Serum Biomarkers of Nutrition Pre and Post-CFTR Modulator Use in Children with Cystic Fibrosis

Helene Kuffel[1], Edith Zemanick[1,2] Jordana Hoppe[1,2], Maxene Meier[1], Jacob Mark[1,2], Elinor Towler[1], Brandie Wagner[1], Timothy Viger[1]
1. Univ. of Colorado School of Medicine, Anschutz Medical Campus, Aurora, CO
2. Children's Hospital Colorado, Aurora, CO

Rationale. People with Cystic Fibrosis (CF) are at risk for malnutrition and fat-soluble vitamin deficiencies due to pancreatic insufficiency and fat malabsorption. Highly effective CFTR modulators, ivacaftor and elexacaftor/tezacaftor/ivacaftor (ETI), substantially improve CFTR activity, lung function and nutritional status (weight and body-mass index) in people with CF with certain genetic mutations. Fat-soluble vitamin levels (vitamins A, D, and E) are assessed annually in children with CF. We sought to determine changes in fat-soluble vitamin levels following treatment with ivacaftor or ETI.

Methods. We performed a retrospective study of children with CF who had at least three annual evaluations including vitamin A, D, and E prior to ivacaftor or ETI start date and at least one evaluation ≥ 3 months post-modulator start date. Data collected included demographics, CF diagnostic data, pancreatic status, nutritional status, and lung function. Summary statistics were calculated and vitamin levels were compared pre to post-modulator within group via signed-rank tests.

Results. There were 36 children with CF prescribed highly effective CFTR modulators who met annual evaluation criteria, 27 on ETI and 9 on ivacaftor. All individuals treated with ETI were pancreatic insufficient, whereas 7/9 (78%) of those treated with ivacaftor were pancreatic sufficient. For children treated with ivacaftor, vitamin levels were not significantly different following treatment with mean (SD) levels before and after modulator treatment: vitamin A 41 (9.8) mcg/dL vs 48 (13.5) mcg/dL, p = 0.05; Vitamin D 40.8 (5.1) ng/mL vs 46.7 (18.1) ng/mL, p = 0.50; and vitamin E (alpha-tocopherol) 13.8 (4.4) mcg/mL vs 12.2 (1.7) mcg/mL, p = 0.04.

For children treated with ETI, mean Vitamin A levels increased following modulator treatment: vitamin A 38 (6.5) mcg/dL vs 45 (10.8) mcg/dL, p <0.01. For vitamin D, we did not detect a difference between pre and post-modulator values: Vitamin D 35 (9.3) ng/mL vs 38.6 (16) ng/mL, p = 0.39. For Vitamin E, the post-modulator average value was statistically significantly lower than pre-modulator values: Vitamin E 10.7 (2.9) mcg/mL vs 9.2 (4.4) mcg/mL, p = 0.01.

Conclusions. Children treated with ETI had improvement in fat-soluble vitamin A following at least 3 months of treatment. Vitamin levels did not change in those treated with ivacaftor, possibly due to small numbers, fewer pancreatic insufficient patients, or less impact on fat absorption compared to ETI. Evaluation of additional children started on ETI and longer follow-ups are needed to determine if significant changes in vitamin levels persist.

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Conflict of Interest. None to report for the study team