The effect of antioxidant vitamin supplementation on anaerobic glycolysis in men

by

Stanislaw Poprzecki[1], Adam Zajac[2], Tomasz Golab[3]
Zbigniew Waskiewicz[4]

The main objective of this research project was to evaluate the influence of antioxidant vitamin supplementation and prolonged aerobic physical exercise on anaerobic glycolysis. The research included 36 healthy students of physical education not engaged in competitive sport. The students were divided randomly into 3 groups of 12 subjects each. Group I was supplemented with daily doses of vitamin C (150 mg), vitamin E – 24 mg, ß-caroten 14,4 mg and selenium (80 µg), while group II 45 mg of Q_{10}-coenzyme and 54 mg of a-tocopherol. Control group did not use any supplements. All of the subjects performed a 1-hour continuous ergocycle effort (Monark 814E) according to the test protocol described by Jeukendrup et al. (1996). The load was constant during the entire test and equaled 60% Wmax yet the pedaling rate was increased during the last 15 min. to individual maximal possibilities. During the first 45 min the subjects pedaled at a rate of 60 rev/min, increasing it over the last 15 min on order to perform the highest possible external work. The test was conducted 3 times, before supplementation, after 3 weeks and following 6 weeks of supplementation. The results showed that increase of glycolytic activity measured by ?LA was significant in group II after 3 and 6 weeks (p£0,01) of supplementation. Statistically significant increase of work in last 15 min. of test was observed in group I after 3 and 6 weeks (p£0,01) of supplementation.
Keywords: Pasteur effect, antioxidants, anaerobic glycolysis

[1] Academy of Physcial Education, Department of Biochemistry, 40-065 Katowice, Mikolowska 72A, Poland
[2] Department of Sport Training, adamzaj@awf.katowice.pl
[3] District Specialistic Hospital, Department of Nuclear Medical Analysis, Tychy, Poland
[4] Department of Team Sports, waskie@awf.katowice.pl

Introduction

Proper functioning of a muscle cell especially during exercise is to a large degree dependent on its ability to produce ATP. This process depends mainly on the availability of energetic substrates, mainly carbohydrates and fat as well as oxygen. Resynthesis of ATP may take place aerobically, where carbohydrates and lipids are metabolized or anaerobically (glycolysis) where only carbohydrates are used (Ainscow and Brond 1999). During anaerobic metabolism, glucose is quickly converted into lactic acid (LA), while in the presence of oxygen the consumption of glucose and the production of LA are diminished. This phenomenon is called the Pasteur's effect (Bangsbo 1996; Petterson and Lundholm 1985; Storey 1985). The reversed reactions have been called the Crabtree effect.

Endurance training with the predominance of aerobic metabolism affects the human organism by stimulating the genetic expression and increased protein synthesis at the transcription level. At the same time the mRNA for glycolytic enzymes is inhibited. Thus the improvement of aerobic endurance usually hinders physical work possibilities based on anaerobic metabolism (Marsin et al. 2002, O'Rourke et al. 1996). The transition from aerobic to anaerobic metabolism and vice-versa is not fully understood and explained. It is well documented that the rate of glycolysis is controlled by activity of its key enzymes such as phosfofructokinase-1 (PFK-1), which is inhibited allosterically, mainly by high concentration of ATP, citrate and hydrogen ions. On the other hand PKF-1 activity is stimulated by AMP, APP, cAMP, fructo 2,6-di-phosphate (F2,6-DP) and pyruvate kinase, which activity is regulated by the phosphorylation and dephosphorylation of the enzyme (Bosca et al. 1985; Dobson et al. 1986; Hochachla 1988; 1998; Winkler et al. 2003). The rate of glycolysis is also stimulated by insulin which effects the activity of glycolytic enzymes and the activity of glycolytic enzymes and the activity of glucose transporters in the muscle (GLUT-4) (Hue at al. 2002). A significant advancement in the explanation of metabolism under hypoxia is the discovery of the factor stimulating transcription during hypoxia HIF-1 (hypoxia-inducible factor –1). It binds with DNA and as a heterodymer it synthesizes specific proteins that regulate glycolysis (Lordo at al. 2002; Seagroves et al. 2001).

