ARCHIVOS LATINOAMERICANOS DE NUTRICIÓN
Revista de la Sociedad Latinoamericana de Nutrición
https://doi.org/10.37527/2024.74.3.007
Publicado: 01/11/2024

Vol. 74 N° 3; julio - septiembre 2024
Artículo de Revisión

Effect of creatine supplementation on muscular function and physical performance in children and adolescents a literature review

Gladys Seleste Ortiz-Barroso[1], *Fernanda Espinoza-López*[1], *Sofía Guadalupe Ocón-García*[1], *Rebeca Montserrat Salazar-Ramos*[1], *Vicente Esparza-Villalpando*[1].

Abstract: Effect of creatine supplementation on muscular function and physical performance in children and adolescents a literature review. Introduction: Creatine (Cr) is an effective and safe ergogenic supplement that enhances post-exercise recovery, prevents injuries, supports thermoregulation, and provides benefits in rehabilitation, as well as spinal and cerebral neuroprotection for adults and older individuals. However, the evidence regarding its benefits in the pediatric population across various contexts has not been conclusive. **Objective:** Analyze the impact of different doses of Cr on physical performance and muscle function in children and adolescents in general through a systematic review of the literature. **Materials and methods:** This review followed the PRISMA reporting guidelines in the electronic databases of PubMed/Medline and Google Scholar. It included controlled clinical trials conducted between 1997 and May 2023 that assessed the effect of Cr supplementation on muscle function and physical performance in children and adolescents. A total of 20 studies were included. **Results:** The subjects included young high-performance athletes from different disciplines and children or adolescents diagnosed with pathologies affecting muscle function. Significant effects were found in athletes' physical performance and muscular function at various doses and periods of supplementation, unlike those involving a pathology, which mainly did not present improvements in these variables. **Conclusions:** Some reports suggest a positive effect on physical performance, specifically in young athletes. However, the Cr doses, posology, and administration protocols vary between studies. **Arch Latinoam Nutr 2024; 74(3): 222-239.**

Keywords: Ergogenic aids, muscle gain, pediatric population, young athletes .

Resumen: Efecto de la suplementación de creatina en la función muscular y rendimiento físico en niños y adolescentes una revisión de la literatura. Introducción: La creatina (Cr) es un suplemento ergogénico eficaz y seguro que mejora la recuperación post-ejercicio, previene lesiones, favorece la termorregulación y proporciona beneficios en la rehabilitación, así como neuro protección tanto espinal como cerebral para adultos y personas mayores. No obstante, la evidencia sobre sus beneficios en la población pediátrica en diversos contextos aún no ha sido concluyente. **Objetivo:** Analizar el impacto de diferentes dosis de Cr sobre el rendimiento físico y la función muscular en niños y adolescentes de forma general mediante una revisión sistemática de la literatura. **Materiales y métodos:** Esta revisión se llevó a cabo mediante la pauta del informe PRISMA en las bases de datos electrónicas de PubMed/Medline y Google Scholar, se incluyeron ensayos clínicos controlados realizados entre 1997 y mayo de 2023 que evaluaron el efecto de la suplementación con Cr en niños y adolescentes sobre la función muscular y el rendimiento físico. Se incluyeron un total de 20 estudios. **Resultados:** Los sujetos incluyeron jóvenes deportistas de alto rendimiento de diferentes disciplinas y niños o adolescentes diagnosticados con algunas patologías que afectan la función muscular. Se encontraron efectos significativos en el rendimiento físico y la función muscular de los deportistas con diferentes dosis y periodos de suplementación, a diferencia de aquellos que involucran una patología que en su mayoría no presentaron mejoras en estas variables. **Conclusiones:** Algunos informes sugieren un efecto positivo en el rendimiento físico, especialmente en jóvenes atletas. Sin embargo, las dosis de creatina, así como los regímenes de dosificación y los protocolos de administración, varían entre los estudios. **Arch Latinoam Nutr 2024; 74(3): 222-239.**

Palabras clave: ayudas ergogénicas, ganancia muscular, población pediátrica, jóvenes atletas.

Introduction

Creatine is a biochemical compound synthesized from the amino acids arginine, glycine, and methionine, primarily in the liver, kidneys, and pancreas. Its primary function is to store and provide energy in the form of phosphocreatine

[1]Universidad Autónoma de Aguascalientes, Health Sciences Center.
Correspondencia: Vicente Esparza-Villalpando, e-mal: vicente.esparza@edu.uaa.mx

(PCr), especially in tissues with high energy demands, such as skeletal muscles and the brain. PCr acts as a phosphate donor to regenerate ATP (adenosine triphosphate), which is the primary source of cellular energy during intense, short-duration physical activities (1). More than 95% of Cr in the human body exists in skeletal muscle, while the remaining 5% is distributed in the brain and testicles. Approximately two-thirds of muscular Cr is found to be PCr, while the remaining third is free. About 1-2% of this muscle Cr is broken down as creatinine and excreted in the urine (2).

Cr reserves in the human body are proportional to muscle mass, and adults consume approximately 1 to 3 grams daily in normal conditions. About half of the requirements are obtained from the diet, mainly from red meat and shellfish (3). The remaining half is synthesized in the liver and kidneys from the amino acids arginine and glycine by the action of the enzyme arginine glycine aminidinotransferase (AGAT) that transforms them into guanidinoacetate (GAA) that is subsequently methylated by guanidinoacetate N-methyltransferase (GAMT) using S-adenosyl methionine to form creatinine (4).

Cr is a popular ergogenic aid among athletes and has been consistently shown to increase muscle availability of Cr and PCr, improving athletes' capacity for acute exercise, as well as training adaptations, allowing performance with greater quality, favoring a better post-exercise recovery, preventing injuries, benefiting thermoregulation, rehabilitation and providing both spinal and cerebral neuroprotection (5–7).

In addition, given its effects on cellular energy balance regulation and reduction of oxidative stress, clinical applications have been attributed to it, finding beneficial effects after its supplementation in neurodegenerative diseases such as muscular dystrophy (8), Huntington's disease (9), Parkinson's disease (10), diabetes (11), osteoarthritis (12), fibromyalgia (13), cerebral or cardiac ischemia (14), depression (15), and aging positively influencing cognitive function (16). Some studies have even found beneficial effects in pregnant women, improving the fetus's growth, development, and health (17).

The Cr supplementation was evaluated in short and long-term effects, as well as among healthy or patients with a particular pathology; Cr supplementation doses range between 0.3 and 0.8 g/kg/day for a maximum of 5 years, with good tolerance, without reporting significant adverse effects. The only consistently reported side effect is weight gain (18).

Cr is an effective and safe ergogenic supplement for adults and older people, but the evidence from the pediatric age group has not been conclusive. Cr has been studied in the pediatric population, particularly in various diseases affecting muscle function and cellular energy. Its use as an ergogenic supplement has been explored in conditions such as muscular dystrophy, metabolic diseases, and neuromuscular disorders. Research has demonstrated that Cr supplementation may offer potential benefits in improving muscle strength, physical function, and quality of life in children and adolescents with these conditions. Additionally, it has been suggested that Cr could play a neuroprotective role, making it an interesting option for the treatment of neurological disorders in childhood (19).

Recently, Jagim & Kerksick (20) and Metzger *et al*. (21) grouped the relevant and available information related to Cr supplementation in children and adolescents. However, the results are inconclusive and widespread. Therefore, this review aims to analyze the impact of different doses of Cr on physical performance and muscle function in children and adolescents in various clinical scenarios.

Materials and methods

Study design

This systematic review is aimed under the Preferred Reporting Items for Systematic Reviews (PRISMA) (22). The study population includes all reports about Cr supplementation during childhood and adolescence between 1997 and May 2023 in the electronic database search.

Selection criteria

The methodological quality assessment where the selection criteria are specified, and the risk of bias

(23) are described in Tables 1 and 2, respectively. The intervention, control, and outcome parameters were selected following the Population, Interventions, Control, and Outcome (PICO) format (24):

Population: Children and adolescents aged 2 to 18 years old with Cr supplementation.

Intervention: Oral Cr supplementation.

Control: Placebo.

Outcome: Muscular function and physical performance

Research question: How does oral Cr supplementation affect muscle function and physical performance in children and adolescents?

Table 1. Methodological quality assessment.

