Particularities of COPD exacerbations in different phenotypes of the disease in Tunisia

Particularités des exacerbations de BPCO dans les différents phénotypes de la maladie en Tunisie.

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RÉSUMÉ

Prérequis : La broncho-pneumopathie obstructive (BPCO) est définie par la limitation des débits aériens. Cette maladie est caractérisée par des exacerbations qui menacent la vie du patient et aggrave le pronostic. En outre, les patients atteints de BPCO sont différents en fonction de nombreux paramètres qui définissent différents phénotypes. Les caractéristiques des exacerbations peuvent dépendre de ces phénotypes selon quelques études récentes.

Objectif : Déterminer les caractéristiques et le pronostic des exacerbations dans chaque phénotype des patients atteints de BPCO en Tunisie.

Méthode: Étude rétrospective incluant 153 patients de sexe masculin hospitalisés pour exacerbation de BPCO de Janvier 2009 à Juin 2012.

Résultats: Les patients ont été divisés en quatre phénotypes selon la classification de Burgel: phénotype (PH) 1: (n = 68), PH2: (n = 33), PH3: (n = 25) et PH4: (n = 27). L'âge moyen des patients de PH 1, 2, 3 et 4 était: 61, 74, 56 et 72 ans. Le nombre d'exacerbations par an était plus élevé dans le PH1. La dyspnée était plus importante dans les PH1 et 4. L'hypercapnie à l'admission était plus élevée dans le PH4. La ventilation non invasive et transfert à l'unité de réanimation étaient plus souvent obligatoires dans les PH 3 et 4. Le décès est survenu chez 2% de patients de PH1 et 5% de PH4. La durée d'hospitalisation était plus importante dans le PH4.

Conclusion : Les patients atteints de BPCO sont hétérogènes et appartiennent à différents phénotypes. Les caractéristiques des exacerbations et leur pronostic diffèrent largement en fonction de ces différents groupes. En Tunisie, les patients ayant une insuffisance respiratoire modérée aux tests fonctionnels, sont les plus faibles répondeurs au traitement avec une fréquence plus élevée de transfert à l'unité de réanimation.

Mots-clés

BPCO, exacerbation, phénotype, pronostic

SUMMARY

Background: Chronic Obstructive Pulmonary Disease is defined by a limitation of airflow. This disease is characterized by exacerbations that threaten the patient's life and worsen his prognosis.

Moreover, COPD patients are different according to many parameters that define different phenotypes. Characteristics of exacerbations may depend on these phenotypes according to few recent studies.

Aim : To determine the characteristics and the prognosis of the exacerbations in each phenotype of COPD patients phenotype in Tunisia.

Methods : Retrospective study including 153 male patients hospitalized for COPD exacerbation from January 2009 to June 2012. Patients were classified into 4 phenotypes according to Burgel's classification.

Results: Patients were divided into four phenotypes: phenotype (PH)1: (n=68), PH2: (n=33), PH3: (n=25) and PH4: (n=27). Mean age for PH1, 2, 3 and 4 was: 61, 74, 56 and 72 years. The number of exacerbations per year was higher in PH1. Dyspnea was more important in PH1 and 4. Hypercapnia on admission was higher in PH4. Non invasive ventilation and transfer to resuscitation unit were more frequently mandatory in PH3 and 4. Death occurred 2% of PH1 and 5% of PH4. Hospitalization duration was more important in PH4.

Conclusion : COPD patients are heterogenous and belong to different phenotypes. The characteristics of the exacerbations and their prognosis widely differ according to these different groups. In Tunisia, it seems that patients who had moderate respiratory functional tests impairment are the lowest responders to treatment with a higher frequency of resuscitation unit transfer.

Key-words

COPD, exacerbation, phenotype, prognosis

Chronic Obstuctive Pulmonary Disease (COPD) is increasing steadily all over the world because of the increase of tobacco smoking. In 2020, it will stand for the third cause of death in the world. Exacerbations are major factors of bad prognosis of COPD. They are major sources of morbidity and mortality (1,2). Moreover, it is nowadays thought that patients with COPD belong to different phenotypes. However, the particularities and prognosis of the exacerbations in each phenotype are not yet evaluated.

The aim of this study is to determine the particularities and the prognosis of COPD exacerbations in different phenotypes of COPD in Tunisia.

