Editorial Comment

Respiration

Respiration 2015;90:353–354
DOI: 10.1159/000441307

Published online: October 20, 2015

VIP: A New Promising Marker for AECOPD – A Fashionable Marker Soon Forgotten?

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It is almost impossible to discuss chronic obstructive pulmonary disease (COPD) without making reference to phenotypes or endotypes. Among COPD phenotypes, there is one which is widely recognized for its clinical and economic implications. This is characterized by a high susceptibility to experience acute exacerbations of chronic obstructive pulmonary disease (AECOPD). AECOPD are natural events occurring in the course of COPD, but still remain a major cause of morbidity and mortality associated with this disease [1]. Clinical criteria that define an acute exacerbation are subjective and open for debate. Hence, it is necessary to identify reliable biomarkers that could help in the early identification of AECOPD, also allowing their clinical progression to be measured. This is especially the case when considering the unfavorable outcomes and the socioeconomic costs that acute exacerbations of the disease predict. Several circulating markers are commonly used in clinical practice for the study of patients with AECOPD, such as white blood count (WBC), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), although these are nonspecific and not particularly sensitive [2, 3]. Furthermore, these clinically available markers are not useful in the early identification of AECOPD, and are therefore not effective in reducing the progression of the disease. Some reports are also available, referring to other new possible markers of AECOPD, such as neutrophil-lymphocyte ratio (NLR) and copeptin [1, 4]. Procalcitonin (PCT) has also been proposed as a fashionable marker for AECOPD, although most experts agree that it is not reliable in predicting bacterial infections in AECOPD [5].

In this issue of *Respiration*, Mandal et al. [6] report the results of their very interesting study about vasoactive intestinal peptide (VIP), properly investigated by these authors and proposed as a promising marker for AECOPD. Indeed, an increased VIP immunoreactivity has been previously found in the airway epithelium and bronchial glands of COPD patients, in comparison to smokers with normal lung function [7]. But are we witnessing the birth of a new clinical tool for the early identification of acute exacerbations of COPD, or will this be the usual fashionable marker that will result in a few publications, but will then be soon forgotten?

The authors of the study detected higher circulating levels of VIP in subjects with AECOPD, when compared to stable COPD patients, and identified a cutoff of 88 pg/ml that could be clinically useful as an indicator of exacerbation. We acknowledge that the results of this study are very stimulating, but we have some questions about the potentiality of VIP as a reliable marker of AECOPD. First, notwithstanding the authors' declaration of a robust performance of VIP in AECOPD diagnosis, how can a single marker be able to identify such different diseases as arthritis, diabetes, cancer, bowel diseases, heart failure,

0025–7931/15/0905–0353$39.50/0

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atopic dermatitis and rhinitis [8–12]? The high specificity of VIP in AECOPD diagnosis reported by the authors refers to a small population of 120 COPD patients with acute disease exacerbations, and we believe the study requires at least a solid confirmation on larger patient populations, possibly to be investigated by multidisciplinary studies. A second question is whether VIP would be validated in the near future, and its dosage standardized in clinical practice.

Finally, we recognize that no single biomarker in COPD, as in all other human diseases, is enough to provide a wide acceptance of clinical information. Therefore, we suggest that there is an urgent need to identify a panel of potential biomarkers, such as VIP, which in combination may increase the singular power of each, thus being potentially useful for AECOPD in clinical practice, in order to allow early recognition of this condition, and also to monitor the effects of treatment.

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