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Q10 coenzyme supplementation effect on heart weight in dysmetabolism and exercise (Note I)
Efectul suplimentării de CoQ10 asupra greutăţii inimii în condiţii de dismetabolism şi efort fizic (Nota I)

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Abstract

Background. The paradoxical effect of exercise as a pro-oxidant at high intensities over short durations and as an antioxidant at moderate intensities over prolonged periods, as well as the influence of nutritional or non-nutritional antioxidant administration on the oxidant-antioxidant balance under exercise conditions are now known.

Aims. The beneficial effect of coenzyme Q10 (CoQ10) as a non-nutritional antioxidant on exercise capacity, its role in weight normalization and cardiovascular protection led us to study experimentally the effect of CoQ10 supplementation on body and heart weight in animals trained to exercise that were given a high calorie diet to achieve dysmetabolic syndrome.

Methods. The experiment was conducted on 12 groups (n = 10 animals/group) of adult male Wistar rats, with three types of food: four groups received a standard diet, four groups were fed a high-carbohydrate diet, four groups a high-fat diet; 6 groups were supplemented with CoQ10. 6 groups were subjected to daily physical exercise (by the swimming test) for 28 days, 60 minutes a day, the other 6 groups being sedentary. At the end of the experiment, the animals were sacrificed, and the body and heart weight was measured. Statistical analysis was performed using SPSS 20 and Excel 2010.

Results. The average daily weight gain was lower in the exercise trained groups, significantly in the groups supplemented with CoQ10. The relative weight of the heart was lower in the groups supplemented with CoQ10.

Conclusions. A normal calorie diet with additional CoQ10 limits weight gain in both sedentary and trained animals. A high calorie diet supplemented with CoQ10 leads to lower weight gain and limits cardiac hypertrophy both in trained and sedentary animals.

Keywords: exercise, dysmetabolism, weight, heart.

Rezumat

Premize. În prezent este binecunoscut efectul paradoxal al efortului fizic-prooxidant la intensităţi mari şi durată scurtă şi antioxidant la intensităţi moderate şi durată prelungită şi influenţa administrării unor antioxidanţi nutriţionali sau nenutriţionali asupra balanţei oxidanţi-antioxidanţi în condiţii de efort.

Obiective. Rolul benefic al coenzimei Q10 (CoQ10), ca antioxidant nenutriţional asupra capacităţii de efort, în normalizarea nivelului ponderal şi în prevenirea şi protecţia cardiovasculară, ne-a determinat să studiem experimental efectul suplimentării de CoQ10 asupra greutăţii organismului şi inimii la animale antrenate la efort, la care s-a administrat o dietă hipercalorică pentru obţinerea sindromului dismetabolic.

Metode. Experimentul s-a desfăşurat pe 12 loturi (n=10 animale/lot) şobolani rasa Wistar masculi adulţi, cu trei tipuri de alimentaţie: patru loturi cu alimentaţie standard, patru loturi cu alimentaţie hiperglucidică, patru loturi cu alimentaţie hiperlipidică; 6 loturi au fost suplimentate cu CoQ10. 6 loturi au fost supuse efortului fizic zilnic (prin proba de înot) timp de 28 zile, 60 minute pe zi, celelelte 6 loturi fiind sedentare. La sfârşitul experimentului, animalele au fost sacrificate, s-au măsurat greutatea corporală şi greutatea inimii. Analiza statistică a fost făcută utilizând programele SPSS 20 şi Excel 2010.

Rezultate. Câştigul ponderal mediu zilnic a fost mai redus la loturile antrenate, semnificativ la loturile suplimentate cu CoQ10. Greutatea relativă a inimii a fost mai scăzută la loturile suplimentate cu CoQ10.

Concluzii. O dieta normocalorică cu suplimentare de CoQ10 determină limitarea câştigului ponderal, atât la animalele sedentare, cât şi antrenate. O dietă hipercalorică şi suplimentare de CoQ10 duce la limitarea câştigului ponderal şi la limitarea hipertrofiei cardiace la animalele sedentare şi antrenate.

