OVER-THE-COUNTER L-ARGININE SUPPLEMENTS

TO IMPROVE HUMAN PERFORMANCE

By

Robert J. Soderman

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Thesis Chair: Dr. Steven J. Albrechtsen

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Thesis Approved

Robert J. Soderman

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Committee Members: _____

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Health, Human Performance and Recreation

Over-the-Counter L-Arginine Supplements to Improve Human Performance

January 17, 2013

Dr. Steven J. Albrechtsen, Thesis Chair

The University of Wisconsin-Whitewater

Over-the-Counter L- Arginine Supplements to Improve Human Performance

The purpose of this research was to evaluate the benefits to human performance of over-the-counter L-arginine supplements. 20 male and 15 female track and field athletes from a NCAA Division III university performed two exercise trials consisting of a thirty second standard Wingate Anaerobic Power Cycle Ergometer Test with a force setting based on 7.5% of body weight. 30 minutes prior to each exercise trial the subjects consumed 5,000 mg of GNC L-Arginine 5000® in eight ounces of water (L-arginine trial) or the equivalent volume of plain water (control trial). The 5,000 mg dosage was based upon the manufacturer's guidelines found on the supplements packaging. Peak power (W/kg) was higher during L-arginine trials compared to control trials, these differences were statistically significant for women ($p=0.0435$) and all subjects (combined, $p=0.0303$), and approached statistical significance for men ($p=0.0811$). Average power (W/kg) was higher during L-arginine trials compared to control trials, but these differences approached statistically significance only for women ($p=0.0520$). Based upon subject weight, men received an average of 57.7 mg of L-arginine per kilogram of body weight while women received an average of 79.9 mg of L-arginine per kilogram of body weight. 15 of 35 subjects (42.9%), including 9 of 20 men (45.0%) and 6 of 15 women (40.0%), reported feeling lightheaded, dizzy or nauseated following the L-arginine trials, while no subjects reported the "muscle pumps" or "excited" feeling advertised by the manufacturer following the L-arginine trials. The manufacturer's

recommended dosage of L-arginine may be an effort to simplify the dosage and avoid calculations for the consumer, but also may be balancing increasing the incidence of feeling lightheaded, dizzy or nauseated against additional improvements in performance that might result from a larger dosage per kilogram. The manufacturer's recommended dosage of L-arginine improved peak performance, but did not improve average performance, during the thirty second standard Wingate Anaerobic Power Cycle Ergometer Test, especially in women who received a higher dosage of L-arginine per kilogram of body weight. The manufacturer's recommended dosage of L-arginine may improve performance in rapid explosive movements, but those improvements may not be sustained over longer periods of exercise.

CHAPTER I

INTRODUCTION

L-Arginine Examined

L-Arginine was first isolated in 1886, reportedly from the extract of a lupine seedling. It is a semi-essential amino acid. Although the body normally makes enough of it, supplementation with additional amounts is sometimes needed. L-Arginine is a chemical precursor to nitric oxide which is a blood vessel-widening agent called a vasodilator. Early evidence suggests that L-arginine might help treat medical conditions that improve with increased vasodilation. These conditions included chest pain, atherosclerosis-clogged arteries, heart disease or failure, erectile dysfunction, intermittent claudication/peripheral vascular disease, and vascular headaches-inducing blood vessel swelling. L-Arginine also triggers the body to make protein and has been studied for healing wounds, bodybuilding, enhancing sperm production, and preventing tissue wasting in people with critical illnesses (Natural Standard Patient Monograph, 2010).

L-Arginine is used in combination with a number of over-the-counter and prescription medications for various purposes. For example, L-arginine is used along with ibuprofen for treating migraine headaches; with conventional chemotherapy drugs for treating breast cancer; with other amino acids for treating weight loss in people with AIDS; and with fish oil and other supplements for reducing infections, improving wound healing, and shortening recovery time after surgery. The Natural Medicines Comprehensive Database (Theraputic Research Faculty, 2012) rates effectiveness based

on scientific evidence according to the following scale: Effective, Likely Effective, Possibly Effective, Possibly Ineffective, Likely Ineffective, Ineffective, and Insufficient Evidence to Rate. The rating for L-arginine on increasing athletic performance fell under the category of Insufficient Evidence to Rate.

L-Arginine treatment prevents the development of hypertension in animals prone to this disease and also causes a rapid reduction in systolic and diastolic pressures when infused into healthy humans and patients with essential hypertension. Furthermore, part of the therapeutic effect of angiotensin converting enzyme inhibitors may be due to their ability to potentiate the duration of action of bradykinin, which stimulates the release of nitric oxide and thus increases its concentration in the vasculature. Endothelium-dependent relaxation is also attenuated in the blood vessels of diabetic animals and in isolated pulmonary arteries obtained from patients undergoing heart-lung transplantation for end-stage chronic lung disease (Epstein, Moncada, & Higgs, 1993).

Nitric Oxide from L-Arginine

Nitric oxide is synthesized from the amino acid L-arginine by a family of enzymes, the nitric oxide synthases, through a previously unrecognized metabolic route, the L-arginine-nitric oxide pathway. The synthesis of nitric oxide by vascular endothelium is responsible for the vasodilator tone that is essential for the regulation of blood pressure (Epstein et al., 1993). The nitric oxide-dependent vasodilator tone seems to be maintained through the physical activation of endothelial cells by stimuli such as pulsatile flow and shear stress (Moncada, 1992). Nitric oxide released from non-adrenergic, non-cholinergic terminals may also contribute to the regulation of blood flow

and pressure (Rand, 1992). The dibasic amino acid L-arginine is a "conditionally essential" amino acid that becomes essential under certain metabolic conditions including muscle trauma and injury. L-Arginine can rapidly induce vasodilatation in skeletal muscle via vascular smooth muscle nitric oxide biosynthesis (Stevens, Godfrey, Kaminski, & Braith, 2000).

