Optimum timing in creatine supplementation for improved sporting performance

José Manuel Jurado-Castro[1]*, Ainoa Navarrete-Pérez[2], Antonio Ranchal-Sánchez[3,4], Fernando Mata Ordóñez[5]

[1]Unidad de Metabolismo e Investigación Pediátrica. Instituto Maimónides de Investigación Biomédica de Córdoba (IMIBIC). Hospital Universitario Reina Sofía. Universidad de Córdoba. [2]Grupo de investigación Neuroplasticidad y Estrés Oxidativo. Departamento de Bioquímica y Biología Molecular. Instituto Maimónides de Investigación biomédica de Córdoba (IMIBIC). Universidad de Córdoba. [3]Instituto Maimónides de Investigación Biomédica de Córdoba (IMIBIC). Hospital Universitario Reina Sofía. Universidad de Córdoba. [4]Departamento de Enfermería, Farmacología y Fisioterapia, Facultad de Medicina y Enfermería. Universidad de Córdoba. [5]CEAN, Centro de Estudios Avanzados en Nutrición. Córdoba.

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Summary

Creatine is a sports supplement with high scientific evidence on its effects on performance and with emerging health's results, including for vegetarian athletes and older adults. The creatine type and effective doses have been well studied, presenting consistent results. However, not many studies have evaluated the ingestion timing in terms of its interaction with the creatine effects. The aim of this review is to analyze the different existing scientific literature on creatine supplementation protocols and their interaction with the timing of ingestion, in order to assess whether there is a greater effect of the ergogenic dose of creatine considered effective when It is ingested before, post workout or at another time of the day. The results of this work presented different types of protocols and doses in creatine supplementation, despite being diverse the protocols shown in the literature, the most effective consisted of a consumption of 0.3 g/kg/d for five days, followed by a consumption of 0.03 g/kg/d, thus achieving a greater reserve of PCr in skeletal muscle. Studies showed greater benefits when creatine intake was carried out in the moments close to workout due to greater blood flow, the studies pointing to significant improvements in post-workout consumption, since creatine can increase the rate of glycogen uptake in muscle and increase insulin sensitivity.

Key words:
Creatine. Sport. Dietary Supplements. Athletic performance.

Timing óptimo en la suplementación con creatina para la mejora del rendimiento deportivo

Resumen

La creatina es un suplemento deportivo con una elevada evidencia científica sobre sus efectos en el rendimiento y con resultados emergentes en la salud, incluida la de deportistas vegetarianos y adultos mayores. El tipo de creatina y las dosis efectivas, han sido bien estudiadas presentando resultados consistentes. Sin embargo, no son muchos los estudios que han evaluado el momento de la ingesta en cuanto a su interacción con los efectos de la creatina. El objetivo de esta revisión, es analizar la diferente literatura científica existente sobre los protocolos de suplementación con creatina y su interacción con el momento de la ingesta, con el fin de evaluar si existe un efecto mayor de la dosis ergogénica considerada efectiva de creatina cuando esta es ingerida antes, después del entrenamiento o en otro momento del día. Los resultados de este trabajo presentaron diferentes tipos de protocolos y dosis en la suplementación con creatina, a pesar de ser diversos los protocolos mostrados en la literatura, el más efectivo constó de un consumo de 0,3 g/kg/d durante cinco días, seguido de un consumo de 0,03 g/kg/d consiguiendo de esta forma, una mayor reserva de PCr en el músculo esquelético. Los estudios mostraron mayores beneficios cuando la ingesta de creatina se realizó en los momentos cercanos al entreno debido al mayor flujo sanguíneo, apuntando los estudios a mejoras significativas en un consumo post-entreno, debido a que la creatina puede aumentar la formación de de glucógeno en el músculo y aumentar la sensibilidad a la insulina.

Palabras clave:
Creatina. Deporte. Suplementos dietéticos. Rendimiento deportivo.

