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 phenotypes[1]. 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 inhaled long acting or ultra-long acting bronchodilators or their combination (LABA, LAMA, LABA+LAMA), regardless to their phenotype, and appropriate non-pharmacologic treatment. Therapeutic choice of LABA or LAMA or LABA+LAMA 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[2]. 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, and prospective study of patients with COPD and post-bronchodilator FEV1≤60% (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.

Aim

The evaluation of effect of COPD therapy based on clinical phenotypes on exacerbations of COPD during 24 months follow-up, using data from the „Czech Multicentre Research Database of COPD".

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 in each cohort 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

A total of 784 patients were enrolled into the Database (572 men, mean FEV1 45%, mean CAT 16). Frequency of COPD phenotypes is shown in Figure 2. All patients were treated by LAMA and/or LABA. Patients treated by phenotype-specific treatment had higher exacerbation rate at the baseline. After 24 months treatment, higher reduction of exacerbations rate was found in a cohort of patients with bronchitic phenotype treated by mucolytics drugs (-0.61 vs -0.17, p=0.028) and in a cohort treated by roflumilast (-1.07 vs -0.08, p=0.043), in comparison to control cohorts. Frequent exacerbators treated by ICS+LABA had a higher reduction of exacerbations (-1.83 vs -1.24), similarly to frequent exacerbators treated by roflumilast (-2.50 vs -1.38). Higher reduction of exacerbations was found in cohort of patients with ACO(S) treated by ICS+LABA (-0.42 vs +0.17) and in cohort of patients with bronchiectasis/COPD overlap treated by mucolytics drugs (-0.57 vs +0.88). There was no difference in reduction of exacerbations between cohort with emphysematic phenotype treated by theophylline and control cohort.(Figures 3-8).

Conclusion

The analysis of baseline data of the „Czech Multicentre Research Database of COPD" showed that phenotype-specific treatment has been preferred in patients with worse health status and with higher exacerbation rate. Analysis of data after 24 months showed that treatment of COPD based on clinical phenotypes was associated with reduction of number of COPD exacerbations.

References:

1. Koblížek V, et al: COPD: Official diagnosis and treatment guidelines of the Czech Pneumological and Phthisiological Society; a novel phenotypic approach to COPD with patient-oriented care. Biomed Pap Med Fac Univ Palacky. 2013 Jun; 157(2):189-201.
2. Global strategy for diagnosis, management and prevention of chronic obstructive pulmonary disease. GOLD Report, Revised 2018. Available from www.goldcopd.org

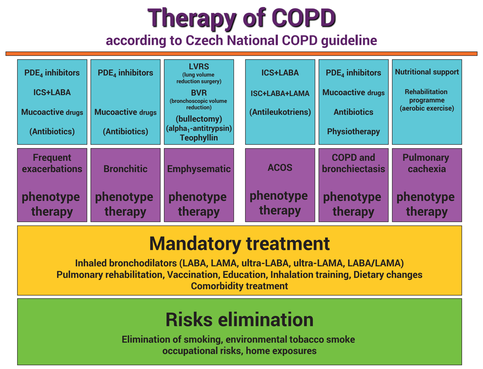

Figure 2: Frequency of COPD clinical phenotypes assessed by physician (total of 784 patients)
One patient can have one phenotype or overlap of more phenotypes

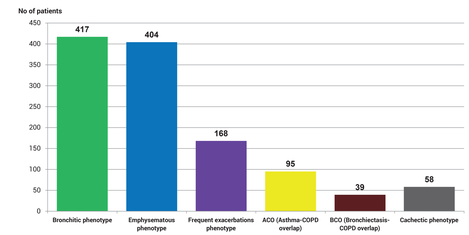

Figure 3: Mean exacerbation rate in patients with bronchitic phenotype treated by mucolytics (Erdosteine in 75% of patients treated by mucolytics) (p=0.028)

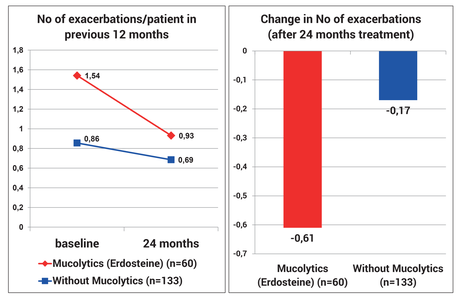

Figure 4: Mean exacerbation rate in patients with bronchitic phenotype treated by roflumilast (p=0.043)

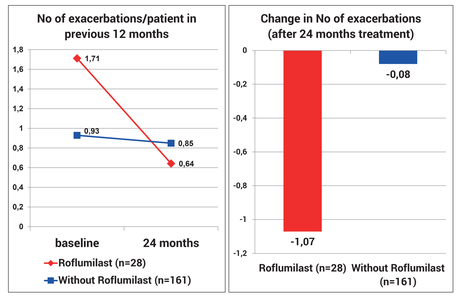

Figure 5: Mean exacerbation rate in frequent exacerbators treated by ICS+LABA (non significant)

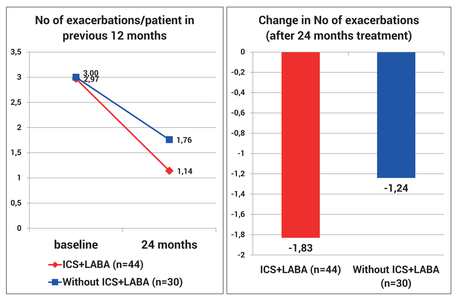

Figure 6: Mean exacerbation rate in frequent exacerbators treated by roflumilast (non significant)

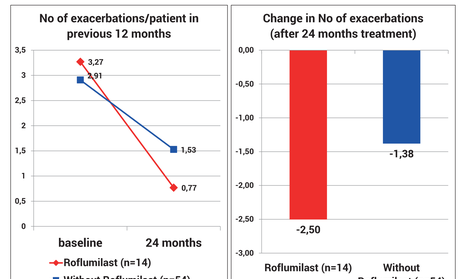

Figure 7: Mean exacerbation rate in patients with ACO(S) treated by ICS+LABA (p=0.044)

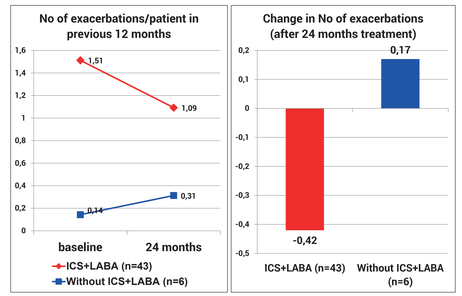

Figure 8: Mean exacerbation rate in patients with Bronchiectasis-COPD overlap treated by Erdosteine (mucolytics) (non significant)