In rings of atherosclerotic coronary arteries as compared with rings of normal coronary arteries, the endothelium-dependent relaxation is decreased and the responses to vasoconstrictors are often enhanced by nitric oxide (Forestermann, 1986). Furthermore, vasodilatation induced by increased blood flow or acetylcholine is impaired in the coronary circulation of patients with atherosclerosis (Cox et al., 1989), smokers, and children with familial hypercholesterolemia (Celermajer et al., 1992). The administration of L-arginine normalizes this vascular dysfunction in patients and animals with hypercholesterolemia (Drexler, Zeiher, Meinzer, & Just, 1991; Creager et al., 1992; Cooke & Tsao, 1992) in animals the effect is accompanied by a reduction in the thickness of the intimal lesions. (Cooke & Tsao, 1992).

Role of Nitric Oxide in the Body

Nitric oxide synthase exists in several isoforms, all of which use L-arginine as the substrate to produce nitric oxide. Endothelium-derived nitric oxide is synthesized by an enzyme and is critical for the preservation of vascular homeostasis (Moncade, Palmer, & Higgs, 1991). The enzyme nitric oxide synthase is associated with low levels of nitric oxide formation, which are continuously generated e.g., basal production (Folts, Stamler, & Loscalzo, 1991). Despite this modest level of nitric oxide production, nitric oxide

released via its constitutive pathway is sufficient to maintain vascular tone and inhibit neutrophil and platelet adhesion to the vascular endothelium under control conditions. These physiological concentrations apparently are between 0.1 and 1 nmol/L in the coronary circulation. Similarly, therapeutic concentrations i.e., 500 nmol/L of agents that release physiological concentrations of nitric oxide e.g., nitric oxide donors also inhibit neutrophil and platelet adhesion to endothelial cells and preserve the ischemic/reperfused myocardium (Folts et al., 1991; Johnson, Tsao, & Lefer, 1991; Lefer, Nakanishi, Johnston, & Vinten-Johansen, 1993). Although low concentrations of nitric oxide clearly have cardio protective effects in ischemic, reperfused hearts, it is not known whether these concentrations exert any direct effect on cardiac contractility (Weyrich et al., 1994).

L-Arginine, has drawn significant attention for its potential role in alleviating endothelial dysfunction and improving exercise performance through increasing nitric oxide production. The vasodilatation effect of L-arginine has been shown in both the central and peripheral circulations. Oral L-arginine supplementation could improve coronary endothelial function in patients with non-obstructive coronary artery disease. Nitric oxide also plays a role in exercise-induced vasodilatation in patients and healthy subjects (Liu et al., 2009).

Gender Considerations with Nitric Oxide and the Heart

Women in the reproductive age group are at a lower risk for developing coronary heart disease as compared with men of similar age (Kannel, Hjortland, McNamara, & Gordon, 1976). Studies in rabbits (Haarbo, Leth-Espensen, Stender, & Christiansen, 1991) and subhuman primates (Clarkson et al., 1990) suggest that estrogen affords

protection against the development of atherosclerosis and estradiol administrated to rabbits that were fed a high cholesterol diet led to decreased aortic accumulation of cholesterol as compared with the control group (Haarbo et al., 1991). In these studies, the beneficial effect of estradiol on atherosclerosis could be explained only partly by its effect in lowering serum total cholesterol or very low density lipoprotein cholesterol. This implies that estradiol possesses additional beneficial effects in inhibiting atherosclerosis, possibly by a direct action on the endothelial cells.

It was recently demonstrated that basal release of nitric oxide from endothelium-intact aortic rings obtained from female rabbits was greater as compared with those obtained from male rabbits. However, this gender difference was not observed when the female rabbits were oophorectomized (Hayashi, Fukuto, Ignarro, & Chaudhuri, 1992). The increase in nitric oxide formation could modulate the early events in the development of atherosclerosis such as adhesion of monocytes to endothelial cells (Gerrity, 1981). However, no well-controlled studies have evaluated the gender differences, if any, in the rate of development of atherosclerosis in animals fed a high cholesterol diet and the role of nitric oxide in this process (Hayashi, Fukuto, Ignarro, & Chaudhuri, 1995).

Effects of Nitric Oxide on the Body

The implications of the existence of a nitric oxide-mediated vasodilator tone are many. The present understanding of the mechanics of the vascular tree consider it either as a system of resistance vessels against which the heart pumps the blood or as a resistance system modulated by neural or hormonal vasoconstrictor and vasodilator

influences. The physiological stimuli for generation of nitric oxide are not yet fully understood, but pulsatile flow and shear stress seem to be two of the main determinants. It is likely that nitric oxide-dependent vasodilator tone is entirely locally regulated and, as such, is probably one of the simplest and yet most fundamental adaptive mechanisms in the cardiovascular system (Moncade et al., 1991).

The available evidence indicates that the cardiovascular system is in a state of constant active vasodilatation dependent on the generation of nitric oxide. Indeed, nitric oxide can now be considered the endogenous nitrovasodilator. Nitrovasodilators have been used clinically for about 100 years and are still widely used in conditions such as angina pectoris, congestive heart failure, hypertensive emergencies, pulmonary hypertension, fibrinolysis, percutaneous coronary angioplasty, and complications following cardiac catheterization (Moncade et al., 1991).

Nitric oxide may be useful in patients with some pulmonary conditions, since inhaled nitric oxide gas reverses pulmonary hypertension. Furthermore, low concentrations of inhaled nitric oxide at 18 to 36 ppm protect against the adult respiratory distress syndrome. Administration of nitric oxide for seven days resulted in sustained improvement in lung function in affected patients, suggesting that inhaled nitric oxide assisted lung healing. Inhaled nitric oxide selectively dilates the vasculature of ventilated lung regions, thus improving ventilation:perfusion ratios. Unlike prostacyclin, another vasodilator, nitric oxide has no effect on systemic hemodynamic (Epstein et al., 1993).