METHODS

We achieved a retrospective study including 153 male patients who were hospitalized in our department for COPD exacerbation during the period from January 2009 to June 2012. We noted from the files the following data: epidemiology, clinical findings, complementary exams finding, treatment and follow-up of the patients concerning the episode of exacerbation studied in the current study. Moreover, the patients were classified in 4 phenotypes according to Burgel's classification (3). For this purpose we used the following parameters : age, tobacco smoking, forced expired volume in the first second (FEV1), body mass index (BMI), number of exacerbations in the year before the study, importance of dyspnea (evaluated according to the modified Medical Research Center (mMRC)), quality of life (QOL) and HAD score of anxiety and depression.

Patients with phenotype (PH) 1 were defined as: young patients (55-63 year-old), thin (BMI: 17-23 kg/m^2), with severe COPD (stage III or IV of the Global Obstructive Lung Diseases (GOLD) classification and mMRC: 3-4), with frequent episodes of depression onset, very altered QOL and a lot of exacerbations and comorbidities (blood hypertension, coronaropathy). Patients with PH2 were defined as: old patients (> 63-year-old), obese, with mild respiratory function impairment, mild depression, QOL slightly altered and few exacerbations. PH3 patients are defined as: young patients, with normal weight, moderate respiratory function impairment, without depression and with a moderate alteration of their QOL.PH4 patients were defined as : old patients, obese, with severe COPD (GOLD III-IV and mMRC: 3-4), with frequent episodes of depression, very altered QOL and many episodes of exacerbations.

Statistical analysis

Data were entered and analyzed on SPSS 17.0 statistics software. Qualitative variables were expressed as frequency and percentage and quantitative variables as mean +/- standard deviation.

To compare groups of patients that present different phenotypes, the Chi2 test or the Fisher exact test when expected count less than 5 were used. These variables were mainly demographic (age, gender), clinical (general history) and therapeutic.

Bivariate analysis was also conducted by calculating odds ratios (ORs) and confidence interval (CI) 95% to quantify the strength of association between these variables and the presence of exacerbations for each phenotype

All tests were performed with a significance level of 5%.

RESULTS

General characteristics of the patients

Patients were classified in 4 phenotypes (PH):

PH1: (n=68), PH2: (n=33), PH3: (n=25) and PH4: (n=27). Mean age of PH1, 2, 3 and 4 was respectively: 61, 74, 56 and 72 years. Tobacco smoking was present in all patients with a mean number of pack-year (PA) more important in PH1 and 2 (58 and 56 PA respectively versus 40 PA in PH3 and 51 in PH4).BMI was more important in PH2 and PH4 patients (25 and 26 kg/m^2 respectively versus 19 in PH1 and 22 kg/m^2 in PH3. Comorbidities were dominated by blood hypertension, diabetes and right heart failure.

Characteristics of exacerbations

Mean number of exacerbations per year was more important in PH1 patients (n=3) than in the other phenotypes (PH2 n=1,4 PH3 n=2,2 PH4n=2 p=0,002).

Table 1: number of exacerbations per year in different phenotypes

	n	min	max
PH1	3	1	10
PH2	1,4	1	4
PH3	2,2	1	6
PH4	2	1	5

Min: minimal number of exacerbations per year for the patients of each phenotype

Max: maximal number of exacerbations per year for the patients of each phenotype

Table 1 shows the number of exacerbations in our patients according to their COPD phenotypes. Dyspnea was the main symptom in exacerbations. It was more important in PH1 and 4 patients (mMRC: 3 and 4 respectively versus: PH2 Mmrc: 2, PH3 mMRC: 1 p=0, 03). On admission for exacerbation, hypoxemia was present in all patients with PaO2 which did not statistically differ from phenotype to another one (p=0, 1). PaCO2 was more important in PH4 phenotype (p=0, 08). Bronchial infection was the leading cause of exacerbation in the four phenotypes but it was more frequent in PH1

phenotype (77% versus 63% in PH2, 70% in PH3 and 61% in PH4 p=0.03). Table 2 shows different causes of exacerbations according to phenotypes. All the patients had oxygen. Noninvasive ventilation was mandatory more frequently in PH4 than in the other phenotypes (PH1= 17%, PH2=9%, PH3=11%, PH4=50%; p=0, 05). Most patients had uneventful follow-up.

Table 2: Etiologies of exacerbations in each phenotype

	PH1	PH2	PH3	PH4
Bronchial infection	77%	63	70	61
Left ventricular heart failure	0	5 %	0	11 %
Pneumonia	4 %	22 %	5 %	11 %
Right heart failure	4 %	0	0	16 %
Other	15%	10%	25%	1%

For the others, resuscitation unit transfer was mainly necessary in PH3 and 4 patients (in 23 and 22% respectively versus 13% in PH1 and 13% in PH2; p=0, 02). Death occurred in 2% among PH1 patients and in 5% among PH4 patients (p=0,08). The difference was statistically not significant Mean duration of hospitalization for exacerbation was for the PH4 phenotype. Table 3 illustrates different clinical and evolutive characteristics of exacerbations according to COPD phenotypes.

