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EVALUATION OF CREATININE AND UREA LEVELS IN CROSSFIT ATHLETES USING NUTRITIONAL SUPPLEMENTS AND ON HIGH-PROTEIN DIETS

Diego Claro de Mello[1], Tatiana Moreira Domingues[1]

ABSTRACT

Background: CrossFit is a modality of high intensity exercise with an increasing popularity. Furthermore, the rising use of nutritional supplements by amateurs and professional athletes of elite sports bring up a new discussion for the safety of both practices. Here, we aim to evaluate whether use of nutritional supplements by CrossFit athletes affect normal renal function. Materials and Methods: We used male CrossFit athletes separated into three groups: a control (C) and a nutritional supplement user group (NSU), and an additional group with NSU who were on a diet (NSDU). The creatinine and urea levels were obtained by two isolated samples of urine (pre and post training) and then analyzed by spectrophotometry. A t test was applied to verify possible differences between C, NSU and NSDU groups. Results: The most used nutritional supplements were creatine and whey protein, and 8 of NSU declared to be on a high protein diet (forming NSDU group). Creatinine levels significantly increased after training, but not urea levels, and samples above normal range were frequently observed after training. However, comparison of creatinine and urea levels among C, NSU and NSDU groups showed no statistical difference in pre and post training conditions. Conclusion: Our data suggest that the use of nutritional supplements and high-energetic diets did not significantly affect urinary creatinine and urea levels, and that the clinical alterations observed here are probably related to a transitory effect of high-intensity training as CrossFit.

Key words: High-Intensity Interval Training. Dietary Supplements. High-protein diet. Creatinine. Urea.

RESUMO

Avaliação dos níveis de creatinina e ureia em atletas de crossfit que usam suplementos alimentares e em dieta hiper proteica

Introdução: CrossFit é uma modalidade de exercícios físicos de alta intensidade com uma popularidade crescente. Além disso, o uso de suplementos alimentares por amadores e atletas de elite, trazem a necessidade de discutir a segurança de ambas as práticas. Aqui, temos como objetivo avaliar se o uso de suplementos alimentares por atletas de CrossFit afeta a função renal. Materiais e Métodos: Atletas de CrossFit do gênero masculino foram separados em três grupos: controle (C) e usuários de suplementos nutricionais (NSU), e um grupo adicional com NSU que estavam em dieta rica em proteínas (NSDU). Os níveis de creatinina e ureia foram obtidos por duas amostras isoladas de urina (antes e após o treino), e então foram analisadas por espectrofotometria. O teste t foi aplicado para verificar possíveis diferenças entre os grupos. Resultados: Os suplementos mais consumidos foram creatina e whey protein, e 8 dos NSU declararam estar em dieta rica em proteínas (compondo o grupo NSDU). Os níveis de creatinina aumentaram significativamente após o treino. No entanto a comparação dos níveis de creatinina e ureia entre os grupos C, NSU e NSDU não apresentaram diferenças significativas nas condições antes e após o treino. Conclusão: Nossos achados sugerem que o consumo de suplementos nutricionais e de dietas altamente energéticas não afetaram significativamente os níveis urinários de creatinina e ureia, e que as alterações clínicas reportadas aqui estão, provavelmente, relacionadas com um efeito transitório do treino de alta intensidade, como o CrossFit.

Palavras-chave: Treinamento Intervalado de Alta Intensidade. Suplementos Nutricionais. Dieta Rica em Proteínas. Creatinina. Ureia.

E-mail dos autores:
mellodc@usp.br
tatiana.domingues@docente.unip.br

1 - Institute of Health Sciences, Universidade Paulista-UNIP, Jundiaí-SP, Brazil.

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INTRODUCTION

CrossFit is a modality of high intensity physical exercise that is on rise nowadays. The training improves muscular effort by combining workouts that involve intensity, variation and functionality in monotonies exercises performed alone and repeatedly, allied to a competitiveness intrinsic, based on Glassman's principles (Cadegiani, Kater, Gazola, 2019; Glassman, 2002; Szeles et al., 2020).