Step	Description
1. Protocol development	Define and register objectives, such as evaluating the effectiveness of creatine supplementation in children and adolescents.
2. Literature search	Conduct searches in relevant databases (PubMed and Googlescholar) using terms like "Creatine supplementation AND children", "Creatine supplementation AND teenagers", "Creatine supplementation AND young athletes", "Creatine Supplementation and adolescent athletes", "Creatine AND Muscular function" and "Creatine AND Physical performance".
3. Study selection	Apply inclusion criteria (clinical trials Cr supplementation on children and adolescents, function and physical performance measurements) and exclusion criteria (unreported data, case reports, and pilot studies).
4. Data extraction	Collect data on dosage, duration of supplementation, and outcomes related to strength and physical performance.
5. Quality assessment	Assess the quality and risk of bias using the Cochrane Risk of Bias Tool.
6. Analysis and synthesis	Perform qualitative analysis of the data on the effects of creatine on strength and performance.
7. Reporting results	Present results clearly, including a flow diagram of study selection and summary tables.
8. Discussion	Discuss findings about previous studies, highlighting the benefits and limitations of creatine in the pediatric population.
9. Conclusions and recommendations	Provide conclusions on the safety and effectiveness of creatine in children and adolescents and suggest areas for future research.
10. Transparency and reproducibility	Document all processes, ensuring methods are reproducible by other researchers.

Table 2. Risk of bias

Study	Randomization	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Assessors	Incomplete Data	Selective Reporting	Other Bias
1997_Grindstaff (25)	Low	Low	Low	Unclear	Low	Low	Unclear
2002_Dawson (26)	Low	Low	High	Unclear	Low	Low	Unclear
2003_Louis (8)	Unclear	Low	Low	Unclear	Low	Low	Unclear
2004_Ostojic (27)	Unclear	Low	Low	Unclear	Low	Low	Unclear
2004_Tranopolsky (28)	Low	Low	Low	Unclear	High	Low	Unclear
2005_Escolar (29)	Low	Low	Low	Unclear	Low	Low	Unclear
2007_Silva (30)	Low	Low	Low	Unclear	Low	Low	Unclear
2007_Wong (31)	Low	Low	Low	Unclear	Low	Low	Unclear
2009_Juhász (32)	Low	Low	Low	Unclear	High	Low	Unclear
2010_Banerjee (33)	Low	Low	High	Unclear	Low	Low	Unclear
2012_Mohebbi (34)	Unclear	Unclear	Low	Unclear	Low	Low	Unclear
2013_Deminice (35)	Low	Low	Low	Unclear	Low	Low	Unclear
2014_Hayashi (36)	Low	Low	Low	Unclear	Low	Low	Unclear
2016_Solis (37)	Low	Low	Low	Unclear	Low	Low	Unclear
2017_Wang (38)	Low	Low	Low	Unclear	High	Low	Unclear
2017_Yañez-Silva (39)	Low	Low	Low	Unclear	High	Low	Unclear
2018_Juhász (40)	Low	Low	Low	Unclear	High	Low	Unclear
2019_Da Silva (41)	Low	Low	Low	Unclear	High	Low	Unclear
2021_Dover (42)	Low	Low	Low	Unclear	High	Low	Unclear
2022_Vargas-Molina (43)	Low	Low	High	Unclear	Low	Low	Unclear

Search strategy and data extraction

The electronic data search of relevant references was performed in electronic databases without publication date restrictions. The electronic databases used were PubMed and Google Scholar. All reviewers retrieved selected studies as full-text reports to be rescreened in detail to confirm whether the studies met the inclusion criteria.

Variables: Because of the heterogeneity of the previous reports and the variety of variables measured in the studies, the variables were classified into two groups:

Muscular function: Hand grip, total manual muscle, quantitative muscle testing, leg press, bench press, segmental lean mass, ankle plantar flexion peak torque, right-hand grip, left-hand grip, manual muscle testing (MMT), and quantitative measure muscle strength (QMT).

Physical performance: Heat, power sprint, swimming, anaerobic work, maximal voluntary contraction (MVC), time to exhaustion, vertical jump (VJ), power test (PT), shuttle run, dribble, time to walk, time to climb stairs, swimming velocity (MSV25), active drag force (Df), hydrodynamic coefficient (Cx), power output (Po), lower limb functional grade, mechanical power output, maximum power, minimum power, fatigue index, time stands, time up-and-go, post-activation potentiation (PAP), pain intensity, rate of perceived exertion (Borg´s Scale), squat jump (SJ), drop jump (DJ), countermovement jump (CMJ), Abalakov jump (ABJ), peak work, moderate vigorous physical activity, vigorous physical activity, max jump, Wingate Anaerobic Test (WAnT), peak power output (PPO), mean power output (MPO), total work, time to stand, time to climb stairs, time to run, repeated sprint test, accuracy of shooting and, dribble.

Reported data finding

The electronic search of databases included 117 potential studies, as shown in Figure 1. After removing duplicates (n=37), the reports with different study designs in the abstract (n= 8) were discarded; after the full-text available studies (n=65), the manuscripts were screened in more detail and assessed to comply with the inclusion criteria, the manuscripts removed after that whit reasons where: age range (n=35) and reporting physical variables (n= 10). Finally, the remaining 20 studies were included (8, 25–43).

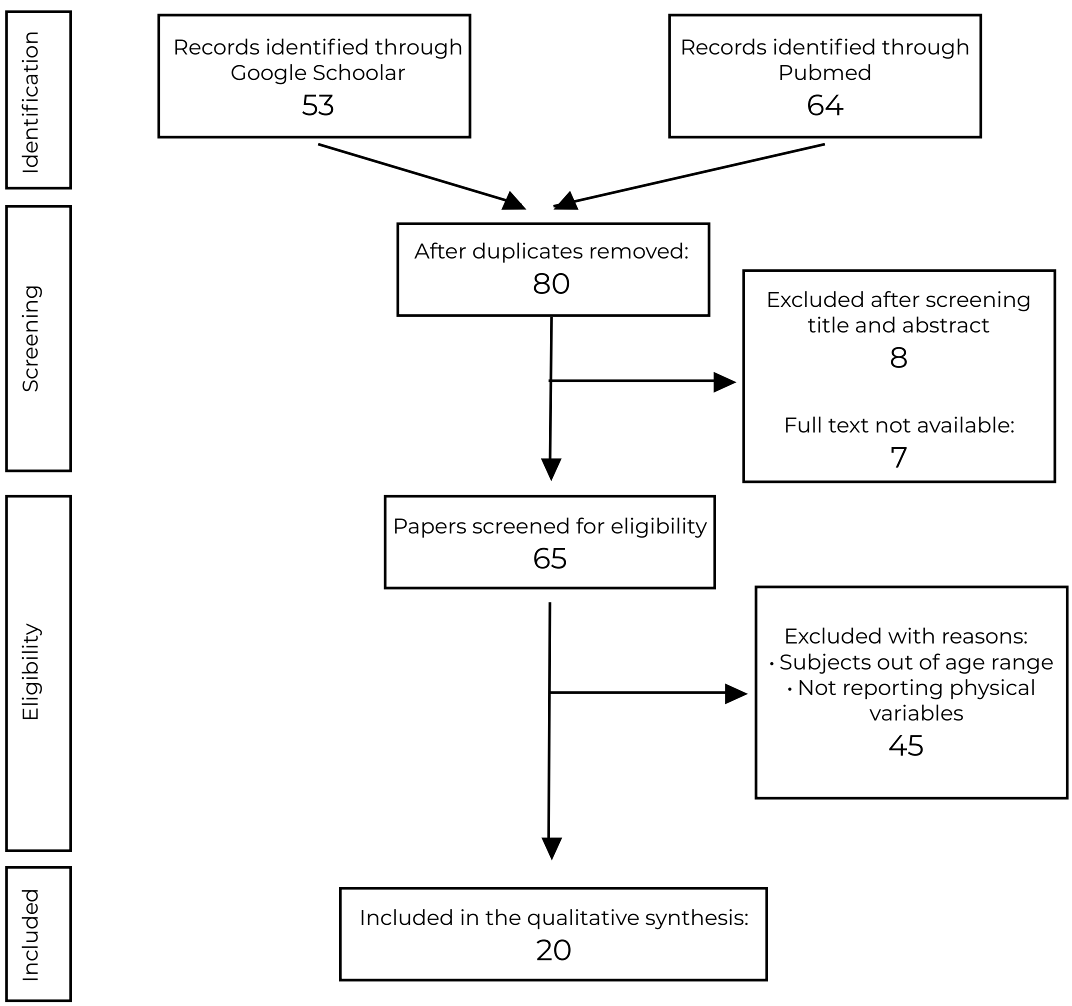

Figure 1. Preferred Reporting Items for Systematic Reviews diagram showing the literature search strategy.