It has been well known that flavonoids produce a vasodilatation effect on the body which is seen through the production of nitric oxide. One prominent study,

showing the effects of flavonoid- rich cocoa, emphasized vasodilatation evident within 90 min of indigestion, suggesting an acute pharmalogical effect on the body (Fisher, Hughes, Gerhard-Herman, & Hollenberg, 2003).

Chronic increases in blood flow can enhance the synthesis and release of nitric oxide from the vascular endothelium of the vessels subject to the high flow. In animal models, endurance exercise training can evoke an increase in nitric oxide synthase gene expression in the endothelial cells of conducting arteries i.e., the aorta that are subject to increased flow during exercise. These vessels also show increased endothelial dependent vasodilatation. However, it has been difficult to determine whether exercise training enhances endothelium-dependent vasodilatation in humans (Joyner & Dietz, 1997).

During mental or emotional stress in humans, there can be skeletal muscle vasodilatation in the forearm. The presence, magnitude and duration of forearm muscle vasodilatation during mental stress are variable and dependent on a wide variety of subject-specific factors. However, this dilation is absent after sympathectomy and it is also blunted by intra-arterial infusions of atropine. These observations suggest that there might be sympathetic-cholinergic innervation to skeletal muscle in humans and that these nerves can be active during mental or emotional stress. Whereas there are pharmacological data to support sympathetic-cholinergic dilation in humans, there is no histological evidence for sympathetic-cholinergic nerves in human skeletal muscle. Beta-Adrenergic-mediated vasodilatation as a result of circulating epinephrine has also been proposed to contribute to the dilation (Roddie, 1977).

Mental stress is also associated with arterial hypertension and tachycardia, and it is possible that these hemodynamic changes mechanically stimulate nitric oxide release from the endothelium. Flow-induced nitric oxide release may be active in the human hand, where a nitric oxide system blockade can reduce finger blood flow in a normothermic human, but not in a cool human with vasoconstricted fingers and limited blood flow to stimulate nitric oxide release. This last possibility is attractive in light of recent observations showing that there can be selective sympathetic withdrawal to the forearm in some subjects who show forearm vasodilatation during mental stress (Halliwill et al., 1997).

Effects of Nitric Oxide on Exercise

Although there has been very limited research done on the effects of pure L-arginine on humans during exercise, some studies have been done on animals. There have also been studies to determine the effects of nitric oxide on humans. The contribution of nitric oxide to the regulation of skeletal muscle vasodilatation during exercise is more difficult to study as a result of multiple mechanisms that might contribute to exercise hyperemia and due to the many potential sources of nitric oxide that might contribute to vasodilatation in active skeletal muscles during exercise (Dyke, Proctor, Dietz, & Joyner, 1995; Gorman, & Sparks, 1991; Jia, Bonaventura, & Stamler, 1996; Kobzik ., Reid, Bredt, & Stamler, 1994; Laughlin, 1987; Shepherd, 1983). It does appear reasonable to suggest that locally released nitric oxide is not essential for the normal rise in flow at the onset of exercise, but that it may contribute modestly as exercise continues, particularly during mild or moderate levels of exercise and in slow-

twitch fibers (Dyke et al., 1995; Hirai, Visneski, Kearns, Zelis, & Musch, 1994; Wilson & Kapoor, 1993).

Animal studies investigating both the peripheral and coronary vasculature suggest that short-term exercise training enhances e-nitric oxide synthase, and nitric oxide production and bioactivity, producing a short-term buffer to the increased shear associated with exercise. After extended training, at least in the peripheral circulation, the increased production of nitric oxide and possibly other mediators induces structural changes in the vessels resulting in an increase in lumen diameter (Brown, 2003; Prior, Lloyd, Yang, & Terjung, 2003).

A study done on humans looking at the mediated dilatation in the brachial artery, which is known to depend on the ability of the vascular endothelium to release nitric oxide, determined that the responses of the brachial artery in young health male subjects were positive for dilatation. (Kannel et al., 1976). The importance of these findings was two-fold. First, the study showed how exercise can potentially affect progression of atherosclerotic vascular disease along with cardiovascular complications. Second, the study showed how ten weeks of generalized training invoked a response from the endothelium of the brachial artery sufficient to be a positive factor for incorporation in all disease prevention strategies.

Athletes and L-Arginine

Although there has been a large amount of research done on animals, L-arginine studies performed with human subjects in an athletic population are still lacking. Most of the previous research done was mostly with clinical populations and not on healthy

populations of athletes. These studies are not able to be linked to non-clinical populations such as athletes. L-Arginine is readily available at modest cost without age restrictions or prescriptions in drug stores, grocery stores, convenience stores and General Nutrition Centers. A recent spike in supplement advertising to athletes has led many to believe that allowing more blood to flow throughout the circulatory system will allow the athlete to perform better due to the availability of additional L-arginine to "boost" nitric oxide pathways. The supplement market also heavily emphasizes an "extreme pumping" feeling to which the user can attribute a higher level of explosive power output during workouts. However, there is insufficient research with athletes to substantiate these claims.

Purpose of the Study

The purpose of this research was to evaluate the benefits to human performance of over-the-counter L-arginine supplements. The intention of this research project was to contribute to further identifying and understanding the possible benefits of over-the-counter L-arginine supplements to improve human performance during exercise.

CHAPTER 2

METHODS

Subjects

Thirty-five male and female track and field athletes from a NCAA Division III university participated in this research project. The safety of exercise was established through the completion of the Physical Activity Readiness Questionnaire (PAR-Q) by each subject. Demographic information, including name, contact information, gender, birthdate, age, height and weight were obtained from each subject.

