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Effects of oral L-arginine supplementation on post-resistance exercise hypotension in normotensive individuals: a double-blind and crossover study

Efeitos da suplementação oral de L-arginina na hipotensão pós-exercício de força em indivíduos normotensos: um estudo duplo-cego e cruzado

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ABSTRACT

Introduction: L-arginine (L-Arg) is an essential precursor for nitric oxide (NO) synthesis and promotes hypotensive effects. However, evidence is limited regarding its role in enhancing post-exercise hypotension (PEH), particularly following resistance exercise (RE) in normotensive individuals, as existing research favors aerobic exercise. Objective: This study investigated whether oral L-Arg supplementation could potentiate PEH after a single RE session in 12 recreationally active, normotensive males. Methods: Participants received 6 g of L-Arg or a placebo at the end of the RE protocol (60% 1RM, 3 sets of 12 repetitions) and 30 min post-RE, with blood pressure (BP) monitored for 60 minutes in two sessions. Statistical analyses utilized repeated-measures ANOVA, Tukey post hoc, and Student's t-test ($p < 0.05$). Results: Participants at baseline [26.5 ± 4.98 years; 22.8 ± 1.80 kg/m2; systolic and diastolic blood pressure 106 ± 5 and 69 ± 9 mmHg, respectively]. The change in BP in the L-Arg condition was significantly greater than in the placebo session at 45 and 60 minutes post-RE ($p < 0.05$). L-Arg supplementation achieved peak reductions of 21.5 ± 8.3 mmHg in systolic BP, 11.3 ± 7.2 mmHg in diastolic BP, and 18.1 ± 8.7 mmHg in mean BP ($p < 0.05$). Plasma NO concentration was significantly higher 60 minutes post-RE in the L-Arg session (Pre: 15.3 ± 1.2 vs. Post: 24.6 ± 3.5 µM/L, $p < 0.05$) compared to the placebo session (Pre: 15.9 ± 3.2 vs. Post: 14.9 ± 0.4 µM/L, $p < 0.05$). Conclusion: The L-Arg supplementation successfully potentiated PEH following RE in normotensive subjects, suggesting its potential as a non-pharmacological intervention for the primary prevention of cardiovascular diseases, likely mediated by increased NO bioavailability.

Keywords: Blood pressure; Ergogenic aids; Nitric oxide; Strength exercise.

RESUMO

Introdução: A L-arginina (L-Arg) é precursora essencial na síntese de óxido nítrico (ON) e promove efeitos hipotensores. Contudo, evidências sobre seu papel na hipotensão pós-exercício (HPE) são limitadas, especialmente após exercício de força (EF) em normotensos, dado que as pesquisas existentes priorizam o exercício aeróbio. Objetivo: Investigar se a suplementação oral de L-Arg potencializa a HPE após uma sessão de EF em 12 homens normotensos e inativos fisicamente. Métodos: Os participantes receberam 6 g de L-Arg ou placebo ao término do protocolo de EF (60% de 1RM, 3 séries de 12 repetições) e 30 minutos após, com monitoramento da pressão arterial (PA) por 60 minutos em duas sessões. As análises estatísticas utilizaram ANOVA de medidas repetidas, post hoc de Tukey e teste t de Student ($p < 0,05$). Resultados: Os participantes apresentaram, na linha de base: 26,5 ± 4,98 anos; 22,8 ± 1,80 kg/m²; PA sistólica e diastólica de 106 ± 5 e 69 ± 9 mmHg, respectivamente. A redução da PA na condição L-Arg foi significativamente maior que no placebo aos 45 e 60 minutos pós-EF ($p < 0,05$), com reduções máximas de 21,5 ± 8,3 mmHg (sistólica), 11,3 ± 7,2 mmHg (diastólica) e 18,1 ± 8,7 mmHg (média). A concentração plasmática de ON foi significativamente superior aos 60 minutos na sessão com L-Arg (pré: 15,3 ± 1,2 vs. pós: 24,6 ± 3,5 µM/L) em comparação ao placebo (pré: 15,9 ± 3,2 vs. pós: 14,9 ± 0,4 µM/L). Conclusão: A suplementação de L-Arg potencializou a HPE após EF em normotensos, sugerindo seu potencial como intervenção não farmacológica na prevenção primária de doenças cardiovasculares, possivelmente mediada pelo aumento da biodisponibilidade de ON.

Palavras-chave: *Pressão arterial; Recursos ergogênicos; Óxido nítrico; Exercício de força.*

Introduction

L-arginine (L-arg), a substrate for nitric oxide (NO) synthesis, has drawn significant attention for its potential role in alleviating endothelial dysfunction and improving exercise performance by increasing NO production[1,2]. L-arg has been shown to have a vasodilatory effect in both the central and peripheral circulation[3,4]. NO also plays a role in acute exercise-induced vasodilation in hypertensive patients and healthy subjects[5]. In addition, oral L-arg supplementation has been shown to have hypotensive effects on different diseases[6].