Characteristics of included studies

The included studies are listed in Table 3. All studies were Randomized Clinical Trials (RCTs), 14 double-blinded, three single-blinded, and two open-labeled; 5 were crossover, and 15 were parallel. All studies reported were in English from 1997 to May 2022. The supplementation periods were from 5 days to 6 months, with doses of 0.03, 0.1, 0.15, 0.3, 2.0, 3.0, 5.0, 10.0, 20.0, 21.0, and 30 gr/day. The principal outcome measures were physical variables divided into two groups: Muscular function using force measures and physical performance using time, distance, and power measures.

Results

Effect of 0.03 g/kg/day of monohydrate creatine

A study with this dose compared the Cr supplementation and maltodextrin as the placebo for 14 days; this was a parallel design. Yañez-Silva *et al*. (35) found that Cr supplementation benefited muscle power output in elite youth soccer players and suggested that the dose used appears to be the lowest effective dose of Cr seen in the literature. They found significant changes in the two groups.

Effect of 0.1-0.15 g/kg/day of monohydrate creatine

Five studies evaluated the effect of Cr supplementation in adolescents (28,36,37,42,43) using variables like muscle function, muscle strength, and aerobic capacity parameters. Three of these were cross-over trials (28,36,43) and two studies were parallel designs (37,42). Four studies used a dose of 0.1g /kg/day (28,36,37,43) another one used 0.15g/kg/day (42), and the placebo was dextrose. Solis *et al*. (37) and Hayashi *et al*. (36) Solis *et al*. evaluated the effect of Cr supplementation on muscular function in 12 weeks in different diseases, (37) found that Cr supplementation did not affect muscle function in juvenile dermatomyositis (JDM) Hayashi *et al*. (36) reported no significant changes between placebo and Cr for any muscle function in systemic lupus erythematosus. However, Tarnopolsky *et al*. (28) reported that four months of Cr supplementation does not improve functional tasks or activities of daily living like walking or climbing stairs in Duchenne muscular dystrophy (DMD). Vargas-Molina *et al*. (43) reported that eight weeks Cr supplementation with resistance and plyometric training increased the lower-limb Abalakov jump power and scoring performance in under 16 years of basketball players. Dover *et al*. (42) used a dose of 0.15 g/kg/day and reported that Cr supplementation in children with JDM did not affect muscle function, strength, and aerobic capacity. In summary, the evidence has shown that Cr supplementation with a dose of 0.1g/kg/day only affected muscular strength in conjunction with resistance training.

Effect of 0.3 g/kg/day of monohydrate creatine

Two studies with this dose versus placebo (35,41) were evaluated. One of the studies was single-blind cross-over design (41), the other was a randomized, double-blind design. The studies evaluated pre- and post-measure with a supplementation time of 7 days, using dextrose and maltodextrin as placebo. The subjects were soccer players aged 15 to 19. Da Silva Azevedo *et al*. (41) evaluated the effect of Cr in 8 males measured by the rate of perceived exertion (with Borg´s scale). The data suggest a possible improvement in shock attenuation and a safer practice of high-intensity interval training (HIIT) under Cr supplementation. On the other hand, Deminice *et al*. (35) they measured the Cr in 25 young high-performance athletes to determine its effect after intense exercise sessions. They analyzed different muscular and metabolic parameters, finding that Cr supplementation favored more excellent muscular function. In summary, supplementing 0.3g/day of Cr for 7 days in young high-performance athletes allows better impact control and excellent discharge attenuation to carry out high-intensity training sessions more safely.

Effect of 2-3 g/day of monohydrate creatine

Cr supplementation was analyzed in children with muscle disease. Wong *et al*. (31) studied patients with spinal muscular atrophy (SMA) aged 2-18 years in a double-blind randomized clinical trial in parallel, administering 2g/day of Cr vs. placebo, in which this dose was only administered when the children were under 5 years for 6 months, the muscular function were evaluated at different times without finding

Tabla 3. Characteristics of Included Studies in Qualitative Synthesis.

Study	Age in years mean (SD)	Design	Study subjects	N Before	Experi-mental groups	N After	Follow-up	Mean (SD) Before	Mean (SD) After	Response variable	Conclusion
1997_ Grindstaff (25)	15.3 (0.6)	Randomi-zed, double-blind	Male (n=7) and female (n=11) regio-nally and/or nationally competiti-ve amateur swimmers.	9	Experi-mental: 21 g/day of CrM mixed with 4.2 g/day of granulated maltodex-trin	9	9 days	31.63 (1.5)	31.77 (1.6)	Heat 1 50 m (s)	Results indicate that 9 days of Cr supplemen-tation during swim training may provide some ergogenic value to competitive junior swimmers during repetitive sprint perfor-mance
								65.05 (3.0)	64.77 (2.5)	Heat 1 100 m (s)	
								32.72 (1.4)	32.47 (1.4)	Heat 2 50 m (s)	
								66.96 (3.4)	66.03 (2.8)	Heat 2 100 m (s)	
								32.50 (1.6)	32.58 (1.2)	Heat 3 50 m (s)	
								66.71 (2.9)	66.34 (3.1)	Heat 3 100 m (s)	
								5,318 (1,510)	5,724 (1,404)	Work sprint 1 (J)	
								5,217 (1,386)	5,428 (1,351)	Work sprint 2 (J)	
								5,256 (1,357)	5,307 (1,280)	Work sprint 3 (J)	
								266 (76)	286 (70)	Peak power sprint 1 (W)	
								261 (69)	272 (68)	Peak power sprint 2 (W)	
								263 (68)	26 (64)	Peak power sprint 3 (W)	
				9	Control: 25.2 g/ day of granulated maltodex-trin	9		31. 93 (1.8)	32.37 (1.6)	Heat 1 50 m (s)	
								65.48 (3.7)	66.34 (3.3)	Heat 1 100 m (s)	
								33.58 (1.4)	33.67 (1.4)	Heat 2 50 m (s)	
								68.84 (2.6)	68.44 (3.1)	Heat 2 100 m (s)	
								34.04 (1.6)	34.01 (1.2)	Heat 3 50 m (s)	
								69.35 (3.1)	69.37 (3.0)	Heat 3 100 m (s)	
								5,782 (1,916)	5,786 (1,785)	Work sprint 1 (J)	
								5,479 (1,644)	5,362 (1,699)	Work sprint 2 (J)	
								5,415 (1,535)	5,441 (1,644)	Work sprint 3 (J)	
								289 (96)	289 (89)	Peak power sprint 1 (W)	
								274 (82)	268 (85)	Peak power sprint 2 (W)	
								271 (77)	270 (82)	Peak power sprint 3 (W)	
2002_ Dawson (26)	Males 16.1 (1.4) Females 16.1 (2.2)	Randomi-zed sin-gle-blind clinical trial	Men and women involved in com-petitive swimming training for 2-11 years. No otter nutritional supple-ments were permitted	10	Experi-mental: 5 g of CrM + 1 g of polymer glucose/ day	10	27 days	30.67 (2.35)	30.20 (2.16)	50 m swim (s)	It was concluded that 4 weeks of Cr supple-mentation did not significantly improve single sprint perfor-mance in competitive junior swimmers but enhanced swim ben-chtest performance.
								68.02 (5.07)	66.03 (4.28)	100 m swim (s)	
								4.0 (1.5)	4.3 (1.5)	Total anaerobic work (kJ)	
				10	Place-bo: 6 g of polymer glucose/ day	10		30.44 (1.94)	30.05 (2.11)	50 m swim (s)	
								66.66 (4.40)	65.60 (4.52)	100 m swim (s)	
								4.0 (1.3)	4.1 (1.3)	Total anaerobic work (kJ)	

Tabla 3. Characteristics of Included Studies in Qualitative Synthesis (cont.).

