Ketone Supplementation Dampens Subjective and Objective Responses to Alcohol in Rats and Humans

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Background: Previous preclinical and human studies have shown that a high-fat ketogenic diet and ketone supplements (KS) are efficacious in reducing alcohol craving, alcohol consumption, and signs of alcohol withdrawal. However, the effects of KS on alcohol sensitivity are unknown.

Methods: In this single-blind, cross-over study, 10 healthy participants (3 females) were administered a single, oral dose of a KS (25 g of ketones from D-β-hydroxybutyric acid and R-1, 3-butanediol) or placebo 30 minutes before an oral alcohol dose (0.25 g/kg for women; 0.31 g/kg for men). Assessments of breath alcohol concentration and blood alcohol levels (BAL) and responses on the Drug Effect Questionnaire were repeatedly obtained over 180 minutes after alcohol consumption. In a parallel preclinical study, 8 Wistar rats (4 females) received an oral gavage of KS (0.42 g ketones/kg), water, or the sweetener allulose (0.58 g/kg) followed 15 minutes later by an oral alcohol dose (0.8 g/kg). BAL was monitored for 240 minutes after alcohol exposure.

Results: In humans, the intake of KS before alcohol significantly blunted breath alcohol concentration and BAL, reduced ratings of alcohol liking and wanting more, and increased disliking for alcohol. In rats, KS reduced BAL more than either allulose or water.

Discussion: KS altered physiological and subjective responses to alcohol in both humans and rats, and the effects were likely not mediated by the sweetener allulose present in the KS drink. Therefore, KS could potentially reduce the intoxicating effects of alcohol. A follow-up preclinical experiment concluded that oral administration of KS and intraperitoneal injection of alcohol did not lead to dampened BALs, suggesting that pharmacokinetic effects of KS are due to delayed absorption of alcohol rather than a faster metabolic rate of alcohol, likely due to delayed gastric emptying with KS.