PHENOTYPE-BASED THERAPY OF COPD: EFFECT ON THE RATE OF COPD EXACERBATIONS

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Background
Several sets of guidelines, statements and strategies for managing and therapy of Chronic obstructive pulmonary disease (COPD) exist around the world. “Czech National COPD Guideline” defines 6 clinically relevant phenotypes. Each patient with COPD can have one clinical phenotype or combination of more clinical phenotypes of COPD. Some patients (usually with milder COPD) can be without expressed clinical phenotype. Further, “Czech National COPD Guideline” recommends therapy of COPD based on clinical phenotype. Treatment of COPD according to “Czech National COPD Guideline” is based on two basic principles: Firstly, all symptomatic COPD patients should have “mandatory therapy”, it means inhalation long acting or ultra-long acting bronchodilators or their combination (LABA, LAMA, LAMAXA) regardless to their phenotype, and appropriate non-pharmacologic treatment. Therapeutic choice of LABA or LAMA or LABAXAMA combination depends on symptoms and lung function severity. Secondly, COPD patients with expressed clinical phenotype of COPD should have added phenotype specific therapy. (Figure 1) Exacerbations of COPD are important events in the management of COPD because they negatively impact health status, rates of hospitalisation and readmission, and disease progression. The reduction of risk and severity of exacerbations is an important goal of COPD therapy. The “Czech Multicentre Research Database of COPD” (COPD Database) is a multicenter, observational, prospective study of patients with COPD and post-bronchodilator FEV1<65% (NCT01923051). The enrollment into the “COPD Database” has been finished. Baseline data include i.a. the parameters used for identification of clinical phenotypes, and information about COPD therapy of each subject. Longitudinal and prospective follow-up (in regular 6-month periods) of patients is planned for 5 consecutive years. To date, 24 months follow up has been completed.

Result
A total of 784 patients were enrolled into the Database (572 men, mean FEV1 45%, mean CAT 16). Frequency of COPD phenotypes was assessed. Proportion of patients using phenotype-specific treatment in the moment of enrollment was specified in each phenotype. Cohorts of patients with distinct phenotype and using phenotype-specific therapy were observed for 24 months and compared with control cohorts of patients with the same phenotype, but without phenotype-specific therapy. Exacerbations were analyzed at the baseline and after 24 months. Categorical variables were described by relative frequency and tested by Fisher’s exact test, continuous variables were described by mean and tested by Mann-Whitney U test.

Methods
Baseline data from 784 patients enrolled into „COPD Database” were analysed. Clinical phenotypes of COPD were determined by objective criteria. Frequency of COPD phenotypes was assessed. Proportion of patients using phenotype-specific treatment in the moment of enrollment was specified in each phenotype. Cohorts of patients with distinct phenotype and using phenotype-specific therapy were observed for 24 months and compared with control cohorts of patients with the same phenotype, but without phenotype-specific therapy. Exacerbations were analyzed at the baseline and after 24 months. Categorical variables were described by relative frequency and tested by Fisher’s exact test, continuous variables were described by mean and tested by Mann-Whitney U test.

Results

Figure 1: COPD phenotypes.

One patient can have one phenotype or overlap of more than one phenotype.

Figure 2: Frequency of COPD clinical phenotypes assessed by physician (total of 784 patients). One patient can have one phenotype or overlap of more phenotypes.

Figure 3: Mean exacerbation rate in patients with bronchitic phenotype treated by mucolytics (Erdosteine) in 76% of patients treated by mucolytics (p=0.028)

Figure 4: Mean exacerbation rate in patients with bronchitic phenotype treated by mucolytics (Erdosteine) (p=0.043)

Figure 5: Mean exacerbation rate in frequent exacerbators treated by ICS+LABA (non significant)

Figure 6: Mean exacerbation rate in frequent exacerbators treated by roflumilast (non significant)

Figure 7: Mean exacerbation rate in patients with ACOS treated by ICS+LABA (p=0.044)

Figure 8: Mean exacerbation rate in patients with Bronchiectasis-COPD overlap treated by Erdosteine (mucolytics) (non significant)