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Q10 coenzyme supplementation effect on relative liver weight and density in dysmetabolism and exercise (Note II)
Efectul suplimentării de coenzimă Q10 asupra greutăţii ficatului în condiţii de dismetabolism şi efort fizic (Nota II)

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Abstract

Background. Data obtained on the administration of coenzyme Q10 (CoQ10) on heart weight in trained animals led us to study the effects of administration on relative weight and density of the liver.

Aims. We aimed to study the changes induced in liver weight and volume by exercise and CoQ10 supplementation in experimental dysmetabolic conditions.

Methods. The experiment was conducted on 12 groups (n = 10 animals/group) of adult male Wistar rats, with three types of diet: standard, high-carbohydrate, and high-fat, supplemented or not with CoQ10, sedentary or exercise trained. 6 groups were subjected to daily exercise (swimming) for one hour per day for 4 weeks, the other half were sedentary. At the end of the experiment, the animals were sacrificed, body weight and liver weight and volume were measured. Statistical analysis was performed using the SPSS 20 and Excel 2010 tools.

Results. The relative liver weight was significantly influenced only by physical training. Liver density was influenced by both physical training and CoQ10 supplementation.

Conclusions. In trained animals with a high calorie diet, a reduction of relative liver weight was observed, regardless of CoQ10 supplementation. Sedentary animals with CoQ10 supplementation had an increased liver density, regardless of the type of diet.

Keywords: exercise, dysmetabolism, relative liver weight, liver density

Rezumat

Premize. Datele obţinute experimental privind administrarea de coenzimă Q10 (CoQ10) asupra greutăţii inimii la animalele antrenate la efort, ne-au determinat să studiem şi efectul administrării acesteia asupra greutăţii relative şi densităţii ficatului.

Obiective. Ne-am propus să studiem modificările greutăţii şi volumului ficatului induse de efortul fizic şi de suplimentarea cu CoQ10 în condiţiile dismetabolismului experimental.

Metode. Experimentul s-a desfăşurat pe 12 loturi (n=10 animale/lot) de şobolani adulţi masculi rasa Wistar, cu trei tipuri de alimentaţie: standard, hiperglucidică şi hiperlipidică, in condiţii de suplimentare sau nu cu CoQ10, la animale sedentare sau antrenate la efort. 6 loturi au fost supuse efortului fizic zilnic (înot) timp de o oră zilnic pentru 4 săptămâni, cealaltă jumătate fiind sedentară. La sfârşitul experimentului, animalele au fost sacrificate, s-au măsurat masa corporală, greutatea hepatică, volumul hepatic. Analiza statistică a fost făcută utilizând programele SPSS 20 şi Excel 2010.

Rezultate. Greutatea relativă a ficatului a fost influenţată semnificativ doar de antrenamentul fizic. Densitatea hepatică a fost influenţată atât de antrenamentul fizic, cât şi de administrarea de CoQ10.

Concluzii. La animalele antrenate, cu dietă hipercalorică, s-a observat reducerea greutăţii relative a ficatului, indiferent de suplimentarea sau nu cu CoQ10. La animalele sedentare, suplimentarea de CoQ10 a dus la creşterea densităţii hepatice, indiferent de tipul de alimentaţie.

Cuvinte cheie: efort fizic, dismetabolism postprandial, greutate hepatică relativă, densitate hepatică.

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Introduction

Morphological changes are a most faithful witness to extrinsic aggressions on the body. Macroscopic changes are often preceded by microscopic ones, as they are preceded by molecular changes. The physical parameters of weight, volume, length were among the first studied, as their measurement is accessible to many laboratories. The development of laboratory medicine led to their high precision measurement, recent studies trying to standardize several parameters in animal species and humans. Although studies began to be conducted 200 years ago, the multitude of experimental parameters and conditions led to current studies in experimental models, adapted to current conditions. These investigate the effect of certain diets (Saraf Bank et al., 2015), different lifestyles (Bach et al., 2015) and supplementation with certain food constituents or toxic substances (Vitaglione et al., 2015; Tsirigoti et al, 2014).

