



Polypharmacy in patients hospitalised for acute exacerbation of COPD

To the Editor:

Chronic obstructive pulmonary disease (COPD) imposes a great burden on health systems, and the expense will increase in the years to come [1]. Medication represents a large proportion of COPD-related costs [2], and has increased by 170% over the past 20 years [3]. Inpatients with an acute exacerbation of COPD and more than four diagnoses after admission are prescribed significantly more drugs and present with polypharmacy more frequently [4]. It is well known that polypharmacy is associated with greater occurrence of adverse effects [5] and worse treatment adherence [6]. It also contributes to greater healthcare expense [7].

This study seeks to determine the prevalence of polypharmacy in patients hospitalised with an acute exacerbation of COPD, as well as the factors associated with its occurrence.

The ECCO study is an observational, cross-sectional and multicentre study, with participation from 26 Internal Medicine Departments throughout Spain. Detailed features of the study have been reported elsewhere [8]. Each researcher included, consecutively, every patient admitted for an acute exacerbation of COPD they attended between January 1, 2007 and December 31, 2008. COPD was diagnosed using spirometry [9] in a stable condition prior to admission. Information gathered included age, sex, smoking history, previous admissions for COPD and number of acute exacerbations of COPD over the previous 12 months. The Charlson index was used to assess associated comorbidities, but other conditions prevalent in COPD not included in that index were also noted. Basal dyspnoea prior to admission was assessed using the modified (five point) Medical Research Council (mMRC) scale. Polypharmacy was defined as the chronic concurrent use, more than 3 months prior admission, of five or more drugs [10], and excessive polypharmacy as the use of 10 or more medications. The study was approved by the Clinical Research Ethics Committee of the coordinating centre (Hospital de la Vega Baja, Orihuela, Alicante, Spain) and all patients signed an informed written consent form. Quantitative data are presented as mean \pm SD. Comparisons of continuous variables between the two groups were performed using the t-test or the Mann-Whitney U-test whenever variables did not show a normal distribution. Categorical variables are presented as absolute frequencies and percentages. Comparisons between both groups were made using Chi-squared and Fisher's exact tests. To compare proportions between drugs prescribed before the admission and at the time of discharge, a Z-proportion test was carried out. A multivariate logistic regression model was constructed using the variables associated with polypharmacy at discharge in the univariate analysis with a p-value <0.10 . In all analyses p-values <0.05 were considered statistically significant.

We included 398 patients, 353 males and 45 females, with a mean \pm SD age of 73.7 ± 8.9 years. At the time of admission, the mean \pm SD number of chronic drugs per patient was 5.0 ± 2.6 . A total of 224 (56.3%) patients presented polypharmacy and 22 (5.5%) excessive polypharmacy. Compared with patients without polypharmacy, those with polypharmacy were more frequently ex-smokers (75.4% *versus* 68.4%, $p=0.0005$) and used long-term oxygen therapy (41.5% *versus* 30.5%, $p=0.02$). They scored higher in the Charlson index (2.8 *versus* 2.3, $p=0.004$), had more comorbidities, and more severe dyspnoea measured with the mMRC scale (3.7 *versus* 3.5, $p=0.02$), although they showed no differences regarding their COPD Global Initiative for Chronic Obstructive Lung Disease stage.

21 patients died during hospitalisation, six (1.5%) of them without and 15 (3.8%) with polypharmacy ($p=0.15$). At discharge, the number of drugs for chronic conditions, excluding systemic corticosteroids or antibiotics administered for the current COPD exacerbation, was 6.6 ± 2.4 and had increased in 272 (72.1%) patients. 296 (78.5%) patients presented polypharmacy and 44 (11.7%) excessive polypharmacy. Factors independently associated with polypharmacy at discharge were polypharmacy at admission, a lower post-bronchodilator forced expiratory volume in 1 s (FEV₁) % predicted and presence of heart failure (table 1).

There were changes in respiratory drug use before admission and at discharge. The use of combinations of long-acting β_2 -agonists with inhaled corticosteroids (50.7% *versus* 69.0%, $p=0.0003$), inhaled anticholinergics (71.9% *versus* 87.5%, $p=0.0001$), diuretics (42.4% *versus* 51.7%, $p=0.01$), proton pump inhibitors (48.0% *versus* 68.7%, $p=0.0008$) and beta-blockers (3.9% *versus* 8.0%, $p=0.02$) had increased.

