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THE USE OF A PRE-WORKOUT SUPPLEMENT CONTAINING AN AMPHETAMINE DERIVATIVE AND ITS EFFECTS ON PHYSICAL PERFORMANCE

USO DE SUPLEMENTO PRÉ-TREINO QUE CONTÉM UM DERIVADO ANFETAMINICO E SEUS EFEITOS SOBRE O DESEMPENHO FÍSICO

USO DE SUPLEMENTO PRE-ENTRENAMIENTO QUE CONTIENE UN DERIVADO ANFETAMÍNICO Y SUS EFECTOS SOBRE EL DESEMPEÑO FÍSICO

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ABSTRACT

Introduction: The quest for better sports performance or simply for esthetic ends has led individuals to seek ergogenic resources indiscriminately to attain their goals. It is believed that nutritional supplements promote better strength, power, focus and better reaction time. Nutritional supplements are used to delay fatigue and increase athletic performance. Also, the anorectics, drugs derived from amphetamines and commonly sought for weight loss, act on the central nervous system by releasing substances that transmit the sensation of not being hungry. Supplements that promise quick solutions to these goals may have compounds in their formulas that compromise health. Objectives: In this study, the potential of creatine and Jack 3D® to boost physical performance and delay muscle fatigue was evaluated in animals that were given the supplements. Methods: The animals underwent 10 weeks of swim training at 80% of the maximum load and received creatine and/or Jack 3D. The muscle contractions were recorded by an electrophysiograph for analysis of muscle fatigue. Results: It was observed that the SED+CR group had significantly different values compared to the SED group and NAT+CR group showed significant differences between groups for the SED, SED+JACK, JACK, NAT and NAT+JACK groups ($p <0.05$). For the two last parameters, the SED group showed a significant difference in relation to the SED+CR, NAT and NAT+CR groups ($p <0.05$). Conclusions: These results demonstrate a possible positive influence of physical exercise associated with the use of creatine, delaying muscle fatigue and making an increase in sports performance possible. ***Level of Evidence III; Development of diagnostic criteria in consecutive patients (with "gold" reference standard applied).***

Keywords: Muscle fatigue; Creatine; Dietary supplements.

RESUMO

Introdução: A busca pelo melhor rendimento esportivo ou simplesmente para fins estéticos tem induzido indivíduos a procurarem indiscriminadamente recursos ergogênicos para atingir o êxito. Acredita-se que a ingestão de suplementos nutricionais pode proporcionar maior resistência, potência, foco e melhor tempo de reação. Os suplementos nutricionais são empregados afim de retardar o surgimento da fadiga e aumentar o desempenho atlético. Também comumente procuradas para emagrecimento estão os anorexígenos, medicamentos à base de drogas anfetamínicas, que agem sobre o sistema nervoso central liberando substâncias que transmitem a sensação de ausência de fome. Suplementos que prometem soluções rápidas para estes objetivos podem conter em suas fórmulas compostos que comprometem a saúde. Objetivos: Neste estudo foi avaliado o potencial da creatina e do Jack 3D® para o desempenho físico e fadiga muscular dos animais que receberam a suplementação. Métodos: Os animais foram submetidos a 10 semanas de treinamento de natação a 80% da carga máxima e receberam creatina e/ou Jack 3D. As contrações musculares foram registradas por um eletrofisiógrafo para análise da fadiga muscular. Resultados: Observou-se que o grupo SED+CR apresentou valores significativamente diferentes em comparação com o Grupo SED e o Grupo NAT+CR apresentou diferenças significativas com relação aos grupos SED, SED+JACK, NAT e NAT+JACK ($p < 0,05$). Nos dois últimos parâmetros, o Grupo SED apresentou diferença significativa com relação aos grupos SED+CR, NAT e NAT+CR ($p < 0,05$). Conclusão: Esses resultados demonstram uma possível influência positiva do exercício físico associado ao uso da creatina, retardando a fadiga muscular e possibilitando um aumento no desempenho esportivo. ***Nível de Evidência III; Desenvolvimento de critérios diagnósticos em pacientes consecutivos (com padrão de referência "ouro" aplicado).***