To improve training performance is quite common that athletes use nutritional supplements (Bemben, Lamont, 2005; Butts, Jacobs, Silvis, 2018).

Despite its benefits and effectiveness (Bemben, Lamont, 2005; Kreider et al., 2017; Wang et al., 2018; West et al., 2017), the safety of using supplements is still controversial (Bemben, Lamont, 2005; Edmunds et al., 2001; Poortmans, Francaux, 2000; Rocha, Pereira, 1998; Vega, Huidobro, 2019), especially when there is no professional indication for its use.

A study by Rocha and Pereira (1998) shows the aberrant lack of prior consultation with a professional for the use of supplements in practitioners in Brazilian gyms.

The unrestricted acquisition of nutritional supplements enhances its unnecessary or improper use, without a professional considering the athletes' health. In this scenario, there is no control over the dosage and frequency of use by the consumer, which can harm their health (Rocha, Pereira, 1998; Vega, Huidobro, 2019).

Creatine and whey protein supplements are the most used by elite athletes and by amateurs (Butts, Jacobs, Silvis, 2018; West et al., 2017).

Some studies warn of the risk of kidney injury with the use of creatine supplements and changes in biochemical blood profiles (Chen et al., 2016; Souza e Silva et al., 2019; Edmunds et al., 2001; Veja, Huidobro, 2019).

On the other hand, some studies attest to its safety, however, disregarding the use of supplements for a long time (Souza e Silva et al., 2019; Kreider et al., 2017; Poortmans, Francaux, 2000).

Despite the vies, there is a consensus about its proper dosage and contraindications in people with previous kidney injuries to preserve their health (Souza e Silva et al., 2019; Edmunds et al., 2001; Poortmans, Francaux, 2000; Vega; Huidobro, 2019).

Edmunds et al., (2001), evaluated the progression of kidneys disease in mice models with oral creatine supplementation and observed greater kidney weights, renal fluid contents, cyst scores, serum urea concentrations and lower creatinine clearances compared to control.

Due to the lack of long-term studies, Han: Sprague-Dawley is a great mice model with the potential to mimic the effect of creatine supplementation in humans.

The study Poortmans and Francaux (2000) is one of the long-term studies that assessed the adverse effects of creatine supplementation, but it is statistically limited by the number of participants in the user group (n=9).

So far, the increased in blood creatinine is related to a transitional effect of creatine supplements intake, but remains unclear whether this effect can bring harm in long-term way (Vega, Huidobro, 2019).

Few and different studies evaluated the acute metabolic effect of CrossFit athletes (i.e., biochemical, inflammatory and hormonal) (Cadegiani, Kater, 2019; Cadegiani, Kater, Gazola, 2019; Choi, So, Jeong, 2017; Jacob et al., 2020; Timón et al., 2019) and none of these considered these effects with both creatine and whey protein supplements users.

Choi, So, Jeong (2017) reported no significant changes in many biochemical parameters (e.g., renal, hepatic, lipidic and glucose levels) in CrossFit athletes after 14 weeks of training in South Korea.

Cadegiani and Kater (2019) registered significant changes in creatinine levels, hematocrit, lymphocyte, neutrophils, platelets and eosinophils, lactate, creatine kinase and total testosterone in CrossFit health athletes compared to sedentary control.

Timón et al., (2019) studied the recovery of different biochemical parameters in 48 hours after two different modalities of CrossFit and showed significant differences in the levels of hepatic transaminases, glucose and creatine kinase.

However, all values recovery to baseline after 48h, concluding that CrossFit workouts did not induce a pathological state.

In addition, Cadegiani, Kater and Gazola (2019) further characterized the effect of biochemical and hormonal response to CrossFit training in health athletes and athletes with overtraining syndrome, reporting elevated

estradiol and reduced testosterone in those CrossFit athletes with overtraining syndrome.

Finally, a systematic review by Jacob et al., (2020) shows the main studies available that evaluated the metabolic characterization in CrossFit, and warn about the lack of studies in this area to understand the effects of high-intensity sports.