Correspondence: José Manuel Jurado-Castro
E-mail: juradox@gmail.com

Introduction

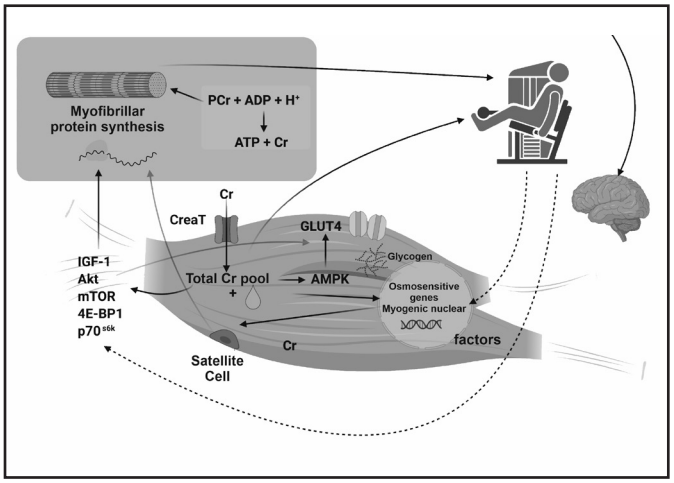
The use of sports supplements (SS) in sport is considerably widespread. In a recent study performed on Spanish athletes from different modalities, it was observed that 64% of them had consumed SS[1]. The reasons behind athletes taking SS are diverse, with the main reported motivation being to improve performance, according to scientific literature[2]. With the aim of finding ways to improve performance, there are some ergogenic aids, such as creatine monohydrate (CrM) with a high level of evidence. In this respect, recently the International Olympic Committee[2] took a positioning in which it assessed the different SS and their degree of evidence, in which creatine (Cr) is considered a SS in Group A, i.e., with a high level of evidence as an ergogenic aid. Over eighty reviews report the ergogenic and therapeutic effect of Cr[3]. Various meta-analyses and systematic reviews[4,5] support these affirmations, observing improvements in lower and upper body strength, in high intermittent intensity training (HIIT), muscle mass and recovery, though few studies indicate positive effects on aerobic performance[6].

Cr (methylguanidoacetic acid) is a natural nitrogenous organic acid[7] which is synthesised endogenously in the liver, pancreas and kidneys from three amino acids: arginine, glycine and methionine, at 1-2 grammes of Cr per day[8], as well as being contributed exogenously through food, which compensates for losses of approximately 2 g/day[9]. Once synthesised, 90% of the Cr is stored in the skeletal muscle in the form of phosphocreatine (PCr) (60%) and free Cr (40%)[10]. The main action of the PCr is linked to the re-synthesis of ATP via the transfer of the phosphate group to ADP. The re-synthesis of ATP measured by the PCr, allows for increased performance during short-duration high-intensity actions, in which the phosphagens channel is the main source of energy. Therefore, the effect of Cr supplementation has been viewed with particular interest in terms of improving performance in high-intensity exercises lasting less than 30 seconds, proving most evident where there are repeated periods of intense exercise, such as strength training, for example[11]. Furthermore, strength training combined with taking Cr, allows for an increase in the intensity of the training, which entails greater adaptations and muscle mass gains[12,13].

Added to the amplifying effect of performance in these kinds of actions, the reaction catalysed by the creatine kinase enzyme has been seen to consume a hydrogen ion (H+), which can contribute to an intracellular buffering action during exercises that entail a high glycolytic pathway activity, and therefore, a lower drop in pH and of neuromuscular fatigue associated (Figure 1).

In terms of the Cr supplementations doses and protocols, a diverse and broad bibliography has been found, however, literary results regarding the most beneficial timing in terms of Cr consumption are not so abundant[14]. The main objective of this review is to analyse the different scientific literature available about Cr supplementation protocols and interaction with intake timing, with the aim of assessing whether there is a greater effect on the ergogenic dose of Cr considered effective when consumed before or after training, or at another time during the day.

Figure 1. Proposed mechanisms of creatine.



Variables to consider in the responses to creatine supplementation

The differences in response to supplementation, must be considered by the different professionals as part of the customisation of the diet and supplementation programme, taking into account variables such as the type of diet and age.

