Beyond creatine: evaluating guanidino acetic acid as a novel ergonutritional aid for basketball players

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Summary

This study investigates the impact of Guanidinoacetic Acid (GAA) supplementation in basketball, a high-intensity sport requiring optimal nutrition and recovery strategies. Ergogenic aids like Creatine (CRM) are common, but GAA, a creatine precursor, may be more beneficial. Involving 31 semi-professional male and female players, the study compared GAA, CRM, and placebo groups. Results showed significant physical performance improvements in females using GAA, particularly in Counter Movement Jump (CMJ) and Handgrip (HG). Male GAA users showed CMJ improvements, while CRM enhanced cognitive functions in males. The study suggests GAA's potential in enhancing physical performance, especially in women, and highlights the need for further research on GAA and CRM effects, considering gender differences.

Más allá de la creatina: análisis del potencial del ácido guanidino acético como nueva ayuda ergogénica de interés para el baloncesto

Palabras clave:
Ergonutrición. Baloncesto. Creatina. Ácido guanidino acético. Nutrición deportiva.

Resumen

Este estudio examina el impacto de la suplementación con Ácido Guanidinoacético (GAA) en el baloncesto, un deporte de alta intensidad que demanda estrategias de recuperación nutricional óptimas. Aunque la Creatina Monohidrato (CRM) es una ayuda ergogénica muy utilizada para este fin, se ha hipotetizado que, el GAA, precursor de la creatina, podría ofrecer mayores beneficios. La investigación, que involucra a 31 jugadores semiprofesionales de ambos sexos, compara grupos que recibieron GAA, CRM y placebo. Los resultados revelan mejoras significativas en el rendimiento físico de las mujeres que utilizaron GAA, especialmente en el Salto con contra movimiento (CMJ) y la Fuerza Manual (HG). Por otro lado, los hombres que emplearon GAA experimentaron mejoras en el CMJ, mientras que la CRM potenció sus funciones cognitivas. Este estudio señala el potencial del GAA para mejorar el rendimiento físico, destacando su relevancia particular en mujeres, y subraya la necesidad de investigaciones adicionales sobre los efectos del GAA y la CRM, considerando las particularidades de género.

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Introduction

In basketball, players must manage intense, fast-paced play with minimal rest, challenging both their physical and mental capacities. They also contend with external pressures such as frequent travel, limited sleep, and a dense game schedule. Thus, prioritizing proper nutrition and effective recovery tactics is essential for optimizing their performance and readiness in this demanding sport[1]. In particular, in certain circumstances, the use of ergogenic aids may also be necessary to support players in achieving their performance goals[2]. Among them, one of the most popular ergogenic aids for the past 30 years has been creatine monohydrate (CRM)[1]. It is widely considered safe and reliable for athletes and also, has been associated with potential beneficial effects on physical conditioning and cognitive performance[1], as well as promoting recovery[1]. Due to these benefits, basketball players have long used CRM supplementation to improve their physical and cognitive performance and recover. However, CRM presents some limitations such as low solubility in water, transportability issues, and heterogeneous response among individuals (non-responders)[1]. To overcome these limitations, researchers are studying studied other novel formats of CRM[3]. Despite the emergence of various alternative forms of this product, none of them have yet surpassed the efficacy of CRM in enhancing muscle uptake and high-intensity exercise performance[4]. While creatine citrate, creatine pyruvate, and magnesium creatine chelate have shown some potential, they do not exceed CRM in terms of muscle uptake and their evidence base is less robust[4]. Other forms, such as creatine ethyl ester, buffered creatine, and creatine nitrate, lack substantial supportive evidence. However, guanidinoacetic acid (GAA), a precursor of creatine, has been proposed as an advantageous and interesting alternative for CRM supplementation[5].

The first evidence of its performance-enhancing effects dates back to the early 1950s[6]. The GAA is naturally synthesized in the kidney and pancreas through an enzyme-catalyzed step from L-arginine and glycine, ultimately leading to the formation of creatine. It is theorized that oral administration of GAA is easily absorbed from the gastrointestinal tract and rapidly metabolized to creatine[6], improving cellular bioenergetics[6] and acting as fuel in high-energy-demand tissues such as skeletal muscle and the brain[7].

