Can Vitamin C and E supplementation ameliorate Post-exercise Protienuria?

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Abstract: Background/aim: Exercise-induced protienuria is a common consequence of physical activity; however, its mechanism is not fully understood. Generation of reactive oxygen species (ROS) during aerobic exercise has been involved. In this work, we aimed to study the effect of exogenous antioxidant supplementation on exercise-induced proteinuria. **Subjects, Material and Methods:** A total of eligible 50 participants were enrolled in this work, conducted in the Faculty of Sport, Egypt, during December 2012. Thorough history taking and clinical examination were done. A total of 8 urine samples were taken from each participant, twice-a day on three successive weeks; one before and one after moderate exercise applied for two hours in the morning. Urine samples were collected using the clean-catch method, then, total urinary protein levels were assayed. One tablet (500 mg) ascorbic acid and one tablet vitamin E (400 IU) was given daily for each volunteer from the first day after the post-exercise urine sample for 3 weeks as an antioxidant supplementation. **Results:** A statistically significant reduction in both pre-exercise and post-exercise protienuria and haematuria was evident when comparing the initial and after 3 weeks results in subjects on anti-oxidant supplementation. No gender differences in both pre- and post-exercise proteinuria and haematuria on comparing the initial and post-3 weeks data in the studied subjects (p>0.05). **Conclusion:** our data revealed a statistically significant amelioration of post-exercise proteinuria on three weeks' exogenous vitamin C and E supplementation in our studied untrained apparently healthy volunteers. For a positive adaptive benefit, it is strongly advised to perform regular moderate intensity exercises especially to untrained subjects, to gain the antioxidant protection.

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1. Introduction

Although the positive effects of exercise on human health has been known for many years, professional sports can still cause complications in renal, cardiovascular and muscular systems (Koning *et al.*, 2003; Neumayr *et al.*, 2005; and Clarkson *et al.*, 2006). Exercise-induced urinary abnormalities are well-documented in humans and have been termed "athletic pseudonephritis", characterized by proteinuria, pigmenturia and haematuria. These transient changes are consistent with nephritis and do not appear to be associated with any pathological structural changes in the kidneys (Schott *et al.*, 1995 and McKeever *et al.*, 2004).

Several mechanisms have been proposed to explain this benign phenomenon including; increased glomerular permeability exceeding the renal maximum renal tubular reabsorption capacity, relative decrease in renal blood flow and glomerular filtration during exercise, with subsequent increased filtration fraction facilitating the passage of proteins into the ultrafiltrate (Poortmans 1985 and1988). Also, lost fixed negative charge of the capillary wall of the glomerular tuft may be another contributing factor (Zambraski *et al.*, 1981).

Neutrophils characterized by their abilities to generate ROS, may be activated during exercise by a variety of factors including growth hormone, muscle damage, and interleukin (IL)-6 with variable inconsistent responses dependent mainly on the exercise mode, participants' fitness level, differences in sampling time and the assay method used to measure *in vivo* neutrophil ROS production (Suzuki *et al.* 1999 and Peake, 2002).

Several studies suggest that ROS may play a role in proteinuria by altering glomerular vascular permeability, causing glomerular basement membrane degradation and impairing the electrostatic barrier in various kidney diseases in humans and in animal models (Tay *et al.*, 1990; Kanwar *et al.,* 1991; and Sananka *et al.,* 1997). Moreover, reduction of protienuria in several experimental renal models has been achieved with administration of anti-oxidant agents as vitamin C, selenium, probucol and vitamin E (Tay *et al.*, 1990; and Sananka *et al.,* 1997).

Despite the well-established close relationship between physical exercise and oxidant stress, however, their association to post-exercise proteinuria has not been fully investigated on our subjects.

Thus, the aim of this work was to study the effect of anti-oxidant supplementation in apparently healthy volunteers with exercise-induced proteinuria during the study period.

2. Subjects, Material and Methods

A total of eligible 50 non smoker, non athlete, non obese [a body mass index (< 25 Kg/m^2)], apparent healthy participants, aged (17-22 years), with an equal sex ratio (25 males, 25 females) were enrolled in this study conducted in the Faculty of Sport, Egypt, during December 2012 after giving well-informed consent.

Thorough history including dietetic, nutritional aspects, especially related to anti-oxidant supplements and clinical examination were done. All participants were on a standardized diet during the study period.

