Creatine Monohydrate Supplementation Improves Microvascular Blood Flow But Not Glucose Homeostasis in Response To A Meal

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Abstract

Consumption of high-carbohydrate (HC) or high-fat (HF) meals is known to increase reactive oxygen species (ROS), which underlie the development of cardiovascular disease (CVD). Furthermore, the consumption of HF meals specifically is known to induce a state of hyperglycemia which can also increase ROS. NADPH oxidase (NOX) is a primary source of ROS in the vasculature, but the effects of NOX-generated ROS on *in vivo* microvascular blood flow following a HC or HF meal are unclear. Recent studies indicate creatine monohydrate (CM) may reduce ROS levels and improve blood flow. **PURPOSE:** The primary aim of this study was to determine whether 5 days of CM supplementation could reduce in vivo ROS concentrations, improve microvascular blood flow in response to a HC or HF meal and reduce hyperglycemia in response to a HC meal. **METHODS**: Young, healthy males and females (n = 6; age: 28 ± 6 yrs.; BMI: 27.4 ± 6.0 kg/m^2) were studied. Microdialysis was utilized to measure local skeletal muscle (vastus lateralis) ROS concentrations and microvascular blood flow at rest and for 4 hours after consumption of either a HC (150 g of glucose) or HF (66 g of fat) meal. A continuous glucose monitor was inserted into the subcutaneous adipose tissue to collect readings of interstitial glucose levels throughout the study. One microdialysis probe was perfused with a control saline solution containing 5 mM ethanol (CON). Microvascular blood flow was assessed by ethanol outflow:inflow ratio (o:i), which is inversely related to blood flow. Microdialysis procedures were repeated after 5 days of CM supplementation (20 g/day). Due to limited sample size, HC and HF groups were combined for data analysis. **RESULTS**: Following 5 days of CM supplementation, ROS concentrations (POST: 3.22 ± 1.76, PRE: 1.94 ± 0.86, p = 0.025) and microvascular blood flow (ethanol o:i, POST: 0.58 ± 0.26; PRE 0.74 ± 0.13, p = 0.038) were significantly increased at 180 mins post HC/HF consumption. No change in interstitial glucose levels were observed with CM supplementation. **CONCLUSION**: CM supplementation increases ROS concentrations but improves microvascular blood flow which may indicate that the increased ROS is beneficial. Furthermore, CM supplementation had no effect on hyperglycemia in response to a HC meal which suggests that a longer supplementation period or exercise intervention may be needed.

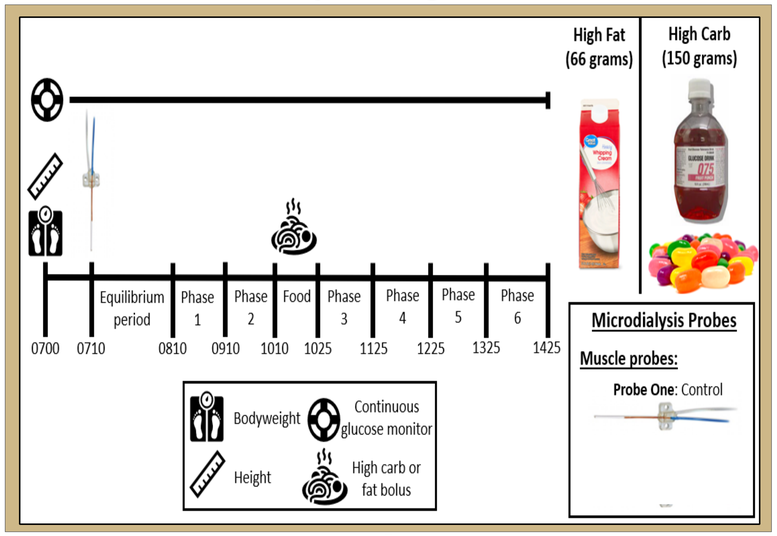
Introduction

Chronic hyperglycemia, characterized by persistent elevations in blood glucose levels, can result in detrimental effects on the vasculature and contribute to the development of debilitating health conditions such as type 2 diabetes and cardiovascular disease. The harmful effects of hyperglycemia primarily stem from its ability to elevate levels of oxidative stress in the form of reactive oxygen species (ROS), which can have deleterious consequences on cellular function and overall health. In turn, excess ROS concentrations can lead to further elevation of blood glucose levels, creating a vicious cycle. Interventions that mitigate hyperglycemia and oxidative stress are more likely to induce significant reductions in disease risk and damage to the body. Creatine monohydrate (CM), a widely utilized sports performance supplement recognized for its capacity to enhance muscular power and performance, might serve as a potent intervention in hyperglycemia and ROS reduction. To date, researchers have had to resort to the utilization of indirect surrogates, or in-vitro (outside a living organism) tissue measurements of ROS to assess oxidative stress. However, a novel microdialysis technique has been developed that can be used to measure in-vivo (in human) production of ROS. Therefore, the main objective of this project is to examine if CM supplementation is able to significantly lower hyperglycemia and ROS concentrations.