The impairment of NO production and endothelial dysfunction are the two major factors that limit exercise capacity in patients with several cardiopulmonary conditions. Via these mechanisms, NO mediates increased blood flow at rest[7,8] and during resistance exercise (RE)[9], which is of particular interest for patients with hypertension. However, it is not clear whether oral L-arg supplementation increases vasodilation via NO synthesis during postexercise hypotension (PEH), via RE in normotensive individuals.

Conversely, oral L-arg supplementation in normotensive individuals with functional endothelium is justified by primary prevention, rather than treating existing vascular dysfunction. By potentiating PEH, this "natural" intervention can optimize the acute hemodynamic response to RE. Such a strategy is crucial to counteract the detrimental process of vascular aging, helping to maintain optimal blood pressure (BP) and reduce long-term cardiovascular risk.[6]

Most previous studies regarding PEH have been performed with an aerobic exercise design[10-13]. However, a significant reduction in BP is also observed following an acute bout of RE[11,14-16] and chronic RE[17,18] programs for normotensive and hypertensive individuals. PEH has been considered clinically relevant and a non-pharmacological antihypertensive strategy for BP control, both in normotensive and hypertensive individuals[5,19,20]

The intersection between oral L-arg supplementation and BP is an emerging field of research[21]. Researchers have investigated whether oral supplementation with L-arg can enhance the PEH effects of aerobic exercise, possibly through an increase in NO production and consequent vasodilation[22,23].

Currently, there is a lack of scientific data specifically examining the effects of oral L-arg supplementation on PEH responses following RE. Although L-arg is known to enhance NO production, leading to vasodilation and reduced BP, the specific impact of L-arg on PEH in the context of RE has not been investigated in normotensive individuals[24]. Further research is needed to explore whether L-arg can augment hypotensive responses after RE in normotensive and hypertensive individuals[9,25].

Despite the established efficacy of L-Arg supplementation combined with RE on PEH in clinical populations, evidence remains limited regarding PEH potentiating in normotensive individuals following RE[8,25]. Specifically, it is unclear whether oral L-Arg supplementation at safe levels can optimize the acute vasodilatory response and subsequent PEH after a single bout of RE in individuals with functional endothelium[9,23].

Therefore, the aim of the present study was to investigate whether PEH is increased after oral L-arg supplementation in normotensive individuals subjected to RE via NO synthesis.

Methods

This study is a double-blind and crossover trial conducted in accordance with the Consolidated Standards of Reporting Trials (CONSORT) checklist[26]. Normotensive individuals were included and assigned to two experimental sessions (L-arg and Placebo) in a 1:1 allocation ratio. A washout period of at least 48 hours was adopted between sessions, which has been described as an adequate time frame for cardiovascular parameters to return to baseline levels. All volunteers provided written informed consent after the experimental procedure, and possible risks were explained in accordance with the ethical standards of the Declaration of Helsinki. The study protocol was approved by the Institutional Review Board of the Catholic University of Brasilia (CEP-UCB CAAE: 79934024.3.0000.0029, under opinion number 6.891.527).

Experimental approach to the problem

This study investigated whether acute 6g L-Arg supplementation potentiates PEH in normotensive individuals. The design tested the hypothesis that L-Arg, as a NO precursor, acts synergistically with exercise-induced shear stress to optimize endothelial function. To verify this mechanism, plasma NO concentrations were measured at baseline, immediately post-exercise, and at 60 minutes. Concurrently, systemic BP was monitored in a supine position at fixed intervals to quantify the hemodynamic response. Ultimately, the design aimed

to confirm if maximized NO synthesis yields a more sustained BP reduction compared to placebo, positioning this protocol as a viable non-pharmacological strategy for primary cardiovascular prevention.

Participants

The volunteers were recruited through local advertising (Taguatinga, Brasilia, Brazil), all were male adults, normotensive, and with at least 6 months of continuous RE experience. Subjects who had taken any dietary supplements in the past 6 months were excluded.

Experimental design

Each subject was randomly assigned to the L-arg or Placebo trial and separated by a 7-day washout period. The L-arg group consumed 6 g/day of L-arg capsules (Sigma, Pittsburgh, PA, USA), 3 g at the end of the RE session, and 3 g at 30 min post-RE. The Placebo trial consumed an equal number of capsules containing starch. The schedule of the RE session, blood sampling, and supplementation is shown in Figure 1.

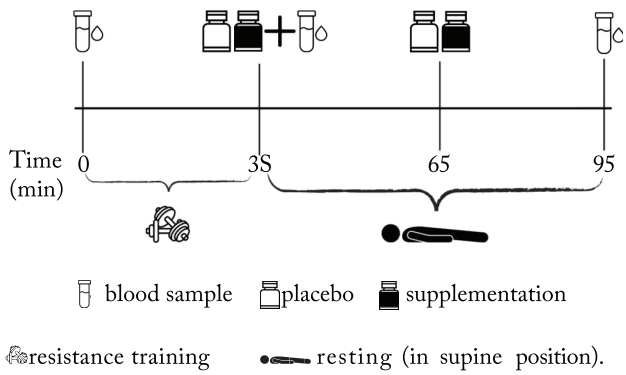

Figure 1 – Diagram of the experimental design and supplementation timeline.

