Original Article

ENGLISH VERSION

Investigation of the effects of oral supplementation of arginine in the increase of muscular strength and mass

Gerseli Angeli¹, Turibio Leite de Barros¹, Daniel Furquim Leite de Barros² and Marcelo Lima³

ABSTRACT

Introduction: Oral administration of arginine has been associated with physical performance improvement due to probable decrease of muscular fatigue derived from the vasodilatation factor of the nitric oxide over the skeletal muscles. Objective: to evaluate the effects of oral administration of L-Arginine during an exercise program with weights. Methods: 20 male individuals, randomly divided in two groups: A and B, were submitted to eight weeks of training with weights (three times per week). Group A used 3 grams of L-Arginine + vitamin C during the eight weeks and group B used only vitamin C (control group). Results: After eight weeks of training, group A presented body weight values and lean mass significantly higher (p < 0.05), body fat percentage significantly lower (p < 0.05), and strength of lower limbs significantly higher (p < 0.05), while group B did not present significant differences for the same period. Conclusion: Oral administration of arginine associated with a training program with weights increased the stimuli of the exercise to the skeletal muscles level, enabling hence, increase of muscular strength and mass.

INTRODUCTION

Oral administration of arginine has been related with improvement of physical performance due to a probable decrease of muscular fatigue. Such fact would be associated with the vasodilation promoted by the nitric oxide, resulting in an increase of muscular perfusion, as well as by the decrease of glucose consumption by the skeletal muscles in activity⁽¹⁾. Nitric oxide (NO) is a molecular gas which consists of the covalent ligation between a nitrogen atom and an oxygen atom. Its production in the human body occurs when the L-arginine amino acid is converted into L-citrulline in a reaction catalyzed by the nitric oxide synthetase enzyme (NOS)⁽²⁾. Since prolonged administration of arginine increases the nitric oxide production, its supplementation has been related with improvement of contraction function of the skeletal muscle⁽³⁾. Santos et al. 2001⁽⁴⁾ demonstrated improvement of resistance to fatigue in individuals submitted to oral supplementation of arginine (3 g per day) during 15 days.

On the other hand, arginine supplementation can also be associated with improvement in contraction strength through greater synthesis of muscular proteins⁽⁵⁾ in periods of more prolonged administration when concomitantly performed with a resisted-exercises program. One may consider the hypothesis that the very effect of perfusion improvement of skeletal muscles contributes to better quality of weight training. As a result to the prolonged time,

- Centro de Medicina da Atividade Física e do Esporte, Universidade Federal de São Paulo, São Paulo, SP.
- 2. Universidade Federal de São Paulo, São Paulo, SP.
- 3. São Paulo Futebol Clube, São Paulo, SP.

Received in 19/7/06. Final version received in 28/9/06. Approved in 21/11/ 06.

Correspondence to: Gerseli Angeli, Rua Rino Pieralini, 175, apto. 83B, Vila Mariana – 04017-010 – São Paulo, SP. Tel./fax: 3887-9105. E-mail: gerseli @uol.com.br

Keywords: Exercise. Nitric oxide. Vasodilatation. Muscle.

boosting of the training effects and more remarkable increase of muscular mass and contraction strength are observed.

OBJECTIVE

This study had the aim to investigate the effects of the oral administration of arginine during 8 weeks associated with a weight exercises program.

METHODS

This study was approved by the Ethics Committee in Research of the UNIFESP, under the resolution number 1188/06. The study's subjects signed the free and clarified consent form and 20 healthy and non-smoker male individuals, age between 17 and 19 years (mean 17.65 \pm 0.8 years), were randomly divided in two groups numerically equal: ARG and CON. They were submitted to eight weeks of a weight training program for lower limbs, with frequency of three weekly sessions, intensity of 70 % of maximal load for each muscular group, and training volume of three sets of ten repetitions. The ARG group received oral supplementation of arginine (three grams – single daily dose) associated with vitamin C (1 g/day) and the CON group received only vitamin C (1 g/day).