Descritores: *Fadiga muscular; Creatina; Suplementos nutricionais.*

RESUMEN

Introducción: La búsqueda por el mejor desempeño deportivo o simplemente para fines estéticos ha inducido a los individuos a buscar indiscriminadamente recursos ergogénicos para alcanzar el éxito. Se cree que la ingestión de suplementos nutricionales puede proporcionar mayor resistencia, potencia, enfoque y mejor tiempo de reacción.

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Los suplementos nutricionales son empleados para retardar el surgimiento de la fatiga y aumentar el desempeño atlético. También comúnmente buscados para adelgazamiento están los anorexígenos, medicamentos a base de drogas anfetamínicas, que actúan sobre el sistema nervioso central liberando sustancias que transmiten la sensación de ausencia de hambre. Los suplementos que prometen soluciones rápidas para estos objetivos pueden presentar en sus fórmulas, compuestos que comprometen la salud. Objetivo: En este estudio fue evaluado el potencial de la creatina y del Jack3D® para el desempeño físico y la fatiga muscular de los animales que recibieron la suplementación. Métodos: Los animales fueron sometidos a 10 semanas de entrenamiento de natación a 80% de la carga máxima y recibieron creatina y/o Jack3D. Las contracciones musculares fueron registradas por un electrofisiógrafo para análisis de la fatiga muscular. Resultados: Se observó que el grupo SED+CR presentó valores significativamente diferentes en comparación con el grupo SED y el grupo NAT+CR presentó diferencias significativas con relación a los grupos SED, SED+JACK, NAT y NAT+JACK (p < 0,05). En los dos últimos parámetros, el grupo SED presentó diferencia significativa con relación a los grupos SED+CR, NAT y NAT+CR (p < 0,05). Conclusión: Esos resultados demuestran una posible influencia positiva del ejercicio físico asociado al uso de la creatina, retardando la fatiga muscular y posibilitando un aumento en el desempeño deportivo. ***Nivel de evidencia III; Desarrollo de criterios diagnósticos en pacientes consecutivos (con estándar de referencia "oro" aplicado).***

Descriptores: *Fatiga muscular; Creatina; Suplementos dietéticos.*

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INTRODUCTION

Several ergogenic resources have been used to increase performance, achieve success in competitions, or just for aesthetic purposes, a very common practice in weight training clubs and gyms.

Many of these supplements promise immediate solutions for those looking for muscle growth, reduction in body fat and increased strength. However, some of these have substances in their composition that can cause damage to ones health, such as amphetamine derivatives[1,2] and regulatory agencies have banned selling them in several countries, but lack of knowledge on the part of the population leads to the indiscriminate use of some of these products.

Ergogenic resources are used to enhance physical performance.[3] Some of these supplements contain several ingredients in their formulas and, when ingested, these ingredients can function synergistically increasing various aspects of exercise performance.[4] The lack of rigorous inspection and standardization of these leads to great variation in composition and permits products of inferior quality and/or combined with other harmful components to reach the user without them knowing what they are actually taking.

One of these supplements used to increase performance, lean mass and delay fatigue is a product marketed as Jack 3D®. This class of supplements, called "pre-workout training" supplements, has aroused interest, given its popularity among physiculturists and other athletes in search of good performance and aesthetics, but it is worth mentioning that, despite easy access, it is not authorized by the National Health Surveillance Agency (ANVISA). According to its label, this product includes the following components: arginine-alpha-ketoglutarate, creatine monohydrate, beta-alanine, caffeine, 1-3 dimethylamylamine and schizandrol A (*Schisandra chinensis*). Some of these components have been described in the literature for their effectiveness, but other still need more studies on their possible benefits and potential side effects, as well as clarification about their action when used alone and/or in association with other substances. One of the components, 1-3 dimethylamylamine (DMAA) is an amphetamine derivative, recognized for its potential for chemical dependency. Derived from the geranium, a species of flower, DMAA is found in dietary supplements, in particular those that promise weight reduction and athletic performance,[6] which are generally used before starting each practice. The interest in drugs derived from amphetamines is associated with physiological factors such as feelings of increased energy, self-confidence, well-being, loss of appetite, euphoria and increased sexual performance,[7] which would explain the sensation of heightened disposition for physical activity reported by users of the supplement mentioned above.