Procedures

- **Physical activity and dietary control**

To mitigate confounding variables, participants were instructed to maintain their habitual diet and physical activity level for 48 hours pre-session. Dietary control was ensured via a 24-hour food record before the first visit, which was replicated prior to the crossover session. Nutritionists instructed subjects to avoid nitrite (NO_2^-) and nitrate-rich (NO_3^-) foods to prevent interference with NO analysis[27]. Participants received a standardized list of permitted and prohibited foods to guide their intake 24 hours before testing[28,29]. Adherence was monitored through dietary recalls. Finally, alcohol, caffeine, and supplements were prohibited for 24 hours pre-test, while normal caloric intake was maintained.

- **Supplementation**

Subjects performed two RE trials separated by a one-week washout, starting at the same time of day. Participants replicated their 24-hour diet before each session and maintained a 12-hour overnight fast. Two hours prior to baseline blood collection, a standardized breakfast (355 mL of non–sugar-fortified orange juice) was provided. In a double-blind design, subjects ingested 6 g of either L-arg (Sigma, New York, USA) or a maltodextrin placebo (Byoformula, Brasilia, Brazil) with 300 mL of water. The identical appearing 1000 mg caplets were free of common allergens and sweeteners, coded by independent personnel. This 6 g dosage was selected for its tolerability and proven efficacy in increasing vasodilation and potentiating PEH[22,30].

- **Preliminary testing**

All volunteers were instructed on the techniques involved in the RE session and BP measurements 1 week before the RE session. The subjects were also familiarized with the Strength Research Laboratory environment. In the laboratory of Catholic University of Brasilia, the air temperature was maintained between 21 and 24°C, and the relative humidity ranged between 50-60%.

- **Anthropometry**

Height and weight were expressed in meters and kilograms, measured using a scale from Sanny® (Welmy W200a, Sanny®, São Paulo, Brazil). Waist circumference was recorded with a Sanny flexible metal tape (Sanny®, São Paulo, Brazil). Body composition was determined via the Jackson and Pollock seven-site skinfold protocol (subscapular, triceps, biceps, chest, abdomen, thigh, and suprailiac)[31] using Lange skinfold calipers (Beta Technology Inc., Santa Cruz, CA, USA). Three measurements with 1-minute intervals were made for each skinfold, and the average value was used to calculate body composition.

- **Assessment of muscle strength**

Maximal isotonic strength was assessed via the one-repetition-maximum technique (1-RM) for seven muscle groups using pin-loaded equipment (Biotech, São Paulo, Brazil). Participants completed three nonconsecutive familiarization sessions (two sets of 12

repetitions at minimum weight) before testing. Following a brief warm-up, 1-RM was determined for the leg press, leg curl, chest press, lat pulldown, shoulder press, bicep curl, and triceps extension. Lifting and gripping techniques followed National Strength and Conditioning Association (NSCA) standards, with 2 kg minimum weight increments[32].

- **Resistance exercise session protocol**

After 48 h of 1-RM testing, subjects completed two randomized experimental sessions (L-Arg or placebo) separated by a one-week washout. To control circadian rhythms, sessions occurred between 08:00 and 12:00. The RE protocol consists of three sets of 12 repetitions at 60% 1-RM for the seven previously described exercises[11,33]. Sets and exercises were separated by 1-minute rests, totaling approximately 35 minutes. An exercise physiologist (MRM) supervised all sessions, ensuring proper technique and hydration (15 mL/kg). Participants were prohibited from additional regular exercise throughout the study.

- **Determination of nitric oxide**

Venous blood was collected at baseline, immediately post-exercise, and 60 minutes post-exercise. Samples were centrifuged at 4°C (15 min at 2,000 g), and plasma was aliquoted and stored at -80°C. Duplicate assays were performed within two months using the Griess reaction[34]. For analysis, plasma was deproteinized with zinc sulfate (20%). Samples (300 µL) were incubated for 40 min at 37°C with vanadium chloride, sulfanilamide, and N-(1-naphthyl) ethylenediamine dihydrochloride. Absorbance was measured at 540 nm using a spectrophotometer (linearity ≤1%, CV ≤10%). Results were expressed in millimolar units. To ensure accuracy, participants maintained a 24-hour nitrate/nitrite-restricted diet prior to testing.