Coenzyme Q10 (CoQ10) is a fat-soluble benzoquinone, whose major role is the production of ATP in the mitochondrial respiratory chain (Crane et al., 1989). The most important quantities have been found in the heart and liver, but its presence is felt in all animal cells, which could not function without it; its absence could even induce apoptosis (Aberg et al., 1992; Folkers et al., 1991). The level of fat solubility determines its absorbance in the small intestine (Bhagavan et al., 2006). In addition to the regeneration of other antioxidants (vitamin E) (Comes, 2001), it has roles in the cardiovascular system (local anti-inflammatory, reduction of LDL-cholesterol) (Singh et al., 2003; Bryce, 2013; Maidell, 1991).

Hypothesis

Experimental data obtained on the effect of CoQ10 on heart weight in physically trained animals subjected to a high-calorie diet to achieve metabolic syndrome and the role of the liver in CoQ10 synthesis, synthesis boosted by vitamin E and selenium, the importance of a balanced diet to ensure the necessary CoQ10 in the body led us to study the effect of CoQ10 supplementation on the relative weight and density of the liver.

Objectives

We experimentally studied the effect of CoQ10 supplementation on relative weight and density of the liver in trained animals, in whom metabolic syndrome was induced by high-calorie (high-carbohydrate and high-fat) diets.

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 the Department of Physiology 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 liver 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

Relative liver weight

Table I shows a decrease in the relative weight of the liver both in the exercise trained and CoQ10 supplementation groups. Statistical significance was high in the trained group (a decrease of 7.71%, $p < 0.001$) compared to the CoQ10 supplemented group, where the magnitude of the changes was of borderline significance (a decrease of 3.3%, p = 0.06) (Table I). The groups were considered sedentary and non-supplemented with CoQ10 (I, III, V), sedentary and supplemented with CoQ10 (VII, IX, XI) or trained without CoQ10 supplementation (II, IV, VI) or with CoQ10 supplementation (VIII, X, XII). There is a cumulative effect of exercise and CoQ10 supplementation on relative liver weight decrease, the groups trained and supplemented with CoQ10 having the lowest relative weight of the liver.

Table II shows an increase in relative liver weight with increased caloric intake. A decline was also observed when CoQ10 was administered. Sedentary groups had at the time of euthanasia a higher relative liver weight than the trained groups.

In the case of the standard diet (group I), the administration of CoQ10 (group VII) or exercise training (group II), although resulting in a decrease of relative weight, was not significant. The most important change was induced by administration of CoQ10 in the sedentary group (p = 0.076).

In the high-carbohydrate diet, exercise training only resulted in a significant decrease of relative liver weight. The changes were significant both for groups without CoQ10 supplementation (group IV vs group III, a 8.47% decrease, p = 0.036) and supplemented with Q10 (group X vs group IX, a 14.34% decrease, p = 0.025), where the most significant change was observed.

In the high-fat diet, exercise only had a statistically significant effect on relative liver weight, both for the groups without CoQ10 supplementation (group VI vs group V, a 7.26% decrease, p = 0.009) and in the case of CoQ10 supplementation (group XII vs group XI, a 5.75% change, p = 0.015). CoQ10 supplementation in sedentary animals did not lead to significant changes.

Liver density

Table III shows an increase of liver density both in the CQ10 supplemented and in the exercise trained groups. The most important changes occurred in the exercise trained groups supplemented with CoQ10.

Both exercise and CoQ10 supplementation resulted in significant liver density changes (an increase of 4.44%, p = 0.004 for exercise, an increase of 5.75%, p = 0.001 for CoQ10 supplementation).

In the standard diet, liver density was also significantly altered by the administration of CoQ10 in the sedentary group (group VII vs group I, an 8.62% increased density, p = 0.019). CoQ10 supplementation in the trained groups was also important, but of borderline significance (group VIII vs group II, a 5.97% increase, p = 0.058).

In the high-carbohydrate diet, there was an increase only in the sedentary group supplemented with CoQ10 (group IX vs group III, 7.02%, p = 0.013) and in the exercise trained group without CoQ10 supplementation (group IV vs group III, 22%, p = 0.006).

