Scottish Government Health Directorates Chief Scientist Office

CHIEF SCIENTIST OFFICE

FOCUS ON RESEARCH

Mannose binding lectin deficiency, bacterial colonisation and disease severity in Chronic obstructive pulmonary disease: towards personalised medicine in COPD

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Aim:
Personalised medicine means giving the right treatment to the right patient. The objective of this study was to find new ways of identifying patients with COPD at higher or lower risk of chest infections to better target COPD treatmetnts. Specific aims were:

1. To determine if a common genetic deficiency in mannose binding lectin (MBL), part of the immune system, is associated with risk of chest infections in COPD
2. To test if bacteria in the sputum or inflammation in the phlegm can be measured to identify patients at higher risk of chest infections

Project Outline/Methodology
DNA samples donated by 1796 patients with COPD in Tayside were genotyped to identify patients with deficiency in the MBL gene. We used electronic medical records to identify patients with admissions to hospital for severe chest infections, or prescriptions from the GP corresponding to mild chest infections. We also examined deaths over up to 10 years follow-up.

We then looked in closer detail at 171 of these patients who were invited to give samples of phlegm and blood and to undergo lung function testing. We used this data and these samples to examine whether patients at risk of chest infections or disease progression could be identified

Key Results
In the large cohort of 1796 patients, genetic deficiency of MBL reduced the risk of being admitted to hospital for a COPD exacerbation by 1/3 and also reduced the risk of developing any exacerbation. MBL deficiency was not associated with risk of death or progression of the disease. This suggests that common genes modify the risk of infections in patients with COPD.

When looking more closely at patients in terms of their lung inflammation and bacteria we could not identify a clear reason why MBL deficiency was so beneficial. However, using new technology to sequence all of the bacteria in the lungs and to measure inflammation, we were able to identify patients at higher risk of infections and disease progression. These patients had more cells called neutrophils, and have less "good bacteria" in their lungs.

Conclusions
We have identified genetic, inflammatory and bacterial modifiers of disease outcome in COPD. These findings provide the basis for future studies to choose the right treatment for the right patient.

What does this study add to the field?
If validated in future studies, the markers identified here could be used to predict and prevent disease progression.

Implications for Practice or Policy
Current COPD guidelines only use the measurement of lung function to decide the best treatment for the patient. Our results suggest that by using relatively simple tests, we can get a more accurate estimate of future risk.

Where to next? The researchers have received funding to perform the next stage of development of these tests and to use them in clinical trials to choose the right treatment for patients.

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