Exclusion criteria: those with documented congenital renal syndromes, cysts (single, multiple, medullary sponge disease), recent (within 1 month) or ongoing urinary tract or upper respiratory tract infection, renal stone disease or stone passers, those with drug-induced nephrotoxicity or receiving anticoagulants, recent intake of oral or parenteral anti-oxidant supplements (within the last 3 months), serious or chronic diseases as diabetes, hypertension and / or major organ impairment. We excluded also those with urine report abnormalities without exercise or with post-exercise persistent protienuria (>48hours).

A total of 8 urine samples were taken from each participant, twice-a day on three successive weeks; one before and one after exercise that was moderate in intensity applied for two hours in the morning. Urine samples were collected using the clean-catch method, then, analyzed using a thin strip of plastic (dipstick) impregnated with chemicals that react with substances in urine and quickly change its color. One tablet (500 mg) ascorbic acid and one tablet vitamin E (400 IU) was given daily for each volunteer from the first day after the post-exercise urine sample for 3 weeks as an antioxidant supplementation.

Statistics:

Statistical Package for Social Sciences (SPSS) 15.0 (SPSS, Chicago, IL, USA) was used for statistical analyses. The variability of results was expressed as mean ± standard deviation (X±SD) Mann-Whitney test was used to test the significance of differences between mean values. A p-value ≤ 0.05 was considered statistically significant.

3. Results

There is a statistically significant reduction in the level of pre–exercise and post-exercise protienuria when comparing the initial and after 3 weeks results in subjects on anti-oxidant supplementation (Tables 1 & 2).

No gender differences exist in both pre- and post-exercise proteinuria on comparing the initial and post-3 weeks data in the same studied subjects (p=0.677).

4. Discussion

Aerobic exercise of sufficient duration can result in increased generation of reactive oxygen/nitrogen species (RONS), if produced in large quantities that overwhelm the endogenous antioxidant defense system; this would be referred to as an oxidant stress (Urso, Clarkson, 2003). Regular muscular training and exogenous antioxidant micronutrient supplementation are the main methods used to reduce RONS formation and subsequent macromolecule oxidation to maintain appropriate health and physical function (Powers *et al*., 1999 and 2004).

In this work, we aimed to clarify the possible role of oxidant stress in apparently healthy subjects with post-exercise proteinuria by using exogenous antioxidant supplements (vitamins C and E) to suppress RONS generation.

Vitamin C is a water-soluble *in vivo* antioxidant and has the ability to protect against lipid peroxidation, a primary target of oxygen radicals, by acting as a ROS scavenger and by one-electron reduction of lipid hydroperoxyl reduction via the vitamin E redox cycle while vitamin E is fat-soluble antioxidant acting by scavenging lipid hydroperoxyl radicles (Halliwell; and Gutteridge, 1999 and Traber, and Stevens, 2011). Thus, combined use of both (Vit C and E) has synergistic biological activities that would complement each other in vivo. Moreover, vitamin C maintains vitamin E in the reduced and active state. (Paker *et al*., 1979).

After 2 months of antioxidant supplementation, Gupta and coworkers noticed significantly increased serum ascorbic acid and alpha-tocopherol levels, increased catalase activity, and decreased malondialdehyde, superoxide dismutase and suggested that oxidant stress could be reduced, after endurance training, by strengthening the antioxidant defense system by an exogenously added dual vitamin supplements (Gupta *et al.*, 2009). Duration, dosage, and cocktail of vitamin supplements and severity of exercises have led to insignificant variations in the final results. Only with trained athletes, the erythrocyte catalase activity insignificantly changed in trained athletes during 4.5 weeks' research activity (Rokitzki *et al*., 1994).

Our data would have revealed obvious clinical effects of exogenous Vitamin C and E supplements for 3 weeks with significantly reduced levels of pre–exercise and post-exercise protienuria and haematuria. Gupta *et al.* (2006) would have probably explained the underlying mechanism of our observed findings.

It has been suggested that females are less susceptible to oxidant stress due to the fact that estrogen has in vitro antioxidant properties. In animal models, female gender would have lower resting level of oxidant stress (Tidus, 2000 and Ginsberg *et al*., 2001). Also, it is suggested that males have a higher metabolic rate leading to increased mitochondrial flux and increased ROS generation (Mastaloudis *et al*., 2004).

