flu Pandemic

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Abstract

Introduction: Chronic obstructive pulmonary disease has been described as an underlying medical cause for the influenza A infection (H1N1). In this study we analyzed the presence of H1N1 virus infection in COPD patients and compliance protocols.

Material and Methods: We identified COPD patients hospitalized for lower respiratory infection (acute exacerbation or pneumonia) in the period of pandemic influenza. The microbiological analysis was performed according to standard clinical practice according to published protocols.

Results: We included 129 episodes in 110 patients, 104 with acute exacerbation and 25 for pneumonia. Pharyngeal samples were studied for detection of H1N1 in 17 patients, of which 5 cases were positive (3.9% of episodes). These patients were younger, more fever, headache and increased need for mechanical ventilation. The patients studied for H1N1 infection were those with clinical worsening and radiographic progression. According to the criteria of clinical suspicion for H1N1 infection of the published protocol, throat swab was performed in 24-44% of episodes of hospital admission in COPD patients during the peak incidence of influenza pandemic.

Conclusion: The study of H1N1 infection was made illegally in COPD patients admitted. Of the patients evaluated, we found no biological data that could guide the virus box. Nor have we observed differences in respect to the severity of COPD based on spirometric data.

Keywords: COPD; Respiratory infection; Acute exacerbation; Pneumonia; A influenza; Hospitalization.

Introduction

In June, 2009, the World Health Assembly announced the first influenza pandemic of the XXI century. It was an outbreak of influenza A virus (H1N1) of pork origin. Although most cases were a mild and subclinical influenza, in Spain, it caused a mortality rate of 0.21 deceased for every 1000 affected [1].

Its duration was of about 8 weeks, with a maximum impact during the week from 15th to 21st November [2], with 372, 7 cases for every 100.000 inhabitants.

Hospitalization was more frequent in children, teenagers and young adults. At least half of patients had a subjacent medical cause [3-6] such as pregnancy, asthma, diabetes mellitus, obesity (which had not been described previously as a factor of risk for other pandemics in the past) and chronic obstructive pulmonary disease (COPD). The influence of this one is unknown, so much so that COPD presence appears in 0.2-8% of the global of infected patients with H1N1virus, and these required hospitalization [4,7]. This proportion rises above 30% if we consider patients who required treatment in the Intensive Care Unit (ICU) [8], and among the ones who deceased, we know that in Spain the 17% had COPD [9].

In this study we analyze the influence of the virus A infection (H1N1) in COPD patients and its clinical and prognostic repercussion based on a group of COPD patients admitted due to a mild respiratory infection during the period of flue pandemic. Therefore, characteristics of the admitted cases are analyzed, considering subjects compliance on those indications and recommendations from published protocols.

Material and Methods

Patient selection

A prospective, longitudinal and observational study of cohorts was made on patients attended in a general hospital, with an influence area of 240.000 inhabitants, and with conditions of regular clinical practice.

Adult patients were identified, no age limit, requiring hospital admission due to a lower respiratory tract infection from 1stOctober, 2009 to 31st December, 2009.

Patients meeting COPD criteria were included by using pulmonary function tests (spirometry: FEV1<80% of normal value and

FEV1/FVC <0.7 after using bronchodilator) [10]. Patients admitted due to a reason other than COPD exacerbation and those unable to make a spirometry or not meeting spirometric criteria were excluded.

In order to value the importance of the Influenza A virus infection (H1N1), COPD patients with lower respiratory tract infection (acute exacerbation and/or pneumonia) were identified. COPD exacerbation (AE-COPD) was defined according to Rodríguez-Rosín definition [11], and assuming infectious etiology by using Anthonisen criteria [12]. For the diagnosis of pneumonia in COPD, the presence of a new radiological consolidation, which evolutionarily behaved like pneumonia, was required.

Procedures

In addition to the identification data related to register, age, sex and reason for the hospital admission, we registered spirometrical values which were obtained in a stable situation and its bronchodilator response, smoking records, previous admissions due to COPD during the previous year, as well as pneumonia and exacerbation episodes.

From all these included patients, a series of clinical and biological basic parameters were obtained (temperature, cardiac frequency, height, weight, body mass index, Modified Medical Research Council Dyspnea Scale (mMRC) [13], arterial blood gas test at admission, hematocrit, hemoglobin, baseline glycaemia, total cholesterol, C-reactive protein [CRP] and fibrinogen).