Additionally, the response to GAA seems to be more significant in terms of performance for individuals compared to non-responders[8]. The administration of guanidinoacetic acid (GAA) is widely recognized as safe and has been associated with beneficial effects that outweigh its potential side effects[9]. While caution must be exercised regarding potential neurotoxicity[10], GAA has demonstrated its efficacy even at low doses, typically ranging from approximately 1.2g/d1.2 g/d to around 5g[6]. In male athletes, GAA was associated with enhanced high-intensity anaerobic performance and increased body creatine levels[11], suggesting its potential as an ergogenic aid. Meanwhile, women with Chronic Fatigue Syndrome experienced improvements in muscular strength and aerobic power following GAA supplementation[12]. Moreover, GAA has been linked to enhanced brain performance, suggesting its potential cognitive benefits[7].

While these outcomes are significant across various athletic disciplines, they hold particular importance in high-intensity, intermittent sports like basketball. In basketball, the fundamental importance of lower body power and force production, particularly for actions such as jumping, is well recognized. This is often measured using the Counter Movement Jump (CMJ) test, which closely mirrors in-game jumping demands. The outcomes from this test highlight the essential role of ample creatine reserves in the lower body for optimal basketball performance[1]. Similarly, the capacity to generate force through explosive upper body movements, crucial for actions like throwing, shooting, and passing, underscores the importance of creatine stores in facilitating strength and power output. Equally, the Medicine Ball throw test provides valuable insights into these upper body strength requirements in basketball. Moreover, cerebral creatine reserves are vital to support cognitive abilities in sports performance[7], including maintaining focus, activating/inhibiting automatic responses, and adapting to changing situations on the court. These cognitive demands can be assessed using specific tests such as reaction time or Stroop On/Off, potentially indicating the use of cerebral creatine reserves. The potential of CRM to facilitate recovery is increasingly recognized, not confined to the court but extending to post-exercise recuperation, which is essential for an ergogenic aid in the context of basketball[2]. This includes its capacity to aid in glycogen restoration and attenuate increases in creatine kinase and delayed-onset muscle soreness[13]. Despite the limited data on GAA's role in recovery, it is postulated to contribute to recovery by enhancing insulin sensitivity, modulating GABA neurotransmission, promoting vasodilation, or being utilized in an unidentified metabolic pathway instigated by intense exercise[11].

The outcomes observed in prior research, in alignment with the unique requirements of basketball, invite the hypothesis that GAA may have a potential ergogenic effect in basketball players. To the best of the authors' knowledge, this study is the first examining the effectiveness of GAA supplementation in the area of basketball performance. The main aim of this study is to investigate the potential effects, of GAA as an effective ergo nutritional in basketball. As a secondary aspect, and parallel to this research, a comparative study will be conducted against CRM to investigate potential differences between these supplementation strategies. Finally, this work also aims to provide detailed information specifically for female basketball players. This is important because most studies in this field are conducted on men, and the data is subsequently extrapolated to the female population. This approach often overlooks the possibility that women's responses could be different.

Design

Thirty-one non-vegetarian basketball players, originally 33 but reduced due to team change and COVID-19, participated in this study. The group comprised 17 semi-professional female players from various Spanish divisions (average 24 years, 1.78m, 67.85kg) and 14 male players (average 23 years, 1.92m, 85.81kg). Inclusion criteria included players aged 16-40 in Spanish divisions, attending most practice sessions, no recent injuries, and no drug/supplement use. Vegetarians, those with metabolic disorders, or recent injuries were excluded.

The study, approved by the Basque Country University Ethics Committee and adhering to the Declaration of Helsinki and EU data regulations, was a simple-blind, placebo-controlled trial during the 2021-2023 seasons. Participants were divided into three groups: guanidinoacetic acid (GAA), creatine Monohydrate (CRM), and placebo, with detailed demographics provided for each group.

Participants were administered either a GAA product (comprising 2g of CRM and 2g of GAA, sourced from CreGAAtine, Applied Bioenergetic Lab and Carnomeda), CRM (4g, Nutrisport), or a Placebo (4g Maltodextrine, Decathlon). The selected doses were based on the safety and efficacy of GAA and CRM in exercise, sport, and medicine. Each product was provided to the participants in sachet form prior to the commencement of the experiment. Instructions were given to consume the product during main meals, allowing them to choose either lunch or dinner to better fit their daily routines. This was done to enhance adherence and minimize the risk of gastrointestinal issues[1].

Each participant underwent two trials and was assessed before and after 4 weeks of supplementation. Physical, cognitive, and body composition variables were measured to evaluate differences induced by the interventions across the three groups (Figure 1).

