Respiratory infections, exacerbations and the microbiome in COPD

Valorisation

VALORISATION

This thesis includes a series of studies to broaden our knowledge of respiratory infections, exacerbations and the respiratory microbiome in patients with Chronic Obstructive Pulmonary Disease (COPD). Practical implications are described in various chapters of this thesis, in order to make this knowledge suitable and available for clinical practice. In the current chapter, these studies and their outcomes are further positioned in a broader economical and societal framework, in order to transfer the scientific knowledge described into clinical practice, as well as to put the findings into future perspective.

RELEVANCE

COPD is a chronic disease, with a high morbidity and mortality, which affects many people. Research in the field of COPD is necessary, in order to gain insight into disease development and management. It is known that the prevalence of community acquired pneumonia (CAP) in patients with COPD is remarkably higher compared to controls, and that subgroups of patients with COPD are susceptible to COPD exacerbations. Both disease conditions influence socially and economically, which warrants the fact that a lot of obstacles need to be taken.

The first part of this thesis focussed mainly on the impact of COPD with concomitant CAP on various health related outcomes. Adverse outcomes are more frequent and more severe in patients with COPD, for example a longer length of hospital stay and higher mortality rates. Targeted diagnostics of patients during hospitalisation play an important role, including microbiological sampling. Especially, the last should be a key component of the management of hospitalised CAP-COPD patients, as therapy can be better targeted to the spectrum of pathogens, which has the potential to reduce unnecessary coverage, increase antimicrobial efficiency and also reduce the economic burden.

Next to CAP, patients with COPD are vulnerable to COPD exacerbations. The concept of COPD exacerbations is still incompletely understood, since there is no clear definition yet. In the second part of this thesis, the impact of exacerbations on disease related outcomes following pulmonary rehabilitation was assessed. The results made clear that pulmonary rehabilitation has a positive effect on health status and exercise capacity, even when exacerbating mildly-to-moderately during the course of treatment. These results emphasise that completing pulmonary rehabilitation is essential, even for patients with a severe exacerbation.

Following the research questions and outcomes of the first two parts of this thesis, it became clear, that many steps should be taken to broaden our knowledge, in order to really understand what are the particular pathophysiologic features of the respiratory system of patients with COPD. Therefore, the last part of this thesis is especially relevant for the future. Respiratory microbiome analysis is a central component in this and is expected to contribute to finding answers to health-related questions. Until now, the focus is on gaining insight into the microbial composition of the lungs in both health and disease. But, for the future, it has the potential to provide guidance in prevention of the disease and acute disease conditions, as well as treatment of the latter.

TARGET GROUPS

Health care professionals

The main target group of this thesis are respiratory physicians, who are involved in the care of patients with COPD. Besides, for other health care providers, such as physician assistants, nurse practitioners and respiratory nurses, this thesis provides important clinical implications. Insight into respiratory infections is important to guide the management of patients with COPD. Therefore, microbiological sampling is an essential part of disease management. Moreover, insight into the microbiology involved in acute conditions of the disease can trigger pharmaceutical companies to develop new treatment options.

On the other hand, we also suggest a shift from treatment towards prevention. Paramedics such as occupational therapists, physiotherapists and dieticians are expected to motivate and stimulate patients to maintain or gain a healthy lifestyle. Even when chronically ill, delaying disease progression can often be accomplished by healthy lifestyle. Furthermore, health care professionals need to create a supportive environment and are encouraged to improve a patient's performance.

Patients with COPD

Unfortunately, patients with COPD do not directly benefit from the research performed for this thesis. However, patients are always the main target, as research questions arise from problems patients encounter. By performing this research, our knowledge is extended, and might result in further research and recommendations for patients with COPD. One direct key message for patients with COPD is the fact that patients should not be withheld from completing pulmonary rehabilitation when exacerbating. For both, patients and health care professionals, this should result in motivation and faith that even after an acute event, encouraging results can be accomplished. Second, it is

worth mentioning, that we observed promising results for microbiome analysis with non-invasive sampling. Non-invasive sampling makes it easier to perform microbiome analysis in clinical practice, but also makes it easier to perform research in this field. We hope our research provides the basis for future research projects more directly targeted to clinical implementation and application.

ACTIVITIES AND PRODUCTS

The findings of this thesis have led to several activities in the field of expertise. The results of chapter 2 to 6 have been presented during the European Respiratory Society (ERS) Congress in 2013 (Barcelona, Spain), 2014 (Munich, Germany), 2015 (Amsterdam, the Netherlands) and 2016 (London, United Kingdom). Furthermore, the findings have been translated into original manuscripts, published in different scientific international journals. Besides, results have been presented at different meetings and courses organized by CIRO, the Maastricht University Medical Centre and other institutions. Following these activities, the current findings have been distributed and may hopefully inspire future research.

FUTURE PERSPECTIVE

For the near future, it is important to distinguish between CAP and exacerbations in patients with COPD. Both acute events present with comparable symptoms and substantially impact on the disease, although treatment options differ. The disease conditions are often mixed in clinical practice, while it is expected that clear definitions would positively contribute to both the societal and economical field, as disease management can be optimised.

Second, respiratory microbiome analysis has a lot of potential, but is still in its infancy, and comprises many aspects which remain to be studied. Especially the technique used for microbiome analysis in this thesis needs to be further explored. Until now, respiratory microbiome analysis changed our perspective concerning the microbial composition of the lungs. In future, microbiome analysis has the potential to shed light on the development of disease and its relationship with health and disease alterations by advanced microbiology. This hopefully leads to new products such as medication, and techniques to prevent disease and/or disease alterations.