Pilegaard et al. (2000) proved that physical exercise temporarily increases the transcription of genes responsible for skeletal muscle metabolism. They also indicate that temporary metabolic adaptations related to physical exercise accumulate, thus increasing the transcription during restitution or following

training sessions. It seems that genes activity is strictly related to the volume and intensity of performed exercise.

During prolonged physical exercise the aerobic system is most effective in producing ATP. Its effectiveness is related to the rate of oxygen delivery into the mitochondria for which the cardiovascular, pulmonary and hemopoetic systems are responsible (Bangsbo et al. 1992; Ebert and Bunn 1999). An increased oxygen uptake is usually accompanied by an increased generation of free radicals, the so-called reactive forms of oxygen (RFO) which are responsible for the oxidative stress. This created the possibility of mitochondrial DNA disruption and diminished ATP resynthesis (Lenaz et al. 2002). Under such conditions the antioxidant mechanisms are triggered in order to protect the DNA. Additionally protein complexes related to aerobic and anaerobic metabolism are activated. The human organism is equipped with a very effective antioxidant mechanism of enzymatic and nonenzymatic character. The last one, among others includes antioxidant vitamins such as: E (α-tocopherol) C (ascorbic acid) ß-caroten, coenzyme Q. They do not influence the rate of enzymatic protein synthesis directly, yet most likely they can influence the level of substrates and coenzymes or help the body eliminate substances inhibiting biochemical reactions related to free radicals or hydrogen ions (Lenaz et al. 2002).

The main objective of this research project was to evaluate the influence of antioxidant vitamin supplementation and prolonged aerobic physical exercise on anaerobic glycolysis.

Material and methods

The research included 36 healthy students of physical education not engaged in competitive sport. The students were divided randomly into 3 groups of 12 subjects each (tab. 1). All of the subjects participated only in their obligatory physical education classes which required close to 2 hours of physical exercise daily. All of the participants gave their written consent of approval after being familiarized with the objectives of research procedures. The research project was accepted by the Regional Ethics Committee for Scientific Research in Katowice.

Before the experiment began and at its termination maximal oxygen uptake [$VO_2max(ml \cdot min^{-1} \cdot kg^{-1})$] was measured in all subjects with the Astrand method on a Monark 829E ergocycle with the application of Jeukendrup et al. (1996) protocol. Maximal power (Wmax) was also evaluated on the 829E Monark

ergocycle during the test of progressive intensity according to the protocol described by Jeukendrup et al. (1996).

Table 1 Somatic and physiological characteristics of tested subjects

Variable	Group I		Group II		Group III	
	$\bar{x}$	SD	$\bar{x}$	SD	$\bar{x}$	SD
Age (years)	20,7	0,6	21,2	1,4	20,7	1,1
Body mass (kg)	75,0	6,9	76,2	7,8	70,8	5,7
Body height (cm)	178,0	6,9	181,2	7,3	175,9	7,5
VO₂max (ml·min⁻¹·kg⁻¹)	51,64	8,9	56,4	10,7	50,4	8,9
Total external work Wmax (W)	277,6	35,6	274,2	25,0	234,5	36,9

The load for the exercise protocol was set at 60% of Wmax. The subjects from groups I and II were supplemented with antioxidant vitamins for 6 weeks (tab. 2) While those from group III did not receive any supplements and were treated as the control group. During the experiment all of the subjects did not take any medications, vitamins or caffeine.

Table 2 Type and composition of supplements

Group	Supplement	Composition of daily dose
I	**Zellschutz** (Fitline, Germany)	Vitamin C – 150 mg, Vitamin E– 24 mg, β-caroten – 14,40 mg, selenium – 80 μg, carbohydrates – 36,4g
II	Emusol CoQ₁₀ Plus (Fitline, Germany)	Coenzym CoQ₁₀ – 45 mg and α-tocopherol – 54 mg
III	Control group	Did not take antioxidant supplements

All of the subjects performed a 1-hour continuous ergocycle effort (Monark 814E) according to the test protocol described by Jeukendrup et al. (1996). The load was constant during the entire test and equaled 60% Wmax yet the pedaling rate was increased during the last 15 min to individual maximal possibilities. During the first 45 min the subjects pedaled at a rate of 60 rev/min, increasing it over the last 15 min on order to perform the highest possible external work. The test was conducted 3 times, before supplementation (A), after 3 weeks (B) and following 6 weeks of supplementation (C).