Procedures

All subjects performed two exercise trials, including an L-arginine trial and a control trial in a randomized order. The orders in which the subjects took either the supplement or control was determined upon their first trial, with each subjects drawing 1 numbered ball from a shaker bottle. This number, either 1 or 2, was linked to the supplement or the control. Thirty minutes prior to each exercise trial the subjects consumed 5,000 mg of GNC L-Arginine 5000® in eight ounces of water (L-arginine trial) or the equivalent volume of plain water (control trial). The 5,000 mg dosage was based upon the manufacturer's guidelines found on the supplement packaging. Subjects were brought in groups of 4, utilizing two cycle ergometers. The subjects were staggered according to time to not allow two subjects to be pedaling at the same time. The subjects completed a warm-up consisting of four minutes of submaximal exercise on a cycle ergometer beginning five minutes prior to each exercise trial. This warm up was done at

cadence of 100 bpm heard from a metronome. Each exercise trial consisted of a standard Wingate Anaerobic Power Cycle Ergometer Test involving thirty seconds of lower body exercise on a computerized cycle ergometer made by Monark. The force setting was based on 7.5% of body weight at the time of the first exercise trail rounded to the nearest 0.5 kg and the same force setting was used for both exercise trials.

Analysis

After all exercise trials were completed, each subject's peak anaerobic power, average anaerobic power, minimum anaerobic power and anaerobic power drop were calculated for both exercise trials. Results from the L-arginine trials and control trials were compared using Student's t-test for paired data. The p value of the data which approach statsitcally significant was $p<0.10$ and statistically significant data was $p<0.05$.

CHAPTER 3

RESULTS

The subjects in this research project were 20 male track and field athletes and 15 female track and field athletes from an NCAA Division III university. The men and women ranged in age from 18-22 with body weights for men averaging 86.6 kg ± 3.7 kg and women averaging 62.6 kg ± 2.3 kg. All except two of the subjects were sprinters, throwers or jumpers. The two exceptions were 800 m runners. All subjects had also previously participated in high school track and field along with various other high school sports. Nine men and six women reported feeling lightheaded, dizzy or nauseated following the L-arginine trials. No subject reported a "muscle pumps" or "excited" feeling following the L-arginine trials.

Figure 1 shows data from the L-arginine trials for men, women and all subjects combined. Figure 2 shows data from control trials for men, women and all subjects combined. Figure 3 shows the peak power from the L-arginine trials and control trials for men, women and all subjects combined. Figure 4 shows the average power from the L-arginine trials and control trials for men, women and all subjects combined. Figure 5 shows the power drop from the L-arginine trials and control trials for men, women and all subjects combined. Figure 6 shows the minimum power from the L-arginine trials and control trials for men, women and all subjects combined.

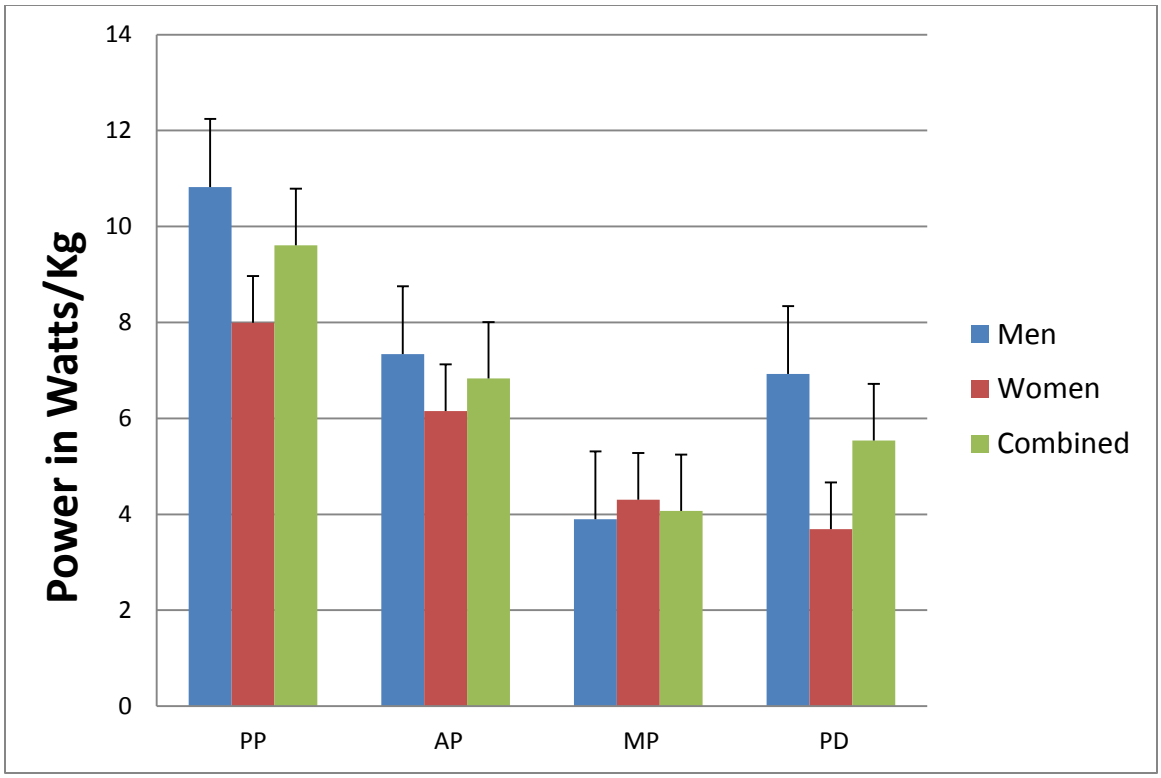

Figure 1. Data from L-Arginine trials for men, women and all subjects combined. PP = peak power; AP = average power; MP = minimum power; PD = power drop. Data are mean plus or minus standard deviation.