Given this context, we aimed to assess the acute biochemical effects of CrossFit exercises by measuring levels of creatinine and urea in the urine of individuals with and without nutritional supplement.

We expected that nutritional supplement users may exhibit signals of kidney injury or overload.

MATERIALS AND METHODS

Study design

We used 20 male CrossFit athletes (33.9 ± 6.46 years old) in our study. The athletes regularly trained at CrossFit boxes in Jundiaí and Itupeva (São Paulo, Brazil), according to Glassman's fundamentals. All study was performed in December 2019.

Data collect

An interview was conducted to obtain athletes' information, which consisted in collecting data about CrossFit practices, physical conditions, if they were on diet and if they used any nutritional supplementation and its related habits. The athletes signed the consent statement and this work was approved by the Research Ethics Committee of Universidade Paulista (São Paulo, Brazil), under protocol 14101219.6.0000.5512.

Biological samples

The athletes provided two isolated urine samples: the first one being the first of the day, or at maximum with a 2-hour retention ('pre-training'), and the second one was collected immediately after the regular training ('post-training').

The athletes were instructed to collect the medium stream of urine. Then, 10 mL of urine were collected in new tubes and then samples were centrifuged to remove impurities.

Creatinine determination was obtained after dilution of the urine with distilled water (1:25), using the colorimetric Alkaline Picrate Jaffé methodology (Labtest Diagnóstica Inc. - MG, Brazil).

For urea determination, the samples were diluted 1:50 with distilled water and enzymatic colorimetric methodology was applied, which urea is hydrolyzed by ammonium ions and CO_2 by urease (Bioclin Quibase Ltd. - MG, Brazil).

Finally, the absorbance was obtained by a spectrophotometry at 510 nm for creatinine and 600 nm for urea (FEMTO, Indústria e Comércio de Instrumentos-SP, Brazil).

Statistical analysis

The athletes were divided into two groups based on their use of supplements: i) in a control group 'C' (n = 7), ii) and a nutritional supplement user group 'NSU' (n=13). Also, the NSU had an additional separation with athletes who were on diet 'NSDU' (n=8).

Then, the t-test was applied within and among the groups to analyze information obtained by the questionnaire and to analyze urinary samples before and after training.

We considered statistically significant if p value was ≤0.05, using GraphPad Prism Version 8.0.2 (GraphPad Software Inc., CA, USA) to analyze the data and elaborate graphs.

RESULTS

Use of nutritional supplements and diet by CrossFit athletes

At first, 20 male CrossFit athletes answered a questionary and 13 declared to use nutritional supplements and 7 declared not to use it (NSU and C groups, respectively).

This questionary consisted in general information about these athletes of both groups and provided us the habits of CrossFit practices and about the use of supplements. As previous papers, the main used supplements were whey protein and creatine (Butts, Jacobs, Silvis, 2018; West et al., 2017) (Table 1, Figure 1A-B).

Significantly, the NSU group practices exercise more frequently than the C group (4.429 ± 1.134 days/week in C against 5.538 ± 0.776 days/week in the NSU group; $p<0.05$). Interestingly, 9/11 creatine NSU consume whey protein supplement (Table S1).

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Table 1 - Main information of CrossFit athletes and about nutritional supplements consumption.

	C (n=7)	NSU (n=13)	
	Mean ± SD	Mean ± SD	p value
Height (cm)	175.857 ± 4.947	177.923 ± 5.235	0.418
Weight (kg)	82.143 ± 9.008	81.000 ± 9.301	0.794
Age (years)	35.571 ± 7.569	33.000 ± 5.902	0.410
Time practicing CrossFit (years)	2.057 ± 1.761	2.308 ± 1.032	0.690
Weekly frequency (days)	4.429 ± 1.134	5.538 ± 0.776	0.018*
Time using supplements (years)		3.708 ± 5.608	
Total supplements (number)		2.769 ± 1.641	
Whey dosage (g)		29.550 ± 10.600	
Whey daily frequency (days)		1.639 ± 0.924	
Creatine dosage (g)		4.524 ± 5.296	
Creatine daily frequency (days)		1.273 ± 0.905	

Our data shows that only 7/13 (53.85%) of participants consulted a nutritionist before using supplements, while the other voluntaries consulted non-specialist to their use, such as coach or supplements salesperson or even themselves (self-prescription) (Figure1C).