Prior and post training program plus supplementation, the following variables were measured: weight (kg), muscular mass (Kg), body fat % (Pollock) and bilateral muscular strength of knee flexextension (psi) in isokinetic dynamometer (BIODEX[®] USA).

Statistical analysis

- Paired 't' test.
- ANOVA.

RESULTS

After eight weeks of weight training, we could observe that the ARG group presented statistically significant increase of body weight ($66.4 \pm 6.1 - 67.84 \pm 6.8$ Kg), and muscular mass ($60.8 \pm 6.05 - 62.07 \pm 5.9$ Kg) (figure 1) and decrease of fat mass ($6.02 \pm 0.6 - 5.77 \pm 0.59$ Kg) and body fat percentage ($9.45 \pm 0.8 - 8.66 \pm 0.77$) (figure 2), p < 0.05.

The CON group did not present significant differences (figures 3 and 4).

Concerning muscular strength for knee flexion and extension of right (R) and left (L) legs, we could observe that the ARG group presented post values significantly higher in both variables (Flexion R 100.2 \pm 9.4 – 108.8 \pm 10.2; L 96.5 \pm 9.3 – 103.3 \pm 10.07; Extension R 184.8 \pm 17.4 – 195.8 \pm 16.3; L 191.1 \pm 18.4 – 199.1 \pm 19.1) (figure 5) (p < 0.05).

Statistically significant differences were not observed for such variables in the control group, which presented pre and post body weight in Kg of 70.59 ± 6.88 and 70.9 ± 7.01 respectively; pre and post lean mass in Kg of 64.88 ± 6.4 and 65.07 ± 6.7 respectively; pre fat and post fat mass (Kg) 5.71 ± 0.4 and 5.83 ± 0.42 respec-

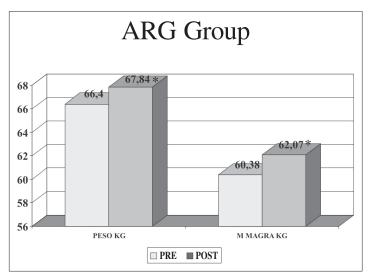


Figure 1 – Body weight and lean mass weight (Kg) pre and post 8 weeks of training in individuals of the ARG group. The Post Weight and Lean Mass values are significantly higher (p < 0.05).

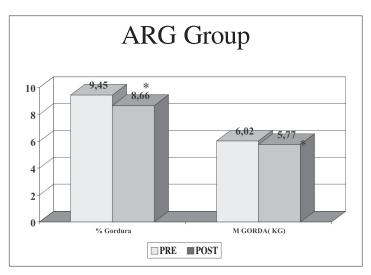


Figure 2 – Body fat percentage and fat mass (Kg) pre and post 8 weeks of training in the individuals of the ARG group. The post body fat percentage is significantly lower (p < 0.05).

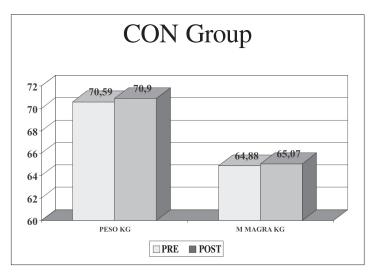


Figure 3 – Body weight and lean mass weight (Kg) pre and post 8 weeks of training in the individuals of the control group. There was no statistically significant difference.

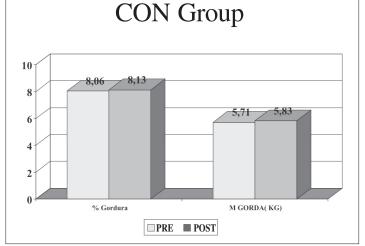


Figure 4 – Body fat percentage and fat mass (Kg) pre and post 8 weeks of training in the individuals of the control group. There was no statistically significant difference.

