Cystic Fibrosis Research News

Title:

YKL-40 as a clinical biomarker in adult patients with CF: Implications of a CHI3L1 single nucleotide polymorphism in disease severity.

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What was your research question?

The purpose of our research was to explore if the circulating inflammatory protein called YKL-40 as well as the specific mutation of its corresponding gene (chitinase 3-like 1) are important biomarkers of disease severity in adults with CF.

Why is this important?

In CF, chronic infection leads to excessive inflammatory response, tissue destruction, and eventually inability to breathe. We previously identified in lung cells from CF patients the presence of an inflammatory gene called chitinase 3 like 1 (CHI3L1), which codes for the YKL-40 protein. Since YKL-40 is considered as a prognostic factor in inflammatory diseases and diabetes and since it is expressed in inflammatory cells like macrophages and neutrophils, we believe it is important to understand if circulating levels of YKL-40 could be a prognostic factor of disease severity in CF.

What did you do?

We established a cohort of 188 adult patients with CF in 2015. Demographic and clinical characteristics as well as blood samples were collected from every patient for a period of 2 years. Patients were also genotyped for specific alternations (single-nucleotide polymorphisms) in the chitinase 3-like 1 gene. Levels of the YKL-40 were measured in blood

samples. We searched for clinical and/or demographic factors that could be associated to high levels of YKL-40 in the blood.

What did you find?

We found that people with CF could be categorized into having either low or high YKL-40 protein concentration in their blood. Compared to the patients in the low YKL-40 group, the patients in the high YKL-40 group had lower lung function, mostly had a double (homozygote) delF508 mutation and were more likely to have abnormal blood sugar. In addition, patients who had high blood levels of YKL-40 were also more colonized with *Pseudomonas aeruginosa* and required more frequent intravenous antibiotic. Finally, we found that a specific genotype of the CHI3L1 gene led to higher blood levels of YKL-40.

What does this mean and reasons for caution?

These findings indicate that in this cohort of adult people with CF, patients with a genetic alteration to express higher blood concentrations of YKL-40, have a more severe disease as well as abnormal blood glucose. Therefore, we suggest that the YKL-40 protein could become a biomarker of disease severity in CF. However, our data did not show that circulating blood levels of YKL-40 are a predictor of lung function decline over time or a predictor of pulmonary exacerbations. Furthermore, these data do not provide any clues about the potential role of YKL-40 in the disease mechanism in CF.

What's next?

Future studies are needed to establish a causal link between higher blood levels of YKL-40 and the CF inflammatory reaction. It would also be interesting to perform a study over longer time in children with different CHI3L1 genotypes to see if CHI3L1 could be a modifier gene of CF disease evolution in children.

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