Is elevating BHB by a Ketone Ester supplement sufficient in reducing alcohol craving and consumption in Alcohol Use Disorder?

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SUBMISSION DETAILS

What is the Methodological Question Being Addressed? The methodological question addressed is whether a one-dose Ketone Ester (KE) drink can be effective in lowering alcohol craving, consumption, and withdrawal in Alcohol Use Disorder (AUD), in the same way a three-week ketogenic diet (KD) intervention is effective. The Ketone Ester drink is an energy drink that, after one dose, elevates plasma levels of the ketone body beta-hydroxybutyrate within 30 minutes to similar levels as a multiple-week KD. Moreover, the KE provides methodological advantages over the KD in terms of blinding (it is easier to blind a one-dose drink than a multiple week diet), timing (a 30-minute intervention will be time effective over a 3-week intervention), and costs (a one-dose KE is by far cheaper to implement than a 3-week diet intervention).

Introduction Individuals with AUD show elevated metabolism of acetate at the expense of reduced glucose metabolism by the brain compared to non-dependent controls. During alcohol intoxication, plasma levels of acetate increase and then decline with detoxification. We hypothesized that a shift in energy substrates during withdrawal may contribute to withdrawal severity and neurotoxicity in AUD. In AUD inpatients, we recently found that a 3-week KD lowered alcohol withdrawal and craving in AUD inpatients undergoing detoxification (Wiers et al, 2021). Moreover, an animal study indicated that KD lowered alcohol intake and increased sensitivity for alcohol (Wiers et al, 2021). A recent preclinical study found that the KE is sufficient to reduce alcohol withdrawal in alcohol-dependent rodents (Bornebusch, 2021). However, it has not been tested whether elevating BHB by means of a KE is sufficient in lowering alcohol craving, consumption, and withdrawal symptoms in humans.

Methods This trial uses the KE ((R)-3-hydroxybutyl (R)-3-hydroxybutyrate (TdelaS, Orlando, FL) drink, and a placebo drink that is equally bitter as the KE, and masks the flavor of the drinks with the smell of rubbing alcohol in the testing room. We will test AUD outpatients in a randomized cross-over trial and test whether a one-dose KE intake elevates plasma and brain BHB to equal levels as the KD. We will also test whether KE lowers alcohol craving (Alcohol Urge Questionnaire) and consumption (Bar Lab procedure).

Results Our first pilot data indicated that intake of a 1.9 kcal/kg of KE elevated BHB to 4.5 mM within 30 min of intake. In our previous study in AUD inpatients, BHB levels were 1.8mM, 4.3mM, and 4.2mM after 1, 2 and 3 weeks of a "classic" 4:1 ratio of grams of fat:grams of carbohydrate and proteins KD. We are currently testing AUD outpatients with 3T MRI and an alcohol self-administration paradigm. Results of 5 individuals tested twice will be presented at the 2021 Autumn ISCTM.

Conclusion KE drinks may offer a unique treatment option in AUD inpatient and outpatient

populations that can be taken as an oral supplement without extensive changes to the normal diet and provide methodological advantages of blinding, timing and costs that can be considered for future trials. If beneficial clinical effects of metabolic ketosis by a KE drink can be documented in humans with AUD, i.e., on alcohol craving and consumption and on brain energetic functioning, then this could be targeted as a therapeutic intervention to enhance success in treatment for AUD.

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Keywords

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alcohol
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Guidelines I have read and understand the Poster Guidelines

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