Cuvinte cheie: efort fizic, dismetabolism, greutate, inimă.

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Introduction

The paradoxical effect of exercise as a pro-oxidant at high intensities over short exercise and as an antioxidant at moderate intensities over long periods, as well as the influence of nutritional or non-nutritional antioxidant administration on the oxidant-antioxidant balance in effort are now known.

Macroscopic changes are often the starting point for some conclusions, but accompanied by histopathological studies they can lead to complex results of body responses. Anthropometry (weight, volume, length) was among the first studied, as access to these values was relatively easy, even before the development of laboratory medicine. Value standardization was a priority for research on human subjects as well as on animals. Simple experimental model studies have been conducted since the 19th century, with the focus of research on different food types (e.g. Mediterranean diet). Supplementation of certain specific items (carbohydrates, food subgroups) was used in simple standard diets, and body weight variations were observed (Palmisciano et al., 2015). Difficulties were encountered when classifying risk factors for some diseases; statistical research was limited and very few studies on large groups were available. The body mass index is still studied due to the increased prevalence of obesity, and obesity animal models induced genetically, by streptozotocin, etc. are used to study diabetes, obesity, in an attempt to find a predictive factor in adulthood (Leibowitz et al., 2007).

CoQ10 is a fat-soluble benzoquinone, involved in all cell breathing, especially in mitochondria, supporting energy generation by the production of ATP in mitochondria (Crane et al., 1989; Mataix J et al., 1997). It is stored in the heart, kidney, liver; the most important quantities in the animal kingdom are found in cattle (Aberg et al., 1992). Absorption takes place in the small intestine within maximum 4 hours postprandially (Bhagavan et al., 2006). There are researchers who maintain its indispensability in the human body, and the absence of CoQ10 can result in cell apoptosis or death of the whole body by blockage of the mitochondrial respiratory chain (Folkers et al., 1991). It is involved in the regeneration of other antioxidants (vitamin E) (Comes, 2001), cardiovascular protection (local anti-inflammatory effect, reduction of LDL-cholesterol, anti-atherogenic role, atherosclerotic plaque stabilization, ischemia-reperfusion injury prevention by maintaining ATP supplies, post-infarction ventricular dysfunction prevention) (Singh et al., 2003), thyroid hormone regulation (Mancini et al., 2005), increase of immunity (Bliynakov & Hunt, 1998; Lieberman & Bruning, 2005), mitochondrial membrane stabilization (Ciocoi-Pop & Tache, 2007).

Hypothesis

While the effects of CoQ10 supplementation on body weight and on exercise capacity are known, its myocardial protective effect, in reducing cardiac hypertrophy induced by exercise, particularly in metabolic syndrome, is not well known.

Objectives

The beneficial influence of CoQ10 as a non-nutritional antioxidant on exercise capacity, weight normalization, cardiovascular prevention and protection led us to study experimentally the effect of CoQ10 supplementation on body and heart weight in exercise trained animals receiving a high-calorie diet to induce metabolic syndrome.

Materials and methods

The study was approved by the Bioethics Committee of the University of Medicine and Pharmacy Cluj-Napoca No 401/5.10.2011. The research was conducted on 120 adult Wistar rats from the biobase of UMPh Cluj-Napoca. The animals were acclimated one week prior to the experiment to adequate vivarium conditions.

Research protocol

a) Period and place of the research

The experiment lasted for 28 days, during October-November 2012, and was carried out in the experimental laboratory of the Department of Physiology of UMPh Cluj-Napoca.

b) Subjects and groups

The following groups were included in the study:

Group I - control, standard diet, sedentary;

Group II - control, standard diet, exercise trained;

Group III - high-carbohydrate diet, sedentary;

Group IV - high-carbohydrate diet, exercise trained;

Group V - high-fat diet, sedentary;

Group VI - high-fat diet, exercise trained.