Our work revealed that no gender differences exist in both pre- and post-exercise tested urinary parameters (p>0.05) after 3 weeks of antioxidant supplementation. This attenuated gender difference observed in our work would be explained by the fact that Estrogen may not be the only factor involved in gender comparisons of oxidative stress as animals' studies revealed differences in vitamins C, E and glutathione levels following an acute bout of exercise as well as at rest (Tidus PM *et al*., 1999 and Tidus, 2000).

In this study, all enrolled participants were untrained students that when practicing acute exercises, increased oxidant levels and oxidant stress was evident. On the contrary, long-term exercises would increase the level of antioxidant enzymes and may counteract the acute already mentioned effects of exercises. Thus, it is advised to perform regular moderate intensity exercise to increase the antioxidant protection (Ji *et al.,* 2006). The upregulation in antioxidant defense would be expected to shift the redox balance in favor of a more reducing environment, thereby potentially explaining the adaptive benefit of pro-health/ anti-pathological effects of exercise (Chung *et al*., 2008 and Radak *et al*., 2008).

Table 1: Comparison between pre and post (Vitamins C & E) before exercise {Mean ± S.D}.

Groups	Blood	Urobilino-gen	Bilirubin	Protein	Nitrite	pH	Leukocytes
Pre-exercise	88.1±15.1	2.5±0.1	3.3±1.1	37.4±3.9	0.09±0.003	7.5±0.4	22.6±2.1
Post 1W Dose	69.9±5.6*	2.3±0.1	2.9±0.1	33.6±3.3**	0.08±0.002	6.6±0.1	19.2±1.9
Post 2W Dose	56.3±4.3*	2.2±0.1	2.5±0.1	31.8±2.8**	0.07±0.002	6.1±0.1	17.3±1.7
Post 3W Dose	20.1±2.7*	2.1±0.1*	2.2±0.1*	30.7±2.2**	0.06±0.001*	5.9±0.1*	16.5±1.5*

**P= ≤ 0.05; *= P ≤ 0.01

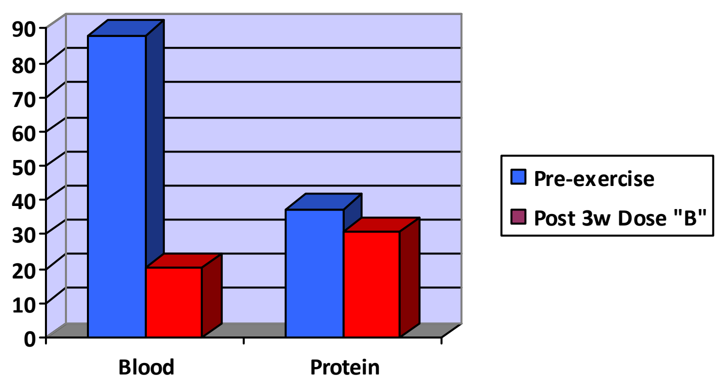

Figure 1: Shows pre and post (Vitamins C & E) pre- exercise parameters

Table 2: Comparison between pre and post (Vitamins C & E) after exercise {Mean ± S.D}.

Groups	Blood	Urobilino-gen	Bilirubin	Protein	Nitrite	pH	Leukocytes
Post-exercise	192.7±13.9	4.1±1.6	3.9±1.3	64.1±5.5	1.01±0.01	7.8±0.4	48.4±4.2
Post 1W Dose	155.6±11.3*	3.6±1.2	3.6±1.2	54.3±4.2**	0.09±0.003	7.1±0.1	39.2±4.1
Post 2W Dose	121.1±9.9*	3.2±0.1	3.3±1.1	46.2±4.1*	0.08±0.002	6.5±0.1	27.3±2.9
Post 3W Dose	98.6±8.8*	2.9±0.1*	3.1±0.1*	36.3±3.8*	0.07±0.002*	6.1±0.1*	19.9±2.1*

**P= ≤ 0.05; *= P ≤ 0.01

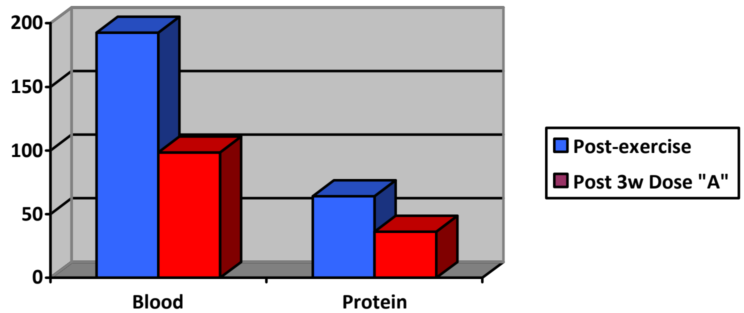

Figure 2: Shows improvement of post exercise haematuria and proteinuria at the end of the study

Table 3: The percentage of enhancement according to (Vitamins C & E) doses Post exercise.