Among the most common characteristics of these substances is the psychoactive action in the central nervous system (CNS), causing changes in mood, behavior, and cognition.[7] The action mechanism of amphetamines occurs in the central nervous system (CNS) through an increase in the availability of biogenic amines serotonin (5-HT), dopamine (DA) and norepinephrine (NE) in the synaptic cleft. These neurotransmitters are released from non-vesicular stores through a connection to the monoamine transporters, functioning as false substrates, and thus effecting reverse neurotransmitter transport.[8] Research in the area demonstrates a chain of reactions that occur in the central nervous system as a result of drug use and that, to some extent, with abusive use, increase dopaminergic transmission in the mesocorticolimbic pathways and in the NAc, which is perhaps the determining factor in the establishment of dependence.[7] Understanding the mechanisms of these drugs in the central nervous system can allow health professionals to make athletes and people participating in physical activities aware of the risks of using certain substances.

Caffeine is consumed by a large part of the population as a regular constituent of the diet as coffee and is arguably one of the most used ergogenic resources in the world.[9] The recommended amount for a caffeine supplement intended for athletes is between 210 and 420 mg per portion. In sports, caffeine has shown an interesting ergogenic effect, as intake reduces muscle pain, increases oxygen consumption during exercise and delays fatigue, mainly due to its lipolytic effect.[10]

The role of creatine during exercise and in its recovery began to be investigated as an ergogenic resource to enhance the physical performance of Olympic athletes.[4] Used alone, creatine supplementation triggers mechanisms that favor the increase of muscle strength, such as an increase in phosphocreatine (PC) muscle content, an increase in the speed of PC regeneration during exercise, greater activity of the glycolytic pathway through the buffering of H+ ions due to the reduced relaxation time associated with improvement in calcium pump activity, as well as an increase in muscle glycogen content.[11] Evidence seems to suggest that physical training combined with creatine supplementation may be effective for better sports performance.[12]

Muscle fatigue can be defined as the inability to maintain the strength required in a contraction.[13] There are several physiological mechanisms that may be responsible for the state of neuromuscular fatigue[12] because it involves several factors, such as the central nervous system, the peripheral nerve, the neuromuscular junction and the skeletal muscles. Initially, any of these systems may be involved in the muscle fatigue process and the significant physiological factor may be of mechanical, metabolic or electrophysiological character.[1]

Measurement of the isometric force of the tetanic muscle contraction can be considered an important tool for the evaluation of strength and muscle fatigue.[14] Using the technique of preparation of the anterior tibial muscle and direct electrical stimulation of the sciatic nerve, it is possible to maintain innervation and vascularization during the experiment maintaining its physiological properties. Understanding fatigue is useful in the search for improving protection of the muscles against overload during sports training. The objective of this study is to analyze the effect of supplements based on amphetamine derivatives, in combination with creatine, as well as other components, on physical activity in mice submitted to swimming.

METHODS

The study was conducted with the approval of the Institutional Review Board (IRB) of the Universidade do Vale do Paraiba Animais/IPD-UNIVAP under protocol A02/CEUA/2013. In the present study, male mice (Swiss), 06 weeks of age, weighing between 20 ± 3 g were used. The animals were kept in polyethylene boxes (five animals per box) with controlled temperature (22 to 25°C), relative humidity (40 a 60%) and photoperiod (12-hour light/dark cycle), and a diet of water and feed ad libitum. The animals were divided into six groups, with five animals per group:

Group 1 (SED): sedentary, Group 2 (SED + CR): sedentary supplemented with creatine, Group 3 (SED + JACK): sedentary supplemented with Jack 3D®, Group 4 (NAT): exercised in the pool, Group 5 (NAT + CR): exercised in the pool and supplemented with creatine, Group 6 (NAT + JACK): exercised in the pool and supplemented with Jack 3D®.