During testing days, participants warmed up at their basketball court for 15 minutes, led by a coach. The warm-up routine included 8 minutes of jogging, 5 minutes of full-body stretches, and 3 minutes of intense running[14].

After warming up, participants performed tests including Medicine Ball throw, Handgrip, Counter Movement Jump, Stroop tests, and LED Reaction time. They were familiar with these tests and practiced each three times. Staff demonstrated correct techniques. Recovery periods of 5 minutes were given between some tests, with 3 minutes for others. No break was provided between Handgrip and Counter Movement Jump tests. Feedback was given during tests to maximize performance.

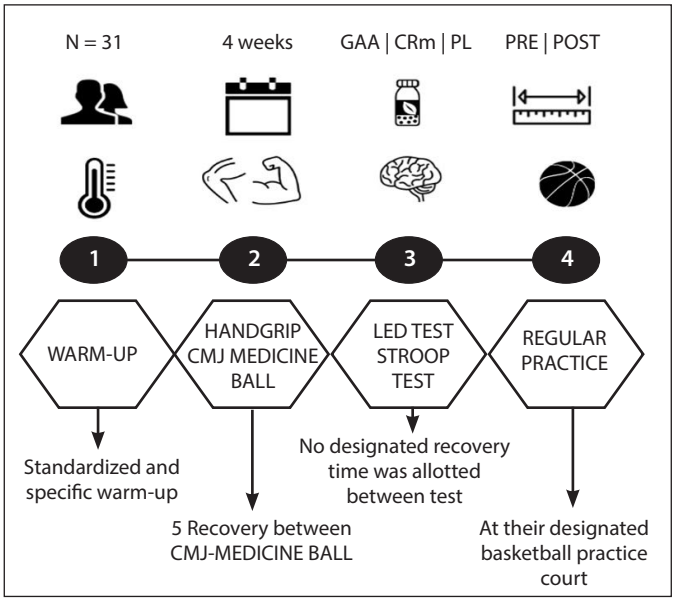
Material and method

To assess lower neuromuscular performance: the CMJ test, a widely used field test in basketball research[15], was employed to assess lower body neuromuscular performance. Each participant performed three maximal jumps with a two-minute rest interval between jumps[15]. To ensure accurate measurement, the validated and reliable smartphone app My Jump Lab®[16] was utilized to record and analyze the jumps. To asses upper Neuromuscular Performance, the Handgrip (HG) test, a widely used method to assess upper body dynamic strength[17], was performed by participants. They executed three maximal handgrip contractions with their dominant hand, and the best attempt was recorded. The Medicine Ball (MB) test, another common test in basketball research, was also conducted. Participants were instructed to perform a horizontal medicine ball throw using a two-hand chest pass movement, following established protocol instructions[18]. Female participants used a 3kg medicine ball, while male participants used a 5 kg medicine ball. To ensure accurate measurement, the throws were recorded using two strategically positioned video cameras for clear visibility. Subsequently, each throw was analyzed by two researchers using the Kinovea analysis software, achieving a high intra-class correlation coefficient of 0.99[19].

Regarding cognitive performance, to assess psychomotor Speed and Cognitive Flexibility, the SO and SOFF tests were employed. These tests have proven to be sensitive in detecting cognitive impairment[20]. To ensure accurate measurement, a validated and reliable smartphone app, the Stroop Smartphone App, was utilized. The test[21] consisted of two tasks: 1) "Stroop Off" (the easier task), where participants matched a color name to the displayed color; and 2) "Stroop On" (the more challenging task), where participants matched the color of the word presented in discordant coloring (e.g., the word "blue" displayed in red color). In both Stroop modes, the test concluded after five consecutive correct runs. However, if a mistake was made, the run was interrupted, and the player had to restart. To assess perceptual and decision-making skills (reaction time), LED test was used to provide insights into the speed and accuracy of player responses[22]. A reliable and validated test designed for fast-action sports such as basketball was administered[22]. Three light sensors with LED indicators were positioned at fixed heights on the left, center, and right side of the player's defensive position (mass center). Players assumed the starting position and promptly touched the illuminated LED indicator with either hand, aiming to react as quickly as possible.