Groups	Blood	Urobilino-gen	Bilirubin	Protein	Nitrite	pH	Leukocytes
Post 1W Dose	19 %	%12	%8	%15	91 %	9 %	19 %
Post 2W Dose	% 38	%22	%15	30 %	92 %	17 %	44 %
Post 3W Dose	%49	%29	%21	43 %	% 93	22 %	59 %

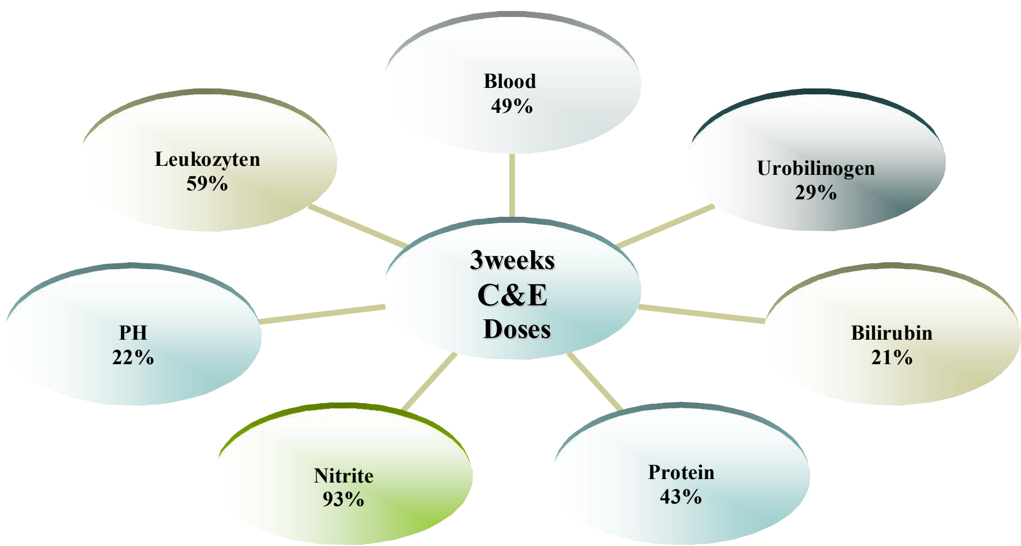

Figure 3: Illustrates the degree of improvement after 3 weeks vitamin supplementation

In conclusion:

Our data revealed a statistically significant amelioration of post-exercise proteinuria on three weeks' exogenous vitamin C and E supplementation in our studied untrained apparently healthy volunteers.

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References

1. Neumayr G, Pfister R, Hoertnagel H, *et al.* Renal function and plasma volume after ultramarthon cycling. Int J Soprts Med 2005; 26: 2-8.
2. Koning D, Schumacher YO, Heinrich L, *et al*. Myocardial stress after competitive exercise in professional road cyclists. Med Sci Sports Exerc 2003; 35: 1679-83.
3. Clarkson P, Kaerns A, Rouzier P. *et al*. Creatinine kinase levels and renal function measures in exertional muscle damage. Med Sci Sports Exerc 2006; 38: 623-7.