In the high-fat diet, liver density increased only in the sedentary group with CoQ10 supplementation (group XI vs group V, 7.02%, p = 0.013) or in the exercise trained group without CoQ10 (group VI vs group V, 6.22%, p = 0.006. CoQ10 supplementation in the trained groups did not induce significant changes (Table IV).

The analysis of the correlation between average daily weight gain and liver density showed a negative Pearson coefficient (-0.386) with a high statistical significance ($p \ll 0.001$). Thus, a greater weight gain is associated with decreased liver density.

Liver density is negatively correlated (Pearson coefficient = -0.204) with relative liver weight (p = 0.025). A high liver mass will be related to its low density.

The correlation between the relative weight of the liver and daily weight gain was significant (p = 0.017), the correlation is positive in this case. A greater weight gain will result in an increase of relative liver weight.

Discussions

Both CoQ10 administration and physical exercise decreased the relative weight of the liver. Statistical

Table I

Comparison of the effect of exercise or CoQ10 supplementation on relative liver weight (in grams liver/100 g body weight).

Group A	Group B	Group A		Group B		Student t test
		Average	Standard deviation	Average	Standard deviation	
Without CoQ10	With CoQ10	3.169748	0.265721	3.065261	0.333573	0.06
Sedentary	Trained	3.242730	0.282588	2.992278	0.275098	<0.001

Table II

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

Group A	Group B	Group A		Group B		Student t test
		Average	Standard deviation	Average	Standard deviation	
I	II	3.152082	0.096284	2.994298	0.301944	0.133
I	VII	3.152082	0.096284	3.012815	0.213548	0.076
II	VIII	2.994298	0.301944	2.860250	0.177023	0.242
VII	VIII	3.012815	0.213548	2.860250	0.177023	0.099
III	IV	3.295603	0.170015	3.016680	0.351265	0.036
III	IX	3.295603	0.170015	3.341573	0.495779	0.785
IV	X	3.016680	0.351265	2.862731	0.373326	0.355
IX	X	3.341573	0.495779	2.862731	0.373326	0.025
V	VI	3.403362	0.23965	3.156461	0.117000	0.009
V	XI	3.403362	0.23965	3.250947	0.161004	0.112
VI	XII	3.156461	0.117000	3.063248	0.151433	0.141
XI	XII	3.250947	0.161004	3.063248	0.151433	0.015

significance was high in the case of exercise training (a 7.71% decrease, p < 0.001) compared to CoQ10 supplementation, where the magnitude of the changes was of borderline significance (a 3.3% decrease, p = 0.06). Concerning liver density, both exercise and CoQ10 administration led to significant changes (a 4.44% increase, p = 0.004 in the case of exercise, a 5.75% increase, p = 0.001 in CoQ10 supplementation).

Standard diet

In the standard diet, administration of CoQ10 or physical exercise, though leading to a relative liver weight loss, was not significant. The most important change was induced by administration of CoQ10 to the sedentary group (p = 0.076). Hepatic density was significantly changed by administration of CoQ10 to the sedentary group (an 8.62% increased density, p = 0.019). CoQ10 supplementation in the trained groups was important, but of borderline significance (up to 5.97%, p = 0.058).

High-carbohydrate diet

In the high-carbohydrate diet, exercise training resulted in a significant decrease of relative liver weight. The changes were significant both for groups without CoQ10 (a decrease of 8.47%, p = 0.036) and for the groups supplemented with Q10 (a decrease of 14.34%, p = 0.025). Liver density increased only in sedentary groups with CoQ10 supplementation (7.02%, p = 0.013) and by physical training (6.22%, p = 0.006) without CoQ10. CoQ10 supplementation in the sedentary groups did not involve significant changes.