All comorbidities referenced in Charlson index were included. Barthel index was used to value the functional capacity of patients.

Finally, data referred to hospitalization was included, such as the days of hospital stay, resources used (admission in ICU) and treatment done. Readmission was defined as a new hospitalization after a minimum of one week from the discharge date of the last exacerbation that required hospital admission.

Microbiology studies for the etiological diagnosis were made during the regular clinical practice at the discretion of the physician in charge, including Gram stain and the conventional sputum culture; serial blood cultures and Antigenuria for Streptococcus pneumoniae and Legionella pneumophila. For the detection of influenza virus, polymerase chain reaction techniques (PCR) were used according to the clinical practice protocol made as a consequence of the flu pandemic [14]. This protocol limited the obtaining of clinical samples in the acute cases of infection, described by Ministerio de Sanidad as follows: acute clinical profile compatible with pandemic virus infection (H1N1) which requires hospital admission and suspect of pneumonia due to pandemic virus. During the clinical practice the Influenza A virus infection was suspected on a patient who suffered temperature above 38°C with acute respiratory infection, or upon pneumonia of unknown etiology diagnosis, or in the event of death from respiratory disease.

Data analysis

With all data obtained, it has been done a descriptive analysis of all variables included in the study by using SPSS 14.00 software. Qualitative variables were expressed as absolute frequencies and percentages (%), while quantitative variables were expressed as measures and standard deviations (SD). It has been done the average comparison by using Student t test for independent samples, applying Bonferroni correction when advised. U-Mann Whitney was used for variables not meeting normal criteria. For proportion comparison, Chi2 test or exact Fisher test was used. In all cases, bilateral hypothesis with a p value below 0,05 was considered to identify differences statistically significant.

Results

During the study period, 141 hospital admissions for acute respiratory infection on patients with COPD diagnosis (acute exacerbation or pneumonia) were identified. COPD diagnosis could not be confirmed on 12 patients. Finally, 129 episodes on 110 patients were included, 104 for acute exacerbation (AE) and 25 for pneumonia.

Among these episodes, 19 were readmissions (15 for AE and 4 for pneumonia).

Figure 1 shows hospital admission evolution during the study period, as well as Influenza A H1N1 diagnosis.

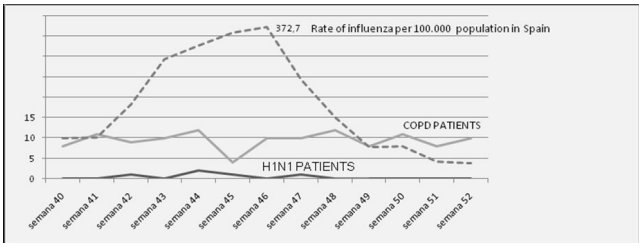

Figure 1: Inclusion of patients during the period of influenza pandemic 2009. Incidence rate of influenza A during the study period [2].

General clinical characteristics of patients are described on Table 1. Mainly, they were men (7 women, 6.4%), with an average age of 71.9 years old (43-91, SD 10.4). A smoking background was identified on most patients (97.3%), being it active in the 27.3%. Average tobacco consumption was of 58.3 packs a year (SD 33.6), and 23.8 cigarettes a day (SD 14.3). 19.1% of the patients had a history of alcohol consumption. According to spirometry data, patients showed an average FVC of 1209 ml (SD 805), and FEV1 1209 ml (SD 491), with the percentage of FVC% 95.6% (SD 19.6) and FEV1% 54.6% (SD 79.7). At baseline, dyspnea grade according to mMRC was 1 in a 33.3%, grade 2 in 41%, grade 3 in a 32% and grade 4 in a 4%. Most patients showed a moderate-severe COPD, and 33 of them (30%) required home oxygen therapy. Of all patients, 9 of them made chronic antibiotic treatment (8.2%), mostly with azithromycin and ciprofloxacin. IECA's use was in 30 patients (27.3%) and statins in 38 (34.5%). A 59.1% had received seasonal influenza vaccination within the study period, and 24 of them got pandemic influenza A vaccination (21.8%). Of all episodes observed, antibiotic treatment was not prescribed only for two of them, with acute exacerbation diagnosis of unknown etiology in both of them. In the rest of infections in the lower respiratory tract, the mainly empirically prescribed antibiotics were levofloxacin (44.2%) and amoxicillin-clavulanic (25,6%), followed by ceftriaxone (12.4%) and imipenem (6,2%). Antiviral treatment was empirically made in 12 episodes (9,3%).