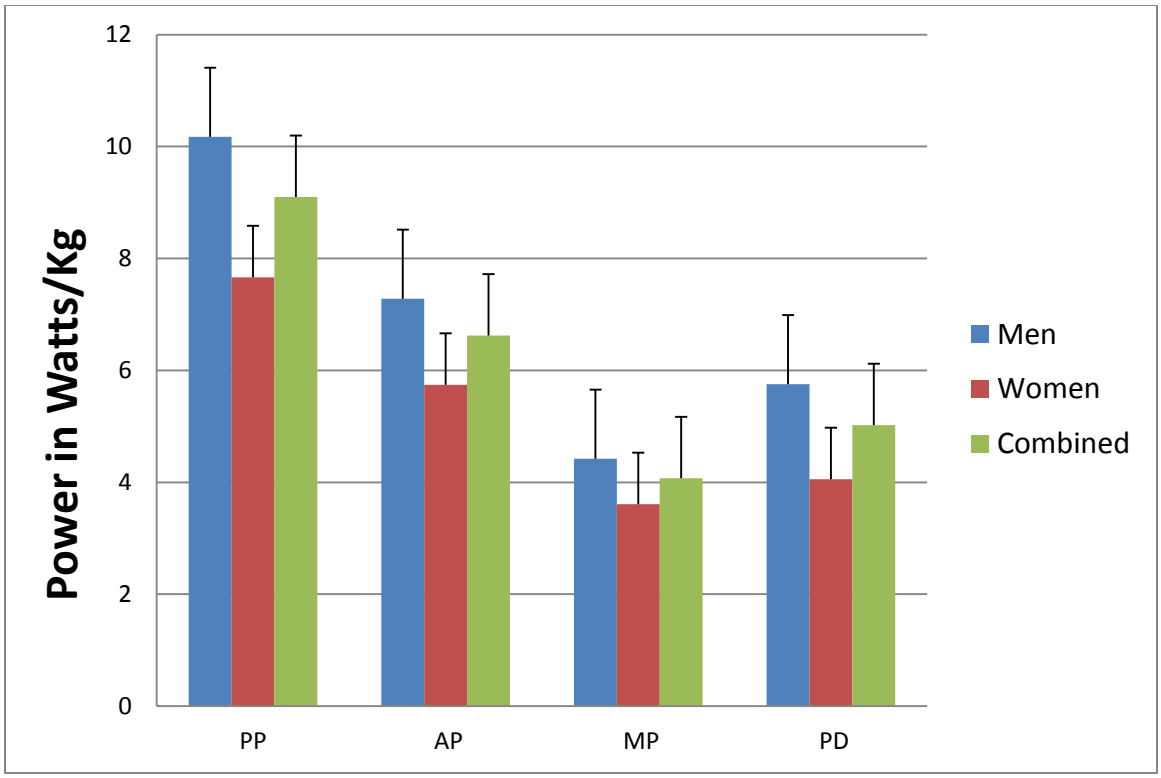

Figure 2. Data from control trials for men, women and all subjects combined. PP = peak power; AP = average power; MP = minimum power; PD = power drop. Data are mean plus or minus standard deviation.

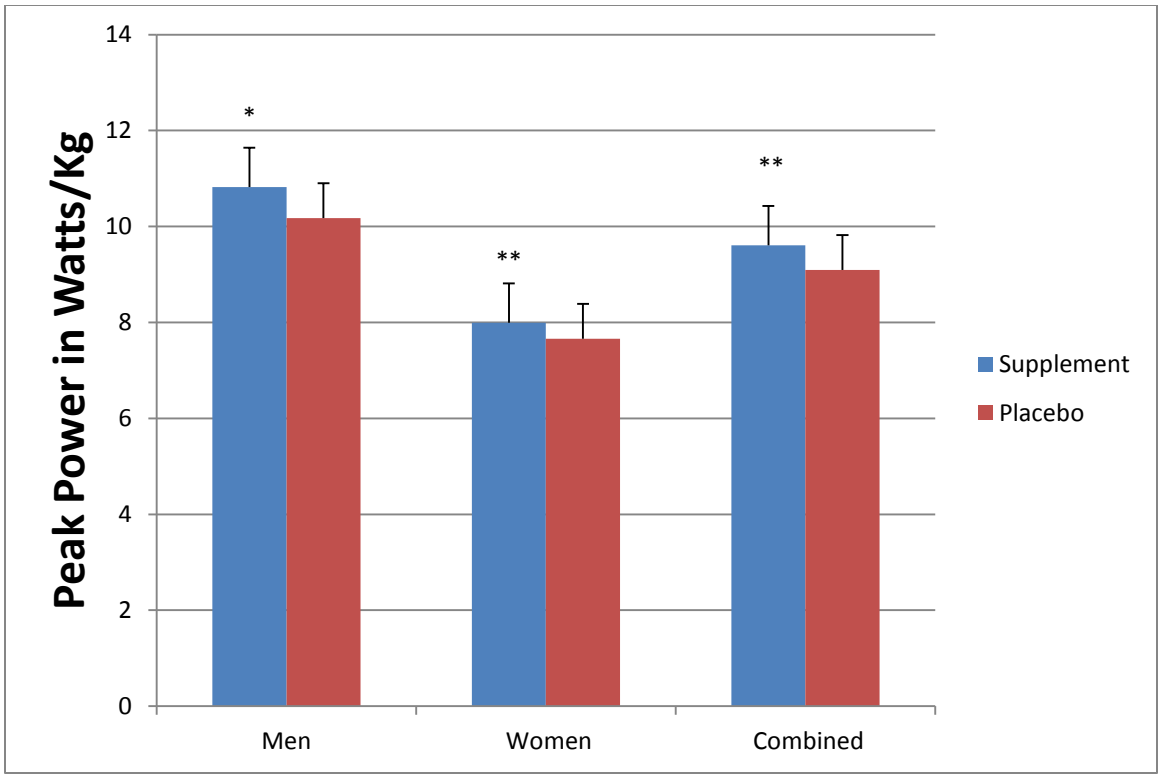

Figure 3. Peak power from L-arginine trials and control trials for men, women and all subjects combined. Data are mean plus or minus standard deviation. *p<0.10, **p<0.05.