High-fat diet

In the high-fat diet, exercise training had a statistically significant effect on relative liver weight, both for the groups without CoQ10 (a decrease of 7.26%, p = 0.009) and in those supplemented with CoQ10 (5.75%, p = 0.015). The administration of CoQ10, unaccompanied by physical training, did not lead to significant changes. Hepatic density was influenced only in the sedentary groups, by CoQ10 administration (an increase of 7.76%, p <<0,001) and by physical training (an increase of 8.21%, p = 0.002). There is a slight difference in favor of exercise.

Correlation between weight gain, density and relative weight of the liver

There is a significant negative correlation between average daily weight gain and liver density. Thus, as daily weight gain increases, liver density decreases. Also, weight gain is positively correlated with relative liver weight increase. A more marked increase in weight gain is associated with a parallel increase in liver weight with the decrease of liver density. This change is consistent with the conclusion that an increased mass index is associated with an increased incidence and intensity of hepatic lipid load or the occurrence of hepatic steatosis. In this experiment, the increase in liver weight was also correlated with decreased liver density. Thus, in all groups, increased relative liver

Table III

Comparison of the effect of exercise or CoQ10 supplementation on liver density.

Group A	Group B	Group A		Group B		Student t test
		Average	Standard deviation	Average	Standard deviation	
Without CoQ10	With CoQ10	1.164105	0.078521	1.231191	0.110235	<0.001
Sedentary	Trained	1.171389	0.081670	1.223907	0.111952	0.004

Table IV

Comparison of liver density depending on 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	1.164260	0.098013	1.221144	0.088020	0.189
I	VII	1.164260	0.098013	1.259991	0.064010	0.019
II	VIII	1.221144	0.088020	1.294209	0.072963	0.058
VII	VIII	1.259991	0.064010	1.294209	0.072963	0.280
III	IV	1.124460	0.042699	1.194241	0.056358	0.006
III	IX	1.124460	0.042699	1.203956	0.080840	0.013
IV	X	1.194241	0.056358	1.238237	0.212031	0.534
IX	X	1.203956	0.080840	1.238237	0.212031	0.639
V	VI	1.095032	0.046097	1.185494	0.061323	0.002
V	XI	1.095032	0.046097	1.180633	0.023666	<0.001
VI	XII	1.185494	0.061323	1.210118	0.092956	0.493
XI	XII	1.180633	0.023666	1.210118	0.092956	0.344

Table V

Correlation of liver density, relative weight and weight gain.

The measured variable	Statistical test	Liver density	Average daily weight gain	Relative liver weight
Liver density	Pearson correlation	1	-.386**	-.204*
	Sig. (2-tailed)		.000	.025
Average daily weight gain	Pearson correlation	-.386**	1	.217*
	Sig. (2-tailed)	.000		.017
Relative liver weight	Pearson correlation	-.204*	.217*	1
	Sig. (2-tailed)	.025	.017	

** Correlation significant at the 0.01 level (2-tailed)
* Correlation significant at the 0.05 level (2-tailed)

weight can be seen as a consequence of hepatic steatosis.

CoQ10 supplementation has been shown to reduce oxidative stress and oxidative stress-related injuries in the liver (including hepatomegaly) in various animal models (Uboh et al., 2009; McNulty et al., 2008). Antioxidant supplementation has been shown to be useful in various types of hepatomegaly in humans (Stewart et al., 2007). The effect may be a consequence of the reduction of hepatic glutathione peroxidase activity and necroinflammatory activity associated with oxidative stress. It has been postulated that antioxidant supplementation may prevent liver ethanol related cirrhosis and hepatomegaly (steatosis) induced by a high-fat diet (Soylu et al., 2006). Thus, a high calorie diet could lead to a decreased hepatic synthesis of CoQ10, which would justify its supplementation in high-calorie diets, in obesity or metabolic syndrome.

Conclusions

1. CoQ10 supplementation leads to hepatic density increases in sedentary animals, in normal or high calorie diets.
2. CoQ10 supplementation does not induce changes in relative liver weight and density in trained animals receiving normal or high calorie diets.
3. Average daily weight gain is negatively correlated with liver density and positively correlated with relative liver weight.
4. Hepatic density is negatively correlated with relative liver weight.

Conflicts of interest

There are no conflicts of interest.

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