Vegetarian or vegan diet

Cr is found naturally in meat and fish, and in very small quantities in some vegetables, which means that due to the reduction or lack of intake of these food groups among vegetarians or vegans, Cr consumption is lowered or practically absent[15]. Furthermore, if vegan athletes do not introduce vitamin B12 supplementation into their diet, they may suffer a deficiency of this micro-nutrient, interfering with their endogenous synthesis of methionine, and with it, a lower biosynthesis of Cr[16].

Among these demographics, it has been observed that the Cr content in different tissues, such as muscle, plasma, red blood cells, is lower than that of omnivores, though not in brain tissue[17]. Studies performed using an analysis of lateral vast muscle biopsy samples, have observed that total Cr levels (Cr + PCr) are lower in vegetarians than in omnivores, specifically: some 10-15% of the total; 7-10% of PCr and 7-26% of the Cr[18]. This could indicate that CrM supplementation could be of interest for athletes who follow this food pattern, because given the low levels of this amino acid on a muscle level, this could affect performance at high intensity due to the premature appearance of fatigue[19]. Likewise, the results from a recent systematic review[18] reveal how Cr supplementation in vegetarians is effective in increasing Cr and PCr to higher levels than those obtained in omnivores. The minimum recommended intake for this demographic, is around 1 g/d (amount equivalent to that found in one fillet of meat)[20]. Therefore, Cr supplementation among vegetarians could be an efficient ergogenic aid to increase performance, with no

current conclusive data available of how this effect may be greater than that observed in omnivores[18].

Age

Despite the vast amount of literature available regarding the effectiveness of Cr supplementation in adult athletes, there is limited data in terms of children or teenagers. This lack of available literature is probably attributable to ethical restrictions, security issues and methodological challenges. Although its use in children and teenagers has commonly been discouraged[21] there is no evidence of any dangers or adverse effects on this demographic[22]. In fact, the only clinically proven side effect is a 1-2 Kg weight increase, with no evidence that its short- or long-term use (as long as the 30 g/d dosage over a period of 5 years is not exceeded) has negative effects on a healthy population from infancy to old age[23].

Some studies have shown that Cr content reduces with age, what is not known is if this is due to low levels of physical activity or the ageing process[24]. Furthermore, the quantity and amount of Type II fibres diminishes progressively with age, with some studies[25] observing that individuals with more type II fibres and a larger transversal session area, respond better to Cr supplementation, which can determine that older adults have an attenuated anabolic response to Cr supplementation[9].

A recent review[26] that assessed Cr supplementation combined with exercise on healthy older adults, reveals a positive effect with at least 12 weeks of resistance training. Its supplementation combined with moderate to high-intensity exercise in older people, would lead to an improvement in muscle health. This issue is particularly important in all countries with progressive ageing, given the special rate of morbidity associated with sarcopenia, such as fractures caused by falls, for example.

In addition to these benefits applicable to training and physical activity in older people, other benefits of Cr supplementation have been found, related to a greater capacity to reason quickly and think abstractly, known as "fluid intelligence", refuting double-blind tests performed on subjects of advanced age, who underwent memory tests[27,28]. A possible useful effect has also been associated, regarding spinal and bulbar muscular atrophy, as during the development of this pathology, there is a drop in intramuscular Cr levels, possibly related to the appearance of muscle weakness in these patients. Clinical trials are currently underway to assess the use of Cr as treatment for this pathology[29]. A relationship has also been observed between supplementing and an improvement in the state of health, despite ageing, with better lipid profile, lower growth of body fat compartment, and a reduction of oxidative stress and bone resorption among other effects[30].

Safety of creatine

To date, not many studies have assessed the safety of Cr with a comparison of its effects on performance or on certain pathologies[31,32]. Studies about safety among males using CrM can be found in scientific literature, observing renal dysfunction, compartment syndrome in the legs, rhabdomyolysis, ischaemia cerebrovascular accident, atrial fibrillation, acute cholestatic hepatitis injury, and toxic hepatitis. However, this data has not been replicated with placebo controlled clinical trials[3].

