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EXTENDED ABSTRACT

Features related to respiratory disability and performance of inhaler technique in COPD population.

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Introduction:

Chronic obstructive pulmonary disease (COPD) is one of the most common respiratory diseases treated in the community setting [1]. If not appropriately managed can result in poorer health, negative societal and economic effects, with a significant burden on patients' quality of life [1].

COPD cannot be cured, but treatment can help slow down disease progression and control of the symptoms. Treatments may include non-pharmacological approaches as smoking cessation, or pharmacological inhaled therapy, pulmonary rehabilitation, and in very few cases surgery or lung transplant [2], depending on medical doctor assessment of each individual case to provide tailored therapy.

This work aimed to explore which features of patients with COPD can be related with respiratory disability and the performance of inhaler technique in Portugal.

Methods:

Data for this work were obtained from the Pilot Project INspira – Study of inhaler use in asthma and COPD (January to November 2019) patients. A cluster randomized controlled trial, was conducted in the community pharmacies affiliated to National Association of Pharmacies to improve inhalation technique among COPD patients with inhaled therapy [3, 4]. Eligible patients were adults aged 18 years or older using at least 1 of the targeted inhalers (both chronic or first user), and a self-reported diagnosis of COPD. The self-reported diagnosis was checked by the pharmacist, using a differential algorithm [4].

Data on sociodemographic features (i.e., sex, age, educational level, occupational status, tobacco exposure), body mass index (BMI), number of comorbidities, number of different medicines and inhalators used by patients to control the disease, respiratory disability, and performance of inhaler technique, were collected prior to any education have been provided. Respiratory disability was quantified according to the modified Medical Research Council dyspnea (mMRC) scale [5, 6]. This tool comprises five statements describing the entire range of respiratory disability from none (score 0) to almost complete incapacity (score 4). Values of mMRC ≥ 2 were classified as more symptomatic. Inhaler technique was considered well performed when all steps (100%) of the inhalation process were executed correctly, and not well performed if patient failed at least one step.

For purposes of descriptive statistics, continuous variables were summarized by median and interquartile range and categorical variables by counts and percentages. Quantitative variables were analysed through the Mann-Whitney Wilcoxon Test and qualitative ones through Fisher's exact test.

Univariate logistic regression was used to select all candidate variables ($p \leq 0.25$) to enter in multivariate logistic regression. Multimodel inference was performed and the models with lowest AIC were proposed as final models. Odds ratios (OR) and 95% confidence intervals (CI) were calculated.

Results were considered statistically significant at $p < 0.05$.

Results and conclusions:

A sample of 84 patients with available mRMC scores and inhaler technique scores was analysed. Patients' main features are summarised in Table 1. The number of medicines taken to control the disease and the educational level, were significantly associated with the respiratory disability and the performance of inhaler technique, respectively.

From the univariate logistic regressions (Table 2), BMI, number of medicines and number of comorbidities were selected to integrate the respiratory disability multivariate logistic regression. Sex, tobacco exposure and educational level were selected to integrate the performance of the inhaler technique multivariate logistic regression.

Keywords:
Chronic disease, COPD, Dyspnea, Inhaler technique, Modeling, Respiratory disability

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Conflict of interest:
The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: ZM, SR and ATR are/were employees of Infosaúde, a company owned by Portuguese National Association of Pharmacies. SM and VA declare no conflict of interests.

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Table 1 – Descriptive Statistics of the chronic obstructive pulmonary disease (COPD) sample by respiratory disability and by performance of inhaler technique.

Variable	Respiratory disability			Performance of inhaler technique		
	More symptomatic	Less symptomatic	p-value	Not well performed inhaler technique	Well performed inhaler technique	p-value
	N (%)	N (%)		N (%)	N (%)	
Sex						
Male	18 (40)	27 (60)	0.384	32 (84)	6 (16)	0.050
Female	19 (50)	19 (50)		18 (62)	11 (38)	
Age						
<65 years old	12 (44)	15 (56)	1.000	16 (70)	7 (30)	0.560
≥ 65 years old	25 (45)	31 (55)		34 (77)	10 (23)	
Educational level						
Primary	14 (47)	16 (53)	0.878	20 (91)	2 (9)	**0.007****
Sixth or ninth grades	8 (50)	8 (50)		14 (88)	2 (13)	
Secondary or university	15 (42)	21 (58)		16 (55)	13 (45)	
Occupational status						
Employed	5 (36)	9 (64)	0.562	8 (73)	3 (27)	1.000
Retired or Unemployed	32 (46)	37 (54)		42 (75)	14 (25)	
Tobacco exposure						
Never smoked	8 (53)	7 (47)	0.790	7 (58)	5 (42)	0.377
Ex-smoker	20 (43)	27 (57)		29 (76)	9 (24)	
Active smoker	9 (43)	12 (57)		14 (82)	3 (18)	
Respiratory disability						
More symptomatic	-	-	-	22 (71)	9 (29)	0.587
Less symptomatic	-	-		27 (77)	8 (23)	
Inhaler technique						
Not well performed	22 (45)	27 (55)	0.587	-	-	-
Well performed	9 (53)	8 (47)		-	-	
	Median (IQR)	Median (IQR)		Median (IQR)	Median (IQR)	
Body mass index (BMI)	27.68 (6.07)	26.18 (5.42)	0.140	27.65 (6.52)	26.64 (5.43)	0.757
Number of inhalators	1.00 (0.00)	1.00 (0.00)	0.565	1.00 (0.00)	1.00 (0.00)	0.599
Number of medicines	2.00 (2.00)	1.00 (1.00)	0.018*	1.00 (1.00)	1.00 (1.00)	0.550
Number of comorbidities	2.00 (3.00)	2.00 (2.00)	0.088	2.00 (2.00)	2.00 (1.00)	0.813