Study	Age in years mean (SD)	Design	Study subjects	N Before	Experimental groups	N After	Follow-up	Mean (SD) Before	Mean (SD) After	Response variable	Conclusion
2003_ Louis (8)	10.8 (2.8)	Double-blind, cross-over.	15 boys with muscular dystrophy (DMD and BMD), aged 6 to 16 years.	8	Experimental:3 g/day of CrM	8	3 months	5.4 (2.1)	6.1 (2.2)	MVC (N·m)	No adverse the effect was observed. Thus, Cr may provide some symptomatic benefits in these patients.
								4.1 (1.3)	7.2 (1.4)	Time to exhaustion (s)	
				7	Control: 3 g/day of maltodextrin	7		5.01(1.5)	4.9 (1.6)	MVC (N·m)	
								4.9 (1.8)	4.2 (1.2)	Time to exhaustion (s)	
2004_Ostojic (27)	16.6 (1.9)	Randomized	Young male soccer players All subjects were in good health (free from musculoskeletal dysfunctions, and metabolic and heart diseases).	10	Experimental: 30 g/day of Cr divided in 3 portions of 10 g	10	7 days	13.0 (1.5)	10.2 (1.8)	SDT (s)	The main finding of the study indicates that supplementation with Cr in young soccer players improved soccer-specific skill performance compared with ingestion of a placebo
								2.7 (0.4)	2.2 (0.5)	PT (s)	
								49.2 (5.9)	55.1 (6.3)	VJ (cm)	
								684.8 (51.2)	654.1 (45.5)	Shuttle run (s)	
				10	Control: An equal number of identi-cal-looking pills that contained cellulose	10		12.9 (1.9)	12.6 (1.7)	SDT (s)	
								2.7 (0.7)	2.8 (0.5)	PT (s)	
								50.1 (8.1)	49.9 (6.1)	VJ (cm)	
								672.9 (47.6)	666.8 (58.3)	Shuttle run (s)	
2004_Tarnopolsky (28)	10 (3)	Randomized, double-blind, cross-over.	31 male patients with DMD.	15	Experimental: 0.10 g/kg/day of CrM (2-5 tablets).	15	16 weeks	NR	NR	Hand grip (N)	Four months of Cr M supplementation led to increases in FFM and handgrip strength in the dominant hand and a reduction in a marker of bone breakdown and was well tolerated in children with DMD.
								NR	NR	Total manual muscle (strength score)	
								6.8(0.55)	7.1(0.55)	Time to walk 30 ft. (s. by functional test)	
								5.9 (0.88)	6.9 (1.2)	Time to climb 4 stairs (s. by functional test)	
				16	Control: 2-5 tablets of dextrose	15		NR	NR	Hand grip (N)	
								NR	NR	Total manual muscle (strength score)	
								7.3(0.67)	7.4(0.64)	Time to walk 30 ft (s. by functional test)	
								5.7 (0.66)	6.0 (0.89)	Time to climb 4 stairs (s. by functional test)	
2005_Escolar (29)	6.74 (1.5)	Randomized Double-blind clinical trial	Ambulant steroid-naive boys with DMD	15	Experimental:5 g/day of Cr powder	15	6 months	6.30 (1.27)	0.24 (0.55)	MMT score (0-10)	There was no statistically significant effect of either therapy based on manual and quantitative measurements. of muscle strength
								8.66 (3.87)	-0.06 (1.52)	QMT score (lb)	
								7.21 (3.31)	0.28 (1.52)	QMT arm (lb)	
								10.84 (5.74)	-0.54 (2.47)	QMT leg (lb)	
								7.97 (4.68)	3.50 (5.25)	Time to stand (s)	
								10.92 (13.27)	0.85 (2.36)	Time to climb 4 stairs (s)	
								8.30 (5.79)	0.44 (0.36)	Time to run 10 meters (s)	
				16	Placebo: NR	16		6.24 (0.70)	-0.08 (0.47)	MTT score (0-10)	
								7.46 (2.16)	-0.53 (1.86)	QMT score (lb)	
								6.92 (2.52)	-0.61 (2.28)	QMT arm (lb)	
								8.30 (1.85)	-0.51 (1.88)	QMT leg (lb)	
								9.21 (5.33)	4.33 (2.38)	Time to stand (s)	
								7.21 (4.17)	4.22 (5.20)	Time to climb 4 stairs (s)	
								6.58 (1.11)	1.41 (1.24)	Time to run 10 meters (s)	

Tabla 3. Characteristics of Included Studies in Qualitative Synthesis (cont.).

Study	Age in years mean (SD)	Design	Study subjects	N Before	Experimental groups	N After	Follow-up	Mean (SD) Before	Mean (SD) After	Response variable	Conclusion
2007_Silva (30)	16.3 (1.8)	Randomized, double-blind placebo-controlled.	16 healthy competitive national-level swimming females.	8	Experimental: 20g/day of Cr divided in 4 portions of 5 dissolved in 150 ml of a colored and flavored 6% maltodextrin solution	8	21 days	1.47(0.6)	1.48 (0.67)	MSV25 (m.s-1)	These data suggest that 21 days of Cr supplementation produced significant effects on gross and/or propelling efficiency during swimming in female athletes. However, Cr supplementation did not influence performance, body weight, and body composition.
								77.3 (23.6)	61.8 (9.08)	Df (N)	
								0.49 (0.16)	0.39 (0.08)	Cx	
								113.9 (35.2)	92.49 (14.2)	Po (W)	
				8	Control: A similar volume of colored and flavored 6% maltodextrin solution	8		1.42 (0.1)	45 (0.15)	MSV25 (m.s-1)	
								61.9 (15.5)	62.5 (13.2)	Df (N)	
								0.46 (0.09)	0.48 (0.13)	Cx	
								88.38 (21.5)	91.15 (14.7)	Po (W)	
2007_Wong (31)	2-18 years	Randomized, double-blind, placebo-controlled trial	Children with a clinical diagnosis of SMA with confirmed mutations of the SMN1 gene.	10	Experimental 2<5 years:2 g/day of Cr	10	6 months	38.7 (8.4)	40.0 (1.3)	GMFM (score)	Cr supplementation for 6 months did not improve motor function, muscle strength, or quality of life in children with SMA.
								59.6 (4.8)	62.7 (3.6)	QOL (score)	
				12	Placebo 2<5 years:NR	12		39.3 (5.1)	40.3 (0.7)	GMFM (score)	
								57.0 (4.9)	59.6 (4.0)	QOL (score)	
				17	Experimental 5>18 years:5 g/day of Cr	17		45.5 (7.3)	54.7 (0.6)	GMFM (score)	
								50.8 (14.9)	59.3 (1.0)	QMT (lb)	
								69.8 (3.7)	66.3 (2.2)	QOL (score)	
				16	Placebo 5>18 years:NR	16		60.6 (8.8)	53.3 (2.6)	GMFM (score)	
								B: 70.8 (12.9)	60.2 (1.11)	QMT (lb)	
								66.8 (2.8)	71.2 (2.6)	QOL (score)	
2009_Juhász (32)	15.9 (1.6)	Randomized double-blind research design	16 Healthy young male fin swimmers.	NR	Experimental: 20 gr/day of CrM divided in 4 portions of 5 g mixed with dextrose, ascorbic acid, and effervescence intensifiers. The total weight of one portion was 12 g	NR	5 days	NR	NR	Mechanical power output (power, kW)	The results of this study indicate that five-day Cr supplementation enhances the dynamic strength and may increase anaerobic metabolism in the lower extremity muscles, and improves performance in consecutive maximal swims in highly trained adolescent fin swimmers
								50.69 (1.41)	48.86 (1.34)	Swimming time 1st 100m (s)	
								50.39 (1.38)	48.5 (1.35)	Swimming time 2nd 100m (s)	
				NR	Control:48 g/day divided in four portions of dextrose-ascorbic acid-flour mixture	NR		NR	NR	Mechanical power output(power, kW)	
								50.13 (1.25)	50.40 (1.28)	Swimming time 1st 100 m (s)	
								50.01 (1.16)	50.14 (1.24)	Swimming time 2nd 100 m (s)	

Tabla 3. Characteristics of Included Studies in Qualitative Synthesis (cont.).

