A pilot study to determine the effects of a ketogenic diet on neuro-recovery and metabolism in individuals with spinal cord injury

Hammad Aslam[1], Adarsh K. Kulkarni[2], Mualla Eraslan[1], Hatice Cetin[4], Baris Cetin[4], Cassandra Renfro[1], Patrick Bosarge[3], Keneshia Kirksey[1], Amie McLain[1], and Ceren Yarar-Fisher[1]
Departments of Physical Medicine and Rehabilitation[1], School of Medicine[2], General Surgery[3], University of Alabama at Birmingham, Birmingham, AL;
Department of Physical Therapy and Rehabilitation[4], Hacettepe University, Ankara, Turkey

INTRODUCTION

- There is a growing need for innovative therapies for improving neuro-recovery following spinal cord injury (SCI).
- A number of pharmacological neuro-protective agents have been subject to intensive investigation; despite promising preclinical animal data, the outcomes of these clinical trials are largely negative.
- There is thus clear rationale for researchers, clinicians, and patients to seek alternative therapies to enhance neuro-recovery and functional status following SCI.
- In rodents, implementing a ketogenic diet acutely after an SCI has been shown to improve forelimb motor function.
- Ketogenic diet (KD) is a high fat, low carbohydrate diet (80-90% fat, 5% carbohydrate, 10-15% protein) that produces increased circulating levels of ketone bodies.
- Ketone bodies are thought to confer neurons with greater ability to resist negative metabolic challenges associated with secondary pathological processes seen in SCI.

PURPOSE

Determine if 8 weeks of KD vs. standard hospital diet (SD) following SCI significantly improves motor and sensory function, and glycemic control in patients with acute SCI.

METHODS

- In a randomized repeated measure design, 7 patients were assigned into one of the two study groups: KD, n=4 or SD, n=3.
- The neurological level of injury ranged from C5-T11.
- Patients with Brown-Sequard and central cord syndromes were not eligible for participation.
- There were 2 motor complete (AIS A and B) and 2 motor incomplete (AIS C) patients in the KD group compared to 1 motor complete (AIS A) and 2 motor incomplete (AIS C and D) in the SD group.
- Clinical outcomes were measured within 72 hours of admission and at discharge; study design and outcome measures are included in Figure 1.
- Diet interventions were initiated within 72 hours of admission and after baseline clinical measures were performed.

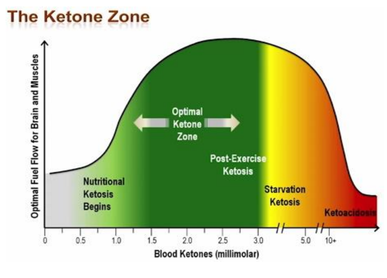
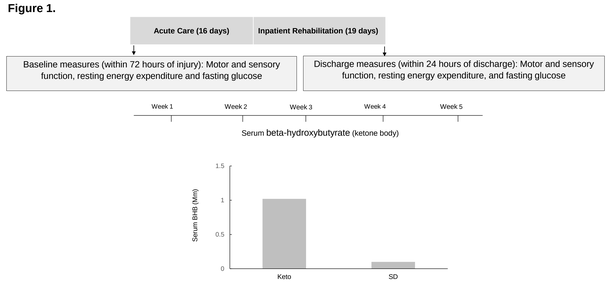


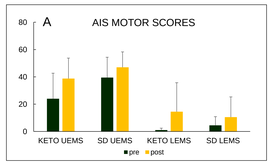
Figure 1.

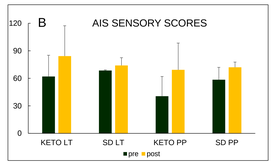


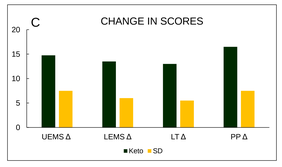
- The KD was a high fat, low carbohydrate diet (lipid to carbohydrate + protein ratio of 3:1) that included ≈72% total energy as fat, ≈25% as protein, and ≈3% as carbohydrate during enteral feeding and ≈65% total energy as fat, ≈27% as protein, and ≈8% as carbohydrate and fiber during solid feeding.
- The SD included ≈35% total energy as fat, ≈27% as protein, and ≈44% as carbohydrate and fiber (none of SD participants received enteral feeding).
- American Spinal Injury Association Impairment Scale (AIS) neurological exam was performed to measure upper and lower extremity sensory and motor function.
- Fasting glucose and insulin levels were measured to determine metabolic status.
- β-hydroxybutyrate (ketone body) was measured weekly to determine nutritional ketosis.
- Patients in both groups underwent an intensive rehabilitation program including respiration therapy, passive and active range of motion, neuromuscular re-education, mobility, transfers, wheelchair mobility skills, bowel and bladder management, tone and spasticity management, and skills for performing other activities of daily living.

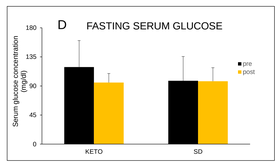
RESULTS

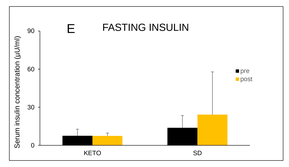
- Mixed model repeated measures analysis was used to assess the effects of group (keto diet, standard diet), time (pre-, post-intervention), and the group-by-time interaction on the outcomes of interest (motor and sensory).
- Statistical tests were two-sided, and p-values less than 0.05 were considered statistically significant.
- All KD patients reached nutritional ketosis (Figure 1, nutritional ketosis ranges from serum β-hydroxybutyrate = 0.5-3.0 mM).
- A main effect of time ($p < 0.05$) was found for upper extremity motor score (UEMS). Keto group demonstrated an increase ($p < 0.05$) in UEMS compared to baseline scores (keto: 24 [pre] vs. 38.7 [post]; SD: 39.5 [pre] vs. 47 [post], Figure 2A).
- Between baseline and discharge time points, 15 UEMS and 13 lower extremity motor score (LEMS) points were recovered in the KD group vs. 8 UEMS and 6 LEMS points were recovered in the SD group.
- The average change of fasting glucose in the KD and SD group were -24 mg/dl and +0.7 mg/dl (Figure 2D), respectively.
- The average change of fasting insulin in the KD and SD group were -0.17 µU/ml and +11 µU/ml (Figure 2E), respectively.
- Light touch (LT), pin prick (PP), and motor recovery scores in the KD group were increased by 28, 22, and 28 points vs. 13, 5, and 13 points in the SD group, respectively (Figures 2C).











DISCUSSION

- Our pilot data showed:
  - A ketogenic diet safely brought KD patients to a state of nutritional ketosis.
  - KD patients demonstrated better improvements in both motor and sensory functions as compared to SD and previous neuro-recovery studies in acute SCI patients.
  - The recovery in motor points in the KD group in 5 weeks was similar or higher compared to the recovery gains reported 6 months to one year after injury.
  - Metabolomic profiling of patients' serum is currently being analyzed for identifying biomarkers of neuro-recovery that may explain differential changes among study groups.

This research was supported by KL2TR001419-01 UAB/CCTS (PI: Ceren Yarar-Fisher); the Department of Physical Medicine and Rehabilitation Functional Neurorehabilitation Research Summer Program and the UAB Medical Student Summer Research Program (NIH/NHLBI T35HL007473).