The animals received creatine monohydrate (Médica Integral, Embu-Guaçu, SP, Brazil) dissolved in water, orally with the aid of a gavage needle, a technique used for the administration of liquid food directly into the stomach, daily for 10 weeks. In the first week of supplementation (loading or overload phase), the dose of creatine was 0.3 g of the body weight of each animal. In the following weeks (maintenance phase), the dose used was 0.075 g. The dosing of Jack 3D used was proportional to that suggested for human intake. It was administered orally by gavage needle 30 minutes before physical activity.

Experimental Protocol

All the animals remained idle in the vivarium for 10 days for adaptation to the environment. The animals in groups G3, G4, and G5 completed a period of adaptation to the water 5 days a week for a week in daily 30-minute load-free swimming sessions and then underwent physical resistance training for 10 weeks, carried out in swimming sessions (30 minutes/day, three days a week, on Mondays, Wednesdays and Fridays, always conducted in the afternoon). Figure 1 shows a flowchart of the experimental protocol.

The training was conducted with an overload of 80% of the maximum load supported by each animal, which was determined through the Maximum Load Test.[16] For the preparation of the loads, lead spheres were weighed on a precision scale (Bel®) and attached to the body of the animals using elastic vests. A fiberglass tank measuring 100 cm (length) X 50 cm (width) X 60 cm (height) was used for the physical activity. Drinking water was used and changed after each training session, always with the temperature adjusted to 33ºC.

For the muscle contraction test, an isometric force transducer was used. The animals were anesthetized and sedated and then the right tibial muscle was dissected, and an incision was made to locate the sciatic nerve, which was connected to an electrode to receive electrical impulses. The tendon was also dissected and connected to an electrophysiograph to record the contractions made by the muscle. The muscle, tendons, and the nerve were kept moistened with saline solution.

After establishing the minimum voltage to which the muscle responded, stimulation was applied in pulses of 1HZ, and the voltage was gradually increased until we found the maximal voltage with a stimulus two minutes in duration. The muscle and tetanic contractions were stimulated using the isometric transducer to induce the tetanic contraction. The frequency was increased to 50Hz for a period of 10 seconds. Muscle fatigue was characterized by the inability to maintain the muscle contraction.

Responses to the stimuli were recorded on an UGO BASILE GEMINI 7070 electrophysiograph. The paper speeds used for the recordings were 005 mm/s and 300 mm/s, respectively.