Study	Age in years mean (SD)	Design	Study subjects	N Before	Experi-mental groups	N After	Follow-up	Mean (SD) Before	Mean (SD) After	Response variable	Conclusion
2010_Ba-nerjee (33)	7.0 (1.2)	Randomi-zed, sin-gle-blind place-bo-con-trolled	33 out-patients with DMD, steroid naïve.	18	Experi-mental: 5g/day of CrM	13	8 weeks	6.2 (0.5)	6.2 (CI 5.9-6.5)	MMT (score)	Cr preserved the muscle strength in short term. This study provides no evidence that creatine will prove beneficial after long-term treatment or have any positive effect on patient lifespan.
								0 (0.0)	NR	Vigno´s lower limb functional grade 2 (%)	
								9 (69.2)	NR	Vigno´s lower limb functional grade 3 (%)	
								4 (30.8)	NR	Vigno´s lower limb functional grade 4 (%)	
				15	Control: 500 mg/ day of vitamin C	14		6.1 (0.7)	5.8 (CI 5.5-6.1)	MMT (score)	
								1 (7.1)	NR	Vigno´s lower limb functional grade 2 (%)	
								8 (57.1)	NR	Vigno´s lower limb functional grade 3 (%)	
								5 (35.7)	NR	Vigno´s lower limb functional grade 4 (%)	
2012_Mo-hebbi (34)	17.18 (1.37)	Dou-ble-blind	17 young soccer players	17	Experi-mental:20 g/day of Cr divided in 4 portions of 5 g	17	7 days	18.89(0.7)	17.79 (0.5)	Repeated sprint test (s)	Cr supplementation improved the perfor-mance of repeated sprints and dribbling in young soccer players.
								3.62 (1.4)	4.25 (1.2)	Accuracy of shooting	
								7.37 (1.09)	6.75 (0.5)	Dribble (s)	
				17	Placebo: 20 g/day of glucose polymer	17		18.77 (0.6)	18.31 (0.4)	Repeated sprint test (s)	
								4.55 (2.2)	5.22 (1.3)	Accuracy of shooting	
								7.06 (0.8)	7.38 (0.4)	Dribble (s)	
2013_De-minice (35)	17.25 (1.3)	Randomi-zed, dou-ble-blind clinical trial	Men pla-yers from a second-di-vision team.	13	Experi-mental:0.3 g/kg of Cr	13	7 days	426.7 (51.3)	531.2 (94.2)	Average power (W)	Average, maximum, and minimum power values were greater in the Cr-supplemented group than in the placebo group. The fatigue index did not differ between groups
								673.4 (105.4)	749.8 (112.3)	Maximum power (W)	
								282.3 (60.5)	396.1 (67.5)	Minimum power (W)	
								5.7 (1.2)	4.2 (2.4)	FI (W/s-1)	
				12	Placebo: Maltodex-trine	12		426.7 (51.3)	531.2 (94.2)	Average power (W)	
								673.4 (105.4)	749.8 (112.3)	Maximum power (W)	
								282.3 (60.5)	396.1 (67.5)	Minimum power (W)	
								5.7 (1.2)	4.2 (2.4)	FI (W/s-1)	

Tabla 3. Characteristics of Included Studies in Qualitative Synthesis (cont.).

Study	Age in years mean (SD)	Design	Study subjects	N Before	Experimental groups	N After	Follow-up	Mean (SD) Before	Mean (SD) After	Response variable	Conclusion
2014_Hayashi (36)	15 (2)	Randomized, double-blind, cross-over placebo-controlled trial	Children with Systemic Lupus Erythematosus.	8	Experimental: 0.1g/kg/day of CrM	8	12 weeks	92 (42)	99 (42)	1-RM leg press (kg)	A 12-week Cr supplementation protocol at 0.1 g/kg/day does not affect muscle function in children with Systemic Lupus Erythematosus
								15 (4)	16 (4)	1-RM bench press (kg)	
								21 (9)	21 (9)	Handgrip (kg)	
								16 (2)	17 (3)	Timed stands (reps)	
								5.88 (1.12)	5.75 (1.22)	Timed up and go (s)	
				8	Placebo: 0.1g/kg/day of dextrose	7		88 (36)	94 (36)	1-RM leg press (kg)	
								15 (4)	15 (4)	1-RM bench press (kg)	
								21 (8)	21 (7)	Handgrip (kg)	
								16 (2)	16 (3)	Timed stands (reps)	
								6.21 (1.79)	6.01(1.53)	Timed up and go (s)	
2016_Solis (37)	13 (4)	Randomized double-blind cross-over clinical trial	Patients with JDM are active or inactive.	18	Experimental: 0.1g/kg/day of CrM	15	12 weeks	34.7 (12.9)	36.9 (14.2)	Leg press (kg)	Twelve weeks of creatine supplementation in JDM patients were well-tolerated and free of adverse effects, but the treatment did not affect muscle function, intramuscular PCr, or any other parameter.
								16.1 (10.4)	16.6 (10.8)	Bench press (kg)	
								20.5 (10.1)	21.5 (10.7)	Handgrip	
								16.5 (3.7)	17.5 (3.5)	Time-stands (reps)	
								5.6 (0.7)	5.4 (0.7)	Timed ug-and-go (s)	
				18	Placebo Dextrose	15		36.6 (13.2)	37.7 (13.6)	Leg press (kg)	
								15.7 (10.5)	16.8 (10.4)	Bench press (kg)	
								20.2 (11.4)	21.4 (10.9)	Handgrip	
								17.1 (3.3)	17.3 (3.9)	Time-stands (reps)	
								5.8 (0.8)	5.4 (0.7)	Timed ug-and-go (s)	
2017_Wang (38)	16.75 (0.70)	Randomized Double-blind	Male high school canoeists	8	Experimental: 20 g of CrM + 20 g of dextrose: divided into 4 portions of 5 g dissolved in 300 ml of water per day	8	6 days	85.63 (8.63)	88.12 (8.36)	Maximum muscle strength (kg)	This study suggests that short-term Cr supplementation in male high school canoeists resulted in improved upper body maximum strength and shortened optimal individual PAP times for training efficiency during a set of complex training bouts involving the upper body
								NR	NR	Distance (m)	
								9.75 (2.31)	8.12 (2.23)	PAP time (min)	
	16.44 (1.13)			9	Control: 20 g carboxymethyl cellulose + 20 g of dextrose divided in 4 portions of 5 g dissolved in 300 ml of water	9		NR	NR	Maximum muscle strength (kg)	
								NR	NR	Distance (m)	
								NR	NR	PAP time (min)	

Tabla 3. Characteristics of Included Studies in Qualitative Synthesis (cont.).

Study	Age in years mean (SD)	Design	Study subjects	N Before	Experimental groups	N After	Follow-up	Mean (SD) Before	Mean (SD) After	Response variable	Conclusion
2017_Yañez-Silva (39)	17.0 (0.5)	Randomized, double-blind placebo controlled	Elite male youth soccer players	20	Experimental: 0.03 g/kg/day of Cr	19	14 days	NR	NR	WAnT	Substantial evidence indicates that a low-dose, short-term oral Cr supplementation beneficially affected muscle power output in elite youth soccer players.
								NR	NR	PPO (W.kg-1)	
								NR	NR	MPO (W.kg-1)	
								NR	NR	FI (%)	
								NR	NR	Total Work (J.kg-1)	
				20	Placebo: Equivalent volume of maltodextrin	19		NR	NR	WAnT	
								NR	NR	PPO (W.kg-1)	
								NR	NR	MPO (W.kg-1)	
								NR	NR	FI (%)	
								NR	NR	Total Work (J.kg-1)	
2018_Juhász (40)	15.1 (1.5)	Randomized, double-blind, placebo-controlled	Injured adolescent male and female competitive fin swimmers	9	Experimental: Loading: 20 g of Cr for 5 days, divided into 4 portions of 5 g Maintenance: Cr 5 g/day for 37 days	9	6 weeks	NR	16.8 (1.7)	PFT (N·m)	Cr supplementation combined wit therapeutic strategy effectively supports the rehabilitation of tendon overuse injury of adolescent fin swimmers
				9	Control: Loading: Placebo 20 g of dextrose, ascorbic acid and flour mixture for 5 days Maintenance: Placebo 5 g/day for 37 days	9		NR	14.7 (2.3)	PFT (N·m)	
2019_da Silva (41)	16.3 (0.5)	Single-blind crossover clinical trial	Soccer players with 2 years of experience in running individuals.	8	Experimental 0.3 g/kg/day of CrM	8	7 days	NR	12.46 (1.3)	RPE (Borg´s Scale)	Cr supplementation has the potential to influence biomechanical parameters related to impact control during a single session of HIIT based on running. In particular, the current study's findings indicate possible improvements in shock attenuation and a safer practice of HIIT under creatine supplementation.
				8	Placebo 20 g/day of dextrose	8		NR	13.24 (2.08)	RPE (Borg´s Scale)	

Tabla 3. Characteristics of Included Studies in Qualitative Synthesis (cont.).