Group VII - control, standard diet, CoQ10 gavage, sedentary;

Group VIII - control, standard diet, CoQ10 gavage, exercise trained;

Group IX - high-carbohydrate diet, CoQ10 gavage, sedentary;

Group X - high-carbohydrate diet, CoQ10 gavage, exercise trained;

Group XI - high-fat diet, CoQ10 gavage, sedentary;

Group XII - high-fat diet, CoQ10 gavage, exercise trained.

At the end, all animals were euthanized and the heart was harvested according to goRENI standards (1).

The animals received three types of diet: standard diet (20 g/day/rat granulated fodder, Cantacuzino Institute, Bucharest, oropharyngeal gavage of 2 ml saline to simulate the stress of gavage), high-carbohydrate diet (standard diet + oropharyngeal gavage of 2 ml glucose syrup 75%) or high-fat diet (standard diet + gavage of 2 ml pork lard). The animals received water ad libitum. CoQ10 supplementation was done by oropharyngeal gavage of pure CoQ10 in suspension, delivered by Alevia Romania, at a dose of 100 mg/kg body weight.

c) Applied tests

The aerobic capacity was determined based on 60 minutes swimming in a pool with an open area larger than 1000 cm^2, 40 cm water depth, to avoid interference of the animals with each other (Kregel, 2006).

The measured indicators were: absolute animal weight expressed in grams at the beginning (T0) and at the end of the experiment (T28), using a Kern Germany KB650-2NM electronic balance, relative heart weight in grams/100 g body weight using an electronic laboratory scale to 2 decimal places (MH-Series Pocket Scale/MH-100 100 g/0.01g).

d) Statistical processing

Statistical data analysis was performed using the SPSS.20 and Excel 2010 tools. Parametric tests were used for groups which were supposed to have a normal distribution, and those with a non-normal distribution were taken into account with their logarithmic values. Student t test, ANOVA, Pearson correlation coefficient were calculated.

Results

a) Average daily weight gain variation

We can see in Table I that both CoQ10 administration and physical exercise led to a decrease in daily weight gain compared to groups that did not receive CoQ10 and sedentary groups, respectively. Statistical tests (Student t) confirmed the statistical significance of this finding, p values being well below the 0.05 value considered statistically significant. The groups considered were the CoQ10 supplementation groups (VII-XII) compared to all groups without CoQ10 supplementation (I-VI), and the exercise trained groups (II, IV, VI, VIII, X, XII) compared to sedentary groups (I, III, V, VII, IX, XI). The greatest weight gain was obtained for sedentary groups and among them, those that had a high-calorie, high-fat diet, without being supplemented with CoQ10 (2.27 ± 0.87 g/day). Opposed to these were the animals in groups that were exercise trained or supplemented with CoQ10. The lowest weight gain was obtained in group VIII (exercise, standard diet with CoQ10 supplementation), 0.79 ± 0.29 g/day.

Table II shows that exercise lowers daily weight gain, CoQ10 also leads to its limitation, while a diet rich in calories leads to a higher average daily weight gain. The groups supplemented with CoQ10 had a lower weight gain than unsupplemented groups in all types of diet. The lowest values were obtained for the trained and CoQ10 supplemented groups.

In the standard diet, physical exercise groups (group II) had limited weight gain compared with sedentary groups (group I) (1.65 ± 0.31 g/day vs 1.25 ± 0.38 g/day). The administration of CoQ10 without exercise resulted in a more significant reduction (1.01 ± 0.16 g/day). In trained and CoQ10 supplemented groups, the decline was most significant (0.79 ± 0.29 g/day). Exercise in CoQ10 supplemented groups resulted in a borderline significant decrease (p = 0.054) (1.01 ± 0.16 vs 0.79 ± 0.29 g/day). The effect of CoQ10 supplementation is thus shown to limit weight gain and consequently to combat obesity. Exercise is effective only in the absence of CoQ10 supplementation, its effect being reduced by CoQ10 supplementation.