Dietary intake and training protocols were closely monitored throughout the study. To assess dietary habits, players completed a validated Food Frequency Questionnaire (FFQ) that has been utilized in previous sports nutrition research[23]. Through a self-administered questionnaire, participants were queried about their health status, dietary style, their perception of the adequacy of their nutritional habits in relation to recommendations, and their perception of their fitness level (Anex 1). To minimize potential interference from dietary changes or the use of other nutritional supplements[23], participants were instructed to maintain their usual dietary intake throughout the study period and avoid the consumption of any dietary supplements that could potentially provide ergogenic benefits. To track their training activities, participants completed a self-administered questionnaire detailing their weekly team practice duration and frequency of resistance training

Figure 1. Chronology of Research Events.



sessions[24]. Additionally, to evaluate the potential side effects associated with GAA, CRM, or PL supplementation, players were asked to report any adverse effects on their gastrointestinal system through an online survey (https://form.typeform.com/to/fks2Xck8). The survey was available until 1st December 2022, with the last access to the link recorded on 10th January 2023 (Survey Close Date: 1-12-2022; Last access to the link 10-01-2023). Participants were also requested to provide subjective assessments of their overall health status, dietary habits, eating patterns, and physical fitness level.

Statistical analysis

Data was analyzed using descriptive statistics (mean, standard deviation) for normality and homoscedasticity. Student's t-tests were applied to normal data, and Wilcoxon rank-sum tests for non-normal data. Group comparisons were conducted, categorizing effect sizes (trivial <0.20 to very large >2.0).

Players' outcomes were classified into responders (>10% difference), quasi-responders (5%–10% difference), and non-responders (<5% difference) based on previous research. Categories included non-responders (≥50% variables reported as "non-responders"), responders (≥50% variables reported as "responders"), and quasi-responders. Significance was set at P <0.05, analyzed with SPSS® 26.0 and R 4.2.2.

The study used a 2-way ANOVA (group × trial) with Bonferroni-corrected post-hoc tests to analyze changes. Effect size was measured using partial eta squared. Responders surpassed the smallest worthwhile change (SWC), set at 0.2 times the between-participant deviation, signifying the minimum change above measurement error at 95% confidence.

Results

A total of 31 semiprofessional basketball players (17 female players from the 1st, 2nd, 3rd, and Spanish Basketball Divisions and 14 male players from the 2nd and 4th divisions) completed the study. No differences were found among groups regarding their health status, diet type, eating habits, fitness level, weekly team practice minutes, or weekly resistance frequency. Only one player (CRM group: 3.2%, P>0.05) reported gastrointestinal adverse symptoms whereas the other volunteers (96.8%) reported no major side effects after they participated in the study. Eleven players (52%) were categorized as responders, five as quasi-responders (24%), and five as non-responders (24%). The secondary outcomes for: 1) Anaerobic neuromuscular performance (MB, HG, CMJ) (Table 1); 2) cognitive performance (SO, SOFF, LED) (Table 2) were assessed at baseline (pre-intervention; T1) and 4-week follow-up (post-intervention; T2).

Table 1. Physical condition outputs in the three study groups at the baseline (T1) and after 4 weeks (T2).

