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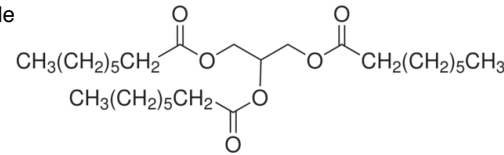
Assessment of caprylic triglyceride for dietary intervention in an amyotrophic lateral sclerosis mouse model

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BACKGROUND

- Amyotrophic Lateral Sclerosis (ALS) or Lou Gehrig's disease
 - Adult-onset progressive degeneration of motor neurons in the spinal cord
 - Patients develop muscle weakness, progressing to paralysis and death
 - Mitochondrial energy metabolism deficiencies contribute to ALS cell death (1-3)
- Ketogenic diet beneficial in a mouse model of ALS, possibly by improving energy metabolism (4)
- Caprylic triglyceride



Medium chain (8 carbon) fatty acid ester of glycerol
Can provide ketone bodies as an alternative energy source to glucose

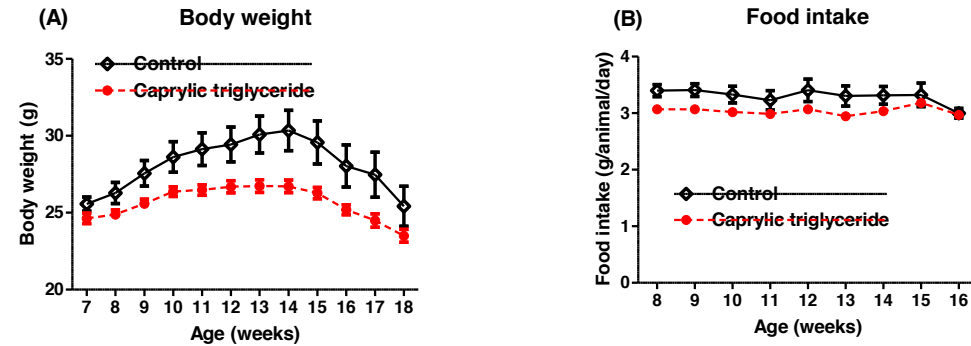
AIMS AND HYPOTHESIS

- To test whether caprylic triglyceride has a beneficial effect on motor performance and survival in a mouse model of ALS
- To investigate whether caprylic triglyceride improves mitochondrial bioenergetic function in ALS spinal cord and in vitro

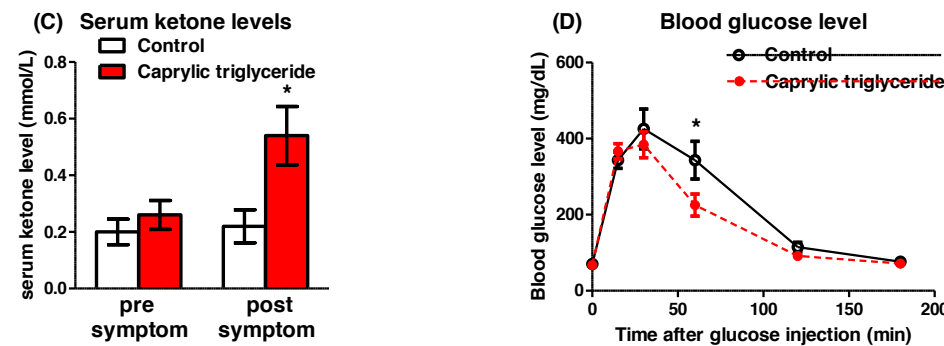
METHODS

- Male ALS superoxide dismutase-G93A transgenic mice starting at six weeks of age till the end of the study were administered
 - Control group: Isocaloric diet (34 kcal% fat)
 - Treatment group: Caprylic triglyceride (10% w/w)
- Body weight and food intake monitored through treatment period
- Serum ketone level measured before and after development of symptoms
- Blood glucose assayed by glucose tolerance test
- Motor performance assessed by accelerating rotarod test
- Survival monitored through course of the study
- Spinal cord mitochondrial respiratory function measured using Seahorse XF24 Extracellular Flux Analyzer
- Cellular energy metabolism after caprylic triglyceride treatment assessed using XF24 in NSC-34 mouse motor neuron-like cell line