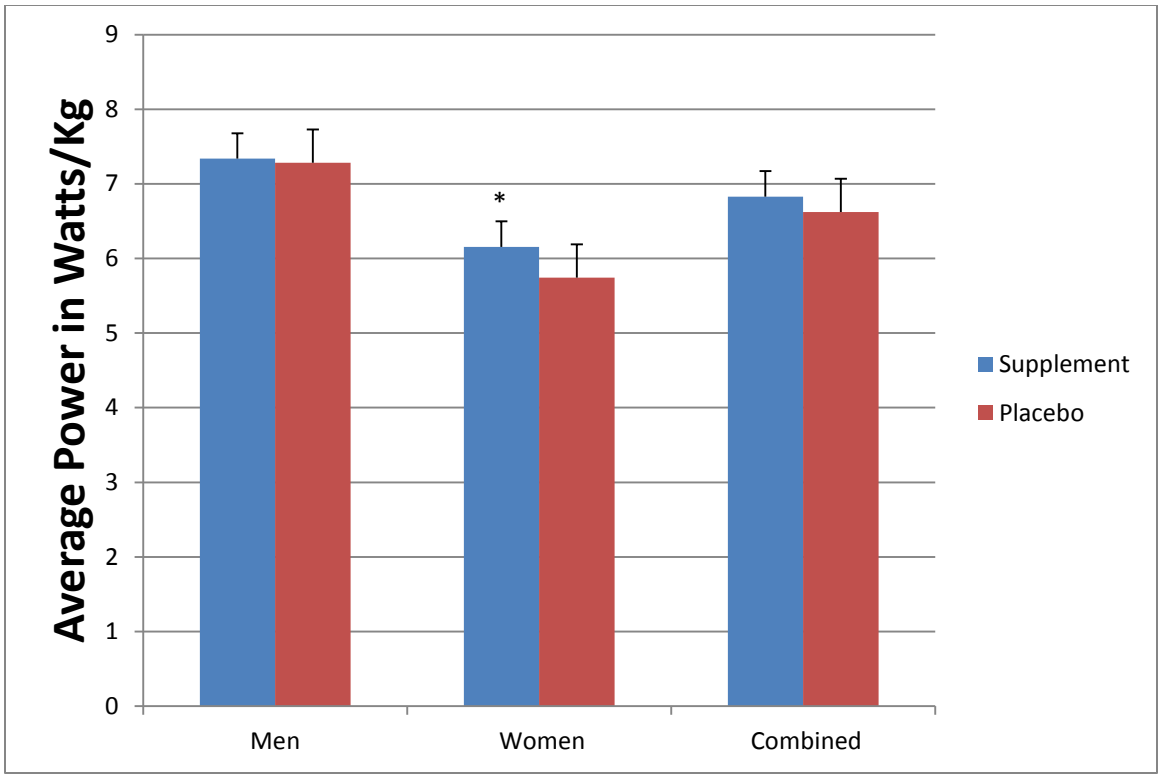

Figure 4. Average power from L-arginine trials and control trials for men, women and all subjects combined. Data are mean plus or minus standard deviation. *p<0.10, **p<0.05.

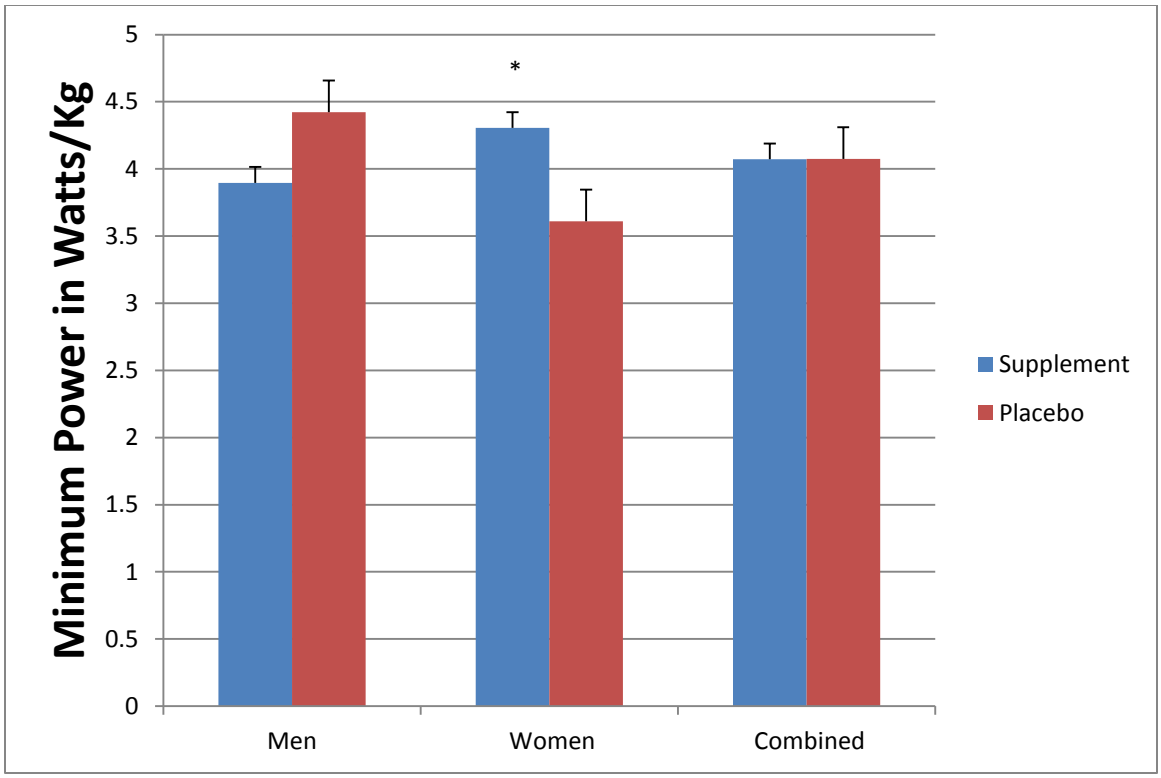

Figure 5. Minimum power from L-arginine trials and control trials for men, women and all subjects combined. Data are mean plus or minus standard deviation. *p<0.10, **p<0.05.