Total n (%)	
Demographic characteristics	
Age, years (± SD)	71,9 ± 10,4
Sex, men	103 (93,6)
Former smokers	30 (27,3)
Occupational history	14 (15,7)
Influenzae / H1N1 vaccination	65 (59,1) / 24 (21,8)
S. pneumoniae vaccination (last 10 years)	51 (46,4)
AE-COPD in the last year	51 (46,4)
COPD hospitalization in the last year	45 (40,9)
Pneumonia in the last year	9 (8,2)
Treatment	
Oxygen long treatment	33 (30)
Oral Corticoids	19 (17,4)
Chronic antibiotics	9 (8,2)
Comorbidities	
Charslon index (± SD)	2,38 ± 1,7
Hypertension	61 (55)
Dyslipidemia	39 (35,5)
Diabetes mellitus	32 (29,1)
Bronchiectasis	31 (28,2)
Arrythmia	23 (20,9)
Ischemic heart disease	21 (19,1)
Apnea hypopnea syndrome	18 (16,4)
Valvular heart disease	16 (14,5)
Osteoporosis	15 (13,6)
Tuberculosis	13 (11,8)
Neoplasm	12 (10,9)
Depression	12 (10,9)
Heart failure	9 (8,2)
Cor pulmonale	5 (4,5)
Obesity	5 (4,5)
Functional status	
Barthel scale (± DS)	89 ± 19,7
mMRC scale (± DS)	1,86 ± 1
COPD severity (GOLD)	

Mild (>80)	5 (4,7)
Moderate (50-80)	36 (34)
Sever (30-50)	32 (30,2)
Very sever (<30)	33 (31,1)

Table 1: Characteristics of COPD patients. Data are expressed as number (%) unless otherwise indicated. Influenza vaccination within the current influenza season; pneumococcal polysaccharide vaccination in the previous 10 years. COPD, chronic obstructive pulmonary disease; AE-COPD: acute exacerbation of COPD; GOLD, Global Initiative for Chronic Obstructive Pulmonary Disease.

Of all studied episodes of hospital admission, 9 required ICU admission (7%), for they needed mechanical ventilation, and 7 patients deceased (5,4% intrahospital mortality) having a poor progress on their respiratory infection (with a lung neoplasia as underlying disease in 2 patients, pneumonia in another 2, acute exacerbation of unknown etiology in one of them, and MRSA bacteremia in one patient and P.aeruginosa bacteremia in another one). Pharyngeal samples were studied for the detection of H1N1 in 17 patients, of which in 5 cases they were positive for epidemic virus H1N1 (3,9% of episodes). First, we analyzed patients with positive throat swab for virus H1N1. Table 2 shows the characteristics of patients who were diagnosed viral infection presence. Hospital stay showed a tendency to be longer in patients with a diagnosis of H1N1 infection (13,6 vs. 8,98; p=0,09), but without any difference statistically significant. Secondly, we analyze patients to whom the physician in charge made a throat swab, observing that criteria for the study were the clinic worsening and the radiologic progression (Table 3).

	H1N1	**Other diagnostics (n=124)**	**P**
	(n=5)		
	n (%)	**n (%)**	
Clinical characteristics			
Age (years)	60,8 ± 10,4	72,2±10	0,015
height (cm)	170 ± 4,1	163 ± 6,5	0,058
Obesity	1 (20)	4 (3,2)	0,238
Non smoker (years)	3 ± 3	8,97 ± 10,2	0,06
Hospitalization last year (n)	2 (40)	16 (12,9)	0,143
Grade obstruction	43 ± 3,5	49,6 ± 13,5	0,019
(FVC/FEV1 post BD)			
Episode clinical			
Peak temperature (ºC)	38,4±0,67	37,1 ± 1	0,027
Congestion	2 (40)	10 (8)	0,068
Headache	2 (40)	3 (2,4)	0,020
Laboratory data			
Total lymphocytes (mm3)	912 ± 379	1498 ± 2198	0,036
Hematocrit (%)	46,5 ± 2,6	42,3 ± 4,7	0,02
Treatment			
Inhaled corticoids	3 (60)	27 (21,7)	0,084
Antipyretics	5 (100)	53 (42,7)	0,017
Mechanical ventilation	2 (40)	7 (5,6)	0,039
Clinical evolution			
Early evaluation	1 (20)	1 (0,8)	0,030
Failure	3 (60)	113 (91,1)	
Improvement			
Clinical failure	2 (40)	115 (92,7)	0,011
No	3 (60)	6 (4,8)	
Respiratory failure			
ICU admission	2 (40)	7 (5,6)	0,039
Change of antibiotics			
No change	1 (20)	78 (62,9)	0,014
Resistance	0 (0)	10 (8)	
Empiric	3 (60)	35 (28,2)	