TABLE 1 Factors associated with polypharmacy at discharge

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age by decade years	1.33 (1.03–1.73)	0.03	1.02 (0.99–1.05)	0.22
10% predicted FEV₁	0.81 (0.67–0.99)	0.038	0.73 (0.57–0.93)	0.01
Charlson index	1.21 (1.01–1.44)	0.03	0.92 (0.76–1.13)	0.43
Heart failure	7.52 (2.95–19.20)	0.0002	3.94 (1.36–11.43)	0.01
Coronary artery disease	3.05 (1.26–7.34)	0.01	2.26 (0.80–6.33)	0.12
Hypertension	3.19 (1.90–5.36)	0.0001	1.71 (0.90–3.26)	0.10
Cardiac arrhythmia	3.49 (1.67–7.29)	0.0009	0.81 (0.33–2.08)	0.68
Diabetes	2.30 (1.23–4.29)	0.009	1.81 (0.85–3.87)	0.12
Osteoporosis	3.37 (1.01–11.28)	0.048	1.39 (0.36–5.39)	0.63
Polypharmacy at admission	19.31 (8.94–41.68)	0.0005	13.10 (5.67–30.28)	0.0002

FEV₁: forced expiratory volume in 1 s.

Our study shows that patients hospitalised with an acute exacerbation of COPD have been prescribed a mean of five drugs before their admission, and that the number increases after their discharge. Comorbidities, especially heart failure, and impaired lung function are the factors associated with a greater use of medication.

Polypharmacy is a frequent problem in elderly patients. A study associated having more than four diagnoses with using seven or more drugs [4]. The same association was observed with certain diagnoses, such as COPD, heart failure, diabetes mellitus, hypertension, ischaemic heart disease and renal failure. Our study has shown similar associations. Old age and comorbidities are frequent among patients of internal medicine departments, and usually these patients are more drug-dependent. In the Registro Politerapi SIMI, carried out in Italian internal medicine departments, COPD was independently associated with polypharmacy [11]. COPD–heart failure and COPD–coronary artery disease clusters were also strongly associated with polypharmacy [11]. In our study, these two comorbidities, heart failure and coronary artery disease, were present in 27% and 17% of COPD patients. A lower FEV₁ % predicted has also been associated with polypharmacy. These results were to be expected, since international clinical practice guidelines recommend using a variety of drugs for the treatment of both COPD and cardiovascular diseases. However, there are some difficulties in adapting and following the guidelines for patients suffering from multiple diseases [12]. Recommendations in the guidelines are based on clinical trials, and it is well known that trials usually exclude elderly patients with multiple diseases [13]. Furthermore, the use of more medication does not necessarily result in better health outcomes. In the case of COPD patients with a reduced life expectancy, rational prescription is paramount [14], assessing interactions, risks and benefits, and prioritising comfort, symptom control and quality of life.

Clinical inertia is a big challenge in chronic diseases including COPD, both from the diagnostic and the therapeutic angle [15]. Up to one third of all patients diagnosed with COPD are not treated. Our study shows an increase in the number of respiratory drugs prescribed at discharge, especially inhaled anticholinergics and combinations of long-acting β_2 -agonists with inhaled corticosteroids. However, we cannot rule out that a negative clinical inertia possibly led to maintenance at discharge of drugs unnecessarily prescribed before admission. The mean number of drugs increased from 5 before admission to 6.6 at discharge, and polypharmacy before admission was the major determining factor of polypharmacy at discharge.

Our study has some limitations. First, patients were recruited in internal medicine departments. In these departments COPD patients are older and suffer from more comorbidities than those attended in respiratory departments. This might limit the widespread generalisation of our conclusions outside this setting. Secondly, female patients were scarcely present in the study. This is common in other studies carried out in Spain, where the prevalence of smoking in females only started increasing after 1960. Thirdly, patients were recruited during hospitalisation for an acute exacerbation of COPD. The frequency of polypharmacy and the profile of drug prescription probably differ between COPD patients with frequent acute exacerbations of COPD and patients without any acute exacerbation of COPD. In the days or weeks prior to their admission, patients with an acute exacerbation of COPD may have experienced increasing symptoms and perhaps been prescribed new drugs. It is also possible that at discharge they were prescribed antibiotics, corticosteroids or other drugs just for a few days, only to have them removed later in a control

visit. However, to limit this factor, only drugs prescribed for chronic conditions were considered and the use of antibiotics, systemic steroids or mucolytics prescribed for the current exacerbation were excluded.

In summary, our study concludes that polypharmacy is frequent among patients hospitalised for an acute exacerbation of COPD and that it is associated with polypharmacy prior to admission, greater spirometric severity and a larger number of comorbidities, particularly heart failure. We propose that the presence of polypharmacy should be assessed in all COPD patients, and that whenever it is present, pharmaceutical care measures should be included in relation to these patients, in order to maximise adherence and reduce the possibility of adverse effects and drug interactions.



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Polypharmacy is frequent in COPD patients with acute exacerbation and is associated with severity and comorbidity <http://ow.ly/wpwzG>

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