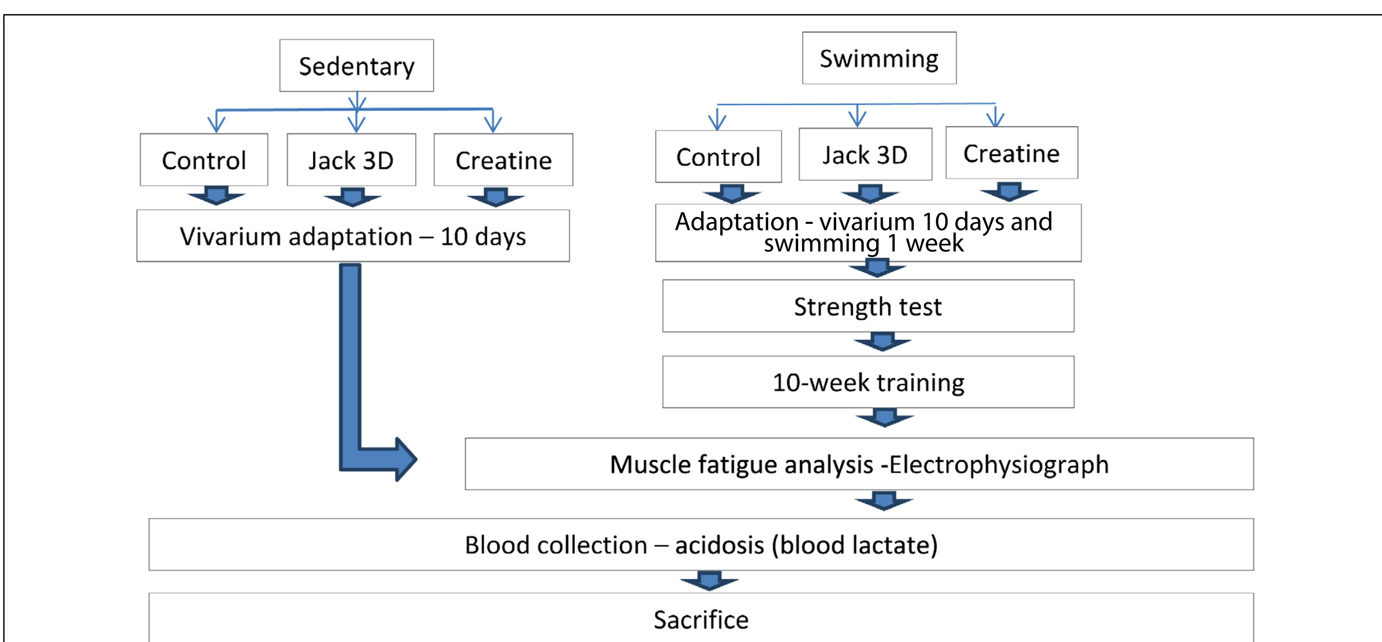

Figure 1. Experimental procedure.

Blood samples (~25μl) were obtained by sectioning the caudal extremity of each animal and placing the samples on test strips for quantification of lactate (BMLactate®). The collections were performed before the muscle contractions and after the last tetanic contraction. The animals were anesthetized and sedated with an intraperitoneal (IP) injection of ketamine 10% and xylazine 2% in a dose of 50 microliters of each. Following the procedure, the animals were sacrificed, still under anesthesia, by intracardiac injection of potassium chloride (KCL) at 20%.

The GraphPad Instat (Version 6.0 GraphPad Software Inc.) statistical program was used. The results were demonstrated using the ANOVA method and the Tukey-Kramer multiple comparison tests were applied to verify the mean values of the different groups. Differences were considered significant for $p<0.05$. For the comparative weight (g) values, the T test was used with differences being considered significant for $p<0.05$.

RESULTS

Through Figure 2 it is possible to demonstrate the behavior of the mean maximum tension (g) or maximum peak obtained for the anterior tibial muscle of the six groups analyzed during the three electrically induced tetanic contractions. There were no significant changes in the means of this variable in the different groups ($p <0.05$).

Figure 3 shows the values of the area under the tetanic curve (cm^2), during 10 seconds of each induced contraction and corresponds to the capacity of the muscle to resist fatigue and maintain its maximum contraction tension, or close to it, for the longest time possible. It is observed that the SED+CR Group had significantly different values when compared to the SED Group and that the NAT+CR Group had significant differences when compared to the SED, SED+JACK, NAT and NAT+JACK Groups for $p <0.05$.

Figure 4 shows the relative percent drop from the initial peak (maximum tension) after 10 seconds of tetanic contraction. With this parameter it is possible to analyze which individuals succeeded in maintaining the contraction with less of a drop after the 10 seconds of tetany. Significant differences were observed between the SED Group and the SED+CR, NAT and NAT+CR Groups ($p < 0.05$).

In Figure 5, the parameter observed relates to the analysis of lactate, where the sedentary group with Jack 3D added to their diet had higher lactate levels than the other groups.