Sex	Group	T1	T2	Delta	%VAR	p	D	P	n2p	MBI
								(TXG)		
MB										
Female	GAA	2.79 ± 0.28	2.81 ± 0.24	0.02 ± -0.04	1.02 ± 3.35	0.530	-0.32; small	0.05 [B]	0.18	Most Likely Trivial Increase.
	CRM	3.07 ± 0.44	3.06 ± 0.37	-0.04 ± -0.01	0.03 ± 5.36	0.900	-0.36; small			Most Likely Large Increase.
	PL	3.86 ± 1.87	3.84 ± 1.94	-0.01 ± 2.62	-1.22 ± 2.49	0.500	0.12; very small			Unclear Difference.
Male	GAA	3.47 ± 0.16	3.52 ± 0.14	0.05 ± 0.02	1.47 ± 1.81	0.200	-0.09; very small	0.65 [B] 0.13 [A]	0.15	Likely Trivial Increase.
	CRM	3.77 ± 0.38	3.91 ± 0.37	0.14 ± 0.1	3.62 ± 1.83	0.010	0.02; very small			Most Likely Trivial Increase.
	PL	3.73 ± 0.41	3.67 ± 0.47	0.06 ± 0.06	-1.52 ± 3.59	0.430	0.01; very small			Most Likely Trivial Decrease.
HG										
Female	GAA	38.71 ± 6.65	41.71 ± 5.77	3 ± -0.88	**8.32 ± 5.19**	**0.003**	-0.38; small	0.743	0.16	Likely Trivial Increase.
	CRM	34.8 ± 3.56	37.2 ± 2.59	-0.88 ± 2.4	7.35 ± 7.56	0.09	-0.18; small			Almost Certainly Very Large Increase.
	PL	41.2 ± 4.97	41 ± 4.95	0.2 ± 0.2	-0.45 ± 2.49	0.700	-0.14; medium			Almost Certainly Very Large Increase.
Male	GAA	55.75 ± 7.23	58.5 ± 7.33	2.75 ± 0.10	5.03 ± 3.02	0.040	-0.48; small	0.072	0.10	Most Likely Trivial Increase.
	CRM	57.6 ± 9.02	59.2 ± 8.56	2.4 ± 0.46	**2.95 ± 3.74**	**0.150**	-0.77; very small			Most Likely Trivial Increase.
	PL	53.4 ± 4.34	54 ± 4.18	0.6 ± 0.16	1.15 ± 1.05	0.070	0.04; very small			Most Likely Trivial Increase.
CMJ										
Female	GAA	28.84 ± 4.36	30.47 ± 3.85	1.63 ± -0.51	**6.01 ± 3.37**	**<0.001**	-0.22; small	0.850	0.16	Most Likely Trivial Increase.
	CRM	30.63 ± 3.06	32.45 ± 5.15	-0.51 ± 1.82	5.55 ± 6.65	0.160	-0.13; very small			Likely Moderate Increase.
	PL	26.83 ± 5.71	26.56 ± 5.74	0.27 ± 0.3	-1.04 ± 1.51	0.200	0.03; very small			Likely Moderate Increase.
Male	GAA	39.4 ± 2.94	40.14 ± 3.77	0.74 ± 0.83	1.79 ± 2.57	0.260	-0.4; small	0.013 [B] 0.263 [A]	0.28	Most Likely Trivial Increase.
	CRM	36.26 ± 4.26	36.88 ± 5.05	0.94 ± 0.79	1.52 ± 4.08	0.410	-0.43; small			Most Likely Trivial Decrease.
	PL	34.17 ± 3.55	34.07 ± 4	0.10 ± 0.45	-0.4 ± 2.68	0.790	0.05; very small			Most Likely Trivial Decrease.

Data are expressed as mean ± standard deviation. Two-factor repeated-measures ANOVA. [A] GAA *Vs* CRE; [B]GAA *Vs* CONT; [C]CRE *Vs* GAA; [D]CRE *Vs* CONT.
*Significantly different between study points (T1 *Vs* T2) P <0.05.
MB: Medicine Ball; HG: Handgrip; CMJ: Counter Movement Jump; GAA: Guanidinoacetic acid group; CRM: Creatine Monohydrate group; PL: Placebo group; %VAR: Percentage of variation; D: Cohen's D; VS: Very Small; S: Small; P (TxG): Group-by-time interaction.

Table 2. Cognitive performance outputs in the three study groups at the baseline (T1) and after 4 weeks (T2).