Most athletes in this research reported having low knowledge about supplements and about the daily dosage to consume (Figure 1D-E). In case of low knowledge or ignorance about the supplement dose, the participants declared to consume a standard dosage indicated at the supplement pack (Table S1).

Importantly, eight CrossFit athletes from NSU group were on a diet, all of them on a high protein diet. Concomitantly, two participants were also on high fats and carbohydrates and one on vegetables diet, forming the 'nutritional supplement and diets users' (NSDU) group (Figure 1F).

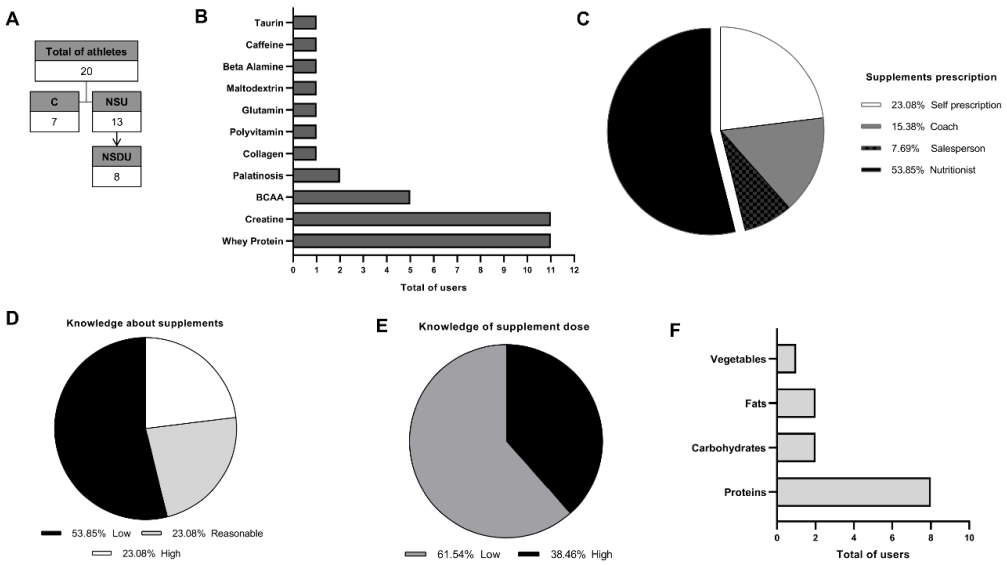

Figure 1 - Use of nutritional supplements and diet by CrossFit athletes. A: Segregation of the 20 athletes into a control, nutritional supplement user and nutritional supplement and diets user groups (C, NSU and NSDU, respectively); B: Types of nutritional supplements and the total used by CrossFit athletes; C: Supplement prescription, separating prescription by a qualified professional (53.85%) and informal prescription (46.15%); D: Knowledge about using supplements; E: Knowledge about the daily dose of supplement consumption; F: Types of diets practiced by supplement NSDU (n=8).

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CrossFit exercises causes changes in creatinine and urea levels

Next, we analyzed creatinine and urea urinary levels before and after usual CrossFit training (Table S2-3).

As expected, creatinine levels significantly increased after training (p=0.0250; t = -2.432) (Feigenbaum, Hoffman, Hunt, 2017). However, urea levels decreased after training but registered no significance difference (Figure 2A).

In order to check an effect on physiology of athletes (clinical signals) we evaluated the percentage of clinical alteration in samples to identify suggestive values for the diagnosis of acute kidney injury and their variation in pre and post-training conditions according to normal ranges to creatinine (39 to 259 mg/dL) and to urea (847 to 2967 mg/dL) (Laboratório Biomédico, [s.d.]; Melo Neto et al., 2017). Values below and above normal range were observed in both groups (Table S2-3). We show that creatinine levels increased when normal-range values decreased after training, while below-range levels of creatinine remained even after high intensity training, similarly to urea below-range levels (Figure 2B).