In the high-carbohydrate diet, the benefits are significant both for physical training (group IV) and CoQ10 supplementation (group IX).The effect is substantially the same in the sedentary groups (2.03 ± 0.27 to 1.32 ± 0.4 g/day in exercise training vs a decrease of 1.34 ± 0.17 g/day in the case of CoQ10 supplementation). CoQ10 administration in the trained group did not result in a significant decrease (1.32 ± 0.4 g/day to 1.02 ± 0.22 g/day, p = 0.055). Exercise training in the groups supplemented with CoQ10 had, however, an additional effect of decreasing weight gain (1.34 ± 0.17 vs 1.02 ± 0.22 g/day, p = 0.003).

In the high-fat diet, both CoQ10 supplementation and physical training led to a limitation of daily weight gain (2.27 ± 0.87 g/day in the sedentary group vs 1.57 ± 0.53 g/day in the trained group vs 1 47 ± 0.24 g/day in the CoQ10 supplemented group). Both CoQ10 administration in the trained group and exercise in the supplemented group, although leading to a greater reduction (up to 1.33± 0.13 g/day), were insignificant.

b) Relative heart weight

CoQ10 administration led to a relative weight loss both in sedentary and trained groups. The effect was more expressed in the latter.

Relative heart weight (Tables III, IV) changed both in the case of CoQ10 administration and physical exercise. There was an increase of 11.45% (p <0.001) for exercise, while CoQ10 supplementation led to a 6.05% decrease, p = 0.003.

Table I

Comparison of average daily weight gain (in grams) by CoQ10 supplementation or physical activity.

Group A	Group B	Group A		Group B		Student t test
		Average	Standard deviation	Average	Standard deviation	
Without CoQ10	With CoQ10	1.689286	0.608665	1.166071	0.31327	<0.001
Sedentary	Trained	1.633929	0.585356	1.221429	0.42266	<0.001

Table II

Comparison of average daily weight gain (in grams) by diet, physical activity and CoQ10 supplementation.

Group A	Group B	Group A		Group B		Student t test
		Average	Standard deviation	Average	Standard deviation	
I	II	1.6536	0.31857	1.2571	0.38568	0.022
I	VII	1.6536	0.31857	1.0179	0.16603	<0.001
II	VIII	1.2571	0.38568	0.7964	0.29693	0.008
VII	VIII	1.0179	0.16603	0.7964	0.29693	0.054
III	IV	2.0393	0.27585	1.3286	0.40329	<0.001
III	IX	2.0393	0.27585	1.3393	0.17107	<0.001
IV	X	1.3286	0.40329	1.0286	0.22449	0.055
IX	X	1.3393	0.17107	1.0286	0.22449	0.003
V	VI	2.2786	0.87268	1.5786	0.53764	0.045
V	XI	2.2786	0.87268	1.475	0.24342	0.012
VI	XII	1.5786	0.53764	1.3393	0.13703	0.189
XI	XII	1.475	0.24342	1.3393	0.13703	0.142

Table III

Comparing relative heart weight (in grams/100 g body weight) based on CoQ10 supplementation or physical activity.

Group A	Group B	Group A Average	Group A Standard deviation	Group B Average	Group B Standard deviation	Student t test
Without CoQ10	With CoQ10	3.998329	0.394618	3.756755	0.466536	0.003
Sedentary	Trained	3.667623	0.347595	4.087461	0.438867	<0.001

Table IV

Comparison of relative heart weight (in grams/100 g body weight) depending on diet, physical exercise and CoQ10 supplementation.

