Área: ANA

Understanding the metabolic changes caused by Preserved Ratio Impaired Spirometry in patients with Chronic Obstructive Pulmonary

Hanna Carvalho de Sá (PG)[1]*, Fabíola Ramos de Jesus (PQ)[2], Massuo Jorge Kato (PQ)[3], Gyselle Chrystina Baccan (PQ)[2], Gisele André Baptista Canuto(PQ).[1]*

***carvalho.hanna@ufba.br**

[1]Departamento de Química Analítica, Instituto de Química, UFBA; [2] Instituto de Ciência da Saúde, UFBA; [3]Instituto de Química, Universidade de São Paulo, USP

Keywords: *(Metabolomics, GC-MS, Chemometrics, COPD).*

Highlights

Untargeted metabolomics demonstrated alterations in serum metabolome of PRISm in comparison to COPD and healthy group.

The major differences are correlated to amino acid metabolism.

Resumo/Abstract

Chronic Obstructive Pulmonar Disease (COPD) it is a disease characterized by airway obstruction caused by different disorders such as asthma and emphysema. It is the fourth leading cause of death in the world according to WHO[1]. A condition that contributes for COPD development is the Preseved Ratio Impaired Spirometry (PRISm) a state of low lung function characterized by the first second of forced expiration (FEV1) < 0.7. PRISm remains underexplored and is often mistaken for COPD, despite its distinct characteristics. Thus, this work aimed to evaluate the metabolic alterations caused by PRISm in comparison to a control group, as well as to differentiate the metabolic profile between PRISm and COPD, aiding in the discovery of potential biomarkers that could improve the efficiency of diagnosis and differentiation between these distinct respiratory disturbs. For this purpose, an untargeted metabolomic study was conducted using serum samples from three groups: PRISm (n=11), COPD (n=18), and Control (n=13). The samples were extracted through protein precipitation using chilled methanol. Before GC-MS analysis, the extract was lyophilized, derivatized through silylation (90 min, room temp.) and oximation (30 min, 40 °C). Metabolite identification was carried out in MS-DIAL software, according to the retention time and correspondence of fragmentation spectra compared to the Fiehn, Kazusa and HMDB databases. Ninety-six metabolites were annotated. Metabolomic data processing is a major challenge, in which several methods can be applied, with no consensus on the best method. In this work, different processing software was evaluated. In addition, different normalization methods were evaluated, since GC-MS data are very susceptible to systematic variations due to instrumental factors, sample preparation steps, and derivatization. The matrix data obtained by the best conditions of processing (Processment Software: MS-DIAL, Normalization: EigenMS, Log Transformation and Pareto Scaling) were applied for multivariate and univariate tests, in which 43 (PRISm x Control) and 34 (PRISm x COPD) significant metabolites were found. Metabolic pathway analysis pointed to significant alterations in the metabolism of amino acids (Glutathione metabolism FDR = 0.01, alanine aspartate and glutamate metabolism FDR = 0.04 and arginine biosynthesis FDR = 0.02). These metabolites are decreased for PRISm group in both comparisons, this kind of alterations was previously reported to respiratory disorders, and may be related to systemic inflammation, immune dysregulation and/or muscle dysfunction[2].

[1] WHO. *Chronic Obstructive Pulmonary Disease (COPD)*. <https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd) > accessed in February 6, 2025.

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Agradecimentos/Acknowledgments

FAPESB, IQ-USP, PPGQuim - UFBA