Following, we verified whether the use of supplements influences the creatinine and urea indices before and after usual training compared to control, which we found no difference between C and NSU groups, despite the increased values in NSU group (Figure 2C).

To evaluate whether dietary intake, especially high-protein diets, causes difference in urinary creatinine and urea levels, we separated 8 users of supplements who were on diet in a new group, 'NSDU', which registered no significance changes in creatinine and urea levels. Interestingly, the NSU group had increased levels of creatinine and urea compared to C and NSDU groups.

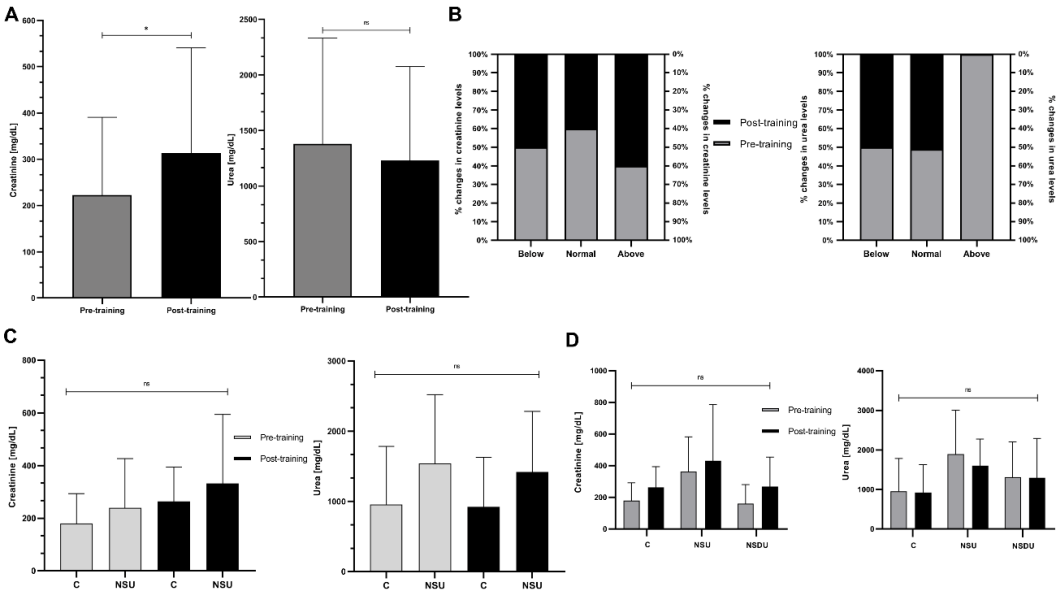

Figure 2 - CrossFit exercise causes changes in creatinine and urea levels. A: Comparison of urinary creatinine (left) and urea (right) levels before and after training for all CrossFit athletes; B: Percentage of clinical alteration in creatinine (left) and urea (right) levels in CrossFit athletes in pre- or post-training conditions classified as 'normal', 'below' or 'above' the normal range; C: Comparison of urinary creatinine and urea levels between Control (C) (n = 7) and Nutritional Supplements Users (NSU) (n=13) groups; D: Comparison of urinary creatinine (left) and urea (right) levels between C, NSU (n=5) and Nutritional Supplements and Diets Users (NSDU) groups (n = 8). *(p=0.0250), ns (not significant).

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DISCUSSION

Here, we compared the urea and creatinine elimination before and after usual CrossFit training in nutritional supplement users (NSU) and those users on high-energetic diets (NSDU) against non-users of nutritional supplements (C), expecting that nutritional supplement users may exhibit signals of kidney injury or overload. We show that urinary creatinine levels exhibited significant changes in CrossFit athletes specially after training, consistent with previous studies (Cadegiani, Kater, 2019; Feigenbaum, Hoffman, Hunt, 2017).