During the last 15 min of the test total external work and temporary peak power were registered with the use of software MCE v-2,3 (IBA, Poland). To determine pulmonary variables several subjects from each group performed the test with the use of gasometric apparatus (Jaeger Germany), which allowed for

the evaluation of minute ventilation (V_E, lmin^{-1}). Before and immediately after each exercise protocol body mass of subjects was registered (± 0.1 kg).

During the research a questionnaire was conducted among all participants related to the diet. Based on the data from the questionnaire the biological value of the diet was calculated with the use of a computer program "Dictus BUI InFit" 1995 (Poland). Blood samples for biochemical evaluations were drawn from the ulnar vein, while blood samples taken from the fingertip at rest and after the exercise protocol were used for evaluation of lactate. The hematocrit value (Ht) was evaluated in the blood with the use of a hematocrit spinner "Seba" PZ (Poland). Plasma lactate concentration was evaluated with commercial kits (BioMerieux), creatine kinase activity (CK, EC 2.7.32) with Analco (Poland) diagnostic kits while. The concentration of malondialdehyde (MDA) was evaluated indirectly with the Buege-Aust's method (1978).

The obtained data was analyzed statistically with the use of a computer program St atistica 5.0 (Statsoft Inc. 1995). Average values ($\bar{x}$) and standard deviations were calculated (SD). Average temporary peak power during the last 15 min of test were normalized every 2 min. for mean values obtained before supplementation.

Pre a post exercise differences were calculated in the concentration of LA and MDA as well as CK activity (ΔLA, ΔMDA, ΔCK). To determine the intergroup differences in relation to independent factors, two-way analysis of variance with repeated measures (ANOVA) were used. The independent variable included the type of supplement (1-Sellschutz, 2-Emusol CoQ, 3-control), and the measurements were repeated 3 times; O(A) – initial, 3(B) – after 3 weeks and 6(C) – after 6 weeks. To determine the relationships between variables, Pearson's linear correlation coefficients were calculated. The values of variables labeled in the blood plasma before and after exercise were corrected for plasma volume (ΔPV) with the application of pre(Ht1) and post (Ht2) exercise hematocrit values according to the formula: ΔPV=(100-Ht2)/(100-Ht1) $\bar{x}$ value of variable.

The significance of results of ANOVA was corrected, considering Bonferronie's correction. The significance level was set at p<0,0167. To determine the significance of differences in relation to pre supplementation values the t-Student test for dependent variables was used while the nonparametric test of Wilcoxon's sequence pairs for ΔCK and ΔMDA were applied. To indicate the significance of differences between groups the students "t" test for independent variables and the U-Mann-Whitney test were applied. The significance level was set at p<0,05.

Results

The biological value of the students diet was similar in all tested groups, while significant differences were observed in vitamin C intake, which was very low, especially in subjects from group II (tab. 3).

Table 3 The average, daily calories value and vitamin intake of meals preceding the exercise protocol

Variable	Group I	Group II	Group III
	$\overline{x}$	$\overline{x}$	$\overline{x}$
Energy intake (kcal)	3856,7	3539,6	3746,0
Vitamin A[1] (µg)	844,6 (+2500)[1]	728,1	710,9
Vitamin C (mg)	59,7 (+150)	49,1	86,5
Vitamin E (mg)	8,4 (+24)	7,7 (+54)	8,5
% Protein	11	12	12
% Fat	27	31	29
% Carbohydrate	62	57	59

[1] equivalents of retinol

[2] in parenthesis – additional amount of supplemented vitamin

The average daily caloric value and vitamin intake of meals preceding the exercise protocol.