Study	Age in years mean (SD)	Design	Study subjects	N Before	Experimental groups	N After	Follow-up	Mean (SD) Before	Mean (SD) After	Response variable	Conclusion
2021_Dover (42)	13.0 (7.0-14.0) Values are median.	Randomized, double-blind, multiple baselines	Children and Adolescents with JDM.	13	Experimental: >40kg weight 0.15 g/kg/day of Cr	13	6 months		* 9.5	Peak work (W)	Creatine supplementation in children with JDM is feasible to study and is safe and well-tolerated; it may lead to improvements in muscle metabolism.
									* 1.09	Fatigue index (%)	
									* 0.11	MVPA (number of 30-minute blocks)	
									* -0.57	VPA (number of 30-minute blocks)	
									* -0.26	Right-hand grip (kg)	
				13	Placebo:NR	13			* -0.90	Left-hand grip (kg)	
									* -0.21	Max jump (inches)	
									* 0.81	MMT score	
2022_ Vargas-Molina (43)	14.3 (0.4)	Randomized open-labeled study	Male basketball players of the Unicaja Málaga reserve team.	12	Experimental: 0.1 gr/kg/day of CrM	12	8 weeks	28.8(5.3)	33.3(4.9)	SJ (cm)	Cr supplementation in conjunction with resistance and plyometric training increased the lower-limb ABJ power and scoring performance in basketball players.
								1.1 (0.3)	1.6 (0.6)	DJ (cm)	
								31.1(6.1)	35.2(6.2)	CMJ (cm)	
								37.0(7.6)	41.1(7.0)	ABJ (cm)	
				12	Control: Non-supplemented	11		32.8(5.3)	36.5(6.3)	SJ (cm)	
								1.3 (0.3)	1.6 (0.4)	DJ (cm)	
								33.6(8.1)	36.7(6.8)	CMJ (cm)	
								41.7(8.0)	43.3(7.3)	ABJ (cm)	

SD: standard deviation; g: grams; Cr: creatine; CrM: creatine monohydrated; s: second; J: Joule; W: Watt; kJ: kilojoule; m: meter; DMD: Duchenne muscular dystrophy; BMD: Becker muscular dystrophy; MVC: maximal voluntary contraction; N·m: Newton·meter; SDT: specific dribble test; PT: power test; VJ: vertical jump; cm: centimeter; kg: kilogram; NR: not reported; N: Newton; ft: feet; FFM: fat-free mass; MMT: manual muscle testing; QMT: quantitative muscle testing; lb: pound; ml: milliliters; MSV25: 25 m swimming velocity; m.s-1: meter per second; Df: active drag force; Cx: hydrodynamic coefficient; Po: power output; SMA: spinal muscular atrophy; GMFM: gross motor function measure; QOL: parent questionnaire for the PedsQL Neurouscular Module; kW: kilowatt; mg: milligrams; CI: confidence interval; W/s-1: Watt/second; 1-RM test: one-maximum repetition test; reps: repetitions; JDM: juvenile dermatomyositis; PCr: phosphocreatine; PAP: post-activation potentiation; min: minute; WAnT: Wingate anaerobic test; PPO: peak power output; W.kg-1:Watts per kilogram of body weight; MPO: mean power output; FI: fatigue index; J.kg-1: Joules per kilogram of body weight; PFT: plantar flexion peak torque; RPE: rate of perceived exertion; HIIT: high intensity interval training; MVPA: moderate-vigorous physical activity; VPA: vigorous physical activity; *: Mean difference between experimental and placebo; SJ: squad jump; DJ: drop jump; CMJ: counter movement jump; ABJ: Abalakov jump.

significant effects, concluding with this that under experimental conditions the supplementation of 2g/day of Cr for 6 months in children with spinal muscular atrophy does not improve motor function and muscle strength of these patients. However, Louis *et al*. (8), in a double-blind cross-over study carried out on children with muscular dystrophy, who were administered 3 g/day of Cr for 3 months compared to placebo, this administration improved muscle strength and resistance to fatigue.

Effect of 5 g/day of monohydrate creatine

Four studies evaluated the effect of Cr versus placebo (26,29,31,33), two studies had a single-blinded design (26,33), and the other was double-blinded (29,31). All studies evaluated a pre and post-measure with a different supplementation time, and only two studies described the placebo group glucose polymer powder (26), and vitamin C (33). Dawson *et al*. (26) evaluated the effect of Cr on male swimmers (16.1 ± 1.4 years) and females (16.6 ± 2.2 years) for 27 days with a maximum speed test of 50 meters (m) and 100 m freestyle, in which no significant differences were found between the Cr and placebo groups, while in the total anaerobic work output score (kilojoule) the Cr group increased their scores after supplementation. Other studies evaluated the effect of Cr on different pathologies, such as those by Wong *et al*. (31) the study included children with SMA (5 to 18 years) and determined that six months of Cr supplementation at this dose did not improve motor function or muscle strength. The remaining studies assessed children with DMD, in the case of Banerjee *et al*. (33) performed an 8-week supplementation and reported a significant difference in MMT score between the Cr and placebo group after the supplementation. On the other hand, Escolar *et al*. (29) supplemented for six months and didn't find a statistically significant difference in the MMT or the QMT scores. In summary, the findings reported by these authors suggest that a 5 gr Cr supplementation effectively increases the scores of total anaerobic works in swimmers, but the effect on different pathologies is not yet apparent.

Effect of 20-21 g/day of monohydrate creatine

Six articles evaluated Cr supplementation versus placebo in adolescents (25,30,32,34,38,40) six articles were double-blind. All studies assessed pre and post-measures with different supplementation times and placebo substances (see Table 1). The subjects range in age from 12 to 19 years. Silva *et al*. (26) evaluated the effect of Cr in 16 females for 21 days, where Df, Cx, Po, and swimming velocity (MSV25) were assessed. The data suggest that Cr supplementation significantly affected gross and/or propelling efficiency during swimming in female athletes. On the other side, Juhász, *et al*. (32) evaluated 16 young men for five days, where swimming time over 100 meters (1st and 2nd) were assessed, having as results that Cr supplementation enhances the dynamic strength and may increase anaerobic metabolism in the lower extremity muscles. Again, Juhász *et al*. (40) measured 18 male and female competitive swimmers with tendon injuries. The data suggest that after six weeks of Cr supplementation and rehabilitation, it effectively supports the rehabilitation of tendon overuse injuries in adolescent fin swimmers. Wang *et al*. (38) identified in 17 male high school canoeists, after six days of supplementation with Cr, that maximum muscle strength and the neuromuscular phenomenon of PAP improves the efficiency during a set of complex training bouts involving the upper body. Mohebbi *et al*. (34) rated 17 young soccer players and concluded that repeated sprints and dribbling performance improved after seven days of supplementation with Cr. Finally, Grindstaff *et al*. (25), evaluated 18 males and females for nine days where heat to 50 and 100 m (three times each), work sprint (three times), and peak power sprint (three times) were measured, where the results indicated that supplementation during swim training may provide some ergogenic value in competitive junior swimmers during repetitive sprint performance. In summary, the evidence shows that Cr supplementation with a dose of 20-21g/day produced significant and positive efficiency effects during swimming and in soccer skills on male and female young athletes.

Effect of 30 g/day of monohydrate creatine

Only One study reported this dose versus placebo (cellulose) in adolescents (27), in a pre-and post-measures design. The subjects ranged in age from 14 to 19, and all were soccer players from the junior league. Ostojic *et al*. (27) evaluated the effects of Cr supplementation in 55 males and females for seven days, where dribble, sprint power, endurance, vertical jump, and shuttle run. The author indicates that supplementation in young soccer players improved soccer-specific skills but not endurance performance.

Discussion

Cr is a popular ergogenic supplement among athletes due to its beneficial effects on muscle and energy metabolism. Likewise, it has also been helpful in some neurodegenerative diseases in the adult population. This systematic review compiles the studies carried out in children and adolescents, demonstrating their benefits in different clinical settings.

The Cr supplementation in athletes from different disciplines like swimmers (25,26,30,32,40), canoeists (38), soccer (27,34,35,39,41), and basketball players (43) improves most of the physical performance and muscle function. This could be explained by the role of the creatine kinase (CK)/PCr system, as Wallimann *et al*. suggest (44). Since the primary metabolic function of Cr is to form PCr from the union with a phosphoryl group (Pi) by the CK enzyme, the Pi released in the degradation of Adenosine triphosphate (ATP) to adenosine diphosphate (ADP) provides energy for metabolic activity, together can use in the resynthesize of ATP and help buffer energy needs, which explains the potential ergogenic and therapeutic benefits of Cr supplementation increasing the availability of muscle Cr.