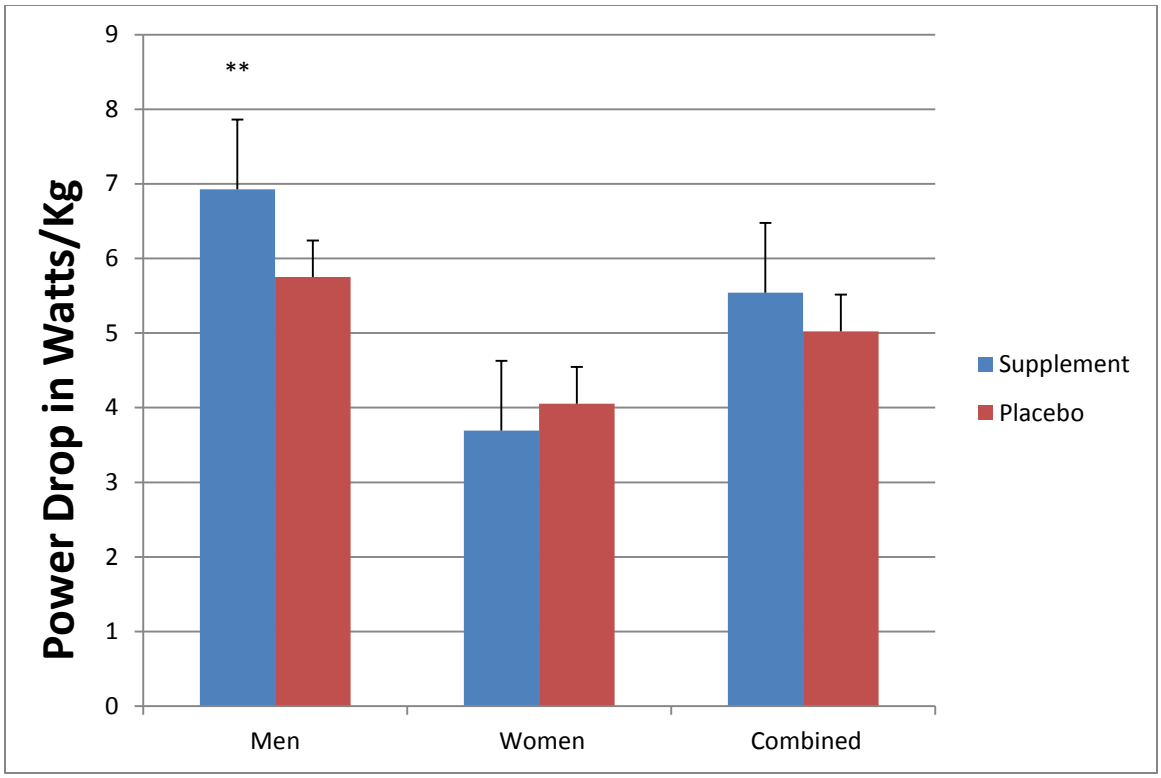

Figure 6. Power drop from L-arginine trials and control trials for men, women and all subjects combined. Data are mean plus or minus standard deviation. *p<0.10, **p<0.05.

Table 1 shows the peak power, average power, power drop and minimum power from the L-arginine trials and control trials for men. Table 2 shows the peak power, average power, power drop and minimum power from the L-arginine trials and control trials for women. Table 3 shows the peak power, average power, power drop and minimum power from the L-arginine trials and control trials for all subjects combined. Table 4 shows the Probabilities from One-Tailed Paired t-Tests for all the power categories.

Table 1

Peak Power, Average Power, Power Drop and Minimum Power for Men

Exercise Trial	PP(W/kg)	AP(W/kg)	MP(W/kg)	PD(W/kg)
L-Arginine (n=20)	10.82±1.97*	7.34±1.12	3.90±2.05	6.93±3.48**
Control (n=20)	10.17±1.12	7.28±1.28	4.42±1.83	5.75±1.89

Note: n = number of subjects; PP = peak power; AP = average power; MP = minimum power; PD = power drop. Data are mean plus or minus standard deviation. *p<0.10, **p<0.05.

Table 2

Peak Power, Average Power, Power Drop and Minimum Power for Women

Exercise Trial	PP(W/kg)	AP(W/kg)	MP(W/kg)	PD(W/kg)
L-Arginine (n=15)	7.99±1.63**	6.15±.1.15*	4.30±0.98*	3.69±0.90
Control (n=15)	7.66±1.59	5.74±1.01	3.61±1.34	4.05±2.31

Note: n = number of subjects; PP = peak power; AP = average power; MP = minimum power; PD = power drop. Data are mean plus or minus standard deviation. *p<0.10, **p<0.05.

Table 3

Peak Power, Average Power, Power Drop and Minimum Power for All Subjects Combined

Exercise Trial	PP(W/kg)	AP(W/kg)	MP(W/kg)	PD(W/kg)
L-Arginine (n=35)	9.61±2.30**	6.83±1.27	4.07±1.67	5.54±3.12
Control (n=35)	9.10±1.82	6.62±1.39	4.07±1.67	5.02±2.22

Note: n = number of subjects; PP = peak power; AP = average power; MP = minimum power; PD = power drop. Data are mean plus or minus standard deviation. *p<0.10, **p<0.05.