In general, the three sedentary groups, whether or not they were given supplements, had higher mean values than the groups that exercised and the acidosis in the swimming + creatine group was lower than all the other groups, although not statistically significantly.

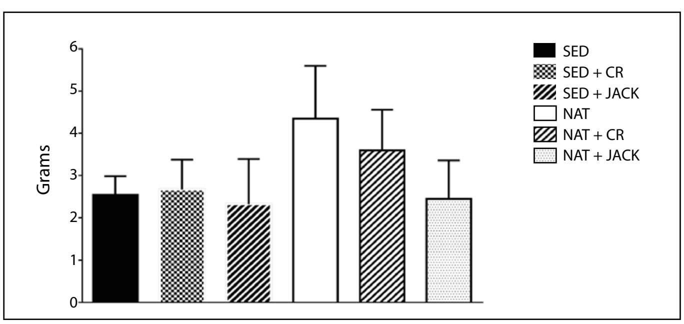

Figure 2. Maximum peak of intensity of the tetanic contraction in mice submitted to 10 weeks of training and supplementation. The data represent the mean ± SD; n=5; * $p < 0.05$ and when compared with the response obtained in the SED control group (ANOVA, followed by the Tukey-Kramer multiple comparison test).

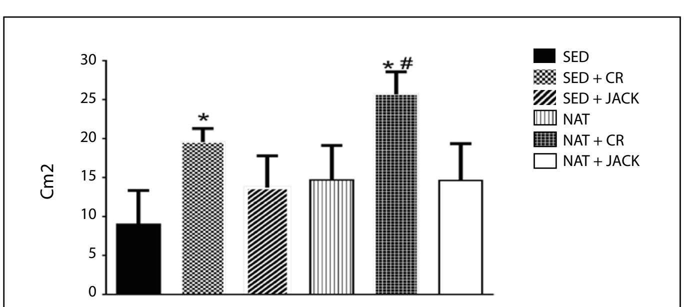

Figure 3. Area under the curve during 10 seconds of tetanic contraction in Swiss mice for the different experimental groups. The data represent the mean ± SD; n=5; * $p < 0.05$ when compared with the response obtained from the control group (SED); # $p < 0.05$ when compared with the response obtained in the group that swam (NAT). (ANOVA, followed by the Tukey-Kramer multiple comparison test).

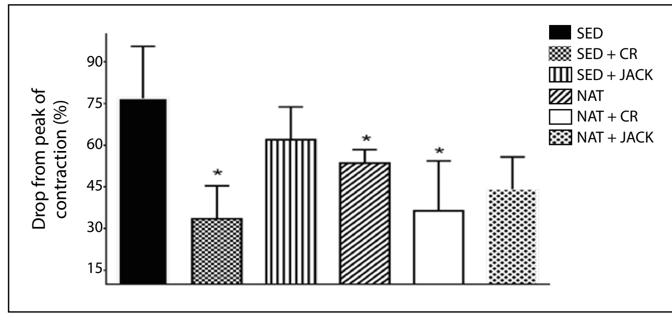

Figure 4. Percent drop in maximum peak 10 seconds after the maximum peak of the tetanic contraction for the different experimental groups. The data represent the mean ± SD; n=5; * $p < 0.05$ and when compared with the response obtained in the SED control group (ANOVA, followed by the Tukey-Kramer multiple comparison test).

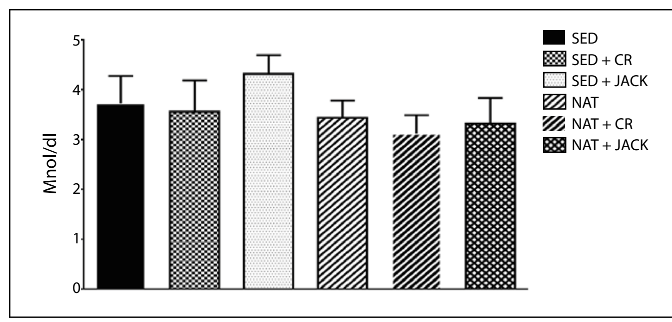

Figure 5. Graph of the concentration of blood lactate in the different experimental groups of Swiss mice after the muscle contraction test. The data represent the mean ± SD; n=5; * $p < 0.05$ and when compared with the response obtained in the SED control group (ANOVA, followed by the Tukey-Kramer multiple comparison test).