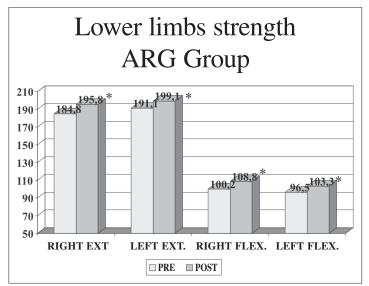


Figure 5 – Maximal extension and flexion strength of the lower limbs pre and post 8 weeks of training in the individuals of the ARG group. The post values are significantly higher (p < 0.05).

tively; pre and post body fat percentage 8.06 ± 0.7 and 8.13 ± 0.73 respectively; and pre and post muscular strength (psi) of 129.9 ± 13.2 and 129.2 ± 12.9 for right knee flexion; 232 ± 20.01 and 221.5 ± 22 for right knee extension, 114.2 ± 10.8 and 118.7 ± 11.2 for left knee flexion; 222.3 ± 21.4 and 216.1 ± 20.2 for left knee extension, respectively (figure 6).

DISCUSSION

The effect of the oral administration of arginine in the strength increase of lower limbs has been already reported⁽⁴⁾. The hypothesis which this increase occurs in short time has been related with the vasodilator effect of nitric oxide, with consequent increase of muscular perfusion. Schaefer *et al.* 2002⁽⁶⁾ affirm in their study that arginine supplementation favors the arginine-nitric oxide mechanism triggered by physical exercise, increasing the formation of nitric oxide from arginine.

However, it is also known that the arginine administration may be related with a second effect associated with muscular strength and mass, the protein synthesis⁽⁵⁾.

The significant increases of lower limbs strength as well as lean mass in the ARG group found in this study, suggest that the argin-

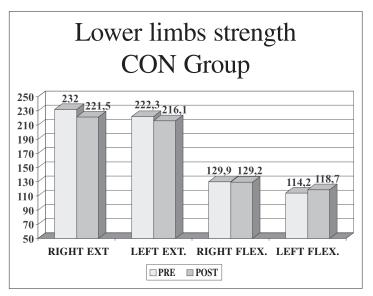


Figure 6 – Maximal extension and flexion strength of the lower limbs pre and post 8 weeks of training in the individuals of the control group. There was no statistically significant difference.

ine supplementation promoted greater increase of proteins synthesis due to the interaction of its effects with resisted exercise ones. This same effect at short term alone could partly answer for the strength increase in isokinetic exercise obtained by Santos *et al.* 2004⁽⁴⁾. Moreover, the results of the present study corroborate the findings by Flakoll *et al.* 2004⁽⁴⁾ who when supplementing women with arginine for 12 weeks, found a significant increase in muscular strength, lean mass, protein synthesis and functionality, reaffirming that arginine supplementation promotes protein synthesis, resulting in strength and muscular mass increase.

The possible explanation for the lack of increase of muscular mass and isokinetic strength of lower limbs in the individuals of the control group must be related with the fact that this group did not improve the weight training quality when associated only with vitamin C ingestion. Since the training program performed during the study's period had already been applied to the athletes for a previous time of 12 weeks, totalizing hence a period of 20 weeks with no frequency, intensity and/or training volume alteration, it would not be expected to find a very significant increase of muscular strength or mass derived from it.

In addition, concerning the apparent strength difference between the ARG and the CON groups, it was not statistically significant (p > 0.05 single t test). Concerning strength in the isokinetic test, we also observed a tendency in the control group to present higher values which are not statistically significant either. Once strength is expressed in absolute value, the tendency to heavier weight in the CON group is reflected by a tendency of higher strength in these individuals.

