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INVITED COMMENTARY

Is there a place for dornase alfa therapy in lung transplantation?

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Dornase alfa is a DNase, produced by recombinant gene technology, that digests extracellular deoxyribonucleic acid (DNA). Nebulized dornase alfa exerts a mucolytic effect. It is indicated for use in cystic fibrosis (CF) which is characterised by the presence of viscous purulent airways secretions rich in highly polymerized DNA. By cleaving DNA, it makes mucus less viscous and easier to expectorate. Compared to placebo, in CF patients dornase alfa improves lung function and reduces number of exacerbations [1]. On the other hand, in comparison to active treatment (hypertonic saline or mannitol), there is no clear evidence of benefit of dornase alfa over other treatments. Nevertheless, current CF guidelines recommend the use dornase alfa in combination with (or without) hypertonic saline in patients with clinical evidence of pulmonary disease [2]. Available data do not support the use of dornase alfa in non-CF diseases [3], although it is often used empirically in some centres to improve atelectasis and bronchial secretions [4].

In lung transplant recipients, increased mucus secretion and decreased mucus clearance may arise because of impaired mucociliary clearance, diminished cough reflex and chronic bacterial airway colonization. This could be predisposing factor for infections and chronic allograft dysfunction [5]. Strategies for coping with this problem vary between centres owing to lack of appropriate studies. Dornase alfa is used in some, hoping to achieve similar benefit as seen in CF patients. In this issue, Tarrant *et al.* [6] published a randomized controlled trial of the use of dornase alfa during lower respiratory tract infection (LRTI) in lung transplant recipients. Included patients – mostly males, who had been transplanted for chronic obstructive pulmonary

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disease (COPD) or CF; and were free from chronic lung allograft dysfunction (CLAD) were admitted to the hospital owing to signs of – mostly bacterial – lower respiratory tract infections and had productive sputum. Dornase alfa or isotonic saline was prescribed for 1 month once daily in addition to other standard of care therapies, including systemic and nebulized antibiotics. The patients were followed up for additional 2 months after the end of intervention. No difference in lung clearance index, lung function, quality of life, readmissions, length of stay, exacerbations or adverse effects was found. The demonstrated lack of efficacy is consistent with other studies performed in non-CF patients [3]. In CF, however, a mutation in CF transmembrane conductance regulator (CFTR) gene causes dysregulation of epithelial fluid transport, resulting in production of viscous mucus, obstructing the airways [7]. Consequently, there is inability of successful airway clearance, a secondary event. On the other hand, primarily impaired mucocilliary function and diminished cough reflex result in a decreased mucus clearance in lung transplantation. This may explain the efficacy of dornase alfa (which alters the sputum structure) in CF, but not in other patients. Be that as it may, the published study did not provide clinical evidence of dornase alfa efficacy LRTI in lung transplant recipients. Given the significant costs of dornase alfa, the routine use of this therapy can therefore not be justified. The authors explored its use mainly in the context of acute events and the treatment time could have been too short. Moreover, the ability to detect its beneficial effects might have been hampered by small sample size and other concurrent interventions, possibly also including the use of azithromycin – a strong inhibitor of epithelial mucin secretion – in this specific population [8]. Finally, patients <2 months after transplantation were not included, yet in those patients beneficial effects could perhaps be more pronounced. Nevertheless, this study should be seen as a first stepping stone towards evidence-based use of specific therapies in lung transplantation, for which the authors should be congratulated. Hopefully, further studies will follow and shed a light on open questions.

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Conflicts of interest

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