DISCUSSION

It was demonstrated that swim training with 80% of the maximum load for 10 weeks, using creatine or the supplement in associative regime (JACK 3D®), did not significantly alter the mean maximum intensity of the contraction (g), even in the group that received the supplement containing DMAA, where, knowing that these derivatives can change the levels of excitatory transmitters, such as serotonin, adrenaline and norepinephrine, a higher peak of power was expected. The data were obtained from the three electrically induced tetanic contractions of the anterior tibial muscle. We emphasize that this parameter relates to power and the ability to produce strength in the shortest period of time possible. The training conducted in this experiment is aerobic in character, corroborating several other studies that demonstrate that in order to increase the production of maximum contractile force resistance training should be prioritized. Additionally, the supplement in question by itself did not demonstrate efficiency for these parameters.

As regards the mean area under the tetanic curve (Graph 2), the results indicate that the SED group had a significantly lower mean than the group that used creatine as an ergogenic resource, SED+CR. For the same variable, the NAT+CR group obtained significantly higher means than SED and NAT groups. These results seem to point to a possible contribution of supplementation with creatine to delaying the process of muscle fatigue.

For muscle tension after 10s of tetanic contraction (Graph 3), the ability to maintain the initial muscle tension after 10s was significantly lower in the sedentary group than in the SEC+CR, NAT and NAT+CR groups, which shows that the groups supplemented with creatine and the groups that performed swimming exercises were able to maintain muscle tension closer to the initial level, demonstrating greater resistance to muscle fatigue. No benefits were observed in the groups that used JACK 3D for this variable.

As regards blood lactate, the trained groups had lower concentrations than their respective control, which highlights the importance of exercise to increase aerobic capacity, providing the muscles with contractile capacity for a longer period. The NAT+JACK group values were greater than those of the NAT and NAT+CR groups, suggesting that this supplement does not contribute to the maintenance of lactate levels. However, none of these lactate values were statistically significant.

We can also suggest that the supplement in associative regime (JACK 3D®) includes DMAA, an amphetamine derivative, has an anorexic effect and can lead to a reduced appetite, an assumption that would compromise adequate intake of nutrients, for example, carbohydrates, an energetic substrate essential for muscle activity. With a reduced store of muscle glycogen, sports training performance will be compromised, not achieving adequate physical adaptations, such as lower performance during the tetanic contraction test and higher metabolic acidosis.

CONCLUSIONS

We conclude that, at least in our experimental conditions, supplementation with creatine associated with physical training promotes better results than the supplement in associative regime (JACK 3D®), with regard to tolerance to muscle fatigue. Additionally, JACK 3D® did not demonstrate any significant differences for the peak of maximum contraction, even though it contains an amphetamine derivative, which could alter the levels of excitatory transmitters.

The indiscriminate use of supplements in addition to causing side effects (chemical dependence, risk of acute myocardial infarction, behavioral changes), may fail to deliver the results promised in their commercial advertising. Further studies are needed to disseminate the knowledge and awareness of professionals who work in this area about the risks of these products.

All authors declare no potential conflict of interest related to this article

AUTHORS' CONTRIBUTIONS: Each author made significant individual contributions to this manuscript. RCAF was responsible for conducting the experiments, preparation for and writing the text. WR was the master's advisor and fundamental in the conception of the study. RALO was fundamental in interpreting the data and assisted with discussion of the data presented in this manuscript. WSF was responsible for statistical analyses and preparation of the graphs. RCAF and WSF conducted the bibliographical research and review of the manuscript. All authors contributed to the intellectual concept of the study.

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