4. Schott HC, Hodgson DR, and Bayly WM. Haematuria, pigmenturia and protienuria in exercising horses. Eguine Veterinary Journal1995;27(1): 67-72
5. McKeever HM. Renal function during exercise. In: Henchcliff K.(ed), Equine Sport medicine and surgery, Saunders, Philalelphia); 2004: 862-865.
6. Poortmans JR. Postexercise proteinuria in humans. J Am Med Assoc 1985; 253: 236-240.
7. Poortmans JR. Evidence of increased glomerular permeability to proteins I during exercise in healthy men. Contrib Nephrol 1988; 68: 236-240.
8. Zambraski EJ, Bober MC, Goldstein JE, Lakas CS, Shepard MD. Changes in renal cortical sialic acids and colloidal iron staining associated with exercise. Med Sci Sports Exerc 1981; 13: 229-232.
9. Peake JM. Exercise-induced alterations in neutrophil degranulation and respiratory burst activity: possible mechanism of action. Exerc Immunol Rev 2002; 8: 49-100.
10. Suzuki K, Totsuka M, Nakaji S, Yamada M, Kudoh S, et al. Endurance exercise causes interaction among stress hormones, cytokines, neutrophil dynamics, and muscle damage. J Appl Physiol 1999; 86: 1360-1367.
11. Tay M, Comper WD, Vassilliou P, Glascow EF, Baker MS, Pratt L. The inhibitory action of oxygen radical scavengers on proteinuria and glomerular heparin sulphate loss in isolated perfused kidney. Biochem Int 1990; 20: 767-778.
12. Kanwar YS, Liu ZZ, Kashihara N, Wallner EL. Current status of the structural and functional basis of glomerular filtration and proteinuria. Semin Nephrol 1991;11: 390-413.
13. Sananka T, Nakano Y, Nishimura H, Shinobe M, Higuchi C, Omata M, Nihei H, Sugino N. Therapeutic effect of a newly dev eloped antioxidantive agent (OPC-15161) on experimental immune complex nephritis. Nephrol 1997; 76: 315-322.
14. Urso MI, Clarkson PM. Oxidative stress, exercise, and antioxidant supplementation. Toxicology 2003; 189: 41-54.
15. Powers SK, DeRuisseau KC, Quindry J, and Hamilton KL. Dietary antioxidants and exercise. J Sports Sci 2004; 22: 81-94.
16. Powers SK, Jt LL, Leeuwenburgh C. Exercise training-induced alterations in skeletal muscle antioxidant capacity: a brief review. Med Sci Sports Exerc 1999; 31: 987-997.
17. Halliwell B; Gutteridge JM. Free radicals in biology and medicine, New York:Oxford University Press; 1999.
18. Traber MG, and Stevens JF. Vitamin C and E: Beneficial effects from a mechanistic perspective. Free Radic Biol Med 2011; 51(5): 1000-1013.
19. Paker JE, Slater TF, and Wilson RL. Direct observation of a free radicle interaction between vitamin E and vitamin C. Nature 1979; 278: 737-738.
20. Gupta C, Gupta P and Singh B. Effect of vitamin supplementation on exercise-induced stress in trained elite Indian cyclists. Am J Biol Sci 2009; 1(2); 166-170.
21. Rokitzki L, Longemann E, Huber G, Keck E, and Keul J. Alpha-tocopherol supplementation in racing cyclists during extreme racing training. Int J Sport Nutr 1994; 4(3): 253-164.
22. Ginsberg GS, O'Toole M, Rim E, Douglas PS, Rifai N. Gender differences in exercise induced changes in athletes participating in Hawaii ironman Triathlon. Ginsburg-gender and exercise-induced lipid peroxidation. Clin Chem Acta 2001; 305(1-2):131-139.
23. Tidus PM. Estrogen and gender effects on muscle damage, inflammation and oxidative stress. Can J Appl Physiol 2000; 25(4): 274-287.
24. Mastaloudis A, Morrow JD, Hopkins DW, Devaraj S, Traber MG. Antioxidant supplementation prevents exercise-induced lipid peroxidation, but not inflammation in ultramarathon runners. Free Radic Biol Med 2004; 36(10): 1329-41.
25. Tidus PM, Bombardier E, Hidiroglou N, Madere R. Gender and exercise influence on tissue antioxidant vitamin status in rats J Nutr Sci Vitaminal(Tokyo) 1999; 45(6): 701-710.
26. Ji LL, Gomes-Cabrera MC, Vina J. Exercise and hormesis activation of cellular antioxidant signaling pathway. Ann N Y Acad Sci 2006; 1067: 425-435.
27. Chung HY, Cesari M, Anton S, Marzetti E, Giovannini S, Seo AY, Carter C, Yu BP, Leeuwenburgh C. Molecular inflammation: Underpinning of ageing and age –related diseses. Age Res Rev 2008.
28. Radak Z, Chung HY, Koltai E, Taylor AW, Goto S. Exercise, oxidative stress and hormesis. Ageing Rev Res 2008; 7(1): 34-42.

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