Table 3: clinical and evolutive characteristics of the exacerbations in each phenotype

	PH1	PH2	PH3	PH4	P
mMRC	3	1	2	4	0,03
VEMS	33	47	62	39	0,05
PaO2 (1)	56	55	54	53	0,1
PaCO2 (1)	50	48	43	53	0,08
Dicrease in the general status	10	19	17	22	0,04
Thoracic distension	84	77	70	66	0,7
Transfer to ressuscitation ward	13 %	13 %	23%(p=0,02)	22 %	0,02
NIV	17 %	9 %	11 %	50 %	0,6
O2	63 %	54 %	64 %	83 %	0,09
Death (h1)	2 %	-	-	5 %	0,08
Pa O2 (2)	63	65	62	69	0,000
Pa CO2 (2)	46	47	45	53	0,001
Duration of hospitalization	15 j	12 j	16 j	22 j	0,07

1: on admission
2: at the end of hospitalization

DISCUSSION

In COPD, exacerbations differ as their clinical presentations and their prognoses according to the phenotype of the disease. Therefore, the knowledge of the characteristics of the exacerbations of each COPD phenotype allows an improvement of the treatment of this disease. COPD have functional definition: a progressive and permanent obstruction of respiratory airways (4). This definition is based only on spirometric criteria which, alone, don't reflect either the diversity of the disease or its reality. This contrasts with the complexity and the heterogenicity of COPD which has multiple components. COPD includes patients who are extremely hetergenous and who can be classified to different phenotypes (4). Phenotypic classification of COPD patients dated back to the fifties, when Dornhorst (5) classified COPD patients into type A or « pink puffers » and type B or « blue bloaters ». Many years later, Burguel (3) identified four phenotypes in patients with COPD. These phenotypes were based on: age, tobacco smoking, FEV1, BMI, number of exacerbation, dyspnea, QOL and HAD score of anxiety and depression.

Exacerbations represent one of the major risks of the disease that can threaten the patient's life. A good knowledge of the characteristics of COPD exacerbations may therefore ameliorate the prognosis of the disease. That is what showed Burgel (3) in his study. In these latest years, many important studies (UPLIFT (6), ECLIPSE (7) and TORCH (8) studies) reported the characteristics of COPD exacerbations according to the severity of the COPD as classified by the GOLD (9). However, studies about the relationship between the phenotypes and the characteristics of the exacerbation are rare.

In our study, we classified our patients in four phenotypes. PH1 was the more frequent one (44%). Exacerbations were more frequent in PH1and PH2. These findings are similar to those of Burgel (3).

In all phenotypes, bronchial infection was the dominant cause of exacerbation. In spite of severe disease, altered QOL, multiplicity of the comorbidities, PH1 patients had favorable clinical and gazometric outcome. In this phenotype resuscitation NIV and transfer to resuscitation unit were less frequent than in the other phenotypes. PH3 patients, who had moderate respiratory functional tests impairment, were the lowest responders to treatment with a higher frequency of resuscitation ward transfer. Table 4 compares clinical and evolutive characteristics of exacerbations in PH3 patients of our series and Burgel's ones (3).

Table 4: characteristics of exacerbation in PH3 patients

	Burgel	Our study
Frequency (%)	28	16
Age (years)	59	56
Number of exacerbations	1	2,2
Comorbidities		
Blood hypertension	20	5 %
Diabetes	3	6 %
Dilated cardiomyopathies	0	5 %
BMI	21	22
mMRC	1	2
VEF1	46 %	62 %
PaO2 (1)/(2) (mm Hg)	-	54/62
Bronchial infection	0	70 %
Follw-up	0	Ressuscitation : 23 %, NIV : 11 %
Death	0	1,3%

CONCLUSION

Through our study, we emphasize on the fact that in COPD, exacerbations differ as their clinical presentations and their prognoses according to the phenotype of the disease. In Tunisia, the patients who had moderate respiratory functional tests impairment are the lowest responders to treatment with a higher frequency of resuscitation unit transfer.

Therefore, the knowledge of the characteristics of the exacerbations of each COPD phenotype allows an improvement of the treatment of this disease.

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