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The effect of pulmonary rehabilitation in salivary microbiota of people with chronic obstructive pulmonary disease: A longitudinal study

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Background: Chronic obstructive pulmonary disease (COPD) is the third leading cause of death worldwide. Pulmonary rehabilitation (PR) is the most cost-effective therapy for this disease with several physical, psychological, and social benefits widely demonstrated. Nevertheless, its impact on the microbiota of people with COPD has not been established. This study aimed to investigate the effect of PR in the salivary microbiota of people with COPD.

Methods: Patients were followed for 6 months. The experimental group undertook a 12-week community-based PR programme and the control group was not submitted to any additional intervention. Saliva samples were collected monthly, and 16S rRNA sequencing of oral microbiota was performed. Bioinformatic and statistical analyses were conducted with QIIME2 v2020.8, R v3.6.0, GraphPad Prism v8, and IBM SPSS Statistics v27. Generalized Liner Mixed Models were used to evaluate microbiota dynamics over time. Relative abundance analyses were conducted with LEfSe and ANCOM. Alpha- and beta-diversities were estimated with Faith and Shannon indexes and Weighted-Unifrac distance, respectively.

Results: Seventy-six patients were included; 38 in each group with no significant differences in their baseline characteristics (control group: 31 male, 70±7.6y, FEV1pp 52.34±19.76 and experimental group: 29 male, 72±9y, FEV1pp 49.15±16). The microbiota of patients undergoing PR changed significantly over time compared to patients of the control group ($p<0.0001$). Moreover, PR seemed to reduce the heterogeneity of the microbiota composition.
At phylum level, most patients submitted to PR presented a significant increase in Proteobacteria ($p=0.030$) and Fusobacteria ($p=0.0007$) and a decrease in Bacteroidetes ($p=0.046$). No significant differences were observed in the control group. An increase in Haemophilus as consequence of PR (LEfSe effect size for significance>2) was also observed.
No significant differences were found on the average microbiota diversity within each patient in response to PR.

Conclusions: Our study suggests that PR modulates the oral microbiota of patients with COPD significantly. In the short term, it seems to become closer to the profile characteristic of the disease mainly due to the increase in Proteobacteria and decrease in Bacteroidetes. Future studies should address the implications and stability of these microbiota modifications.

Poster 12