During the 1-hour endurance exercise protocol a differentiated minute ventilation (VE) was observed. At rest it equaled $11,24 \pm 1,36$ l·min^{-1} and rose until the 10th min of exercise until reaching $55,49 \pm 6,58$ l·min^{-1}. After the 10th min of exercise VE stabilized at 58 l·min^{-1} until the 45t[h] min of the test.
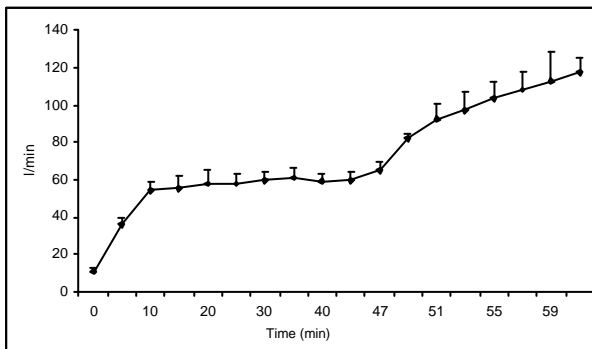

Fig. 1 Changes in pulmonary ventilation (VE) during the 1 h exercise protocol

This part of exercise was performed at intensity below the anaerobic threshold (AT) (aerobic metabolism). During the last 15 min of the test VE increased up to $117,53 \pm 7,74$ $l \cdot min^{-1}$. At this point the intensity of exercise was above the AT and ATP resynthesis occurred at first from both aerobic and anaerobic pathways while during the end of the exercise protocol anaerobic glycolysis was dominant (fig. 1).

During the 1-hour exercise protocol, body mass of all tested subjects decreased by 0,67 kg before supplementation and by 0,62 kg after 3 weeks of supplementation. It can be assumed that such insignificant dehydration (below 1% BM) did not effect physical work capacity.

Average relative power (ARP) obtained in the last 15 min of the test reached 2-2,5 $W \cdot kg^{-1}$ of body weight during the last minute of the test when the exercise was performed with maximal intensity ARP increased significantly in all groups up to 4 $W \cdot kg^{-1}$ b.w. (fig. 2-4). The average values of relative temporary peak power obtained during the last 15 min of the test after 3(B) and 6(C) weeks of supplementation, normalized for values registered before supplementation indicate that in group I the exercise was performed with higher values of relative temporary peak power, both after 3 and 6 weeks of supplementation during initial stages of the effort and with lower values of ARP at the end of the protocol in comparison to initial values (fig. 2).
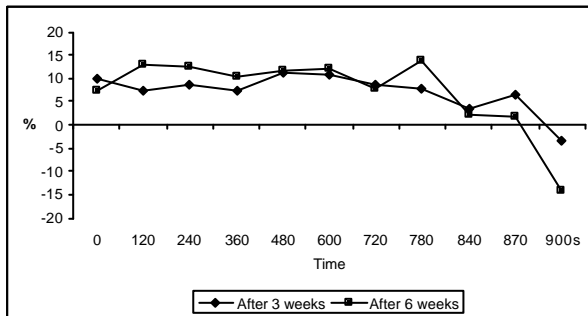

Fig. 2 Percent changes in relative temporary peak power during the last 15 min. of the 1 h test after 3 and 6 weeks of research, normalized for values of ARP obtained at initial measurement in group I.

In group II (fig. 3) the subjects increased the exercise intensity after 6 weeks of supplementation with CoQ and vitamin E compared to initial values. No changes were observed in relative temporary peak power during the last 15 min

of the test in the control group and a decrease of ARP after 3 and 6 weeks was registered in the final stage of the test.
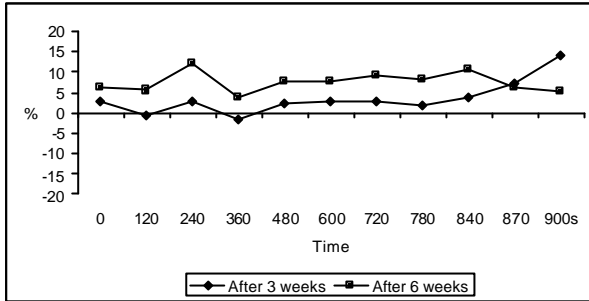