Table 4

Probabilities from One-Tailed Paired t-Tests for Peak Power, Average Power, Power Drop and Minimum Power for Men, Women and All Subjects (Combined)

	PP(W/kg)	AP(W/kg)	MP(W/kg)	PD(W/kg)
Men(n=20)	0.0811*	0.4159	0.1335	0.0481**
Women(n=15)	0.0435**	0.0520*	0.0797*	0.2218
Combined(n=35)	0.0303**	0.1263	0.4964	0.1269

Note: n = number of subjects; PP = peak power; AP = average power; MP = minimum power; PD = power drop. *p<0.10, **p<0.05.

CHAPTER 4

DISCUSSION

Peak power (W/kg) was higher during L-arginine trials compared to control trials for men, women and all subjects (combined). These differences were statistically significant for women (p=0.0435) and all subjects (combined, p=0.0303), and approached statistical significance for men (p=0.0811). Average power (W/kg) was higher during L-arginine trials compared to control trials for men, women and all-subjects (combined). These differences approached statistically significance for women (p=0.0520).

Differences in minimum power (W/kg) and power drop (W/kg) between L-arginine trials and controls trials were inconsistent between men, women and all subjects combined. Minimum power was higher during control trials compared to L-arginine trials for men; minimum power was higher during L-arginine trials compared to control trials for women; and minimum power was similar during L-arginine trials and control trials for all subjects combined. The higher minimum power during L-arginine trials compared to control trials for women approached statistical significance (p=0.0797). Power drop was higher during L-arginine trials compared to control trials for men and all subjects combined; and power drop was higher during control trials compared to L-arginine trials in women. The higher power drop during L-arginine trials compared to control trials for men was statistically significant (p=0.0481).

The dosage of L-arginine, 5,000 mg in eight ounces of water, was the same for all subjects and based upon the manufacturer's guidelines found on the supplement

packaging. Based upon subject weight, men received an average of 57.7 mg of L-arginine per kilogram of body weight while women received an average of 79.9 mg of L-arginine per kilogram of body weight. The 38.5% higher dosage of L-arginine per kilogram of body weight for women compared to men is important to understanding the results and applications of this research.

Both peak power and average power were higher during L-arginine trials compared to control trials for men, women and all subjects (combined). The differences in peak power were statistically significant for women and all subjects (combined), but only approached statistical significance for men, and the differences in average power only approached statistical significance for women. The stronger statistical evidence for women may be a consequence of the higher dosage per kilogram of L-arginine consumed by women compared to men during the L-arginine trials.

Peak power was consistently achieved during the first 10 seconds of the 30 second standard Wingate Anaerobic Power Cycle Ergometer Test. The stronger statistical evidence for differences in peak power compared to average power suggests that the advantages gained in peak power from L-arginine in the first 10 seconds were not sustained during the remaining 20 seconds of the 30 second standard Wingate Anaerobic Power Cycle Ergometer Test. While L-arginine might help a sprinter to accelerate more quickly out of the blocks at the start of a race, that advantage may not be sufficiently sustained at the finish line to make a difference in the outcome of the race. However, in events lasting less than 10 seconds, such as shot put and javelin throw, L-arginine might

facilitate a higher peak power in a rapid explosive movement that could provide a measureable advantage in performance.

15 of 35 subjects (42.9%), including nine of 20 men (45.0%) and 6 of 15 women (40.0%), reported feeling lightheaded, dizzy or nauseated following the L-arginine trials, while no subjects reported the "muscle pumps" or "excited" feeling advertised by the manufacturer following the L-arginine trials. The incidence of feeling lightheaded, dizzy or nauseated following the L-arginine trials was similar in men and women, and may impose a practical limitation on the use of L-arginine to enhance performance. The manufacturer's recommended dosage of L-arginine, 5,000 mg in eight ounces of water, rather than a dosage per kilogram, may be an effort to simplify the dosage and avoid calculations for the consumer. The manufacturer also may be balancing increasing the incidence of feeling lightheaded, dizzy, or nauseated against additional improvements in performance that might result from a larger dosage per kilogram.

Future research should utilize higher fixed dosages of L-arginine to maintain simplicity and avoid calculations for the consumer, and higher dosages of L-arginine per kilogram of body weight with all subjects receiving the same dosage per kilogram of body weight to more clearly determine the dose-response relationship. Future research should also utilize a wider range of exercise, including rapid explosive movements that may have greater potential to be improved by the use of L-arginine and exercises of longer durations that may have potential to be improved through different mechanisms.

The potential limitations of feeling lightheaded, dizzy or nauseated should also be explored since this may limit the willingness of consumers to utilize L-arginine in

dosages sufficient to provide measureable advantages in performance. In addition to the effects of single dosages of L-arginine, future research should explore repeated dosages, including the possibility that potential limitations of feeling lightheaded, dizzy or nauseated might be overcome with repeated dosages. Hemodynamic measurements would also be useful to more fully understand the potential limitations of feeling lightheaded, dizzy or nauseated as they apply to the cardiac system. The subjects of this test were not instructed to refrain from food or drink prior to the test. This may have limited some of the results if prior to testing the subjects had food or drink up hours before the test. This would also limit the potential of intensified side effects from the supplement.

Conclusion

The manufacturer's recommended dosage of L-arginine, 5,000 mg in eight ounces of water, improved peak performance, but did not improve average performance, during the thirty second standard Wingate Anaerobic Power Cycle Ergometer Test, especially in women who received a higher dosage of L-arginine per kilogram of body weight. The manufacturer's recommended dosage of L-arginine, 5,000 mg in eight ounces of water, may improve performance in rapid explosive movements, but those improvements may not be sustained over longer periods of exercise.

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