Asthma-COPD overlap syndrome and precision medicine

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Differentiation of asthma and chronic obstructive pulmonary disease (COPD) in symptomatic patients has been extremely difficult clinically in many instances. This situation led to the formulation of the so-called "Dutch hypothesis" in 1961,[1] cited by Christenson.[2] The theory postulates that obstructive lung disease occur in a continuum, with asthma and COPD being expressions of the same disease taking place on the opposite ends of the same spectrum. Although there is no consensus on the definition of asthma-COPD syndrome (ACOS), current understanding would suggest that ACOS is a common clinical and biological manifestation of a separate disease entity with higher morbidity and worse outcomes than COPD or asthma in general with regard to quality of life and increased use of medication. There is hope that clinical variability and biomarkers, such as eosinophilia and type 2 inflammatory markers which are used to identify an ACOS molecular phenotype, would tenably help target therapies for this group of patients.

The following information is focused on current evidence on how precision medicine plays a role in the diagnosis of and therapeutics for ACOS. Despite limited understandings of the syndrome, the author proposes precision medicine as a medical application model for identifying individuals by their disease susceptibility, pathobiology, and response to specific treatments. The followings are the possible current practices for this purpose.

Clinical phenotypes

The ACOS umbrella: There are numerous combinations of ways in which ACOS is currently being diagnosed, namely using clinical, spirometric, and imaging data, as well as biomarkes (e.g., blood or sputum eosinophils and gene expression) to define ACOS subgroups.

For making a provisional diagnosis, age of onset, respiratory pattern (e.g. history of wheezing), personal or family history of exposures and asthma or atopy, lung function, radiographic patterns, and time course, all furnish important data. In general, most ACOS cases are associated with more frequent exacerbation, hospitalization, and emergency room visits than COPD patients. Encountering COPD patients with bronchodilator reversibility on spirometry and lack of emphysema on CT scan would often suggest ACOS.

On using biomarkers to define ACOS: While the immune profile of COPD is dominated by neutrophils, macrophages, and type 1 (Th1) inflammation, in asthma, it is dominated by eosinophils and type 2 (Th2) inflammation. Notwithstanding these aspects, there are conflicting results suggesting that blood eosinophils may be capturing some but not the whole range of ACOS patients.

Towards Better Therapeutics for ACOS

Recently, global gene expression profiling of airway cells obtained from bronchoscopy in COPD patients has been used to identify a subgroup exhibiting increased type 2-related gene expression similar to asthma, which could provide substantiation of ACOS.

Understanding that biomarkers in COPD and asthma disclose multiple biologics targeting circulating IL-5, or the IL-5 receptor, provides knowledge tenable for implementing personalized approaches to making therapeutic decisions on airway diseases. In this regard, two drugs, mepolizumab and reslizumab which target circulating IL-5 or the IL-5 receptor, now available for use in severe asthma, along with benralizumab, which targets the IL-5 receptor or eosinophils and basophils, are being used in an ongoing trial in COPD.

Conclusions

Asthma-COPD overlap syndrome is a clinical entity that causes higher morbidity than simple asthma and COPD identities. In this article, the reviewer addressed current knowledge of ACOS in the context of making precise diagnosis and providing targets for personalized therapeutic responses.

Documents used for the preparation of this article:

1. Brightling CE, McKenna S, Hargadon B, Birring S, Green R, Silva R, et al. Sputum eosinophilia and the short-term response to inhaled mometasone in chronic obstructive pulmonary disease. Thorax 2005; 60(3): 193-8.
2. Christenson SA, Steiling K, van den Berge M, Hijazi K, Hiemstra PS, Postma DS, et al. Asthma-COPD overlap. Clinical relevance of genomic signature of type 2 inflammation in chronic obstructive pulmonary disease. Am J Resp Crit Care Med 2015; 191:758-66.
3. Christenson SA. The reemergence of the asthma-COPD Overlap Syndrome: Characterizing a syndrome in the precision medicine era. Curr Allergy Asthma Rep 2016;16:81-8.
4. Consentino J, Zhao H, Hardin M, Hersh CP, Crapo J, Kim V, Criner GJ. Analysis of asthma-COPD overlap syndrome when defined on the basis of bronchodilator response and degree of emphysema. Ann Am Thorac Soc 2016; 13(9): 1483-9.

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The Adademy of Science, The Royal Society of Thailand, Bangkok 10300

[1] Orie NGM, Sluiter HJ, editors. Bronchitis. Royal van Gorcum; 1962.
[2] Christenson SA. The reemergence of the asthma-COPD Overlap Syndrome: Characterizing a syndrome in the precision medicine era. Curr Allergy Asthma Rep 2016;16:81-8.

5. Ghebre MA, Bafadhel M, Desai D, Cohen SE, Newbold P, Rapley L, et al. Biological clustering supports both "Dutch" and "British" hypotheses of asthma and chronic obstructive pulmonary disease. J Allergy Clin Immunol 2015; 135: 63-72.

6. Peters MC, Mekonnen ZK, Yuan S, Bhakta NR, Woodruff PG, Fahy JV. Measures of gene expression in sputum cells can identify Th2-high and Th-2-low subtypes of asthma. J Allergy Clin Immunol 2014; 133(2): 388-94.

7. Posma DS, Rabe KF. The asthma-COPD overlap syndrome. N Engl J Med 2015; 373(13): 1241-9.

8. Wurst KE, Rheault TR, Edwards L, Tal-Singer R, Agusti A, Vestbo J. A comparison of COPD patients with and without ACOS in the ECLIPSE study. Eur Respir J 2016; 47(5): 1559-62.