Journal of Cystic Fibrosis
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CYSTIC FIBROSIS FOUNDATION
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Cystic Fibrosis Research News

Citation:

Baker E, et al., Tobacco Smoke Exposure Limits the Therapeutic Benefit of Tezacaftor-Ivacaftor in Pediatric Patients with Cystic Fibrosis. J Cyst Fibrosis 2020

What was your research question? (50 words maximum)

Research in animals and in people who do not have CF shows that exposure to tobacco smoke leads to the CF gene not working correctly. We wanted to see if exposure to tobacco smoke reduces the treatment benefit of CFTR modulators, we specifically focused on the tezacaftor/ivacaftor (Symdeko).

Why is this important? (100 words maximum)

One-third of children and adolescents with CF in the United States are exposed to second hand smoke, and this proportion is higher in other countries. As CFTR modulators become a first-line treatment for CF, children and adolescents who are exposed to smoke may see less benefit from these novel treatments. Tremendous resources have been deployed to develop CFTR modulators and make them available to all people with CF. It is important to know if their effect is lessened by environmental tobacco smoke.

What did you do? (100 words maximum)

We analysed data from the U.S. CF Foundation Patient Registry (2016-2018). We compared how lung function changed after treatment in children and adolescents with CF who are exposed to tobacco smoke versus to those who are not. Exposure to tobacco smoke was determined by caregiver self-report. We accounted for the prior use of lumacaftor/ivacaftor (Orkambi) and for interruptions in tezacaftor/ivacaftor (Symdeko) use.

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What did you find? (100 words maximum)

The sample included 6,653 individuals. Those taking Symdeko who were smoke exposed had a lower baseline lung function and experienced a quicker decline in lung function compared to those who were not exposed to smoke. Over two years, the difference in lung function between smoke-exposed and unexposed users of Symdeko increased by 1.2%, from 7.6% at baseline to 8.8%. Statistical models taking sociodemographic and clinical characteristics into account and found that treatment with Symdeko was linked to an improvement in lung function of approximately 1.5% among children and adolescents who were not exposed to smoke but provided no benefit to smoke-exposed children.

What does this mean and reasons for caution? (100 words maximum)

We found that exposure to tobacco smoke cancels the benefit of Symdeko. A major limitation is the self-reported nature of the smoke exposure information. Biochemical tests that measure actual exposure would be preferred to confirm our conclusions. We only assessed the effect of smoke exposure rather than active smoking. We also acknowledge the large variation in duration of treatment with Symdeko (from 0 to 672 days) and number of lung function tests (from 1 to 44) before and after drug initiation.

What's next? (50 words maximum)

This finding demands programs and services to eliminate tobacco smoke exposure in children and adolescents with CF, particularly those who take CFTR modulators. Future studies will determine the effect of smoke exposure on the therapeutic benefit from ivacaftor (Kalydeko) and elexacaftor/tezacaftor/ivacaftor (Trikafta).