Sex	Group	T1	T2	Delta	%VAR	p	D	P	n2p	MBI
								(TXG)		
SON										
Female	GAA	47.14 ± 6.15	46.95 ± 6.05	-0.19 ± -0.1	-0.4 ± 0.9	0.370	0.01; very small	0.008[A]	0.27	Most Likely Trivial Decrease.
	CRM	52.21 ± 2.14	54.66 ± 6.78	-0.1 ± 2.45	4.49 ± 9.34	0.340	0.69; medium			Possibly Small Increase.
	PL	48.14 ± 2.42	47.66 ± 2.34	0.48 ± 0.10	-0.81 ± 6.6	0.750	0; very small			Possibly Moderate Increase.
Male	GAA	50.05 ± 4.78	49.99 ± 4.5	0.06 ± 0.28	-0.07 ± 1.79	0.900	-0.04; very small	0.001[A]	0.33	Most Likely Trivial Decrease.
	CRM	57.38 ± 2.05	54.99 ± 4.47	2.39 ± -2.42	-4.08 ± 8.01	0.310	-0.47; small			Possibly Small Decrease.
	PL	51.3 ± 4.43	51.3 ± 4.67	0 ± -0.24	0 ± 2.73	0.990	0.6; medium			Most Likely Trivial Increase.
SOFF										
Female	GAA	44.96 ± 4.59	45.12 ± 4.44	0.16 ± -0.15	0.39 ± 0.94	0.320	0.01; very small	0.338	0.26	Most Likely Trivial Increase.
	CRM	52.12 ± 0.95	54.18 ± 6.16	-0.15 ± 2.06	3.84 ± 10.14	0.440	0.36; small			Possibly Small Increase.
	PL	45.1 ± 2.54	36.4 ± 2.48	8.7 ± 0.6	-19.72 ± 44.89	0.380	0.06; very small			Unclear Difference.
Male	GAA	45.45 ± 4.01	45.39 ± 4.15	0.06 ± -0.14	-0.15 ± 1.98	0.900	0.03; very small	0.001[D]	0.59	Most Likely Trivial Decrease.
	CRM	57.81 ± 3.2	55.77 ± 7.47	2.04 ± -4.27	-3.82 ± 9.02	0.390	-0.49; small			Possibly Trivial Decrease.
	PL	47.44 ± 4.21	47.22 ± 3.32	0.22 ± 0.89	-0.35 ± 1.79	0.621	0.2; small			Most Likely Trivial Decrease.
LED										
Female	GAA	69.43 ± 9.61	64.86 ± 6.72	-4.57 ± -2.89	**-6.03 ± 6.6**	**0.040**	0.02; very small	0.637	0.14	Possibly Trivial Decrease.
	CRM	74.8 ± 6.46	71.2 ± 4.21	-2.89 ± -3.6	-4.45 ± 6.89	0.220	0.41; small			Likely Moderate Decrease.
	PL	70 ± 4	70.4 ± 3.13	0.4 ± 0.87	0.64 ± 1.72	0.470	0.32; small			Likely Trivial Increase.
Male	GAA	68 ± 3.74	67.94 ± 3.2	0.06 ± 0.54	-0.05 ± 1.32	0.900	0.55; medium	0.857	0.37	Most Likely Trivial Decrease.
	CRM	67.4 ± 6.5	64.16 ± 9.02	3.24 ± -2.52	-4.52 ± 12.58	0.430	0.66; medium			Possibly Trivial Decrease.
	PL	76.2 ± 6.61	74.49 ± 3.89	1.71 ± 2.72	-1.99 ± 4.21	0.350	-0.11; very small			Likely Trivial Decrease.

Data are expressed as mean ± standard deviation. Two-factor repeated-measures ANOVA. [A]GAA *Vs* CRE; [B]GAA *Vs* CONT; [C]CRE *Vs* GAA; [D]CRE *Vs* CONT.
*Significantly different between study points (T1 *Vs* T2) *P* <0.05.
SON: Stroop On; SOFF: Stroop Off; LED: Reaction Time; GAA: Guanidinoacetic acid group; CRM: Creatine Monohydrate group; PL: Placebo group; %VAR: Percentage of variation; D: Cohen's D; VS: Very Small; S: Small; P (TxG): Group-by-time interaction.

In terms of anaerobic neuromuscular performance, female group players who supplemented with GAA exhibited notable and statistically significant enhancements in their CMJ results (6.01+3.37%; *P* <0.001; ES = 0.22, small), and HG (8.32+5.19%; *P* = 0.003; ES = 0.38; small) performance. No differences were found in the MB (1.02 + 3.35%; *P* = 0.53; ES = 0.32; small). However, for the MB, ANOVA revealed a significant effect of the group, regarding treatment *Vs.* time. Post-hoc comparisons indicated that the GAA group showed significant (0,05) improvements in the MB compared to the control and CRM groups. In contrast, CRM supplementation did not yield significant improvements in any measured anaerobic neuromuscular performance variables. Comparatively, the PL group did not show any significant differences. Regarding male group, while no significant differences were initially comparing GAA, CRM and PL groups, the application of one-way ANOVA tests revealed statistically significant differences. Specifically, these differences favored the GAA group when compared to the PL group in CMJ (0.,013). Furthermore, effect size calculations using eta squared (η^2) showed a significant interaction (0.28) effect for CMJ.

When it comes to cognitive performance, the inclusion of GAA supplementation in the female group also yielded a beneficial effect on LED (-6.03+6.6%; *P* = 0.040; ES = 0.02; very small) whereas SOFF (0.39 + 0.94%; *P* = 0.32; ES = 0.01; very small) and SO (-0.4 + 0.9; *P* = 0.37; ES = 0.01; very small) did not show significant differences. Regarding SO, the ANOVA did detect significant interactions regarding treatment *Vs.* time, and the posterior Bonferroni corrected post hoc test revealed significant improvements in favor of the GAA group (0.008). No differences were found in both the CRM and PL group. In the male group, initial raw data analysis did not reveal any noticeable differences in cognitive performance among the GAA, CRM, and PL groups, further analysis using one-way ANOVA tests revealed nuanced variations. Specifically, the ANOVA tests detected a significant difference in the SOFF, favoring the CRM group over the PL group (0,001), and the GAA group over the CRM group (0,001).