Table 2: Characteristics of H1N1 patients. Data are expressed as number (%) unless otherwise indicated. COPD, chronic obstructive pulmonary disease; AE-COPD: acute exacerbation of COPD. FEV1, force expiratory volume in the first second; FVC, force vital capacity; GOLD, Global Initiative for Chronic Obstructive Pulmonary Disease.

H1N1 Swab	**No swab**		**P**
(n=17)	**(n=122)**		
n (%)		**n (%)**	
Clinical Características			
Age (years)	66,5 ± 9,5	72,5 ± 10,1	0,024
Clínical episode			
Fever	11 (64,7)	27 (22,1)	0,003
Sore thorat	3 (17,6)	6 (4,9)	0,097
Headache	4 (23,5)	1 (0,8)	0,001
Arthromyalgia	4 (23,5)	2 (1,6)	0,002
Peak temperature (ºC)	37,9 ± 0,88	37 ± 1.1	0,06

Temperature in ED (ºC)	37,4 ±0,9	36,6 ± 0,97	0,02
Laboratory data			
Albúmina (g/dl)	3,28 ± 0,77	3,5 ± 0,78	0,5
Creatinine kinasa (%)	157 ± 249	82,7 ± 60	0,46
Hematocrite (%)	45,6 ± 4,1	42 ± 4,7	0,002
Creatinine (mg/dl)	0,71 ± 0,22	0,93 ± 0,47	0,074
Fibrinogen (mg/dl)	484 ± 66,7	590 ± 169	0,010
Sputum culture	10 (58,8)	35 (28,6)	0,04
Negative	1 (5,8)	33 (27)	
Positive			
Blood culture	8 (47)	35 (28,6)	0,004
Negative	3 (17,6)	2 (1,6)	
Positive			
Treatment			
Mechanical ventilation	4 (23,5)	5 (4,1)	0,018
Clinical evolution			
Early assessment	3 (17,6)	8 (6,5)	0,077
Failure	13 (76,5)	103 (84,4)	
Improvament			
Clinical worsening	11 (64,7)	105 (86)	0,001
No	5 (29,4)	4 (3,3)	
Respiratory failure			
ICU admission	4 (23,5)	5 (4,1)	0,018
Radiological progression	11 (64,7)	97 (79,5)	0,04

Table 3: Characteristics of patients with laryngeal swab for H1N1 study. Data are expressed as number (%) unless otherwise indicated. ED: emergency department.

Finally, given the few studied cases during the pandemic period, in order to analyze the compliance with protocols, we value the main criterion for the H1N1 infection study, which was the fever on the total of patients admitted due to an COPD exacerbation in this study period. Depending on how fever was registered, we obtained different results. Of those who had a temperature above 38°C according to their clinic records (17 patients), in a 23.5% a H1N1 swab was made. If they informed us about them having temperature at home (38 patients), in a 28.9% an H1N1 swab was done. Finally, if a temperature above 38°C was noticed upon admission in the emergency room (10 patients), in a 40% the study with swab for H1N1 detection was made.

Discussion

Nowadays there is a lot of information about the impact of influenza A pandemic in 2009, as well as the risk factors of fatal evolution (ICU admission or mortality) or even hospitalization. But still, even though the chronic pulmonary disease is a known risk factor with a bad progression of the viral infection, for data about more aggressiveness on young people there is little information about the influence of the pandemic in COPD patients admitted due to a respiratory infection.

The aim of this study is to value the impact of the influenza 2009-2010 pandemic on the admissions of COPD patients for exacerbation in Spain.

Up to now we only have obtained indirect data from the published series of patients with H1N1 infection, in which a 30% of the admitted patients have COPD [15,16] and this study tries to analyze those hospitalized COPD patients due to an infection in the lower respiratory tract, so that we can consider the compliance of the established protocols for the diagnosis of influenza A (H1N1) in this patients subgroup.