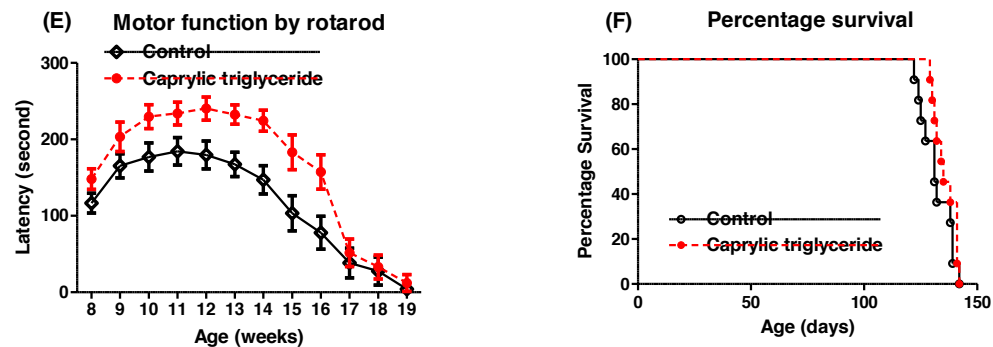
RESULTS



(A) Body weight of ALS mice on caprylic triglyceride was lower than control diet mice ($p < 0.05$ by two way ANOVA, $n = 17-18$)
(B) Food intake was comparable in caprylic triglyceride treated mice compared to controls ($n = 18$)

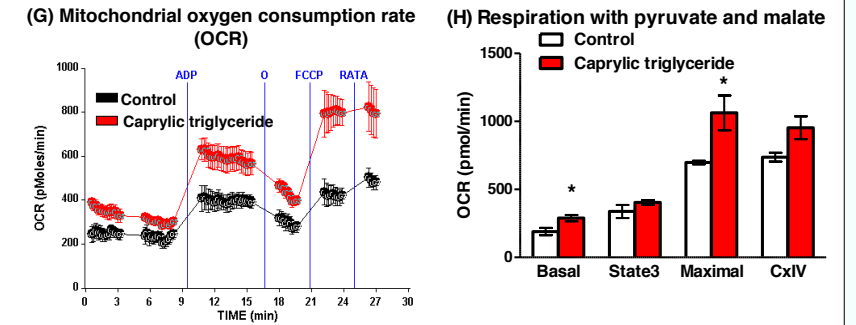


(C) Serum ketone levels were elevated in post-symptomatic ALS mice on caprylic triglyceride but not mice on control diet ($*p < 0.05$ by t-test, $n = 5$)
(D) Blood glucose was lower in caprylic triglyceride treated mice at 60 min post-injection ($p < 0.05$ by t-test, $n = 4-5$)

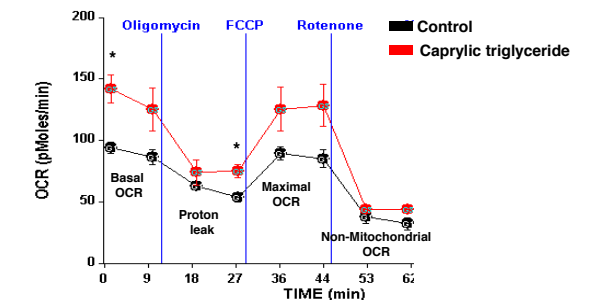


(E) Mice on caprylic triglyceride showed better motor function on the accelerating rotarod compared to ALS mice on control diet ($p < 0.05$ by two way ANOVA, $n = 13-14$)
(F) Caprylic triglyceride treatment had no significant beneficial effect on the survival of ALS mice ($n = 11$)

RESULTS



(I) Cellular oxygen consumption rate



(G) An example of XF24 experiment in spinal cord mitochondria from control and caprylic triglyceride treated mice.
(H) Caprylic triglyceride treatment in ALS mice increased basal and maximal OCR in presence of complex I substrates ($p < 0.05$ by t-test, $n = 3$)
(I) Increased OCR was observed in NSC-34 cell line after treatment with caprylic triglyceride (0.5% v/v overnight) ($p < 0.05$ by t-test, $n = 3$)

CONCLUSION

Caprylic triglyceride improved motor function and energy metabolism in ALS mice but did not beneficially modify the time of survival. As a combination treatment for improving metabolic efficiency in ALS, it may improve quality of life along with drugs that target survival.

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