This suggests that some physical activity is necessary to take advantage of the Cr reserves generated by supplementation, concurring with Harris *et al*. (45) who evaluated the interaction between exercise and Cr supplementation in subjects who performed 1 hour of bicycle ergometer exercise daily with only one leg, while the other leg served as a control. It was shown that there is an increase in Cr muscle reserve when supplementation is combined with regular exercise. However, in the most recent review in this field, Metzger *et al*. (21) concluded that more well-conducted trials are needed to determine whether Cr supplementation is effective in young athletes.

The dose of Cr is essential to the observed variables because some authors found the best results at specific doses. Vargas *et al*. (43), administrated a 0.1gr/kg/day dose. They evaluated basketball players undergoing a resistance and plyometric training program and suggested that de Cr supplementation might benefit strength-training adaptations and sports performance. Mills *et al*. (46) found similar effects because they evaluated physically active young adults during training sessions, finding that this is an effective strategy for increasing muscle strength and endurance. However, Pakulak *et al*. (47) evaluate young adults, and they did not find the effects of Cr supplementation on muscle strength and endurance. They only report that Cr supplementation and resistance training slightly improve knee extensor muscle accretion.

When the Cr supplementation was evaluated in patients with an associated pathology, the reports did not demonstrate significant improvements, for example, in patients with DMD (8,28,29,33), SMA (31), juvenile dermatomyositis (37,42), or lupus erythematosus (36). Additionally, the protocols were very heterogeneous, and the doses differed between studies. Banerjee *et al*. specifically reported Cr as a treatment for some diseases, like DMD, to alleviate the symptoms of muscular dystrophy (33). They evaluated children with DMD who were administered 5 gr/day of Cr for eight weeks and concluded that Cr improved the cellular energetics of their calf muscle with the preservation of muscle strength. However, they suggest no evidence of a beneficial effect after long-term treatment, concurring with Walter *et al*. (48), which showed little to no benefit of Cr supplementation in patients with myotonic and muscular dystrophies. Still, their patients were adults and not only with DMD, but they also included sarcoglycan-deficient limb-girdle muscular dystrophy and Beker dystrophy, while Tarnopolsky *et al*. (28) It was reported that Cr supplementation in children at a dose of 0.1 gr/kg/day for four months increased fat-free mass and handgrip strength in the dominant hand. Hence, Cr supplementation has a beneficial effect on DMD after long-term treatment.

One of the biggest problems in Cr supplementation is the dose and frequency. Each study uses a different administration protocol in different subject contexts, which makes summarizing the evidence difficult. Additionally, the response variables are very heterogeneous regarding evaluation method and timing. The authors must consider the CONSORT guidelines (45) to improve the quality of the trials and answer whether Cr applies to children and adolescents.

Some researchers suggest that higher doses of Cr may yield more pronounced effects, particularly in enhancing athletic performance and muscle recovery. However, this potential benefit must be weighed against the possibility of increased adverse effects, emphasizing the urgent need to establish clear and comprehensive guidelines for supplementation. Additionally, the current literature reveals a notable gap in long-term studies investigating the impact of Cr on children's physical and cognitive development, which raises significant concerns among healthcare professionals regarding its safety and efficacy (19).

The studies included in this review exhibit considerable variability in their methodologies, populations, and outcome measures. This heterogeneity complicates the ability to draw definitive conclusions and limits the generalizability of the findings across different groups. Additionally, the quality of the included studies varies; some lack rigorous design, control groups, or adequate randomization. Most studies focus on specific populations, such as athletes or individuals with particular health conditions, which may not represent the broader population. Consequently, this specificity limits the applicability of the findings to other groups.

Conclusions

Current evidence leaves the effects of Cr supplementation in children and adolescents uncertain. Most studies indicate a positive impact on physical performance, particularly among young athletes, with higher doses showing more significant benefits during physical activity. However, the dosages, administration regimens, and protocols vary widely across studies.

Establishing optimal protocols is crucial to determining effective and safe dosages for the pediatric population, considering age, weight, physical activity level, and existing health conditions. Advancing these research areas could lead to a better understanding of the effects and benefits of Cr in children and adolescents and the development of evidence-based guidelines for its use.

References

1. Clark JF. Creatine and phosphocreatine: a review of their use in exercise and sport. J Athl Train. 1997;32(1):45-51. PMID: 16558432
2. Hultman E, Soderlund K, Timmons JA, Cederblad G, Greenhaff PL. Muscle creatine loading in men. J Appl Physiol. 1996;81(1):232–327. https://doi.org/10.1152/jappl.1996.81.1.232
3. Brosnan ME, Brosnan JT. The role of dietary creatine. Amino Acids. 2016;48(8):1785-1791. https://doi.org/10.1007/s00726-016-2188-1
4. Paddon-Jones D, Børsheim E, Wolfe RR. Potential ergogenic effects of arginine and creatine supplementation. J Nutr. 2004;134(10):2888S-2894S. https://doi.org/10.1093/jn/134.10.2888s
5. Buford TW, Kreider RB, Stout JR, Greenwood M, Campbell B, Spano M, *et al*. International Society of Sports Nutrition position stand: creatine supplementation and exercise. J Int Soc Sports Nutr. 2007; 4:6. https://doi.org/10.1186/1550-2783-4-6
6. Galvan E, Walker DK, Simbo SY, Dalton R, Levers K, O'Connor A, *et al*. Acute and chronic safety and efficacy of dose dependent creatine nitrate supplementation and exercise performance. J Int Soc Sports Nutr. 2016; 13:12. https://doi.org/10.1186/s12970-016-0124-0
7. Volek JS, Ratamess NA, Rubin MR, Gómez AL, French DN, McGuigan MM, *et al*. The effects of creatine supplementation on muscular performance and body composition responses to short-term resistance training overreaching. Eur J Appl Physiol. 2004;91(5–6):628–637. https://doi.org/10.1007/s00421-003-1031-z
8. Louis M, Lebacq J, Poortmans JR, Belpaire-Dethiou MC, Devogelaer JP, Van Hecke P, *et al*. Beneficial Effects of Creatine Supplementation in Dystrophic Patients. Muscle Nerve. 2003; 27:604–610. https://doi.org/10.1002/mus.10355
9. Bender A, Klopstock T. Creatine for neuroprotection in neurodegenerative disease: end of story? Amino Acids. 2016;48(8):1929–40. https://doi.org/10.1007/s00726-015-2165-0
10. Tarnopolsky MA. Potential benefits of creatine monohydrate supplementation in the elderly. Curr Opin Clin Nutr Metab Care. 2000;3 (6): 497–502. https://doi.org/10.1097/00075197-200011000-00013
11. Gualano B, De Salles Painelli V, Roschel H, Artioli GG, Neves M, De Sá Pinto AL, *et al*. Creatine in Type 2 Diabetes: a randomized, double-blind, placebo-controlled trial. Med Sci Sports Exerc. 2011;43(5):770–8. doi: 10.1249/MSS.0b013e3181fcee7d.
12. Neves M, Gualano B, Roschel H, Fuller R, Benatti FB, De Sá Pinto AL, *et al*. Beneficial Effect of Creatine Supplementation in Knee Osteoarthritis. Med Sci Sports Exerc. 2011;43(8):1538–43. doi:10.1249/MSS.0b013e3182118592.
13. Alves CRR, Santiago BM, Lima FR, Otaduy MCG, Calich AL, Tritto ACC, *et al*. Creatine Supplementation in Fibromyalgia: A Randomized, Double-Blind, Placebo-Controlled Trial. Arthritis Care Res (Hoboken). 2013;65(9):1449–59. doi: 10.1002/acr.22020.
14. Balestrino M, Sarocchi M, Adriano E, Spallarossa P. Potential of creatine or phosphocreatine supplementation in cerebrovascular disease and in ischemic heart disease. Amino Acids. 2016;48(8):1955–67. doi: 10.1007/s00726-016-2173-8.
15. Toniolo RA, Fernandes F de BF, Silva M, Dias R da S, Lafer B. Cognitive effects of creatine monohydrate adjunctive therapy in patients with bipolar depression: Results from a randomized, double-blind, placebo-controlled trial. J Affect Disord. 2017; 224:69–75. doi: 10.1016/j.jad.2016.11.029.
16. Rawson ES, Venezia AC. Use of creatine in the elderly and evidence for effects on cognitive function in young and old. Amino Acids. 2011;40(5):1349–62. doi: 10.1007/s00726-011-0855-9.
17. Ellery SJ, Walker DW, Dickinson H. Creatine for women: a review of the relationship between creatine and the reproductive cycle and female-specific benefits of creatine therapy. Amino Acids. 2016;48(8):1807–17. doi: 10.1007/s00726-016-2199-y.