Apparently the oral administration of arginine is provided among quality of training through three mechanisms interrelated and interdependent simultaneously triggered by the vasodilation: the increase of blood perfusion⁽⁷⁻⁹⁾ – making the oxygen and nutrients arrival to the tissues easier; greater glucose disposal for the muscle in activity⁽⁸⁾ – providing more energy substrate for the muscular contraction; and the reduction of the plasma concentration of ammonia and lactate⁽⁶⁾ – delaying fatigue and decreasing the discomfort caused by the accumulation of these catabolites in the muscles. This last idea takes grounding in the principle that first, the accumulation of lactate is an indication of the glycogen depletion, with high concentrations of lactate in the fatigue point⁽¹⁰⁻¹²⁾; and second, the lactic acid is the great responsible for the muscular pain mentioned during exercise practice. Besides that, Yaspelkis and Ivy 1999⁽¹³⁾ affirm that arginine supplementation reduces the

oxidation of post-exercise carbohydrate being able thus to increase the glucose availability for the reestablishment of muscular glycogen supplies during recovery.

Smith, Smith and Criwell 2002⁽¹⁴⁾ besides having demonstrated the importance of nitric oxide for the muscular hypertrophy, also evidenced its role as stimulator and booster for the transition between the two types of muscle fibers in overload situations. This mechanism can be the responsible or booster of the muscular strength increase found when arginine – precursor of nitric oxide – is used in the present study.

A literature review conducted by Maréchal and Gailly 1999⁽¹⁵⁾ suggests that the nitric oxide effects over the muscle fibers may be classified in two groups: direct action and mediated by the cyclic guanidine monophosphate (cGMP). In the former group, the nitric oxide acts directly over the proteins leading to depression of the isometric strength, decreasing the velocity of the resisted or not resisted contractions, glycolysis and mitochondria breathing. The effect over the release of the calcium channels varies, being inhibiting in low and exciting in high concentrations. The general consequence of the direct effects of the nitric oxide is the break of the muscular contraction and its metabolism. In the latter group, the NO effects are mediated by the cGMP - responsible for the straight muscles relaxing, as well as for mediating the hormonal effects (such as the growth hormone – GH), inhibiting the endothelium release (vasoconstrictor) and leading to velocity increase of muscular shortening during contractions with or without overload; maximal mechanical power; initial strength development; fusion tetanic frequency; glucose consumption; glycolysis and the mitochondrial breathing; and decrease of the titanic relaxing and contraction and the calcium release stimulus-associated. All these effects have as consequence the increase of power and muscular mechanics, similarly to the slow fibers transformation in fast ones.

Wang *et al.* 2001⁽¹⁶⁾ found a severe and progressive reduction over walk velocity, muscular mass as well as horizontal section area of muscles of rats submitted to inhibition of the nitric oxide synthetase (NOS).

The regeneration and growth of the muscle fibers injured during physical activity depend on the cells activation-satellite. The genes responsible for the production of these cells are activated between 3-6 hours after the beginning of the physical activity, and 3 extra hours are needed so that the genes regulator of the muscular activity are also expressed. The expression of these genes releases the growth factor and, 24 hours later, activates the synthesis of factors and muscular growth. Nitric oxide is responsible for mediating the cells activation – satellite, accelerating the process⁽¹⁷⁾.

Apparently, all the physical activity-related metabolic processes are improved and boosted with the use of arginine, once better blood perfusion at muscle level occurs, providing a greater release of nutrients (the muscles are able to produce energy for a longer time) and of oxygen (avoiding and/or delaying the anaerobioses process); while they favor the clearance of toxic substances accumulated during physical activity practice, making the muscular recovery process easier. Therefore, it seems important to associate the arginine consumption to the resisted-exercises programs.

Nevertheless, there is still an issue to be better investigated. Is there really an anabolic effect occasionally associated with greater release of GH as a consequence of arginine supplementation, directly determining an increase of lean mass and a consequent strength increase, or the arginine effect during 8 weeks of training improved the training quality due to the perfusion increase, boosting thus the exercise stimulus? Regardless of the answer, we consider the increase of muscular mass obtained important, which may actually provide an indication of arginine use not only in physical fitness programs but also in rehabilitation programs where the increase of muscular mass becomes a priority.

