Elexacaftor/ivacaftor/tezacaftor effect on microbial density and the microbiome composition.

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Abstract

Introduction Previous generations of CFTR modulation have been shown to temporarily decrease the frequency of culture positivity of *P. aeruginosa* and other respiratory pathogens. Recently, a three-drug combination Trikafta (elexacaftor/ivacaftor/tezacaftor) was approved for individuals with at least one F508del mutation. There is limited data on the effect of CFTR modulators on bacterial density and CF microbiome. Methods Our study included 2 separate forms of data collection: Firstly, a retrospective chart evaluation of routine respiratory cultures 1.5 years before and after initiation of Trikafta. Respiratory culture density was recorded based upon the growth fraction of standard respiratory plate: none (0/4), scant (1/4), light (2/4), moderate (3/4), and large (4/4). The second data measurement included obtaining next-generation sequencing (NGS) for bacterial and fungal abundance of post-Trikafta initiation patients only. Results There was a significant density decrease in *P. aeruginosa* (1.5 vs 1.19, p= 0.01), *S. aureus* (2.47 vs 1.9, p= 0.002), *A. denitrificans* (1.39 vs,1.14, p=0.02), *E. coli* (1.09 vs 1.00, p=0.045) before and after initiation of Trikafta. On the NGS the 5 most abundant bacteria after Trikafta initiation were *: S. salivarius*, *S. parasanguinis*, *R. mucilaginosa*, *V. atypica*, and *P. histocola*. Conclusion Our study results demonstrate that there is a significant decrease in the density of known CF pathogenic bacteria. NGS post-Trikafta has shown abundance of anaerobic bacteria (*S. salivarius*, *S. parasanguinis*, *R. mucilaginosa*, *V. atypica*, and *P. histocola*) that have been linked to improved clinical lung stability, lower airway inflammation and increased polymicrobial diversity.

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