

SPECIALIZED SUPPLEMENTATION INCREASES BLOOD KETONE LEVELS AND IMPROVES COGNITION IN MILD COGNITIVE IMPAIRMENT: A CASE REPORT

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RATIONALE

Compensating the decline in the brain energy metabolism is an emerging strategy aimed at delaying the onset and/or progression of **Alzheimer's Disease (AD)** (Cunnane et al., 2020). Our previous preclinical data (Siqueira et al., 2020; 2021) showed that a **specialized supplement, which provides ketone bodies (KB)** as an alternative source of energy along with additional antioxidant and anti-inflammatory nutrients, prevents memory deficit in an animal model of AD. Previous clinical studies have shown that ketogenic supplements have a direct and statistically significant dose-response relationship between brain uptake of ketones and plasma ketone levels (Fortier et al., 2019). At plasma KB values around 1 mM, the percentage of brain energy consumption supplied by KB is about 10–15% (Cunnane et al., 2016). Here we discuss a clinical case of a patient under this supplementation.

METHODS

A 56-year-old female patient, civil servant, graduated in law, started **complaining of inattention and difficulties in organization** and planning for 5 years. The complaints got worse over the years and impacted work activities. In September 2021, a neurologist started an investigation for causes of cognitive decline. She underwent Cranial Magnetic Resonance in 2012, within the normal range, and in 2020, with rare foci of hypersignal on T2 and periventricular and subcortical white matter FLAIR, compatible with microangiopathy.

Given the context, the neuropsychological assessment (NA) showed:

- October 2021: **impairment of the entire explicit memory system**, largely deficient attentional processes and changes in executive functions.

Given the suspicion of **ongoing neurodegenerative disease (ND)**, she underwent Cerebrospinal fluid (CSF) analysis, PET-FDG and genetic exams:

- CSF analysis Dec/2021: Total TAU protein 401.70 (RV: 116 to 370) // Amyloid Beta Peptide 42: 640.70 (RV: 562 to 1018) // Amyloid Beta Peptide 40: 358,20 (VR > 547,6) // Indices: IAT 0.9 Indicative of AD // TAU/Bamyloid Index 42: 0.63 (RV>0.52 abnormal value).

- Brain PET-FDG Dec 2021: Decreased glycolytic metabolism in the mesial temporal, parietal, and posterior cingulate gyrus regions.

- Genetic: Deletion and duplication analysis for 42 genes listed for AD and other ND. Result of uncertain meaning.

Diagnosis: Mild Cognitive Impairment (MCI) multiple domains secondary to AD

In February 2022, she started the **specialized supplement containing 35 grams of capric and caprylic acid (C8 and C10), 300mg of phosphatidylserine, 180mg of DHA** (Instanth Neo, Prodiet Medical Nutrition). After 6 months, the patient underwent a new NA and ketone body measurement (Mayo Clinic). For dosing, she was instructed to eat her usual breakfast, without changes, and undertook venous forearm blood samples at baseline and every 30-45 min during a 2h15min study period to measure beta-hydroxybutyrate (beta-HB) plasma after supplementation.

