Mental Health and Cystic Fibrosis

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Introduction: This review highlights cystic fibrosis (CF) mental health research and case reports, as well as important mental health initiatives. Research that may be of interest to multidisciplinary CF team members is the focal point.

Depression and Anxiety: The prevalence of depression and anxiety, as well as the negative impact of these symptoms in CF, led to the formation of an International Committee on Mental Health in CF that established clinical practice guidelines for the screening and treatment of depression and anxiety in individuals with CF and their caregivers (1).

The Mental Health Advisory Committee (MHAC): In 2016, the CF Foundation (CFF) formed a national advisory committee to oversee implementation of the mental health guidelines and continue to identify best practices. The MHAC is dedicated to promoting the mental well-being of individuals with CF and their families through a partnership with CF care centers to support screening, preventative interventions, and innovative services. Three working groups were formed to meet these goals. The education working group is responsible for an inventory of resources which includes: identifying gaps and creating new CF-specific educational materials and addressing training needs of CF teams and community mental health providers to promote emotional well-being, identify those at risk, and treat diagnosed disorders in individuals with CF. The consultation working group is responsible for supporting, partnering and consulting with care centers. This group developed a mental health screening/tracking log (available on CF Smart Reports) and a Mental Health Quality Improvement Change Package with tools, resources, and examples for CF teams. The research working group is investigating barriers to, as well as facilitators of, dissemination and implementation of the mental health guidelines. (For access to tools or a consultation for implementation support contact mental-health@CFF.org).

Mental Health Coordinator (MHC) Awards: To further aid in the implementation of the depression and anxiety recommendations, and promote development of a collaborative care model, the CFF established a competitive grant process for MHC Awards. The goal is for MHCs to implement screening based on CFF guidelines, provide and/or coordinate follow-up, and track outcomes. MHC awards were granted to 84 programs in 2015, 36 programs in 2016 and applications for 2018 awards are currently under review. The MHAC research working group has evaluated implementation of the mental health guidelines at 84 CF centers and found a universal uptake in the screening guidelines, an increased awareness of mental health concerns, reduced stigma for patients and families, greater identification of clinically significant symptoms, and appreciation by patients and families (2). The CFF is sponsoring a MHC Mentoring Program to provide support, guidance and increased engagement of MHACs in care centers across the country.

New Research: Since the mental health guidelines were published, new research on depression and anxiety in CF is being conducted. An important follow-up study of over 1000 participants from the International Depression Epidemiologic Study (3) found that patients who screened positive for depression had a 60% higher 5-year mortality than those with a negative screen (4). In addition, a study of scores predicting risk of death or lung transplant (LT) found that patients with CF who died or received a LT were more likely to have been diagnosed with depression (5). These studies together underscore the importance of identifying and treating depression across the CF population.

Further, as new therapies become available, providers need to consider their impact on mental health and the potential for adverse drug reactions, including drug-drug
interactions with psychotropic medications. CF transmembrane conductance regulator (CFTR) modulators, specific to a patient's mutations, are increasingly available. A study of ivacaftor’s receptor pharmacology and effects in a chronic mouse model of depression found an anti-depressant like profile. Ivacaftor-treated mice had less immobility in a forced swim test (a similar finding to mice treated with the antidepressant fluoxetine) and more swimming and climbing activity than the fluoxetine controlled mice, highlighting the CNS activity of ivacaftor (6). However, multiple clinical case reports have found emergence or worsening of depression and/or anxiety with the initiation of CFTR modulators, suggesting the need for close mental health monitoring (7,8). In addition, the combination CFTR modulators lumacaftor and ivacaftor may negatively impact drug levels of certain antidepressants, requiring higher doses of these medications to achieve therapeutic benefit. (https://pi.vrt.com/files/uspi_lumacaftor.ivacaftor.pdf).

Lastly, there are two important investigations in process that will provide important answers about the treatment of depression and anxiety in CF. Drs. Friedman and Georgiopoulous are conducting a randomized controlled trial of a CF-specific cognitive behavioral therapy intervention to promote well-being for adults that is integrated into routine CF care. Additionally, Dr. Schechter is conducting a randomized controlled trial of a group telephone/web-based intervention to reduce anxiety and depression in adolescents and adults with CF (Project Uplift). There is also emerging evidence on the role of inflammation on the mental symptoms of depression. There is a study in progress in CF examining the link between inflammatory markers and depression (principal investigator: Dr. Ted Lieu). In some cases, this may contribute to the nonresponsiveness to current antidepressant therapies and focus on the immune system may become a therapeutic option to treat depression in the future.

Beyond Anxiety and Depression:

Sleep: Understanding the mechanisms of sleep disturbance and treatments in CF continues to be an area of investigation, with multiple research articles published in 2017. A pilot study suggested that the sleep phase delay in individuals with CF may be due to circadian rhythm abnormalities secondary to manifestations of CFTR dysfunction in the brain (9); suggesting interventions aimed at CFTR dysfunction may hold promise for new target symptoms, such as sleep. Clinically stable children with CF sleep less than their peers, with lower total sleep time and sleep efficiency (ratio of total time asleep to total time in bed; ref 10) and that poor sleep quality is related to both lung health and comorbid conditions, such as CF-related diabetes, asthma and behavioral disorders (11). Additionally, impaired sleep quality and excessive daytime sleepiness were associated with higher depression scores and poorer health-related quality of life in children with CF (12).

Attention Deficit Hyperactivity Disorder (ADHD): ADHD is a chronic neurobehavioral disorder featuring inattention, impulsivity and/or hyperactivity that interferes with function or development. It carries a high rate of comorbid psychiatric problems including depression, anxiety and substance misuse. ADHD can impact school, work, and CF management through impairments in working memory and recall, problem-solving and organization. In 2018, two articles published in the Journal of Cystic Fibrosis, and privileged with an editorial (13), found an increased prevalence of ADHD in youth and adults with CF compared to the general population (14,15). Both articles discuss CF-related factors that could increase expression of ADHD in individuals with a genetic predisposition including inflammation, effects of hypoxia and disease burden, or differential expression of CFTR in neurons. The management of ADHD often incorporates pharmacotherapy, which can have additional implications for CF (e.g., appetite suppression). Although further investigations are needed, these findings suggest that individuals with CF are vulnerable to ADHD and its effects.

Conclusions: New studies confirm that the mental health guidelines have been widely implemented in routine CF care in the US and shed light on the link between depression and mortality in CF, and the potential for CFTR modulators to affect mental health. Future efforts include sustaining these mental health initiatives and disseminating effective treatments, identifying other mental health vulnerabilities beyond depression and anxiety, and continuing to conduct high quality research.