Investigating the Efficacy of Ketogenic Diets in Reducing COVID-19 Severity

Abstract

Background

The use of ketone bodies as a potential treatment of acute respiratory distress system (ARDS) and cytokine storm caused by COVID-19 has not been thoroughly investigated. The aim of this observational study is to determine if patients with COVID-19 symptoms on the ketogenic diet will experience reduced inflammation.

Methods

Enroll 120 patients infected with COVID-19, hospitalized but not in ICU, and administer a 4:1 ketogenic formula for 10 days. Measure their levels of biomarkers associated with inflammation such as IL-6, fibrinogen, TNF-α.

Hypothesized Results

Due to the anti-inflammatory effects of introducing ketone bodies, most hospitalized patients infected with COVID-19 will exhibit significantly lower levels of fibrinogen, IL-6, and TNF-α.

Conclusion

Ketone bodies are a promising treatment for reducing COVID-19 severity, but more research on their effects on respiratory viral infection is required.

Introduction

COVID-19 mortality is highly correlated with cytokine storm [1], an overproduction of cytokines, and the presence of comorbidities like obesity and diabetes [2]. To reduce mortality by COVID-19 induced immunopathology, it is necessary to find ways to reduce the inflammatory response. A possible therapy to combat the increased inflammation is the ketogenic diet. The ketogenic diet is a high fat, low carbohydrate diet that promotes the production of liver ketone bodies. Ketone bodies (AcetoAcetate and Beta-hydroxybutyrate) have been shown to inhibit NLRP3/inflammasome activation triggered by SARS-CoV-2 antigens [3]. Individuals on a ketogenic diet had a decrease in such cytokines as TNF-α, IL-1, and IL-6 [4]. In a study involving obese individuals, the ketogenic diet caused increased expression of adiponectin, leading to a decrease in weight and blood TNF-α level [5]. TNF-α is important in nearly all acute inflammatory reactions, acting as an amplifier of inflammation. TNF-α blockade has been used to treat more than ten different autoimmune inflammatory diseases, suggesting that this might be a potential therapeutic approach to reduce organ damage in patients with COVID-19 [6].

Methods

Setting

I plan to conduct this study in the ICUs of Keck Hospital of USC, Texas Medical Center, and Cedars Sinai Medical Center.

Data Sources

I will obtain clinical data using the databases from each respective hospital.

Variables Assessed

1. **Interleukin 6 (IL-6) in picograms per milliliter (pg/mL):** A biomarker associated with cytokine storm and severe COVID-19 symptoms. Interleukin 6 upregulates C-reactive protein, fibrinogen, and haptoglobin. It downregulates fibronectin, albumin, and transferrin. IL-6 also promotes specific differentiation of naive CD4+ cells [7]. Increasing levels of interleukin 6 correlate to disease severity and respiratory failure [8].
2. **Tumor necrosis factor-alpha (TNF-α) in picograms per milliliter (pg/mL)**: A pro-inflammatory cytokine that operates by binding to tumor necrosis factor receptor 1 (TNFR1) and tumor necrosis factor receptor 2 (TNFR2) [9].
3. **Fibrinogen in milligrams per deciliter (mg/dl):** A protein that plays a role in blood clotting, fibrinolysis, cellular and matrix interactions, inflammatory response, wound healing, and neoplasia [10]. An increased fibrinogen median value has been shown in COVID-19 patients with Acute respiratory distress syndrome(ARDS) [11].

End Point

The primary endpoint is overall survival. The co-primary endpoint is the decrease in levels of fibrinogen, IL-6, and TNF-α compared to levels prior to the start of the study.

Statistical Analysis

A paired t-test will be used to compare the levels of fibrinogen, IL-6, and TNF-α before the administration of the ketogenic formula to the levels of fibrinogen, IL-6, and TNF-α after 10 days. A Kaplan-Meier estimator will be used to calculate the median overall survival.

Hypothesized Results

Due to the anti-inflammatory effects of ketone bodies, most of the hospitalized patients infected with COVID-19 will exhibit significantly lower levels of fibrinogen, IL-6, and TNF-α. In addition, they will have a lower risk of ARDS and cytokine storms.

Discussion

Ketone bodies have the potential to reduce the severity of COVID-19 symptoms such as ARDS and cytokine storms through their anti-inflammatory effects. This study will be one of the first to investigate the efficacy of ketone bodies in reducing COVID-19 symptoms. Data collected from this study will be valuable in determining if ketone bodies are a safe, viable treatment for COVID-19, especially for obese and diabetic patients. As the pandemic continues, it is crucial to develop therapies such as ketone bodies that will prevent the progression of COVID-19. However, the characteristics of ketone body metabolism and their biological effects in the context of respiratory viral infections such as COVID-19 are not well known [12]. Questions such as “How do ketone bodies affect replication of SARS-CoV-2?” and “How do ketone bodies interact with lung cells?” are still unanswered. COVID-19 infection can trigger ketoacidosis, the production of excess ketone bodies in patients, which often results in death [13]. Going forward, it will be important to fully research the effects of ketone bodies in respiratory viral infections.