A recent study has assessed the adverse outcomes of CrM supplementing on non-pregnant post pubertal females, concluding that this supplement is safe for this demographic[3]. A similar conclusion to the results of other reviews performed on males or in mixed-sex studies, in which CrM taken within the dose and guidelines recommended by the different manufacturers and sporting-nutrition organisms around the world, appear to be safe, with no advantages revealed of using other forms of Cr[31], which furthermore tend to have a higher market cost.

Supplementation protocols and optimum consumption dose

The study by Roger Harris *et al.*[20] revealed how CrM supplementation increased muscular Cr content by around 20%. Most of the studies with Cr commonly used a protocol based on the study by Hultman *et al.*[33], in which they compared different protocols and discovered the most effective was supplementing with a load phase of 5-6 days, with a standard dose of 20 g/d or 0.3 g/kg/d, followed by a maintenance phase of 2 grammes a day or 0.03 g/kg/d.

With regards to the Cr load protocol, a recent study performed on 17 trained males, revealed how intakes of 20 g/d over 5 days combined with strength training, produced an increase in performance[34]. However, the vast majority of studies that have assessed the effects of Cr supplementation with the load and maintenance phase, have been performed on males. In the case of females, another trial has been carried out with the aim of assessing an increase in physical aptitude, performance or body composition, in response to four weeks of HIIT training combined with Cr supplementation. In this case, the initial supplementation was 0.3 g/kg/d over 5 days, followed by a maintenance phase of 0.1 g/kg/d for 23 days, combined with HIIT. The study concluded that the addition of Cr did not improve cardiorespiratory aptitude, nor did it improve the body composition of the females tested[35]. However, more studies are required that analyse the influence on both sex and gender of Cr supplementation.

The Cr load phase may increase body weight by approximately 2% due to an increase of intracellular water caused by the osmotic effect of the Cr[36]. It is important to advise that this effect is necessary as different studies have revealed the activation of specific osmosensitive genes in response to Cr supplementation, and therefore, it forms part of the action mechanism[37].

In other supplementation protocols, an intake of only 0.1 g/kg/day has been chosen, though this final protocol requires more days to cause an ergogenic effect[38]. In this respect, Galvan E, *et al.*[32], performed a trial on 13 healthy and physically active adults, who were split into 4 groups, each supplemented with a different dosage of CrM (1.5 g, 3 g, 5 g

and placebo, respectively), with the aim of assessing the dependent effects of the doses on safety and performance rates of exercise. The authors conclude that up to 3 g/day is a safe and effective dose in terms of changes in strength and body composition.

Yáñez-Silva A, *et al*.[39] performed a study on young elite football players with the aim of establishing the effects of CrM supplementation on muscle power. To do this, they used low consumption doses, with 0.03 g/kg/d for 14 days. The footballers were split into two groups, with one group consuming Cr the other a placebo. This was also a double-blind study. The anaerobic Wingate test was used to measure the results. Significant improvements were observed comparing power before and after the supplementation period. The placebo group also obtained improvements (influenced by training or external factors), but not as significant as those in the group that consumed Cr.

Another study performed on men40 examined the effect of the so-called "load phase", analysing two methods of dosing daily intake. The subjects were split into two groups, and over 5 days they consumed CrM, the first group taking 4 x 5 g/d and the second group consuming 20 x 1 g/d, which obtained a lower urinary excretion of Cr and methylamine, leading to an estimated increase of Cr in the entire body and most probably in the muscle. The authors concluded that an intake of small doses, distributed evenly throughout the day, generated an improvement in the body and muscle retention of Cr.

Optimum timing in creatine supplementation

Attempts have been made to clarify the optimum timing for Cr consumption, however, studies to this effect are more limited (Table 1) compared to those performed for other supplements[14,41].

Regarding the most beneficial timing for Cr consumption, most studies take Antonio y Ciccone[42] as reference, in which they compare the effects of supplementing before and after training. 19 body-building males participated in this study, competing 5-day programmed training for 4 weeks. The study showed that consuming 5 gr of CrM post-training, generated greater benefits in strength and improvements to body composition compared to pre-training consumption.