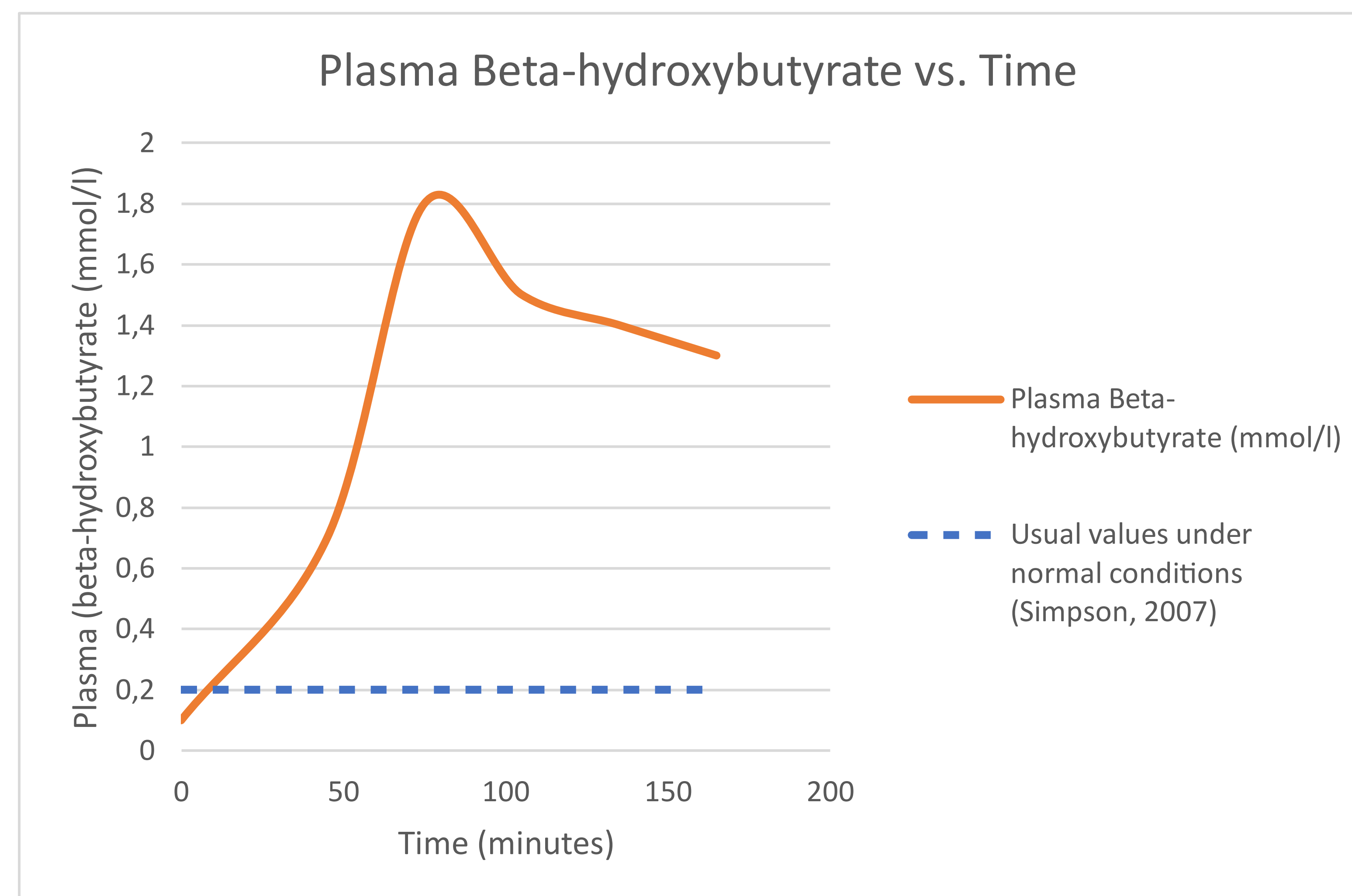


Figure 1. Plasma total ketone response beta-hydroxybutyrate (beta-HB) throughout the 2 hour 15minutes study period.

The patient consumed her usual breakfast and came to the lab at which time a blood sample was drawn (Time 0). After the supplement consumption undertook blood samples every 30-45 min during a 2h15min study period to measure beta-HB plasma after supplementation.

CONCLUSION

In conclusion, we demonstrate that a **specialized supplement** with C8C10 taken for 6 months probably provided enough ketones **to improve brain energy status in this MCI patient and improve aspects of cognitive function.**

RESULTS

Before taking the supplement, KB (beta-HB) levels were within the expected range under normal conditions, 0.1 mmol/L. After 43 minutes of supplement consumption, which happened after usual food consumption, beta-HB reached 1.8 mmol/L after 73 minutes, (Figure 1). In comparison, studies in humans concerning kinetics of ketones showed 2.5 mmol/L after 3 days of fasting.

The NA showed a **qualitative and quantitative improvement**, and in the clinical assessment a **subjective improvement in cognition, mood and work performance** was detected.

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DISCLOSURE

This study was presented at the ASPEN 2023 Nutrition Science & Practice Conference

<https://aspenjournals.onlinelibrary.wiley.com/doi/epdf/10.1002/jpen.2491>

[df/10.1002/jpen.2491](https://doi.org/10.1002/jpen.2491)