18. Kreider RB. Effects of creatine supplementation on performance and training adaptations. Mol Cell Biochem. 2003;244(1–2):89–94. PMID: 12701815.
19. Jagim AR, Kerksick CM. Creatine supplementation in children and adolescents. Nutrients. 2021;13(2):664. doi: 10.3390/nu13020664.
20. Jagim AR, Kerksick CM. Creatine Supplementation in Children and Adolescents. Nutrients. 2021 Feb 18;13(2):664. doi: 10.3390/nu13020664.
21. Metzger GA, Minneci PM, Gehred A, Day A, Klingele KE. Creatine supplementation in the pediatric and adolescent athlete-- A literature review. J Orthop. 2023; 38:73–8. doi: 10.1016/j.jor.2023.03.010.
22. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, *et al*. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ. 2009;339: b2700. doi: 10.1136/bmj. b2700.
23. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JA; Cochrane Bias Methods Group; Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343: d5928. doi: 10.1136/bmj.d5928.
24. Roever L. PICO: Model for Clinical Questions. Evid Based Med Pract. 2018; 4:115. doi: 10.4172/2471-9919.1000115
25. Grindstaff PD, Kreider R, Bishop R, Wilson M, Wood L, Alexander C, *et al*. Effects of Creatine Supplementation on Repetitive Sprint Performance and Body Composition in Competitive Swimmers. Int J Sport Nutr. 1997;7(4):330–46. doi: 10.1123/ijsn.7.4.330.
26. Dawson B, Vladich T, Blanksby BA. Effects of 4 Weeks of Creatine Supplementation in Junior Swimmers on Freestyle Sprint and Swim Bench Performance. J Strength Cond Res. 2002;16(4):485–90. PMID: 12423175.
27. Ostojic SM. Creatine Supplementation in Young Soccer Players. Int J Sport Nutr Exerc Metab. 2004;14(1):95–103. doi: 10.1123/ijsnem.14.1.95.
28. Tarnopolsky MA, Mahoney DJ, Vajsar J, Rodriguez C, Doherty TJ, Roy BD, *et al*. Creatine monohydrate enhances strength and body composition in Duchenne muscular dystrophy. Neurology. 2004;62(10):1771–7. doi: 10.1212/01.wnl.0000125178.18862.9d.
29. Escolar DM, Buyse G, Henricson E, Leshner R, Florence J, Mayhew J, *et al*. CINRG randomized controlled trial of creatine and glutamine in Duchenne muscular dystrophy. Ann Neurol. 2005;58(1):151–5. doi: 10.1002/ana.20523.
30. Silva AJ, Machado Reis V, Guidetti L, Bessone Alves F, Mota P, Freitas J, *et al*. Effect of creatine on swimming velocity, body composition and hydrodynamic variables. J Sports Med Phys Fitness. 2007;47(1):58–64. PMID: 17369799.
31. Wong BL, Hynan LS. A Randomized, Placebo-Controlled Trial of Creatine in Children with Spinal Muscular Atrophy. J Clin Neuromusc Dis. 2007; 8:101–10. doi: 10.1097/CND.0b013e3180315c99
32. Juhász I, Györe I, Csende Z, Rácz L, Tihanyi J. Creatine supplementation improves the anaerobic performance of elite junior fin swimmers. Acta Physiol Hung. 2009;96(3):325–36. doi: 10.1556/APhysiol.96.2009.3.6.
33. Banerjee B, Sharma U, Balasubramanian K, Kalaivani M, Kalra V, Jagannathan NR. Effect of creatine monohydrate in improving cellular energetics and muscle strength in ambulatory Duchenne muscular dystrophy patients: A randomized, placebo-controlled 31P MRS study. Magn Reson Imaging. 2010;28(5):698–707. https://doi.org/10.1016/j.mri.2010.03.008
34. Mohebbi H, Rahnama N, Moghadassi M, Ranjbar K. Effect of Creatine Supplementation on Sprint and Skill Performance in Young Soccer Players. Middle East J Sci Res 2012;12(3):397–401. http://doi.org/10.5829/idosi.mejsr.2012.12.3.64214
35. Deminice R, Rosa FT, Franco GS, Jordao AA, de Freitas EC. Effects of creatine supplementation on oxidative stress and inflammatory markers after repeated-sprint exercise in humans. Nutrition. 2013;29(9):1127–32. doi: 10.1016/j.nut.2013.03.003.
36. Hayashi AP, Solis MY, Sapienza MT, Otaduy MCG, De Sá Pinto AL, Silva CA, *et al*. Efficacy and safety of creatine supplementation in childhood-onset systemic lupus erythematosus: A randomized, double-blind, placebo-controlled, crossover trial. Lupus. 2014;23(14):1500–1511. doi: 10.1177/0961203314546017.
37. Solis MY, Hayashi AP, Artioli GG, Roschel H, Sapienza MT, Otaduy MC, *et al*. Efficacy and safety of creatine supplementation in juvenile dermatomyositis: A randomized, double-blind, placebo-controlled crossover trial. Muscle Nerve. 2016;53(1):58–66. doi: 10.1002/mus.24681.
38. Wang CC, Lin SC, Hsu SC, Yang MT, Chan KH. Effects of creatine supplementation on muscle strength and optimal individual post-activation potentiation time of the upper body in canoeists. Nutrients. 2017;9(11):1169. doi: 10.3390/nu9111169.
39. Yáñez-Silva A, Buzzachera CF, Piçarro IDC, Januario RSB, Ferreira LHB, McAnulty SR, *et al*. Effect of low dose, short-term creatine supplementation on muscle power output in elite youth soccer players. J Int Soc Sports Nutr. 2017;14(1). doi: 10.1186/s12970-017-0162-2.
40. Juhász I, Kopkane JP, Hajdu P, Szalay G, Kopper B, Tihanyi J. Creatine Supplementation Supports the Rehabilitation of Adolescent Fin Swimmers in Tendon Overuse Injury Cases. J Sports Sci Med. 2018;17(2):279–88. PMID: 29769829
41. da Silva Azevedo AP, Michelone Acquesta F, Lancha AH, Bertuzzi R, Poortmans JR, Amadio AC, *et al*. Creatine

supplementation can improve impact control in high-intensity interval training. Nutrition. 2019; 61:99–104. doi: 10.1016/j.nut.2018.09.020.

42. Dover S, Stephens S, Schneiderman JE, Pullenayegum E, Wells GD, Levy DM, *et al*. The effect of creatine supplementation on muscle function in childhood myositis: A randomized, double-blind, placebo-controlled feasibility study. J Rheumatol 2021;48(3):434–441. doi: 10.3899/jrheum.191375.

43. Vargas-Molina S, García-Sillero M, Kreider RB, Salinas E, Petro JL, Benítez-Porres J, *et al*. A randomized open-labeled study to examine the effects of creatine monohydrate and combined training on jump and scoring performance in young basketball players. J Int Soc Sports Nutr. 2022;19(1):529–42. doi: 10.1080/15502783.2022.2108683.

44. Wallimann T, Schlosser T, Eppenberger HM. Function of M-line-bound creatine kinase as intramyofibrillar ATP regenerator at the receiving end of the phosphorylcreatine shuttle in muscle. J Biol Chem. 1984;259(8):5238–5246. PMID: 6143755.

45. Harris RC, Soderlund K, Hultman E. Elevation of creatine in resting and exercised muscle of normal subjects by creatine supplementation. Clin Sci (Lond). 1992;83(3):367-374. https://doi.org/10.1042/cs0830367

46. Mills S, Candow DG, Forbes SC, Neary JP, Ormsbee MJ, Antonio J. Effects of creatine supplementation during resistance training sessions in physically active young adults. Nutrients. 2020;12(6):1880. https://doi.org/10.3390/nu12061880

47. Pakulak A, Candow DG, Totosy de Zepetnek J, Forbes SC, Basta D. Effects of Creatine and Caffeine Supplementation During Resistance Training on Body Composition, Strength, Endurance, Rating of Perceived Exertion and Fatigue in Trained Young Adults. J Diet Suppl. 2022;19(5):587–602. https://doi.org/10.1080/19390211.2021.1904085

48. Walter MC, Lochmüller H, Reilich P, Klopstock T, Huber R, Hartard M, *et al*. Creatine monohydrate in muscular dystrophies: A double-blind, placebo-controlled clinical study. Neurology. 2000;54(9):1848-1850. https://doi.org/10.1212/WNL.54.9.1848

Recibido: 08/08/2024
Aceptado: 30/10/2024