GMDI 2022, May 5-7, Lake Las Vegas, NV
Abstract deadline: December 15, 2022 (time of day not stated)

Current word count: 350/350 (count includes headers)

Dietary goals and current challenges in the management of classical homocystinuria: insights from multinational real-world experience

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Background

Cystathionine beta synthase (CBS)-deficiency, also known as classical homocystinuria (HCU), is a rare, progressive, autosomal recessive disease caused by mutations in the CBS gene. CBS is required for processing homocysteine (Hcy) in methionine (Met) metabolism. Deficient CBS results in toxic accumulation of Hcy causing clinical manifestations of HCU. Patients require reduced dietary Met-intake to decrease Hcy levels and avoid complications. The aim of this project was to collect current practices in HCU treatment as well as discuss future considerations for treatment from seven national and international metabolic centers of excellence.

Methods

Eight metabolic dietitians who manage patients with HCU from four countries (USA, UK, Ireland, Germany) met virtually to discuss real-world treatment practices and challenges for HCU patients.

Results

Older children and adults receiving treatment for HCU at these centers were discussed. Dietary management practices to decrease Met while providing sufficient protein intake, from medical food or diet as needed, were shared. Participants agreed that prescribed Met-restricted diets for HCU need to be highly personalized to minimize negative effects on patients' quality of life as well as to prevent a catabolic state that would negatively impact clinical outcomes. Across centers, patients were assessed biochemically and clinically at 3- to 6-month intervals. Treatment goals included free Hcy <5 μM, total (t)Hcy reduction

(target <50 µmol/l, upper limit 100 µmol/l) and Met levels <1,000 µmol/l. Betaine treatment, which increases re-methylation of Hcy to Met, was used in 6/7 centers. Across centers, challenges to optimal dietary management included poor adherence to prescribed diets and medications (including medical food), lack of home testing options, lack of accurate food-tracking tools, poor palatability/unavailability of medical food and low-protein foods, and financial burden of diet due to lack of insurance coverage (Germany/USA).

Conclusions

Dietitians experienced in treating patients with HCU agreed on the importance of restricting Met while providing a personalized diet for HCU patients. Despite intensive dietary management, patients frequently had poor adherence with a Met-restricted diet. Improved tracking/testing tools, more palatable medical and low-protein foods, and financial coverage of medical food and low-protein food options may improve adherence and outcomes in patients with HCU.

Funding: Travere Therapeutics, Inc.

Author Disclosures

Casey Burns: Paid consultant for Travere Therapeutics, Inc.

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