- **Measurement of blood pressure and heart rate**

Resting BP and heart rate (HR) were measured (Microlife AFIB200, Microlife AG, Widnau, Switzerland) after 20 minutes of supine rest. Following American Heart Association procedures, three measurements were averaged[35]. Participants avoided exercise, caffeine, and alcohol for 24h. Data were collected pre-exercise (sitting) and 5, 10, 15, 30, 45, and 60 min post-exercise (supine). HR was recorded beat-by-beat via a Polar Vantage NV monitor (Polar Electro Oy, Oulu, Finland).

Sample size

To provide a quantitative appraisal of the achieved power, a *post-hoc* calculation was performed using the observed baseline of systolic BP in our sample (systolic BP 106 ± 5 mmHg). Considering a two-sided $\alpha = 0.05$ and a clinically relevant mean difference of 5 mmHg in systolic BP between conditions, the standardized effect size (Cohen's d) is 1.0 (5/5) and the corresponding post-hoc power for a paired design with n = 12 is approximately 93%**.** For smaller, but still clinically meaningful differences (for example, $\Delta = 3$ mmHg with SD = 5 mmHg), a conventional a priori design targeting 80% power and $\alpha = 0.05$ would require approximately 22 participants. These calculations justify the interpretation of the present positive systolic BP findings while highlighting that future studies aiming to detect smaller effects should enroll larger samples.

Statistical analysis

Analysis of variance with repeated measurements (group, treatment, and time interaction) was used for statistical analyses, and the Tukey *post hoc* test was used to identify significant data points ($p < 0.05$). All pre- and post-comparisons were performed using Student's t-test. Statistical analyses were performed using the Prism 5 software package. Differences were considered significant at $p < 0.05$. The data are expressed as the mean ± standard-deviation.

Results

The experiments were conducted between August and December 2024. A total of 25 candidates were initially screened for eligibility. Of these, 13 were excluded prior to randomization: 11 participants failed to meet the inclusion criteria (7 reported current use of dietary supplements and 4 were under pharmacological treatment), and 2 individuals did not complete the mandatory preliminary stages of the protocol. Thus, a total of 12 participants (100%) completed both experimental arms and were included in the final analysis. The flow of participants is detailed in Figure 2.

Table 1 presents the baseline anthropometric, hemodynamic, and biochemical data of the volunteers.

The systolic BP values were significantly different in the L-Arg session at the "45 minutes post-exercise" and at "60 min post-exercise" in relation to rest, on average 21.5 ± 8.3 mmHg ($p < 0.05$), and at 60 min post-exercise in relation to the placebo session (Figure 3A). The diastolic BP (Figure 3B) values were signifi-

cantly different only in the L-Arg session at the "45 minutes post-exercise" and at "60 min post-exercise" in relation to rest, approximately 11.3 ± 7.2 mmHg ($p < 0.05$). With the reductions in systolic BP and diastolic BP, consequently, there was a reduction in mean arterial pressure (MAP), but only in the L-Arg session at the "45 minutes post-exercise" and at "60 min post-exercise" in relation to rest, a reduction of 18.1 ± 8.7 mmHg in MAP ($p < 0.05$) (Figure 3C).

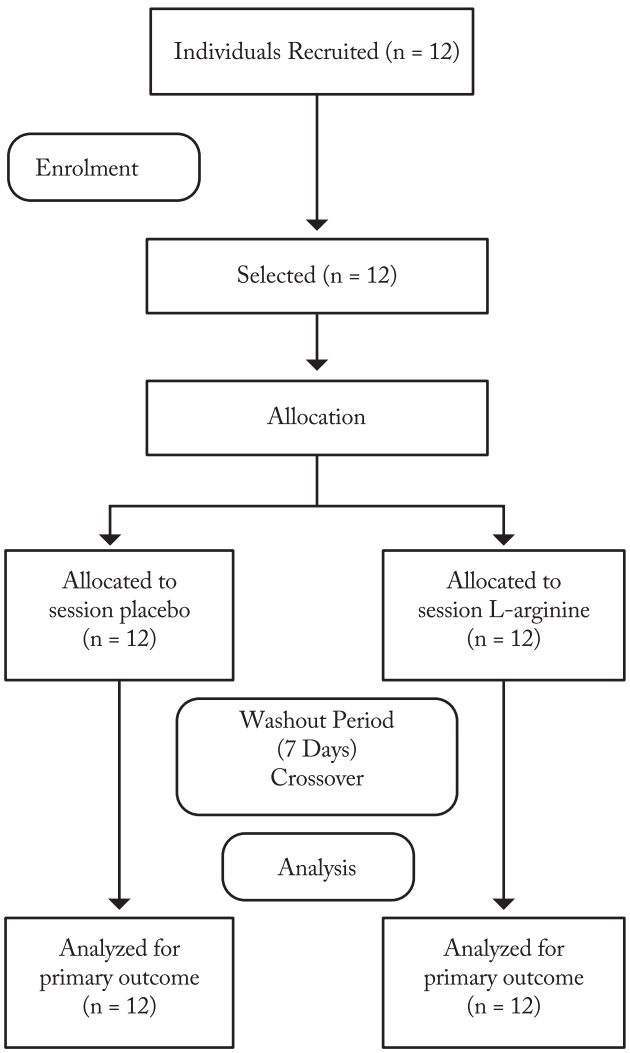

Figure 2 – Flow diagram of participants through the phases of the double-blind and crossover study.