In a later study performed by Candow *et. al*[43], they observed that 32 weeks of Cr supplementation (0.1 g/kg) in healthy older adults (50-71 years) immediately after strength training, led to greater lean mass compared to consumption immediately before exercise. However, the muscle strength increases produced by the Cr occurred regardless of the intake timing.

The observation from the Antonio y Ciccone[42] study was not confirmed by the other study performed by Candow *et al*.[44], whose aim was to compare the effects of Cr supplementation before *vs*. after strength training exercise. This time, the sample constituted 22 healthy older adults (9 males, 13 females, between 50-64 years), performing strength training over 12 weeks (3 days a week). They were divided into two groups: with some consuming Cr before training and some after training, compared to a placebo group. During the 12-week training period, both groups experienced a significant increase in lean mass in the whole body, as well as an increase in strength in the lower and upper body without differences between groups. The authors concluded that changes in muscle mass or strength were similar regardless of the timing of consumption.

The same occurred in the study by Cooke *et al*.[45], which assessed the effects of consuming Cr (with 5 g of additional carbohydrates) after exercise on body composition and muscle strength in 20 older adult males (55-70 years) over 12 weeks, participating in a programmed high

Table 1. Study characteristics about the optimum timing for sports supplementation with creatine.

Author	Participants (Number/gender/age)	Type of training	Supplement	Doses	Duration	Time of taking supplement	Results / Conclusions
Cribb and Hayes (2006)	23 / males / 18 -28 years	Strength training	Creatine + protein + glucose	1 g/kg (7 g/100 g de creatine)	10 weeks	Pre-training / post-training vs dawn / dusk	Greater muscle mass gain and increases in muscle strength at times near training
Antonio and Ciccone (2013)	19 / males / 23.1± 2.9 years	Bodybuilding	Creatine	5 g	4 weeks	Pre-training vs. post-training	Improvement in strength and body composition with post-training consumption
Candow *et al*. (2014)	22 (9 males; 13 females) / 50-64 years	Strength training	Creatine	0,1 g/kg	12 weeks	Pre-training vs. post-training	Changes in muscle mass or strength similar regardless of the timing of consumption.
Candow *et. al* (2015)	64 / (38 females; 26 males) / 50-71 years	Strength training	Creatine	0,1 g/kg	32 weeks	Pre-training creatine vs. post-training creatine vs. pre- and post-training placebo	Increases in muscle mass with post-training creatine. Increases in muscle strength with creatine regardless of timing.

intensity strength training plan. After the initial 7-day "load" phase, participants received instructions to take the supplement within 60 minutes after exercise. Taking CrM after exercise did not provide a greater improvement in body composition and muscle strength than the strength training alone. Although this study did not compare different timing of supplement consumption, these results should be considered in this review.

The aim of another study[46] was to examine the effects of supplementation before and after training, with supplementation at another time of the day (morning and night) on muscle hypertrophy, strength and body composition, in a 10-week strength programme, demonstrating greater muscle mass gains and muscle strength increases when the supplement was taken around the time of training. In this case the supplement contained protein, Cr and glucose.

One review[14] focused on assessing the effect of the timing of Cr consumption on muscle hypertrophy and strength, including some of the studies described linked to timing in our review, and although to date this literature is limited, it appears that Cr supplementation before and after resistance training sessions increases the mass and strength of lean tissue. The review suggests that taking Cr after training, provides greater muscular benefits than when it is taken prior to training[14]. Taking this supplement around the time of training may be more beneficial than taking Cr at another time of day, due to the increased blood flow and the sodium-potassium pump activation[46] following the entry of Cr into the muscle.

In turn, studies are required that demonstrate the influence of circadian rhythms on Cr supplement timing, to discover the effects on performance in morning versus evening training.

Conclusion

The most effective Cr supplementation protocol comprised the consumption of 0.3 g/kg/d over five days, followed by a consumption of 0.03 g/kg/d, thus achieving a better PCr reserve in the skeletal muscle.

The studies revealed greater benefits when the Cr consumption was performed around training times, due to greater blood flow, with studies indicating significant improvements in post-training consumption, as Cr may increase the formation of glycogen in the muscle and increase sensitivity to insulin.

Conflict of interest

The authors claim to have no conflict of interest whatsoever.

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