Dietary cholecalciferol at tenfold the adequate intake attenuates the decline in paw grip endurance and motor performance in the transgenic G93A mouse model of ALS.

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Background: Amyotrophic lateral sclerosis (ALS) is a multi-faceted neurodegenerative disease characterized by heightened oxidative stress, neuroinflammation, glutamate excitotoxicity and apoptosis. The destruction of motor neurons results in progressive paralysis and death. Cholecalciferol (vitamin D₃) and its metabolites have antioxidant, anti-inflammatory and neuroprotective properties, and mitigate the severity of inflammatory, neurodegenerative and autoimmune diseases in humans and animal models that share some common pathophysologies with ALS. Pilot Study Objective: To determine the effects of dietary vitamin D₃ at tenfold the adequate intake (AI) on functional (paw grip endurance – PaGE, motor performance, ability to move – ATM) and disease outcomes (clinical score – CS, disease onset, disease progression, body condition – BC) and lifespan in the transgenic G93A mouse model of ALS. Methods: Starting at age 40 d, 32 G93A mice (21 M, 11 F) were provided ad libitum with either an adequate (AI; 1 IU D₃/g feed) or high (HiD; 10 IU D₃/g feed) vitamin D₃ diet. Differences were considered significant at P ≤ 0.10, since this was a pilot study. Results: For PaGE, HiD mice had a 7% greater score over time vs. AI mice (P = 0.071). For motor performance, HiD mice had a 17% greater score over time (P = 0.079) and a 15% greater area under the curve (AUC; P = 0.025) vs. AI mice; these were due to changes observed in male mice, where HiD males had a 23% greater score over time (P = 0.059) and a 22% greater AUC (P = 0.014) vs. AI males. Between the sexes, males reached disease onset 2.7 fold faster (HR = 2.7, 95% CI: 1.6, 8.1; P < 0.001) and endpoint 2.5 fold faster (HR = 2.5, 95% CI: 1.4, 6.8; P = 0.002) vs. females. There were no significant differences in ATM, CS, disease onset, disease progression, BC or lifespan between the diets. Conclusion: Vitamin D₃ supplementation at tenfold the adequate intake attenuates the decline in paw grip endurance and motor performance in the transgenic G93A mouse model of ALS, specifically in males. However, higher vitamin D₃ supplementation may be required to elicit robust changes in functional and disease outcomes in this disease model. Supported by NSERC and Faculty of Health - York University