

SAFETY OF 28 DAYS OF CREATINE NITRATE SUPPLEMENTATION

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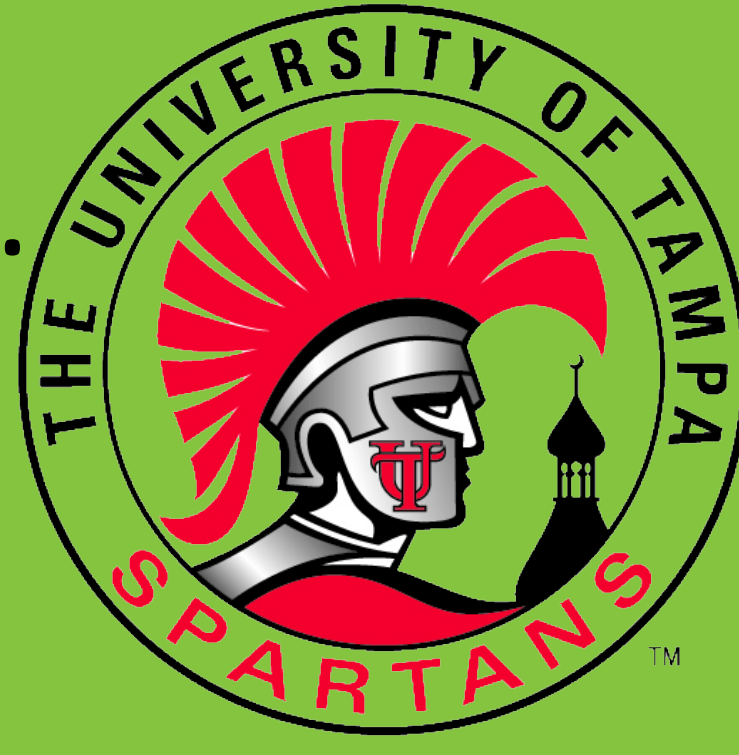
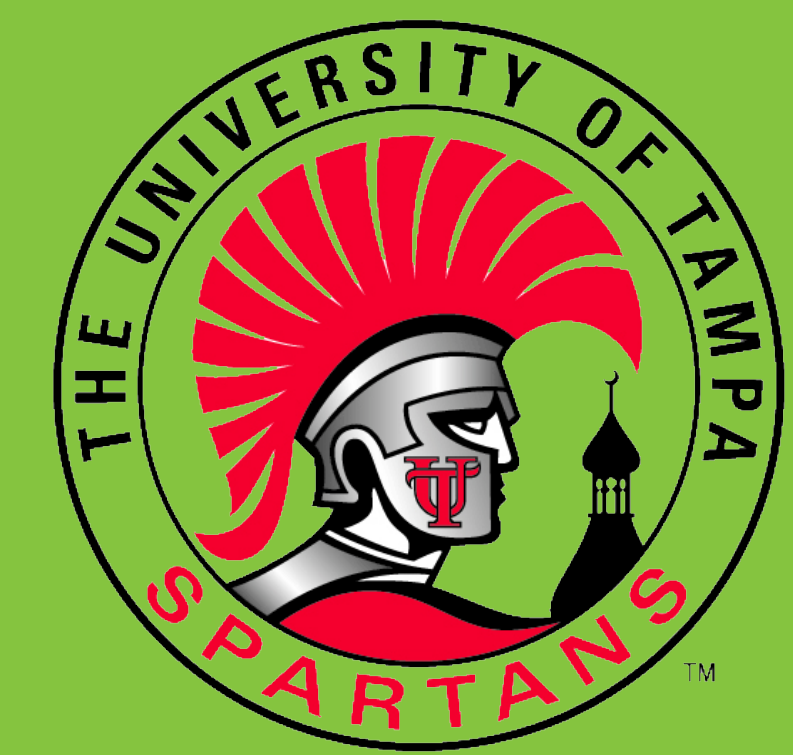
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Introduction

Creatine monohydrate was first observed as an ergogenic aid over 30 years ago when it was reported to increase myosin biosynthesis. Since, it has become a very popular ergogenic aid for its capabilities to increase strength, reduce fatigue, and increase lean mass. Thus, a great number of athletes and recreational fitness enthusiasts have reported consuming creatine. The safety of creatine monohydrate has previously been confirmed. However with each novel form of creatine that emerges, its safety must be verified.

Purpose

The purpose of this study was to examine the safety of a novel form of creatine, creatine nitrate (CN), over a 28 day period.

