The Effects of a Ketogenic Diet on Alcohol Consumption in a Mouse Model

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Ketogenic Diets

Ketogenic diets have been used as a therapy for epilepsy since the 1920's (Paoli 2014). Ketogenic diets are characterized by a reduction in carbohydrates, usually less than 50g/day and relative increase in the proportions of proteins and fats (Jagadish 2019).

After a few days of fasting from carbs, your body can't use glucose for energy and is forced to find a new energy source. This alternative energy source is derived from the overproduction of acetyl coenzyme A (CoA) and includes fatty acids and ketone bodies. This process is what is known as ketosis (Paoli 2014).

Alcohol Use Disorder

Alcohol is one of the leading causes of preventable death worldwide, with 3 million deaths per year attributed to alcohol (Witkiewitz 2019). Binge drinking, intermittent and heavy use of alcohol, is associated with increased problem and risk-taking behaviors, and is often a precursor of Alcohol Use Disorder (AUD). AUD is defined by a loss of control over alcohol consumption, which is accompanied by neurological changes due to overconsumption. Treatments for alcohol use disorder such as use of benzodiazepines have a high abuse liability, so other options need to be investigated. Therefore, a non-invasive diet-based therapeutic intervention to reduce binge drinking could be useful. Research on the introduction of a ketogenic diet (KD) as a potential treatment option for many conditions such AUD are currently unknown. A KD diet could be a therapeutic treatment/intervention for alcohol use disorder.

Recent animal studies have shown promising evidence to suggest ketogenic diets as interventions for AUD, such as work by Dencker et al., 2017. They found that a KD diet caused a decrease in alcohol withdrawal symptoms such as irritability.

Purpose of Study

In the present study, we aim to investigate if introduction of a ketogenic diet will decrease alcohol consumption in mice.

Hypothesis: Mice that are introduced to KD will drink less EtOH while in ketosis.

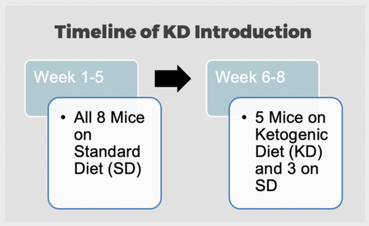

Figure 1. Shows timeline for the entirety of the experiment. Week 6 indicates the start of the Ketogenic Diet (KD).

Results

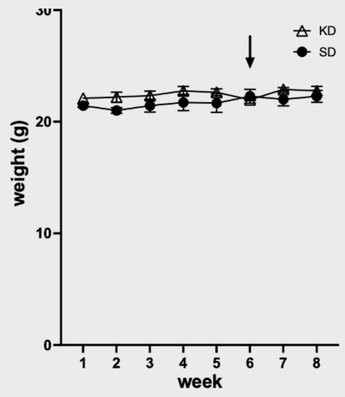

Figure 2. Shows the average weights per week for standard diet (SD) and ketogenic diet (KD) mice were not significantly different (p > 0.05).

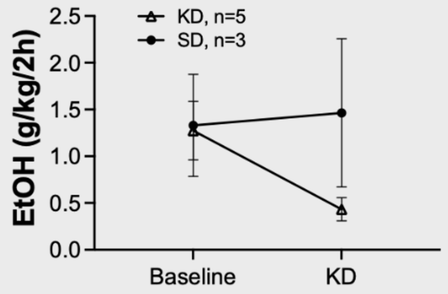

Figure 3. Shows the average self administration of alcohol between standard diet (SD) and ketogenic diet (KD) before and after KD period. There was a significant interaction between time and diet ($F(1,6)=6.538$, $p=0.0431$).

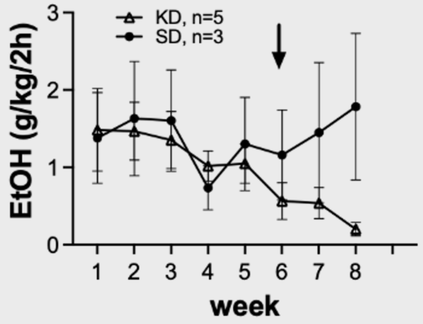

Figure 4. Shows self administration of alcohol over a period of 8 weeks. The black arrow indicates the time when the ketogenic diet (KD) was introduced (week 6-8). There was a significant interaction between time and diet ($F(7,42)= 2.72$, $p=0.019$).

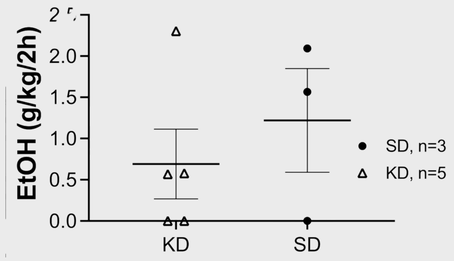

Figure 5. Shows the relapse data after alcohol was reintroduced after the KD diet. The results from a t-test showed an insignificant difference.

Materials

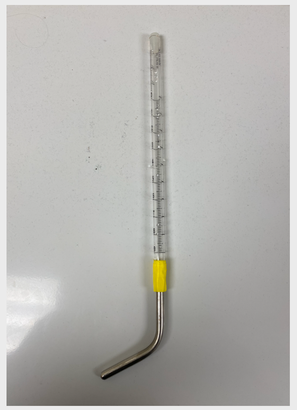

Figure 6 & 7. The picture on the left shows the cage where the mice were kept during the duration of the experiment. The picture on the right shows the sipper that was filled with EtOH and placed through the spaces in the bar.

Methodology

For this experiment, there were 6 female and 2 male C57BL/6 mice. Each mouse was assigned a bar/cage and sipper (shown in figures 6 & 7). 3 days a week, each mouse was weighed, and put into a habituation chamber for 20-30 minutes. This allowed for adjustment to a new environment.

The mice were then placed in their assigned bar for 2 hours. They had access to a sipper filled with 10% EtOH. Pre and Post Volumes, as well as weights were recorded over the duration of the 8-week experiment.

In relation to their diet, all 8 mice (male and female) were given a standard diet (SD) of food for the first 5 weeks of the experiment. At week 6, 5 of the mice were introduced to a ketogenic diet, including both male mice.

Statistical analysis subjected data to a Repeated Measures ANOVA was used to assess diet, time and diet by time effects.

Conclusions/limitations

The results indicate that KD did have an effect on alcohol consumption, as mice on the KD diet drank significantly less over time. This suggest that a ketogenic diet may be a therapeutic treatment option for alcohol use disorder. Through results from the relapse, it can be concluded that a KD diet is more effective in the short term, but might not be a long term treatment option for AUD.

Limitations include a small sample size (n=8). In addition, there were only male mice in one of the treatment groups. Therefore, sex differences couldn't be accounted for.

Future directions include testing the mice in a larger sample size for more accurate results. In addition, an alternate option for longer term treatments should be explored.

References

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