Discussion

This study investigated the ergogenic effects of GAA in basketball players, comparing its impact on males and females and against CRM. Results indicate GAA enhances anaerobic performance in females (MB, HG, CMJ) and CRM improves cognitive functions in males. However, varied gender responses suggest more research is needed to understand GAA and CRM effects and to optimize supplementation strategies in sports performance, particularly exploring gender-specific impacts.

Basketball is a sport characterized by many intermittent high-intensity actions[1] in which the aerobic energetic system is quantitatively higher, but the anaerobic pathways are qualitatively decisive[1]. Both male and female basketball players must deal with numerous situations requiring their maximum physical effort throughout a game, leading to high levels of fatigue. Consequently, to cope with these demands, proper physical condition is crucial to develop optimal performance. Specific actions based on jumps or throws are usually measured to describe the players' physical readiness because the tests involve physical demands like those of the game.

In the context of the MB test, the effects of GAA and CRM supplementation showed distinct differences between male and female groups. The GAA group demonstrated significant improvements over time, hinting at a positive impact of GAA supplementation on upper body neuromuscular performance in basketball players, irrespective of gender. For the female group, the possibility of a heightened sensitivity to GAA[12] supplementation may have underpinned these improvements. This holds substantial implications given that upper body strength is a pivotal aspect of basketball performance, primarily in actions such as rebounding and shooting, which necessitate robust arm and shoulder movements. The male group also exhibited a positive response to GAA supplementation, albeit less pronounced than their female counterparts. This may be attributable to the typically higher initial muscle mass and strength in male athletes[25], potentially resulting in a less noticeable impact of GAA supplementation.

Comparatively, between the GAA and CRM groups, GAA appeared to have a superior effect on MB performance, suggesting that GAA might offer additional ergogenic benefits in the context of basketball performance.

The CMJ test is one of the most commonly used field tests in the basketball literature to assess lower body neuromuscular performance. Our findings suggest that supplementing with GAA may improve it, particularly among female athletes. The male group, on the other hand, showed only marginal improvements after CRM supplementation.

Dietary GAA has been observed to improve cellular bioenergetics by stimulating creatine biosynthesis, which may be the primary mechanism[6] driving the observed enhancements in CMJ performance. This mechanism has been widely observed in CRM supplementation reporting explosive/strength gains in the lower body and aerobic power. Creatine raises levels of intramuscular PCr, in combination with a phosphoryl group (Pi) via the enzymatic reaction of creatine kinase (CK)[26]. This rephosphorylation of the adenosine diphosphate acceleration resynthesis and maintain ATP bioavailability which as result allows muscle fiber to develop fast and strong muscle contractions. Another mechanism that would explain these results is, the role of creatine in calcium recapture in the sarcoplasmic reticle, leading to a more rapid actin-myosin cross-cycle, and therefore enhancing muscle strength and endurance[26]. However, the physiological roles of GAA extend beyond creatine synthesis. It has been found to stimulate hormonal release and neuromodulation, alter the metabolic utilization of arginine, and adjust oxidant-antioxidant status[6]. This hypothesis is supported by creatine´s ability to reduce the formation of reactive oxygen species through an ADP-recycling mechanism via mitochondrial CK[27]. Also, regarding the protective effect on glycogen storage, oral CRM supplementation increases GLUT4 protein content[28] and therefore increases the ability to uptake glucose[29]. This way, GAA may promote faster recovery and better performance.

For instance, the stimulation of hormonal release could induce higher levels of growth hormone or testosterone, which are known to enhance muscle strength and power. The neuromodulator role of GAA[30] could potentially improve the efficiency of neuromuscular transmission, leading to more effective force production during the CMJ. The physiological mechanisms underlying this observation could be multiple and complex. Dietary and pre-existing muscle creatine status can influence the efficacy of CRM supplementation[1]. Given that males typically have higher baseline creatine levels due to higher muscle mass[25] it's plausible that they might not experience the same degree of benefit from CRM supplementation as females do from GAA. Finally, it's unclear whether GAA offers a superior benefit in terms of enhancing handgrip strength and the differences between males and females.