Methods

A pre-post study design study design was implemented to determine if 5 days of 20 g of CM supplementation could lower ROS concentrations, improve microvascular blood flow, and lower hyperglycemia at rest and in response to a HC or HF meal. Participants completed a baseline visit in which bodyweight, height, and body composition were obtained. In addition, a continuous glucose monitor was inserted into the subcutaneous adipose tissue to collect readings of interstitial glucose levels throughout the study. Following the baseline visit, participants came in for a testing day in which 1 microdialysis probe was inserted into the vastus lateralis. The microdialysis probe contained a control solution of ethanol and saline. Dialysate samples were collected at baseline and up to 4 hours following the consumption of a HC (150 g of carbohydrate; 600 kcal) or HF (66 g of fat; 600 kcal) meal. All dialysate samples were immediately assessed in a fluorometer to determine ROS concentrations. In addition, the remainder of each dialysate was stored at 4˚C and analyzed for ethanol concentration within 24 hours, which is displayed as a percent change in ethanol outflow:inflow ratio to determine microvascular blood flow. After the completion of the visit, participants were sent home with 5 days of CM supplementation (20 g per day). Following the 5 days, participants returned for a second experimental day, in which the same procedures were performed.

Study Design



Results

6 participants (28.17 ± 6.24 yrs, 85.53 ± 27.32 kg, 27.35 ± 5.96 kg/m^2, 30.85 ± 9.86 % bodyfat) completed the study. ROS concentrations were significantly increased following 5 days of CM supplementation at 180 mins (POST: 3.22 ± 1.76) compared to pre supplemented conditions (PRE: 1.94 ± 0.86, P = 0.0248) (**Figure 1**). Microvascular blood flow was improved at 160 mins (ethanol o:i, POST: 0.65 ± 0.19; PRE: 0.72 ± 0.18, P = 0.0269) and 180 mins (ethanol o:i, Post: 0.58 ± 0.26; Pre: 0.74 ± 0.13, P = 0.0375) post carb/fat consumption (**Figure 2**). Baseline and peak interstitial glucose was not different after CM supplementation compared to pre supplementation (**Figure 3**).

Figure 1: Concentration of ROS PRE and POST CM Supplementation

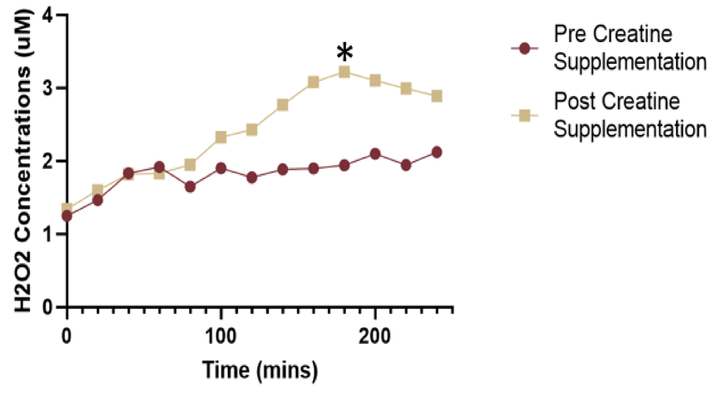


Figure 2: Microvascular Blood Flow Pre and Post CM Supplementation

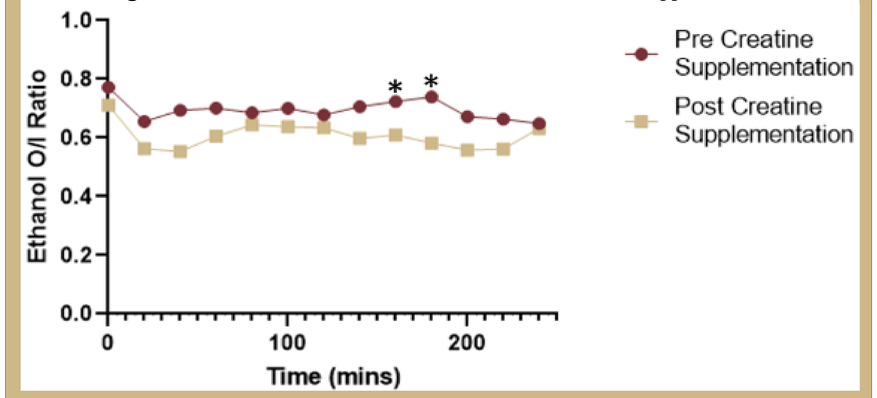
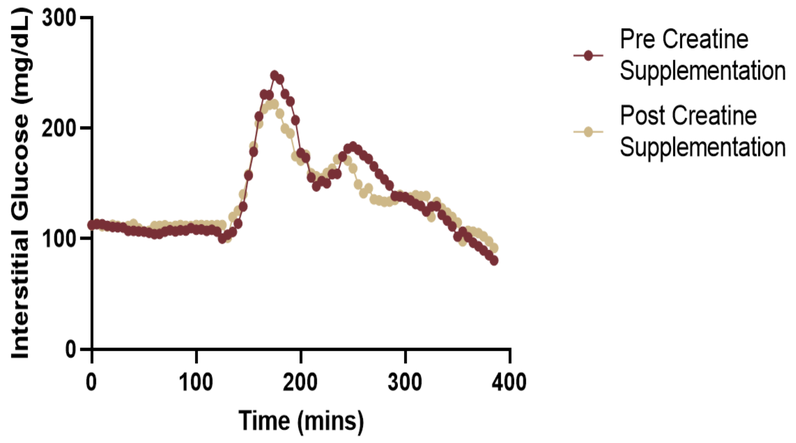


Figure 3: Interstitial Glucose Levels PRE and POST CM Supplementation



Conclusions

To our knowledge, this was the first study to examine in-vivo ROS, microvascular blood flow, and interstitial glucose levels in response to a HC/HF meal PRE and POST CM supplementation. Findings from this study highlight that the administration of CM may ameliorate the impairment of microvascular blood flow induced by a HC/HF meal which would otherwise impede proper blood flow. Further studies are needed to ascertain the potential utility of CM supplementation in mitigating the risks associated with hyperglycemia.

References

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