ACUTE HEMODYNAMIC, HEMATOLOGIC AND DOSE EFFECTS OF INGESTING TWO CREATINE NITRATE BASED DIETARY SUPPLEMENTS

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Abstract

Our aim was to examine the acute (5 hr) hemodynamic (HR and BP) and hematologic profiles for a (1) Placebo (PL), (2) Creatine Monohydrate (CrM, 5 g), (3) Creatine Nitrate (CrN1.5; 1 g CR; 0.5 N), and (4) Creatine Nirtrate 2x (CrN3.0; 2 g CR; 1.0 g N) formula administered in a randomized, double-blind manner with 7 days of washout between treatments. Participants (N=13; 22±2 y) presented for testing after abstaining from exercise and fasting for 8 hrs. Initial unsupplemented measures (Time 0) were assessed, followed by supplement ingestion and serial sampling (0.5, 1, 2, 3, 4, 5 hrs). Variables included heart rate, blood pressure, liver (ALP, AST, ALT), kidney (creatinine, BUN), and muscle (CK, LDH) enzymes, glucose and blood lipids. Analysis included GLM and LSD post-hoc procedures. Significant within group perturbations were noted for LDL-C (CrM, PL), HDL-C (CrN1.5, CrN3.0), triglycerides (CrN3.0, PL), glucose (CrN3.0), creatinine (all), CK (CrN3.0, PL), BUN (all), ALT (PL) over the 5 hr study period (all, $P < 0.03$). Corresponding between group differences (all, $P < 0.05$) were noted for LDL-C (CrN3.0 vs. PL, 5hr), HDL-C (CrN1.5 vs. CrN3.0, 4h) triglycerides (CrN3.0 vs. PL, T0), glucose (CrN1.5 vs. CrN3.0, 2hr), CK (CrN1.5 vs. PL, 2 hr), and ALT (CrM vs. CrN3.0, 4hr). At no time did any analyte exceed clinically normal ranges. Given a lack of consistent patterning for any analyte we have demonstrated that CR, CrN, and CrN2X are well tolerated and do not adversely affect hemodynamic or hematologic function when acutely ingested.

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Rationale

Although use of dietary supplements among U.S adults is common and continues to grow, some state that little research exists on the safety of dietary supplements. It was estimated that dietary supplement sales reached $11.5 billion in 2012, and forecasts suggestion sales will reach $15.5 billion by 2017. Although the safety and efficacy of creatine monohydrate has been established and thoroughly studied, the safety of the combination of creatine monohydrate and nitrate has limited research. Dietary supplement consumption leading to consistent changes in heart rate, blood pressure, liver, kidney, and muscle enzymes, glucose, and blood lipids could be interpreted unsafe. The purpose of this experiment is to examine the heart rate, blood pressure, and blood profile response to four treatments—(1) Placebo (PL), (2) Creatine Monohydrate (CR, 5 g), (3) Creatine Nitrate (CrN; 1 g CR; 0.5 N), and (4) Creatine Nirtrate 2x (CrN2X; 2 g CR; 1.0 g N)—administered in a randomized, double-blind manner with 7 days of washout between treatments.

Methods and Procedures

- Subjects were recruited through flyers and email using the university's Listserv.
- Body mass and height, resting blood pressure, and heart rate were obtained during the familiarization session.
- Fasting blood samples were obtained after an 8 hr fast (Time= 0).
- Blood samples were donated before (0) and after (0.5-hr, 1-hr, 2-hr, 3-hr, 4-hr, and 5-hr) supplementation.
- 4-day food records were obtained at each visit and analyzed.

Statistical Analysis

- Analysis included GLM and LSD post-hoc procedures using IBM SPSS for Windows version 22.0 software (Chicago, IL) and are presented as means ± SD% change from baseline for each treatment group.

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Experimental Design

Subjects

- 13, apparently healthy males (N=13; 22±2 y) were recruited for this study.
- Subjects were informed of experimental procedures and signed a consent statement in adherence with the human subject guidelines of Texas A&M University.
- A standard medical exam and review of subject medical history was performed by a research RN for clearance to participate in the study.

Testing Protocol

- During the familiarization visit, subjects completed a physical exam, medical history form, and signed the informed consent statement.
- After the familiarization, subjects returned to the lab four more times. Subjects were asked to refrain from exercise, alcohol, and non-steroidal anti-inflammatory drugs 48 hrs. prior to each lab visit.
- At each visit, subjects consumed 1) Placebo (PL), (2) Creatine Monohydrate (CR, 5 g), (3) Creatine Nitrate (CrN; 1 g CR; 0.5 N), or (4) Creatine Nirtrate 2x (CrN2X; 2 g CR; 1.0 g N). There was at least a one-week washout period between supplementations.
- Subjects arrived to the lab after an 8-hr fast.
- Blood pressure (auscultatory method) and heart rate were taken in a seated position, immediately prior to each blood sampling time point.
- Blood samples were donated prior to supplementation (Time = 0) and 0.5-hr, 1-hr, 2-hr, 3-hr, 4-hr, and 5-hr post-supplementation.
- EDTA blood collection tubes were pre-chilled on ice. Blood samples were centrifuged immediately and serum was stored in –80°C until analysis.
- Blood variables were analyzed on the Cobas c111 analyzer (Roche Diagnostics, Indianaplis, IN).
- All measurements throughout the study were obtained by lab personnel.
- Self-reported 4-day dietary records were recorded 1-wk prior to each lab visit.

Supplementation Protocol

- Subjects consumed one supplement at each visit.
  1) Placebo (PL)
  2) Creatine Monohydrate (CR, 5 g)
  3) Creatine Nitrate (CrN; 1 g CR; 0.5 N)
  4) Creatine Nirtrate 2x (CrN2X; 2 g CR; 1.0 g N)

Results

- Significant within group perturbations were noted for LDL-C (Cr, PL), HDL-C (CrN, CrN2X), triglycerides (CrN2X, PL), glucose (CrN2X), creatinine (all), CK (CrN2X, PL), BUN (all), ALT (PL) over the 5 hr study period (all, $P < 0.03$).
- Corresponding between group differences (all, $P < 0.05$) were noted for LDL-C (CrN2X vs. PL, 5-hr), HDL-C (CrN vs. CrN2X, 4-hr) triglycerides (CrN2X vs. PL, T0), glucose (CrN vs. CrN2X, 2-hr), CK (CrN vs. PL, 2-hr), and ALT (Cr vs. CrN2X, 4-hr).

Conclusions

- Given a lack of consistent patterning for any analyte we have demonstrated that CR, CrN, and CrN2X are well tolerated and do not adversely affect hemodynamic or hematologic function when acutely ingested.

Tables