Figure 4 represents the NO concentrations in plasma; there was a significant increase in the oral L-Arg supplementation at the session RE 60 min post-exercise. There were no significant differences when taking oral placebo supplementation.

Safety and tolerability

No adverse events or side effects were observed at the dosage administered, confirming the safety and tolerability of the supplementation protocol in this cohort.

Table 1 – Descriptive characteristics of participants enrolled in the study.

Variables	Mean ± standard deviation
Antropometrics	
Age (years)	26.5 ± 4.98
Training time (years)	4.0 ± 1.60
Weight (kg)	73.8 ± 6.50
Height (cm)	179.8 ± 2.76
Body mass index (kg/m^2)	22.8 ± 1.80
Hemodynamics	
Systolic blood pressure (mmHg)	106 ± 5
Diastolic blood pressure (mmHg)	69 ± 9
Mean blood pressure (mmHg)	78 ± 9
Biochemistry	
Nitric oxide (µM/L)	16 ± 3

Values are presented as mean ± standard-deviation

Discussion

The findings of this study demonstrate a significant hypotensive effect of L-arg supplementation in normotensive individuals following a single session of RE. This finding is consistent with the literature on the role of NO in mediating vascular responses. L-arg, a precursor for NO synthesis, has been shown to enhance NO production, which in turn promotes vasodilation and reduces BP[6,36].

The primary mechanistic pathway explaining the enhanced PEH observed in the L-Arg group centers on the optimization of the NO pathway[37,38]. L-Arg is the direct substrate for the endothelial NO synthase (eNOS) enzyme, whose activity is crucial for NO production in vascular cells[30]. While RE exercise alone induces increased *shear stress* on arterial walls, thereby stimulating eNOS[37,39], oral L-Arg supplementation provides greater availability of circulating substrate. This synergistic action (increased substrate plus heightened enzymatic activation) results in a supra-additive increase in plasma NO bioavailability, a potent vasodilator that relaxes vascular smooth muscle. The subsequent increase in peripheral vasodilation decreases total vascular resistance, which is the main factor sustaining PEH[20]. Furthermore, NO plays a critical role in the modulation of central sympathetic tone, inhibiting its activity and thus contributing to the maintenance of reduced systemic BP in the PEH period[37].

In the present study, the NO plasma concentration was significantly greater in the L-arg group than in the