Fig. 3 Percent changes in relative temporary peak power during the last 15 min. of the 1 h test after 3 and 6 weeks of research, normalized for values of ARP obtained before supplementation in group II**.**

Fig. 4 Percent changes in relative temporary peak power during the last 15 min. of the 1 h test after 3 and 6 weeks of research, normalized for values of ARP obtained before supplementation in group III**.**
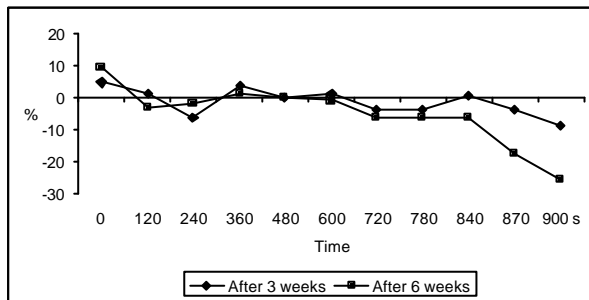
After 3 weeks of research a significant increase in total relative external work obtained in the last 15 min of the exercise protocol was observed only in group I (p<0,001). After 6 weeks of supplementation a significant increase in this variable was observed in all tested group in comparison to initial values (group I p<0,05 group II p<0,05 and group III p<0,01).

Two factor analysis of variance (ANOVA) with repeated measures for the variable, total external work, showed a significant influence of time on results (F=15,55, p=0,0000003). On the other hand, supplementation did not effect the results significantly and no interaction between the two factors was observed.

The greatest increase in total external work (p<0,01) was registered in group I after 3 weeks of supplementation (tab. 4). The results of ANOVA for post exercise changes in lactate concentration during 3 phases of evaluation also showed a significant influence of time of measurements on results (F=7,98, p=0,00078) and no effect of supplementation. No interaction between factors was observed. Statistically significant changes in post exercise LA increment were registered only in group II after 3 weeks (p<0,01) and 6 weeks (p<0,01) of supplementation with CoQ and vitamin E (tab. 4). No significant relationship was observed between total external work performed and the post exercise lactate concentration (ΔLA). The results of ANOVA did not show an effect of supplementation or time of evaluation on post exercise values of CK (ΔCK). After 3 weeks of supplementation a tendency for decreased CK activity was observed in groups I and II (tab. 5).

Table 4 Total external work during the last 15 min. Of the 1h exercise protocol and the differences in post exercise lactate concentration (Δ LA), during initial measurement (A) after 3 (B) and after 6 weeks of supplementation (C), in group I, II and III

Group		Relative external work (J·kg^{-1}m.c.)			Δ LA (mmol/l)		
		A	B	C	A	B	C
I	$\bar{x}$	2128,7	2326,2**#	2353,4*	5,8	6,5	6,2
	SD	335,8	348,1	346,8	1,7	1,4	1,0
II	$\bar{x}$	2039,0	2105,0	2191,1*	5,0	6,7**	6,8**
	SD	286,1	283,9	345,3	1,4	0,6	0,7
III	$\bar{x}$	2001,6	2052,0	2125,3**	6,3	6,7	6,8
	SD	269,6	261,1	248,8	0,8	0,8	0,8

* differences before and after supplementation statistically significant at p≤0,05
** differences before and after supplementation statistically significant at p≤0,01
\# differences before and after supplementation statistically significant at p≤0,01

The results of ANOVA were similar for changes in malonedialdehyde (ΔMDA), were neither supplementation nor time of evaluation effected the results significantly. After 3 weeks of supplementation a slight increase in the level of this metabolite was observed in groups I and II (tab. 5).