If we take into account that analyzed patients needed an admission for an exacerbation or pneumonia within the period of higher incidence of the influenza pandemic in our environment, we should emphasize first the low influenza H1N1 incidence we obtained, which could be attributed to the low affectation on patients older than 65, being the age group with the most incidence the one formed by young patients [17].

We note how our patients were identified during the week of the highest rate of influenza A incidence, as Figure 1 shows [12]. However, of all patients with higher suspect of influenza A because of its clinical features and severity, H1N1 was identified in only a 29.4% (5 out of 7). Diagnostic performance, understood as the prevalence of positivity on all samples analyzed, is similar to the one found in other studies in general population [18].

We can't attribute to influenza vaccination this low incidence. Seasonal influenza vaccination started from September to October, and the campaign for pandemic influenza A vaccination began in November.

Still, if we consider all the included patients from the date that the campaign started, the actual rate of vaccination was the 23.5%. Vaccination rates for seasonal influenza in adult population within the period 2009-2010 in Spain were the 71%, and for influenza pandemic the 28.5% [19], much higher for seasonal influenza but similar to pandemic influenza. Given this similarity of vaccination rate for influenza pandemic, we do not believe this information could have influenced in the different influenza A prevalence in this subgroup of patients.

Another possible explanation to the low incidence of viral infection could be the incorrect compliance of the used protocols. López Garcia et al. proved a low compliance of the published protocols in Castilla y León during the pandemic [16], where only the 42% of the studied cases had severity criteria. According to published protocols, suspect criteria of influenza A were fever presence, pneumonia of unidentified etiology or respiratory infection with a bad evolution or even death. If we analyze these criteria in the identified patients, only in a 40% of the patients with respiratory infection and fever in the emergency room, pharyngeal swab was made for the study of the H1N1 infection.

Of all patients admitted in ICU, only in a 44.4% a pharyngeal swab was made, of the 5 not studied patients, in 2 of them the cause of the respiratory infection was not identified.

Finally, of all patients that died during hospitalization, only in a 28.5% a pharyngeal swab was made. Therefore, of the 7 deceased

patients, H1N1 infection was studied only in two of them. To the other of patients study was not made; of them, 2 died, were not admitted in ICU, probably due to advanced disease, but the cause of death was an exacerbation of unknown etiology and a pneumonia of unknown etiology during the weeks 46 and 47, in which there was a higher incidence of influenza A in our environment.

Of the total of admitted patients during the study period, those patients with H1N1 diagnosis were younger, which had been already described in the numerous publications in which the early age was a risk factor for the viral infection in 2009 pandemic, in comparison to influenza pandemic of previous years when the most affected population was the older one. Other underlying comorbidities, such as obesity, have not proven any statistical significance in our data, probably as a result of the limited number of patients.

According to our data, affected patients of an H1N1 infection had a greater level of high temperature, and needed more resources of ICU admittance (and mechanical ventilation), and a longer hospital stay. This can be explained because those patients with a bad clinical progression were candidates to the study of influenza A infection. Likewise, we have observed that patients to whom swab was made had more influenza clinical features (headache, sore throat, arthromyalgias) and a worse clinical progression.

This study has several limitations. Firstly, since this is a study based only in one center and given the small size of the sample, it limits the value of the results. Likewise, we must emphasize that since it is an observational study, the study criterion for H1N1 infection and also the hospital admission criterion depended on the physician in charge. Moreover, since diagnostic test for H1N1 infection is at the discretion of the physician, this can bring a bias of selection because it is made to younger patients and those with greater clinical severity, even though the existence of action protocol.

In conclusion, of the total of 129 episodes in COPD patients admitted due to a respiratory infection, a 4% of them were diagnosed an episode of infection due to H1N1 influenza pandemic. Only 17 episodes were studied, being positive a 29.4%.

According to criteria of clinical suspect of H1N1 infection of the published protocol, pharyngeal swab was made in the 24-44% of the episodes of hospital admission in COPD patients during the period of maximum incidence of influenza pandemic, depending on how data about fever presence was valued, which exposes the low compliance of protocols in the healthcare.

Presence of high temperature and headache stands out as clinical data of the episode, as well as the greatest severity of the episode and the need of resources of intensive care, as criteria for the determination of the infection due to H1N1, bringing a longer hospital stay in these patients. We have not found biological data that can direct the viral condition. We have not observed any difference in relation to COPD severity depending on spirometric data either.

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