CONCLUSION

Oral administration of L-Arginine (3 g/day) seems to boost the effects of weight training, providing greater strength and muscular mass gain besides contributing to the decrease of body fat percentage.

All the authors declared there is not any potential conflict of interests regarding this article.

REFERENCES

- McConell GK, Huynh NN, Lee-Young RS, Canny BJ, Wadley GD. L-arginine infusion increases glucose clearance during prolonged exercise in humans. Am J Physiol Endocrinol Metab. 2006;290(1):E60-E66.
- 2. Feldman PL, Griffith OW, Stuehr DJ. Chem Eng News. 1993;71:26.
- Schrage WG, Joyner MJ, Dinenno FA. Local inhibition of nitric oxide and prostaglandins independently reduces forearm exercise hyperaemia in humans. J Physiol. 2004;(Pt 2):599-611.
- Santos R, Pacheco MTT, Martins RABL, Villaverde AB, Giana HE, Baptista F, et al. Study of the effect of oral administration of L-arginine on muscular performance in health volunteers. An isokinetic study. Isokinetic Exerc Sci. 2004;153-58.
- Flakoll P, Sharp R, Baier S, Levenhagen D, Carr C, Nissen S. Effect of betahydroxy-methylbutyrate, arginine, and lysine supplementation on strength, functionality, body composition, and protein metabolism in elderly women. Nutrition. 2004;20(5):445-51.

- Schaefer A, Piquard F, Geny B, Doutreleau S, Lampert E, Mettauer B, et al. Arginine reduces exercise-induced increase in plasma lactate and ammonia. Int J Sports Med. 2002;403-7.
- Meneilly GS, Battistini B, Floras JS. Contrasting effects of L-arginine on insulinmediated blood flow and glucose disposal in the elderly. Metabolism. 2001;50(2): 194-9.
- Meneilly GS, Elliott T, Battistini B, Floras JS. N(G)-monomethyl-L-arginine alters insulin-mediated calf blood flow but not glucose disposal in the elderly. Metabolism. 2001;50(3):306-10.
- Rådegran G, Saltin B. Nitric oxide in the regulation of vasomotor tone in human skeletal muscle. Am J Physiol. 1999;276 (6Pt2):H1951-60.
- Sales RP, Miné CEC, Franco HD, Rodrigues EL, Pelógia NCC, Silva RS, et al. Efeitos da suplementação aguda de aspartato de arginina na fadiga muscular em voluntários treinados. Rev Bras Med Esporte. 2005;11(6):347-51.
- Baldwin J, Snow RJ, Gibala MJ, Howarth K, Febbraio MA. Glycogen availability does not affect the TCA cycle or TAN pools during prolonged fatiguing exercise. J Appl Physiol. 2003;94:2181-7.
- Billat VL, Sirvent P, Py G, Koralsztein JP, Mercier J. The concept of maximal lactate steady state: a bridge between biochemistry, physiology and sports science. Sports Med. 2003;33:407-26.
- Yaspelkis BB, Ivy JL. The effect of a carbohydrate-arginine supplement on postexercise carbohydrate metabolism. Int J Sport Nutr. 1999;9(3):241-50.
- Smith LW, Smith JD, Criswell DS. Involvement of nitric oxide synthase in skeletal muscle adaptation to chronic overload. J Appl Physiol. 2002;92(5):2005-11.
- Maréchal G, Gailly P. Effects of nitric oxide on the contraction of skeletal muscle. Cell Mol Life Sci. 1999;55(8-9):1088-102.
- Wang MX, Murrell DF, Szabo C, Warren RF, Sarris M, Murrell GA. Nitric oxide in skeletal muscle: inhibition of nitric oxide synthase inhibits walking speed in rats. Nitric Oxide. 2001;5(3):219-32.
- Renault V, Piron-Hamelin G, Forestier C, Didonna S, Hentati F, Saillant G. Skeletal muscle regeneration and the mitotic clock. Exp Gerontol. 2000;35:711-9.