Methods

27 college aged males and females (76.4 ± 7.2 kg, 172.7 ± 8.89 cm, 20.2 ± 2.1 yrs) participated in this study. Subjects were equally and randomly assigned to consume either 1g (n=14) or 2g (n=13) of CN daily. Blood draws for full safety panels were conducted by a trained phlebotomist prior to and at the conclusion of the 28-day supplementation period. For all variables, see table 1. Dependent samples T-tests were used to determine within condition differences.

Variable	Treatment	PRE	POST	Reference Interval
WBC (x10E3/uL)	2g	6.51 ± 1.56	5.92 ± 1.40	3.4-10.8
	1g	7.73 ± 1.47	6.86 ± 1.72	
RBC (x10E6/uL)	2g	4.60 ± 0.14	4.64 ± 0.27	4.14 - 5.80
	1g	4.64 ± 0.40	4.78 ± 0.37	
Hemoglobin (g/dL)	2g	13.18 ± 1.02	13.35 ± 1.00	12.6 - 17.7
	1g	13.64 ± 1.24	13.96 ± 0.97	
Hematocrit (%)	2g	39.80 ± 2.24	39.58 ± 2.74	37.5 - 51.0
	1g	41.21 ± 3.67	41.67 ± 2.62	
MCV (fL)	2g	86.61 ± 4.77	85.31 ± 4.53	79 - 97
	1g	89.07 ± 2.81	87.29 ± 3.71	
MCH (pg)	2g	28.67 ± 2.09	28.78 ± 1.77	26.6 - 33.0
	1g	29.44 ± 1.37	29.25 ± 1.64	
MCHC (g/dL)	2g	33.01 ± 0.88	33.72 ± 0.78	31.5 - 35.7
	1g	33.09 ± 0.85	33.49 ± 0.76	
RDW (%)	2g	13.78 ± 0.57	13.92 ± 0.63	12.3 - 15.4
	1g	13.11 ± 0.40	13.74 ± 1.20	
Platelets (x10E3/uL)	2g	251.92 ± 65.19	261.62 ± 51.19	155 - 379
	1g	249.50 ± 72.64	259.29 ± 70.50	
Neutrophils (%)	2g	53.92 ± 6.87	54.77 ± 4.88	40 - 74
	1g	55.79 ± 9.10	50.93 ± 11.56	
Lymphs (%)	2g	34.92 ± 6.08	33.38 ± 3.25	14 - 46
	1g	31.21 ± 8.38	34.64 ± 10.70	
Monocytes (%)	2g	8.54 ± 2.07	9.69 ± 2.81	4 - 12
	1g	9.79 ± 2.75	10.79 ± 2.99	
Eos (%)	2g	2.00 ± 0.707	1.77 ± 0.93	0 - 5
	1g	2.93 ± 2.34	3.29 ± 3.56	
Basos (%)	2g	0.62 ± 0.51	0.38 ± 0.51	0 - 3
	1g	0.29 ± 0.47	0.36 ± 0.75	
Neutrophils (Absolute) (x10E3/uL)	2g	3.58 ± 1.28	3.28 ± 0.93	1.4 - 7.0
	1g	4.39 ± 1.53	3.62 ± 1.60	
Lymphs (Absolute) (x10E3/uL)	2g	2.23 ± 0.49	1.97 ± 0.42	0.7 - 3.1
	1g	2.33 ± 0.44	2.24 ± 0.47	
Monocytes (Absolute) (x10E3/uL)*	2g	0.53 ± 0.13	0.55 ± 0.17	0.1 - 0.9
	1g	0.78 ± 0.26	0.74 ± 0.27	
Eos (Absolute) (x10E3/uL)	2g	0.12 ± 0.06	0.10 ± 0.04	0.0 - 0.4
	1g	0.23 ± 0.13	0.23 ± 0.25	
Baso (Absolute) (x10E3/uL)	2g	0.008 ± 0.03	0.008 ± 0.03	0.0 - 0.2
	1g	0.01 ± 0.04	0.01 ± 0.04	
Glucose (mg/dL)	2g	81.77 ± 8.31	83.23 ± 5.73	65 - 99
	1g	81.93 ± 7.80	86.36 ± 6.06	
BUN (mg/dL)	2g	15.92 ± 1.61	17.92 ± 4.57	6 - 20
	1g	14.93 ± 4.63	16.86 ± 6.21	
Creatinine (mg/dL)	2g	0.88 ± 0.11	0.85 ± 0.12	0.76 - 1.27
	1g	0.92 ± 0.17	0.87 ± 0.14	
eGFR If NonAfrican Am (mL/min/1.73)	2g	108.54 ± 14.27	112.31 ± 15.54	>59
	1g	101.93 ± 13.71	107.07 ± 12.55	
eGFR If African Am (mL/min/1.73)	2g	125.15 ± 16.78	128.23 ± 19.21	>59
	1g	117.50 ± 15.88	122.64 ± 15.60	
BUN/Creatinine Ratio	2g	18.07 ± 2.02	21.15 ± 5.58	8 - 19
	1g	16.14 ± 4.24	19.00 ± 5.90	
Sodium (mmol/L)	2g	138.61 ± 2.53	137.85 ± 1.63	134 - 144
	1g	137.93 ± 1.49	138.57 ± 1.55	
Potassium (mmol/L)	2g	3.98 ± 0.28	4.16 ± 0.19	3.5 - 5.2
	1g	3.96 ± 0.22	3.94 ± 0.25	
Chloride (mmol/L)	2g	101.08 ± 2.06	101.31 ± 1.89	97 - 108
	1g	100.71 ± 1.38	100.93 ± 1.49	
Carbon Dioxide (mmol/L)	2g	24.00 ± 1.87	22.30 ± 1.49	19 - 28
	1g	23.14 ± 2.71	22.57 ± 1.22	
Calcium (mg/dL)	2g	9.58 ± 0.27	9.44 ± 0.23	8.7 - 10.2
	1g	9.53 ± 0.28	9.71 ± 0.28	
Protein (g/dL)	2g	6.91 ± 0.26	6.92 ± 0.26	6.0 - 8.5
	1g	6.94 ± 0.35	7.18 ± 0.45	
Albumin (g/dL)	2g	4.50 ± 0.18	4.48 ± 0.23	3.5 - 5.5
	1g	4.38 ± 0.24	4.59 ± 0.20	
Globulin (g/dL)	2g	2.41 ± 0.31	2.43 ± 0.31	1.5 - 4.5
	1g	2.56 ± 0.34	2.59 ± 0.37	
Albumin:Globulin Ratio	2g	1.89 ± 0.27	1.88 ± 0.30	1.1 - 2.5
	1g	1.74 ± 0.25	1.80 ± 0.22	
Bilirubin (mg/dl)	2g	0.68 ± 0.35	0.48 ± 0.18	0.0 - 1.2
	1g	0.59 ± 0.43	0.50 ± 0.15	
Alkaline Phosphatase (IU/L)	2g	82.08 ± 18.40	67.00 ± 23.67	39 - 117
	1g	77.14 ± 32.05	74.93 ± 30.97	
AST (IU/L)	2g	28.00 ± 10.82	29.92 ± 21.37	0 - 40
	1g	30.54 ± 10.30	25.92 ± 8.04	
ALT (IU/L)	2g	21.08 ± 5.07	30.38 ± 38.53	0 - 44
	1g	25.31 ± 6.18	20.54 ± 9.49	