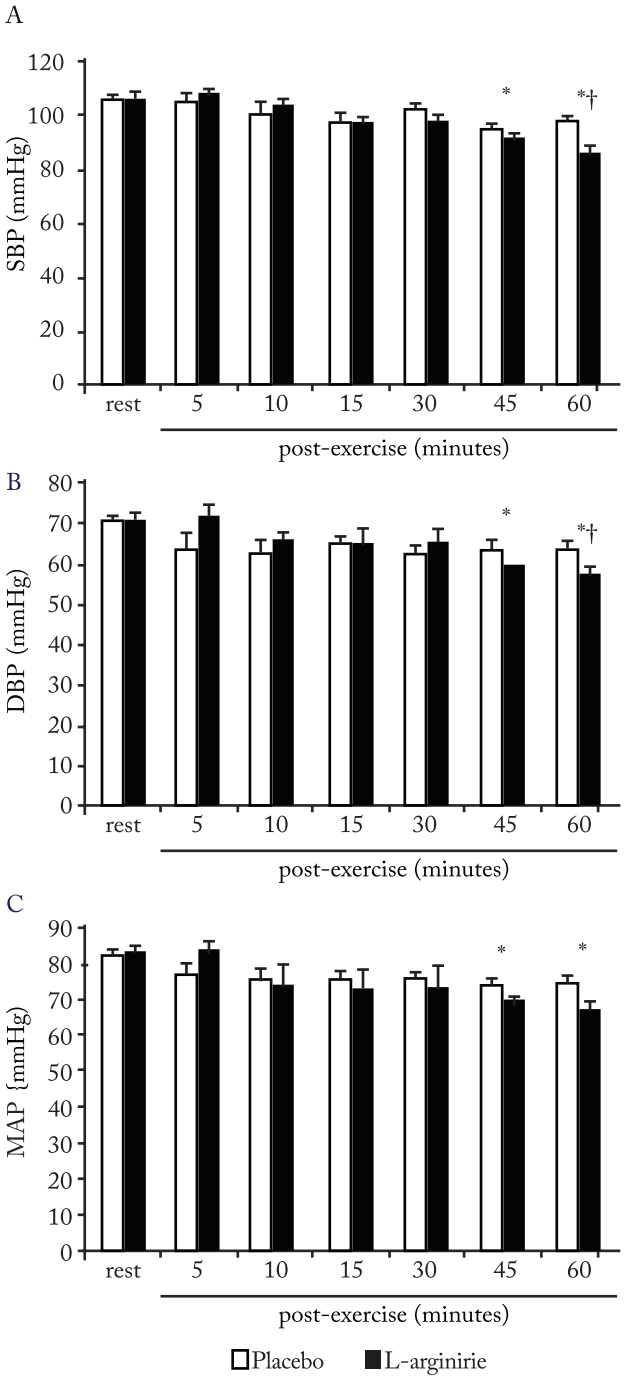

Figure 3 – Comparison of the placebo session (white bars) and the L-arginine supplementation session (black bars) on blood pressure responses in physically active normotensive individuals. SBP: Systolic blood pressure (A); DBP: diastolic blood pressure (B); MAP: Mean arterial pressure (C). * p < 0.01 Compared to rest. † p < 0.05 Compared to placebo 60' post-exercise.

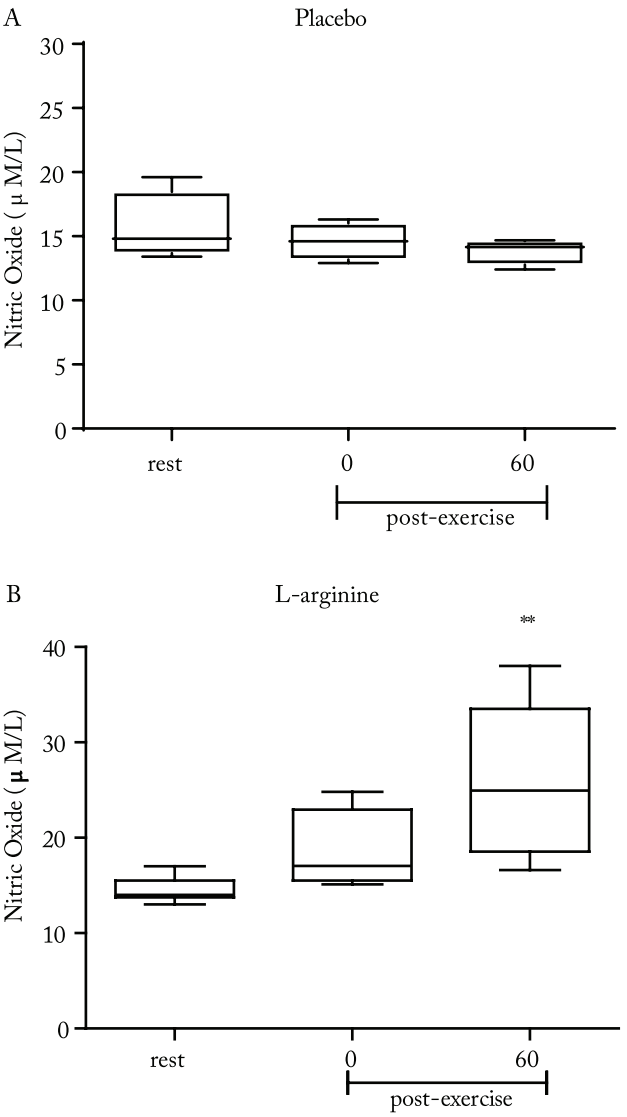

Figure 4 – Comparison of plasma nitric oxide concentrations at rest, 0 min and 60 minutes post-resistance exercise in physically active normotensive individuals. (A) Placebo supplementation session; (B) L-arginine supplementation session. ** p < 0.01 compared to rest.

placebo group 60 minutes after the RE session. This finding aligns with previous research indicating that increased NO availability leads to vasodilation and subsequent BP reduction[6]. The mechanism underlying this effect involves the activation of the NO pathway, which enhances endothelial function and reduces peripheral vascular resistance[37].

While aerobic exercise is widely recognized for its cardiovascular benefits, including BP reduction[38], resistance training (chronic) also positively impacts cardiovascular health[15,18,40]. However, the combination of RE (acute) and L-arg supplementation, which specifically enhances PEH in normotensive individuals, is a novel finding. This finding suggested that NO-mediated vasodilation can be potentiated by L-arg even in the absence of underlying hypertension, highlighting its potential preventive effects on primary cardiovascular diseases[1].

Our findings, demonstrating that acute oral L-Arg

supplementation potentiates PEH with RE in young, normotensive men, are consistent with the known mechanism of NO-mediated vasodilation. This result extends previous work in several crucial aspects. Firstly, our data corroborates the results of studies utilizing RE with L-Arg supplementation, such as that by Casonatto et al.[40], which reported an enhanced systolic PEH following isokinetic RE combined with an oral L-Arg (8 g). However, the Casonato et al.[40] study targeted an elderly women population with pre-hypertension and hypertension, a group known to have impaired endothelial function and lower basal NO production. The observation of a significant synergistic effect in our population of young, healthy normotensive men suggests that the 6 g acute oral L-Arg dose is sufficient to maximize the already optimal NO pathway, indicating a mechanism highly sensitive to precursor availability even in the absence of manifest endothelial dysfunction.