The reasons for this difference are not fully understood but may relate to neural, muscular, or motor learning traits.

Basketball places significant cognitive demands on players, requiring quick, accurate responses to unpredictable events in high-uncertainty conditions. This leads to psychobiological fatigue, impacting motor skills and decision-making. Our study on GAA supplementation offers insights to address these challenges.

Female participants who took GAA showed notable improvements in LED task performance, indicating better reaction time and eye-hand coordination. This aligns with the fact that females typically have a smaller creatine pool in the upper body compared to males, highlighting the potential benefits of increased creatine synthesis from GAA supplementation in such situations.

Another possible mechanism that may explain the improvement is the elevation of GAA concentrations in specific brain regions such as cerebellum[31]. While CRM supplementation increases muscle storage to a greater degree than in brain tissue[32], this small contribution seems to protect athletes from mental fatigue[33].

When mental fatigue occurs (low PCr among other things), a feedback signal controls the suppression of the excitatory transmission, preventing exhaustion and fatal damage. In periods of high neuronal activity, adenosine, acting through A1R and A2AR receptors, plays a key role in brain function by balancing excitatory and inhibitory signals, and fostering synaptic plasticity[34]. In the event of a brain insult, A1R initiates a protective response, but prolonged activation can lead to desensitization. Conversely, A2AR is upregulated potentially triggering adaptive changes, yet this might worsen brain damage, making A2AR blockade a potential neuroprotective strategy[34]. GAA's ability to raise the brain's total creatine storage, and particularly in the cerebellum[31] can acts as a rapidly accessible energy reserve for the regeneration of ATP, leading to a protective neural excitability effect, showing, therefore, meaningful differences when compared with CRM.

In contrast, the male participants did not initially exhibit any significant cognitive performance improvements following supplementation. However, deeper analysis using a one-way ANOVA revealed significant enhancements in the SOFF task performance in the groups supplemented with CRM and GAA, with GAA displaying a superior efficacy. This difference could be rooted in the metabolic role of GAA, thereby

enhancing energy metabolism in high-energy demand tissues such as the brain[31].

Furthermore, GAA may also stimulate nitric oxide production, improving cerebral blood flow, and consequently, oxygen and nutrient delivery to the brain, bolstering cognitive function[35].

The observed gender-based differences in the responses to GAA supplementation underscore the role of physiological characteristics and gender-specific creatine distribution in influencing cognitive performance. The evidence that females, typically characterized by lower upper body creatine levels[25], may stand to benefit more from GAA supplementation, stresses the potential utility of gender-tailored supplementation strategies in sports performance. Our findings invite us to hypothesize that GAA may also be superior to CRM to facilitate cognitive recovery in basketball players who are typically exposed to chronic mental fatigue, such as sleep deprivation. However, new research lines would be necessary to support this hypothesis.

This article acknowledges limitations, including a small sample size, challenging to increase in elite sports and amid the COVID-19 pandemic. Despite this, the study's strength lies in its real-world setting during the 2020-2022 competitive period, adding ecological validity to the GAA and CRM behavior analysis. A notable drawback is the inability to track women's hormonal phases, yet the research still contributes valuable insights for female basketball players. The study duration was limited to four weeks.

The study's findings are relevant for high-level sports requiring quick results. While it didn't use biological techniques like blood tests for primary outcomes, it utilized non-invasive, cost-effective methods for assessing nutritional interventions. A key strength is the study's ecological validity and its replicable methodology, beneficial for sports scientists, trainers, nutritionists, and coaches.

Future research should focus on comparing GAA and CRM, particularly their cognitive effects, for more conclusive evidence. More studies are needed to understand GAA and CRM's impact in basketball, uncover their mechanisms, and refine supplementation strategies. It's important for researchers and sports professionals to consider gender and individual differences in exploring these supplements to enhance basketball performance.

Conclusions

GAA supplementation improved physical performance in females, notably in CMJ, handgrip strength, and medicine ball throw. CRM showed cognitive benefits for males, enhancing attention and control. Further research should examine these supplements' specific effects in basketball, considering gender differences. Thus, female players could use GAA to boost physical abilities, particularly lower body and upper body strength. Male players might also benefit from CRM and GAA's cognitive enhancements.

Conflict of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

- SMO serves as a member of the Scientific Advisory Board on Creatine in Health and Medicine (AlzChem LLC).
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