Table 1. Hematology Values

Results

Within condition differences existed for RBC, MCV, MCHC, RDW, % monocytes, serum glucose, BUN, serum creatinine, BUN:creatinine, serum calcium, total serum protein, serum albumin, AST, and ALT in the 1g condition (p<0.05). Within condition differences existed for MCV, MCHC, % monocytes, absolute lymphocytes, serum creatinine, eGFR, BUN:creatinine, CO2, and total bilirubin in the 2g condition (p<0.05). In the 1g condition, RBC, MCHC, RDW, % monocytes, serum glucose, BUN, BUN:creatinine, serum calcium, serum albumin, and total serum protein increased, yet MCV, creatinine, AST, and ALT decreased (table 1). In the 2g condition, MCHC, % monocytes, eGFR, and BUN:creatinine increased, yet MCV, absolute lymphocytes, creatinine, CO2, and total bilirubin decreased (table 1). Common increases for MCHC, % monocytes, and BUN:creatinine were observed between conditions, and common decreases for MCV and creatinine were observed between conditions.

Conclusions

Surprisingly, creatinine decreased in both conditions, which explains the increase in BUN:creatinine. The increase in MCHC and decrease in MCV could be attributed to the nitrate portion of CN, which has been known to augment hemodynamics, but it is more likely that changes in MCHC and MCV were due to variability, as hematocrit, hemoglobin, and RBC did not have the same magnitude of change for both conditions. Despite significant changes in these hematological measures with CN supplementation, all values remained within normal ranges. Therefore, CN appears to be safe in both 1g and 2g servings daily for 28 days.

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