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Editorial

Editorial for effect of dornase alfa on inflammation and lung function: Potential role in the early treatment of cystic fibrosis

Treat or lose?

The review by Konstan and Ratjen in this issue of the Journal of CF underlines the importance of early treatment of CF lung disease using dornase alfa [1]. Dornase alfa has been important as mucolytic therapy for CF lung disease since the mid-nineties. Dornase alfa was the first drug developed specifically for the treatment of CF patients [2]. The dornase alfa development program included the two-year randomized controlled Pulmozyme Early Intervention Trial (PEIT) [3]. The PEIT included patients with well-preserved lung function (Forced Vital Capacity > 85%). In the dornase alfa group lung function was maintained over the two-year study period. As reviewed by Konstan and Ratjen a large body of evidence on the efficacy of dornase alfa and its potential mechanisms has been added to the pivotal studies. Based on this evidence dornase alfa has been recommended in guidelines as a standard of treatment for children 6 years and above with mild to severe lung disease. Despite these recommendations a large number of young patients with high lung function but without dornase alfa treatment could be found in the database of the Epidemiologic Study of CF (ESCF). In an analysis of the ESCF database by Konstan elevated risk of immediate rapid decline in these untreated patients was shown underscoring the need for early and aggressive treatment to preserve lung function. Why is it that, despite all the evidence on dornase alfa in early disease, its implementation is incomplete? Some patients are probably considered too good to benefit from the treatment by their clinicians. This reminds me of a discussion I had 15 years ago with one of the inventors of dornase alfa. We discussed the results of the PEIT study and he challenged me on my conclusion that I was reluctant to start dornase alfa treatment in CF patients with normal lung function. 'So you want patients with well-preserved lung function to lose function' he argued. He was right, the PEIT data showed us that we should aim for preservation of 'healthy' lungs and not only focus on the obviously sick lungs. It is now well recognized that normal spirometry does not exclude chronic lower airway inflammation, infection, and structural damage.

Unfortunately, large randomized controlled trials like the PEIT have major limitations. It does not help us to determine whether a patient sitting in front of us in our outpatient clinic will be a responder or non-responder. It only teaches us that patients who met the PEIT inclusion criteria and who were randomized to dornase alfa had on average no loss of FEV_1 over a 2-year study period in contrast to the placebo treated patients. Hence, evidence-based medicine defines for us what works for a *group* of patients that meet certain inclusion characteristics. Until we have developed reliable prediction models that allow us to predict outcome from an intervention for an individual based on key characteristics we are stuck to 'one size fits all'. Hence, as advocated by Konstan and Ratjen in their review there is 'a greater role for dornase alfa therapy in the early treatment of CF, where it may help preserve lung function and potentially extend survival'.

References

[1] Konstan MW, Ratjen F. Effect of dornase alfa on inflammation and lung function: potential role in the early treatment of cystic fibrosis. J Cyst Fibros 2012 e-pub 2011/11/19.

[2] Bakker EM, Tiddens HA. Phamacology, clinical efficacy and safety of recombinant human DNase in cystic fibrosis. Expert Rev Resp Med 2007;1(3):317–29.

[3] Quan JM, Tiddens HA, et al. A two-year randomized, placebo controlled trial of dornase alfa in young cystic fibrosis patients with mild lung function abnormalities. J Pediatr 2001;139:813–20.

Harm A.W.M. Tiddens
Department of Pediatric Pulmonology and Allergology, Erasmus Medical Center-Sophia Children's Hospital, The Netherlands
Department of Radiology, Erasmus Medical Center-Sophia Children's Hospital, The Netherlands
Dr. Molewaterplein 60, 3015 GJ Rotterdam, The Netherlands.
Tel.: +31 10 7036263; fax: +31 10 7036800.
E-mail address: h.tiddens@erasmusmc.nl.

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