Table 5 Post-exercise changes in creatine kinase activity (ΔCK) and malondialdehyde (ΔMDA) in groups I, II and III, before (A), after 3 (B) and after 6 weeks of supplementation (C)

Group		ΔCK (U/l)			ΔMDA (µmol/l)		
		A	B	C	A	B	C
I	$\overline{x}$	20,6	14,2	7,58	0,86	0,93	0,67
	SD	21,5	21,9	11,5	0,58	1,07	0,31
II	$\overline{x}$	36,5	14,9	27,1	0,47	0,68	0,54
	SD	60,8	14,9	28,9	0,80	0,44	0,73
III	$\overline{x}$	20,9	21,7	14,1	0,54	0,51	0,56
	SD	18,2	11,7	19,6	0,56	0,48	0,49

Discussion

Oxidation and reduction consist the basis of energy metabolism in which electrons travel from a donor to a acceptor. The energy produced during these reactions is proportional to changes in electron donor affinity to recipient. The most efficient energy production includes the aerobic metabolism in which molecular oxygen serves as the acceptor of electrons. During this reaction energy is stored in the form of ATP (Lenaz et al. 2002). About 1-4% of oxygen is reduced to superoxide anion radical (O_2^-) and further to a very reactive hydroxylic radical (OH).

During intensive physical exercise free radicals are generated to the point of development of oxidant stress.

Free radicals damage biological membranes through peroxidation of fatty acids, mitochondrial as well as nucleous DNA, thus decreasing the efficiency of the organism. The human organism is equipped with a antioxidant mechanism, which consists of a enzymatic and non-enzymatic system. The last one includes antioxidant vitamins (vitamins C, E, B-caroten, Coenzyme Q_{10}). They do not influence the production of energy directly, yet indirectly they may increase the rate of biochemical reactions through the increase of enzyme activity or the removal of inhibitors of this activity (Sen 1995). Besides the aerobic pathway of producing energy the human organism and especially skeletal muscles can generate ATP under hypoxic conditions. During fermentation organic compounds may act as donors and acceptors of electrons. The efficiency of such a metabolic pathway is much lower than that of oxidative phosphorylation (Hochachka 1998). When muscles are deficient in oxygen, pyruvate is converted to lactate, and the rate of this process is related to the amount of glucose

metabolized under hypoxic conditions. Prolonged exercise under such conditions causes muscular acidosis, which slows down the rate of biochemical reactions (Bangsbo et al. 1992; Dobson et al. 1986; Freund et al. 1991). Living organisms have developed the possibility to produce energy through utilization of oxygen and through fermentation. Skeletal muscles use both of these processes. A regulatory mechanism has evolved which allows the conversion from aerobic to anaerobic metabolism and vice versa. Most likely the basis for this regulatory mechanism lies in the genetic expression and biosynthesis of enzymatic proteins significant to glycolysis. It seems that oxygen is an important regulator of genetic expression in mammals and may indirectly influence chemical reactions of different metabolic pathways. Recently a regulator of transcription released under hypoxia has been described (HIF-1 – hypoxia-inducible factor –1), which combines with DNA creating a heterodymer responsible for the production of erythropoetin a transporter of glucose (GLUT-1), phosphofructokinase-L, aldolase-A, phosphoglicerin kinase-1 (PGK-1) lactate dehydrogenase-A (LDH-A), adenylate kinase (Lando et al. 2003; Pilegaard et al. 2000; Seagroves et al. 2001).

The regulation of energy production (ATP) from aerobic to anaerobic pathways is a significant phenomenon is sport and physical exercise. In sport short physical efforts of maximal intensity are performed as well as prolonged ones of low intensity. In many cases prolonged efforts performed at low intensity are finished of by several minutes of intensive effort, which relies on the anaerobic system to produce ATP. All performances are preceded by a specific warm-up, which stimulates particular metabolic pathways. It can be stated that proper functioning of a particular metabolic pathway effects sport results while antioxidant vitamin supplementation can indirectly influence those processes.

During this experiment the intensity of anaerobic glycolysis was evaluated directly by post exercise lactate concentration during the last 15 minutes of the 1 h test. Indirectly it was evaluated on the basis of total external work performed in that period of time. Minute ventilation registered during the test indicated a significant rise during the last 15 min. The dietary habits of all tested subjects were similar. The greatest differences occurred in the intake of vitamin C, which were far from recommended allowances (Ziemlanski 1998).