This synergistic effect may be particularly valuable in RE protocols, as L-Arg supplementation overcomes potential limitations inherent to RE, such as the temporary vascular occlusion and transient spikes in BP during the eccentric phase[11,14,15]. By maximizing NO synthesis, the acute supplementation of L-arg effectively converts the post-exercise period into a potent therapeutic window for PEH[22], narrowing the gap between the acute hypotensive efficacy of RE and aerobic exercise and highlighting RE as an equally important non-pharmacological strategy for cardiovascular health maintenance.

Casonatto et al.[40] investigated the effects of L-Arg supplementation on PEH, femoral artery area, and heart rate variability in twenty elderly women, prehypertensive and hypertensive adults, who were divided into two groups (placebo and L-Arg). The participants ingested 8 g of inert substance (placebo group) or 8 g of L-arg dissolved in water 90 min prior to the experimental session. The experimental session consisted of an isokinetic maximal strength test. BP was measured every 10 minutes for 60 minutes after the experimental session. The femoral artery area (ultrasound) and heart rate variability were also analyzed. The L-Arg supplementation plus exercise group exhibited a significant decrease in systolic BP. No significant differences were identified in the femoral artery area or heart rate variability. The authors concluded that acute L-Arg supplementation can increase PEH effects in elderly women. However, acute L-arg supplementation is not related to either the femoral artery area or HR variability.

The clinical implications of these findings are significant. PEH is an important physiological response that contributes to long-term BP control. The enhancement of PEH through L-arg supplementation could be particularly beneficial in normotensive individuals who are at risk of developing prehypertension or hypertension. By augmenting the hypotensive effects of RE, L-arg may help maintain optimal BP levels and reduce the risk of cardiovascular events[9].

Despite these promising results, further research is needed to elucidate the long-term effects of L-arg supplementation combined with RE on BP and cardiovascular health. Future studies should also explore the optimal dosage and timing of L-arg administration to maximize its hypotensive effects and save. Additionally, examining the effects of L-arg supplementation in diverse populations, including hypertensive individuals and different age groups, would provide a more comprehensive understanding of its benefits[36].

The clinical relevance of L-Arg-potentiated PEH, even in normotensive individuals, lies in its potential cumulative effect on long-term cardiovascular risk reduction[22,23,25]. While the acute magnitude of the systolic BP reduction observed in this study may appear modest in absolute terms, literature demonstrates that a sustained decrease of just 5 mmHg in systolic BP is associated with an approximate 10% relative risk reduction in major cardiovascular events (such as stroke and myocardial infarction)[38,39], regardless of baseline hypertension status or pre-existing cardiovascular disease[39].

By acting to optimize the NO pathway, oral L-Arg supplementation may enhance the acute vasodilatory response to RE. These findings suggest that the combination of L-Arg and RE induces favorable acute hemodynamic adjustments, representing a potential tool for vascular health maintenance. While our results focus on acute effects, they align with lifestyle intervention strategies aimed at risk mitigation in healthy populations.

Despite the inherent strengths conferred by its rigorous double-blind, crossover design, this study is subject to several critical limitations essential for accurate interpretation and generalization. Foremost is the small, highly homogeneous sample, which severely restricts the generalizability of the oral L-Arg potentiated PEH to populations of different age groups, sexes, or fitness levels. Fundamentally, given that the efficacy of L-Arg is intrinsically linked to the reversal of baseline

NO bioavailability impairment[4,27], our exclusive focus on normotensive individuals, who possess already-optimal endothelial function, may substantially underestimate the true therapeutic potential expected in clinically relevant groups, such as the pre-hypertensive or hypertensive. Methodologically, the acute nature of the study only captures immediate hemodynamic responses for only 1 h (resting BP) and was limited, thereby failing to provide insight into the optimal response to long-term cardiovascular adaptations. For this purpose, ambulatory BP monitoring will be recommended. Furthermore, while plasma NO metabolites were assessed, the absence of the vascular gold standard, flow-mediated dilation, prevents a definitive mechanistic confirmation of improved peripheral endothelial function.

In conclusion, L-arg supplementation significantly reduced BP in normotensive individuals after RE, likely due to increased NO concentrations. This finding underscores the potential of L-arg as a nonpharmacological intervention to enhance cardiovascular health and prevent primary cardiovascular diseases. The integration of L-arg supplementation with regular RE regimens could be a practical approach for maintaining cardiovascular health in normotensive individuals.

Conflict of interest

The authors declare no conflict of interest.