However, no significance difference was obtained comparing NSU, NSDU and C groups. Interestingly, the non-dieting NSU had higher creatinine and urea levels compared to the C and NSDU groups, suggesting that NSDU metabolized the energy supplied by intake of supplements and diets in better way, since creatinine and urea indices were matched with the C and mostly within normal range, as opposed to non-dieting NSU.

The misuse of nutritional supplements may increase the percentage of fat and consequent weight gain, considering that will be an excess of ingested amino acids for the recovery of muscle (Martin, Armstrong, Rodriguez, 2005).

This excess will be eliminated in the urine, which may explain the high levels of both creatinine and urea found in non-dieting NSU. However, as we found no significant differences in the comparisons, a deeper approach to supplement consumption in CrossFit athletes should be considered.

Interestingly, in all groups were observed clinical alterations with increased and decreased creatinine and urea levels before and after training, which can cause or even mean acute kidney injury.

This data suggests that CrossFit intense exercise caused changes in urine creatinine and urea levels in both groups observed here. However, intense exercises, protein-based diet and supplementation, hydration and muscle mass must be taken into account to a precise diagnose for acute kidney injury.

In sporting context, the raise in urinary creatinine levels may be related to the constant conversion of creatine and phosphocreatine into creatinine in skeletal muscle as well as dehydration and non-renal fluid loss (e.g., sweating) that could cause more concentrated excretion of metabolites, which are favorable conditions for acute kidney injury (Bongers et al., 2018; Guyton, Hall, 2006; Huidobro, Tagle, Guzmán, 2018; Siqueira et al., 2009).

According to literature, the acute increase in creatinine effect caused by high-intensity sports and also by supplementation intake is transitory, with the baseline values restoring within ~24-hours (Feigenbaum, Hoffman, Hunt, 2017; Timón et al., 2019; Vega, Huidobro, 2019).

Although we have not evaluated creatinine and urea recovery, increased creatinine was also found in the first urine sample, which is expected to have less interference from exercise and/or use of supplements or diets, suggesting that either CrossFit practices and/or supplementation/diet may be compromising kidney function.

Not least, we also pointed out values below normal range in urinary levels of creatinine and urea, which drew our attention to the fact that users of protein-based supplements or diets also presented values below the reference.

Unlike the increased values, hydration can dilute these metabolites concentrations (Bongers et al., 2018) or, in extreme terms, it can be related to renal insufficiency (Lima, Macedo, 2018), considering the constant excretion of urea and creatinine, the latter being also decreased in the same athletes whose urea level was below normal range (Table S2-3).

Therefore, our data suggest that the use of nutritional supplements and energy-rich diets did not significantly affect urinary creatinine and urea levels in CrossFit athletes.

Even though we have not found significant differences in supplement users, it is important to emphasize that nutritional supplements should be recommended by a professional considering the need and adequate dosage for their use. 76.93% of NSU claimed to use supplements aiming to increase muscle mass (Table S1), presenting us an aesthetic goal that can harm health of these athletes in different ways (Hameed, Sahu, Johnson, 2016, Helms, Aragon, Fitschen, 2014).

In this scenario, athletes are more likely to develop overtraining syndrome (Rogero, Mendes, Tirapegui, 2005) or even rhabdomyolysis (Hopkins et al., 2019), increasingly frequent problems within elite

athletes, reversing the benefits that physical activity should provide.

CONCLUSION

Here, for the first time we assessed whether consumption of nutritional supplementation and energy-rich diets causes kidney injury in CrossFit athletes by analyzing creatinine and urea clearance before and after usual training.

Our data suggest that CrossFit training causes changes in creatinine levels regardless of supplement intake or diet.

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AUTHORS' CONTRIBUTIONS

Mello DC and Moreira TM equally contributed to this work.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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Corresponding author:
Diego Claro de Mello.
mellodc@usp.br
Institute of Biomedical Sciences.
Department of Cell and Development Biology (Room 414).
University of São Paulo-USP, São Paulo, Brazil.

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