Average temporary peak power values registered after 3 and 6 weeks of the experiment differed significantly between the tested groups. The greatest increase in temporary peak power in relation to initial values occurred in group I after 3 and 6 weeks of supplementation, yet this variable decreased during the last 30 s after 6 weeks of supplementation. Very intensive pedaling during the

first part of the 15 min anaerobic exercise protocol most likely caused this effect. In group II increases in temporary peak power were observed only after 6 week of supplementation and did not change in the final stages of the test. No changes were observed in temporary peak power in the control group throughout the experiment.

After 3 and 6 weeks of supplementation with antioxidant vitamins (group I) a significant increase in total external work was registered during the last 15 min of the test (p<0,01 and p<0,05), which was accompanied by slight increase in glycolytic activity measured by post exercise lactate concentration (ΔLA). The increment in total external work after 3 weeks of supplementation was significantly different from the control group (p<0,05). In group II, supplemented with vitamin E and CoQ a significant increase in this variable occurred after 6 weeks (p<0,05). A significant rise in glycolytic activity was observed in this group both, after 3 (p<0,01) and 6 weeks of supplementation (p<0,01). In the control group a significant increase in total external work was observed after 6 weeks of research yet no changes in glycolytic activity were observed. Correlation coefficients calculated between lactate concentration and total external work did not show significant relationships. It seems that the amount of external work performed during the last 15 min of the test were influenced by other factors such as motivation or experience. This was supported by the results of two way ANOVA with repeated measurements which indicated that supplementation did not influence total external work yet time of measurements did (p<0,0001 and p<0,001). Most likely the rising intensity of exercise during the last 15 min of the test allowed for the transition from aerobic to anaerobic metabolism without disturbing the homeostasis of the organism (steady state).

It seems that glycolysis was not inhibited by earlier aerobic physical work, thus the Pasteur effect was not observed (Bangsbo 1996; D'Aurelio at al. 2001). Antioxidant supplements most likely support this process indirectly since no changes in post exercise concentration of malonedialdehyde (ΔMDA) (marker of lipid peroxidation) and creatine kinase (ΔCK) a marker of muscle cell disruption. The results of ANOVA for ΔCK and ΔMDA also did not indicate a significant effect of supplementation and time of measurements.

In conclusion it must be stated that the results of this research do not support the hypothesis indicating the inhibition of anaerobic metabolism by preceding exercise of aerobic nature (Pasteur's effect). Supplementation with antioxidants over a prolonged period of time should cause a shift towards aerobic metabolism, thus decreasing post exercise lactate concentration. This was not supported fully by results of this study. In groups supplemented with

antioxidant vitamins and selenium as well as in the group receiving coenzyme Q_{10} with vitamin E a symptom of increased post exercise lactate concentration was observed. This was caused most likely by stimulation of glycolysis. The increase in the amount of work performed under mixed and anaerobic conditions was highest in the supplemented groups after 6 week of the experiment. It thus seems logical to recommend antioxidant supplementation to athletes for periods of 6 weeks.

References

Ainscow E.K., Brand M.D. 1999. Top-town control analysis of ATP turnover, glycolysis and oxidative phosphorylation in rat hepatocytes. Eur. J. Biochem. 263(3):671-679.

Bangsbo J. 1996. Regulation of muscle glycogenolysis and glycolysis during intense exercise: In vivo studies using repeated intense exercise. In Biochemistry of Exercise. (Eds R.J. Maughan, S.M. Shirreffs) Human Kinetics pp. 261-275.

Bangsbo J., Graham T.E., Johansen L., Strange S., Christensen C., Saltin B. 1992. Elevated muscle acidity and energy production during exhaustive exercise in man. Am. J. Physiol. 263:R891-R899.

Bosca L., Aragon J.J., Sols A. 1985. Modulation of phosphofructokinase at physiological concentration of enzyme. J. Biol. Chem. 260: 2100-2107.