Group A	Group B	Group A Average	Group A Standard deviation	Group B Average	Group B Standard deviation	Student t test
I	II	3.560629	0.172831	4.123771	0.268202	<0.001
I	VII	3.560629	0.172831	3.530799	0.577955	0.877
II	VIII	4.123771	0.268202	3.763843	0.731065	0.161
VII	VIII	3.530799	0.577955	3.763843	0.731065	0.439
III	IV	3.804417	0.137946	4.457563	0.312734	<0.001
III	IX	3.804417	0.137946	3.628009	0.316295	0.123
IV	X	4.457563	0.312734	3.890994	0.229686	<0.001
IX	X	3.628009	0.316295	3.890994	0.229686	0.047
V	VI	3.769030	0.303013	4.274563	0.246447	0.001
V	XI	3.769030	0.303013	3.712854	0.384071	0.721
VI	XII	4.274563	0.246447	4.014034	0.295205	0.046
XI	XII	3.712854	0.384071	4.014034	0.295205	0.065

In the standard diet, physical exercise led to a significant heart hypertrophy (a growth of 15.8%, $p < 0.001$). Exercise training and CoQ10 supplementation caused a lower growth, thus limiting the exercise-induced myocardial hypertrophy (a growth of 6.6%, $p = 0.439$). Also, CoQ10 supplementation in the exercise trained groups led to a decrease in the relative weight of the heart (a decrease of 8.7%, $p = 0.161$), but with no statistical impact.

In the high-carbohydrate diet, myocardial hypertrophy was important in the exercise trained group without CoQ10 supplementation (an increase of 17.16%, $p \ll 0.001$). Exercise induced hypertrophy in CoQ10 supplementation (group VIII), although statistically significant ($p = 0.047$), was less important than in the groups without CoQ10 supplementation (7.22%) (group IV). Antioxidant administration limits such exercise-induced myocardial hypertrophy.

In the high-fat diet, physical exercise induced myocardial hypertrophy (growth of 13.39%, $p < 0.001$) (group VI). CoQ10 supplementation (group XII) led to statistically insignificant hypertrophy (a growth of 8.1%, $p = 0.065$). CoQ10 supplementation in the exercise trained groups led to a decrease of 6.08% ($p = 0.046$) in relative heart weight.

Discussions

Average daily weight gain

ORAC (Oxygen Radical Absorbance Capacity) scale is a scale used alongside Trolox equivalents to measure the antioxidant capacity of biological elements (especially food). On that scale, the hypothesis has been discussed that a diet with a high ORAC (30,000 units) along with physical exercise may be beneficial in the management of obesity. Obesity is correlated with oxidative stress, which depends on general inflammation and atherosclerosis, high levels of TNF and IL-6 being found in obese patients (Higdon & Frei, 2003). Antioxidant supplementation, by lowering the antioxidant and inflammatory level, can improve intracellular mitochondrial energy use, speeding up metabolism. Weight reduction is also accompanied by a decrease of pro-inflammatory status (Ziccardi et al., 2002). The result supports the idea that a healthy diet is essential in maintaining optimum weight.

Relative heart weight

Myocardial hypertrophy is recognized as a result of physical training. Concentric left ventricular hypertrophy is a necessary consequence of increased cardiac output and increased afterload due to the contraction of skeletal muscles. Influencing this by various factors is an important study direction in sports medicine (Takemoto et al., 2001) (Choudhary et al., 2006), as this can spiral out of control in endurance athletes (obstructive hypertrophic cardiomyopathy, dilated cardiomyopathy, ischemic heart disease). Improving ventricular hypertrophy may be related to improving the local energy chain, with increased contractile force for the same myocardial perfusion, with increased exercise capacity. Some studies have shown that the combination of antioxidants with a high calorie diet is beneficial in reducing hypertrophy and slowing the development of heart failure (Chess et al., 2008). Exercise may influence the oxidant-antioxidant balance locally, by activating proteins that regulate gene transcription involved in encoding antioxidant activity (Muthusamy et al., 2012). It can be seen that CoQ10 supplementation has a favorable effect on exercise capacity, weight normalization and prevention of adverse effects of exercise on the heart.

Conclusions

1. CoQ10 supplementation leads to a decrease in average daily weight gain in both sedentary and exercise trained animals subjected to a normal calorie diet.
2. In sedentary animals with a high calorie diet, CoQ10 supplementation leads to the limitation of average daily weight gain.
3. In trained animals, a high calorie diet with CoQ10 supplementation reduces heart weight.

Conflicts of interest

There are no conflicts of interest.

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