IQR – Interquartile Range; * p-value < 0.05; **p-value < 0.01.

Table 2 – Univariate Logistic regression results for respiratory disability and performance of inhaler technique outcomes.

Variable	Respiratory disability			Performance of inhaler technique		
	OR	CI	p-value	OR	CI	p-value
Sex (Male)	1.50	0.63-3.62	0.362	0.31	0.09-0.94	**0.044***
Age (>=65)	0.99	0.39-2.50	0.986	0.67	0.22-2.15	0.493
Body mass index (BMI)	0.90	0.81-0.99	**0.038***	0.99	0.89-1.09	0.807
Number of inhalers	0.71	0.25-1.87	0.493	0.83	0.21-2.40	0.759
Number of medicines	0.63	0.40-0.94	**0.031***	0.90	0.53-1.41	0.650
Number of comorbidities	0.73	0.52-0.98	**0.046***	0.93	0.62-1.36	0.726
Respiratory disability	-	-	-	0.72	0.23-2.20	0.568
Performance of inhaler technique	0.72	0.23-2.20	0.568	-	-	-
Tobacco exposure (Active Smoker)	0.99	0.35-2.85	0.981	0.69	0.14-2.74	0.618
Tobacco exposure (Never smoked)	0.65	0.20-2.09	0.467	2.30	0.56-9.15	**0.233***
Occupational status (Retired or Unemployed)	0.64	0.18-2.06	0.467	0.89	0.22-4.48	0.874
Educational level (Sixth or ninth grades)	0.88	0.26-2.98	0.829	1.43	0.16-13.10	0.736
Educational level (Secondary or University)	1.23	0.46-3.28	0.684	8.13	1.89-57.00	**0.012***

OR – Odds Ratio; CI – confidence interval; * p-value ≤ 0.25

Due to the existence of incomplete cases in the initial data set, the multivariate logistic regression analysis was performed with 66 COPD patients. In the respiratory disability multivariate model, only the number of medicines showed to be significant ($p = 0.044$), when adjusted to BMI. As the number of medicines used increases, the respiratory disability increases. In the performance of the inhaler technique multivariate model, only the educational level showed to be significant ($p = 0.005$), when adjusted to tobacco exposure. Patients with a secondary or university degree were 14 times more likely to perform the inhalation technique correctly than individuals with primary school (Table 3).

The positive association between the number of medicines used by patients and the respiratory disability is an interesting result, since the prescription of a greater number of medicines by the doctors will have

Table 3 – Multivariate logistic final models of respiratory disability and performance of the inhaler technique in people with chronic obstructive pulmonary disease (COPD).

	Coefficients Estimate	SE	OR	95% CI	p-value
Respiratory disability					
(Intercept)	3.33	1.56	28.01	1.62-785.42	0.032*
Body mass index (BMI)	-0.09	0.05	0.92	0.82-1.01	0.094
Number of medicines	-0.49	0.24	0.61	0.37-0.96	**0.044***
Performance of Inhaler technique					
(Intercept)	-2.79	0.89	0.06	0.00-0.26	0.002**
Tobacco exposure (Active Smoker)	-0.85	0.82	0.43	0.08-1.99	0.300
Tobacco exposure (Never smoked)	1.72	0.95	5.60	0.96-46.82	0.070
Educational level (Sixth or ninth grades)	0.19	1.14	1.20	0.11-12.33	0.870
Educational level (Secondary or University)	2.71	0.95	14.97	2.86-140.00	**0.005****

* p-value < 0.05; ** p-value < 0.01

the objective of greater effectiveness in controlling the disease or reduce its severity. However, it is known that polypharmacy tends to increase poor medication adherence [7, 8], and thus reducing the effectiveness of the medication, and consequently worsening disease.

On the other hand, as expected, according to previous literature [9–13], our results show that educational level is significantly associated to the performance of the inhaler technique. The correct inhaled technique favors therapeutic effectiveness and consequently better outcomes, namely better symptom control, lower risk of exacerbations, and improved quality of life [14, 15].

Ethics committee and informed consent:

The current research was approved by an independent ethics committee and patients gave their informed consent before they were enrolled in the study. Ethics compliant 10/12/2018, Ethics Committee Institute of Bioethics of Universidade Católica Portuguesa (Instituto de Bioética, Universidade Católica Portuguesa, Porto, Rua de Diogo Botelho, 1327, 4169-005 Porto, Portugal).

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