Buege J.A., Aust S.D. 1978. Microsomal lipid peroxidation. In Methods in Enzymol.. Eds. S.Fleisher, L.Packer, Academic Press, New York 52:302-310.

D'Aurelio M., Pich M.M., Catani L., Sgarbi G.L., Bovina C., Formiggini F., Castelli G.P., Baum H., Tura S., Lenaz G. 2001. Decreased Pasteur effect in platelets of aged individuals. Mech. Ageing Dev. 122(8):823-833.

Dobson G.P., Yamamoto E., Hochachka P.W. 1986. Phosphofructokinase control in muscle; Nature and reversal of pH-dependent ATP inhibition. Am. J. Physiol. 250: R71-R76.

Ebert B.L., Bunn H.F. 1999. Regulation of the erythropoietin gene. Blood 94(6):1864-1877.

Freund H., Oyono-Enguelle S. 1991. The effect of supramaximal exercise on the recovery kinetics of lactate. 39(2):65-76.

Hochachka P.W. 1988. Patterns of O_2-dependence of metabolism. Adv. Exp. Biol. 222:143-151.

Hochachka P.W. 1998. Mechanism and evolution of hypoxia-tolerance in humans. J. Exp. Biol. 201 (Pt 8):1243-1254.

Hue L., Beauloye C., Marsin A.S., Bertrand L., Horman S., Rider M.H. 2002. Insulin and ischemia stimulate glycolysis by acting on the same targets trough different and opposing signaling pathways. J. Mol. Cell Cardiol. 34(9):1091-1097.

Jeukendrup A., Saris W.H.M., Brouns F., Kester A.D.M. 1996. A new validated endurance performance test. Med. Sci. Sports Exerc. 28(2):266-270.

Lando D. Gorman J.J., Whitelaw M.L., Peet D.J. 2003. Oxygen-dependent regulation of hypoxiainducible factors by prolyl and asparaginyl hydroxylation. Eur. J. Biochem. 270:781-790.

Lenaz G., Bovina C., D'Aurelio M., Fato R., Formiggi G., Genova M.L., Giuliano G., Pich M.M., Paolucci U., Castelli G.P., Ventura B. 2002. Role of mitochondria in oxidative stress and ageing. Ann. NY Acad. Sci. 959 pp. 199-213.

Marsin A.S., Bouzin C., Bertrand L., Hue L. 2002. The stimulation of glycolysis by hypoxia in activated monocytes is mediated by AMP-activated protein kinase and inducible 6-phosphofructo-2-kinase. J. Biol. Chem. 277(34):30778-30783.

O'Rourke J.F., Pugh C.W., Bartlett S.M., Ratcliffe P.J. 1996. Identification of hypoxically inducible mRNA in HeLa cells using differential-display PCR. Role of hypoxia - inducible factor-1. Eur. J. Biochem. 241:403-410.

Pettersson G., Lundholm L. 1985. Pasteur effect in vascular and intestinal smooth muscle. Artery 12(5):312-323.

Pilegaard H., Ordway G.A., Saltin B., Neufer P.D. 2000. Transcriptional regulation of gene expression in human skeletal muscle during recovery from exercise. Am. J. Physiol. Endocrinol. Metab. 279(4):E806-E814.

Seagroves T.N., Ryan H.E., Lu H., Wouters B.G. Knapp M., Thibault P., Laderoute K., Johnson R.S. 2001. Transcription factor HIF-1 a necessary mediator of the Pasteur effect in mammalian cells. Mol. Cell Biol. 21(10):3436-3444.

Sen C.K. 1995. Oxidants and antioxidants in exercise. J. Apl. Physiol. 79(3):675-686.

Storey K.B. 1985. A re-evaluation of the Pasteur effect: New mechanism in anaerobic metabolism. Mol. Physiol. 8:439-461.

Winkler B.S., Sauer M.W., Starnes C.A. 2003. Modulation of the Pasteur effect in retinal cells: implication for understanding compensatory metabolic mechanism. Exp. Eye Res 76(6):715-723.

Ziemlanski S. 1998. Podstawy prawidlowego zywienia czlowieka. IZiZ Warszawa.