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Author's contributions

Moraes MR; Almeida PM; Rosa TS; Corrêa HL; Neves RVP; Barbosa JMS; Vargas DA; Moraes TCC; Martins TO; Rios-Neto DF and Souza MK: Methodology; Investigation; Writing – original draft; Approval of the final version. Rosa TS, Correa HL; Silva AS and Moraes MR: Conceptualization; Methodology; Software; Validation; Formal analysis; Investigation; Resources; Data curation; Supervision; Project administration; Visualization; Writing – original draft; Writing – review & editing; Approval of the final version. Bacurau RFP and Aoki MS: Are dieticians and revised the manuscript for important intellectual content. Writing – original draft; Writing – review & editing; Approval of the final version. Araujo RC and Silva AS: Supervision; Project administration; Visualization; Writing – original draft; Writing – review & editing; Approval of the final version. All the authors have read and approved the final manuscript.

Declaration regarding the use of artificial intelligence tools in the article writing process

The authors did not use artificial intelligence tools for preparation of the manuscript.

Availability of research data and other materials

After publication the data will be available on demand to authors.

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Reviewers' assessment

The reviews of this article were originally conducted in Portuguese. This version has been translated using ChatGPT and subsequently reviewed by the Chief Editors.

Reviewer A

Anonymous

Abstract

- Considering the specific number of publications on the subject, it would be more interesting, rather than pointing out the role of L-arginine, if the authors focused on the novelty of the work. What is the differentiating factor of your work? You mentioned that the supplementation involved PHE, but what was the delta reduction? Also, there was an increase in NO bioavailability, but by how much was that increase?

Introduction

- Your entire argumentative basis at the beginning of the introduction is based on diseases that present endothelial dysfunction, but you justify that you will evaluate normotensive individuals. If they have a functional endothelium, wouldn't this improvement be expected?
- How do you justify this with a reduction in risk? Or the benefit of supplementation? Why did you choose this dose? Why evaluate it in relation to strength training? I think all these points could be better discussed in the introduction.

Experimental approach to the problem

- I felt this section was still superficial; that is, the methodological decisions that motivated the team to develop their hypotheses are not well explained.
- For example, the dosage used, the parameters established in strength training, the dosage chosen for the use of L-arginine, the timing of blood pressure measurements... the maximum amount of decision-making with scientific backing is lacking.
- I don't identify the number of ethical committee Diet and Physical Activity Control - believe that this action to descrition with more details.

Results

- It is possible insert the absoluty values baseline in the intervention and control session? is so importante. Be interessity exposy the values of hypotension by the delta, for to permite identify the clinical effect response.

Final Decision

- Major revision required

Reviewer B

Gustavo Oliveira Silva

Faculdade Pernambucana de Saúde, Recife, Pernambuco

Comments to the authors

- This study aimed to investigate whether post-resistance exercise hypotension is increased after oral L-arginine supplementation in normotensive individuals subjected to resistance exercise. The results suggested that L-arginine supplementation reduced the blood pressure of normotensive individuals after resistance exercise, likely through an increase in the nitric oxide concentration.
- The study is interesting and adds relevant information on the subject, however I would suggest some minor changes to improve readability and understanding. Below are specific suggestions and comments

Title

- Authors should present the study type at the end of the title.

Abstract

- Page 3, Lines 8-9: Authors should briefly present sample characteristics here.
- Page 3, Lines 14-16: This is a crossover study in which all participants received both L-Arg and placebo and performed the RE session. Thus, it would be more appropriate to call it L-Arg and placebo sessions or conditions.
- Page 3, Lines 14-16: It is important to present the numerical values of the outcome variables here in the abstract.

Background

- The introduction presents important information on L-arginine, nitric oxide, and post-exercise hypotension. However, the rationale leading to the aim

could be better developed. It would benefit from a more focused articulation of the specific gap in the literature (why investigating L-arginine supplementation after resistance exercise in normotensive subjects is important), and a better logical connection between current evidence and the research question.

Methods

- Page 7, Line 22: This should read "Twelve participants".
- Page 7, Line 23: This information is already presented in Table 1. This format should be included in the abstract, as previously suggested.
- Page 8, Line 8: This abbreviation needs to be defined at first mention, as it was not defined before.
- Page 12, Line 2: I believe this should read "were obtained" in the past sense.
- Page 12, Line 13: I believe this should also read "were used" in the past tense.

Results

- Page 14, Line 6: I believe this should read "the mean age".
- Page 14, Lines 13-24; Page 15, Lines 1-3: Authors need to present the numerical values of the outcomes for figures 2 through 5.

Discussion

- The discussion highlights the main findings and relates them to previous studies, but it is somewhat descriptive. A better exploration of the physiological mechanisms responsible for the observed effects and a clearer comparison with aerobic and resistance exercise studies would make the interpretation stronger. Also, it could present a better assessment of clinical relevance and study limitations to better contextualize the results.
- Page 16, Line 21: This seems out of place.

Final Decision

- Major revision required