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The effect of coenzyme Q_{10} administration on metabolic control in patients with type 2 diabetes mellitus

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Abstract. A possible relationship between the pathogenesis of type 2 diabetes and coenzyme Q_{10} (CoQ_{10}) deficiency has been proposed. The aim of this study was to assess the effect of CoQ_{10} on metabolic control in 23 type 2 diabetic patients in a randomized, placebo-controlled trial. Treatment with CoQ_{10} 100 mg bid caused a more than 3-fold rise in serum CoQ_{10} concentration ($p < 0.001$). No correlation was observed between serum CoQ_{10} concentration and metabolic control. No significant changes in metabolic parameters were observed during CoQ_{10} supplementation. The treatment was well tolerated and did not interfere with glycemic control, therefore CoQ_{10} may be used as adjunctive therapy in patients with associated cardiovascular diseases.

1. Introduction

Type 2 diabetes is one of the most common non-communicable diseases in the world. Despite the high – and increasing – prevalence of the disease worldwide the underlying pathogenetic mechanisms are not well understood. Both genetic and environmental factors are of importance [3,7].

The cornerstones in the treatment regimen of type 2 diabetes are diet, exercise and antidiabetic drug therapy [2]. However despite maximal antidiabetic treatment optimal blood glucose control is often difficult to achieve.

The energy metabolism in type 2 diabetes differs in several aspects from that of healthy individuals. Both oxidative and non-oxidative glucose metabolism are decreased [3,5]. Likewise basal metabolic rate and thermogenetic response to food is decreased compared to non-diabetics.

A close association between type 2 diabetes and coenzyme Q_{10} (CoQ_{10}) deficiency has been hypothezised and CoQ_{10} has been proposed as having an important role in the pathogenesis of type 2 diabetes [8,9,11]. Until this date there are however few studies on diabetes and CoQ_{10} published. In one double-blind study on type 1 diabetic patients CoQ_{10} supplementation did not interfere with glycemic control [1].

Based on the present knowledge of the pathogenesis of type 2 diabetes as well as on the knowledge of the effects of CoQ_{10} a close relationship between type 2 diabetes and CoQ_{10} seems probable. The aim

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of the present study was to investigate the effect of CoQ_{10} on glycemic and metabolic control in type 2 diabetic patients.

2. Materials and methods

Twenty-three type 2 diabetic subjects were enrolled into this 6 months double-blind placebo-controlled trial. The diabetics were treated with diet alone or diet in combination with sulphonylureas. No other diabetes medication was allowed.

The subjects were randomised into two groups, one group receiving capsules containing 100 mg CoQ_{10} bid the other received matching placebo bid. The concomitant medication was not changed during the study period. Baseline measurements, as well as measurements at 3 and 6 months of height, weight, blood pressure, fasting blood glucose, HbA_{1c}, total cholesterol, HDL-cholesterol, triglycerides, vitamin E and CoQ_{10} were obtained.

The total amount of CoQ_{10} and vitamin E was determined by means of HPLC with electrochemical detection [4].

Coenzyme Q_{10} (Bio-Quinone®) was provided by Pharma Nord, Vejle, Denmark which is gratefully acknowledged.

Results are presented as means ± SE.

Differences between groups were compared using t-tests for unpaired data and t-tests for paired data when appropriate. Spearman's rank sum analysis was used for calculating correlations. p-values <0.05 were considered significant.

3. Results

No differences in baseline characteristics existed between the groups regarding age, duration of diabetes, degree of obesity and serum CoQ_{10}.

Table 1

Metabolic parameters assessed at baseline and at 6 months in the coenzyme Q_{10} (Q_{10}) group and placebo-group. Numbers are given as mean ± SEM

	Q_{10}		Placebo	
	Baseline	6 months	Baseline	6 months
Number	12		11	
Age (year)	65 ± 5		64 ± 7	
BMI (kg/m^2)	29.0 ± 4.2	28.6 ± 4.2	29.8 ± 3.4	29.3 ± 3.5
Blood glucose (mmol/l)	11.7 ± 2.8	11.0 ± 3.0	11.3 ± 1.9	10.6 ± 2.1
HbA_{1c} (%)	8.7 ± 1.5	9.1 ± 1.9	7.9 ± 0.9	8.1 ± 0.8
Cholesterol (mmol/l)	5.6 ± 0.8	5.6 ± 0.8	5.4 ± 0.8	5.7 ± 1.1
HDL-cholesterol (mmol/l)	1.07 ± 0.26	1.16 ± 0.29	1.18 ± 0.28	1.27 ± 0.27
Triglycerides (mmol/l)	1.9 ± 1.1	1.7 ± 0.8	2.6 ± 2.0	1.9 ± 0.7
Systolic BP (mm Hg)	142 ± 14	137 ± 16	155 ± 27	151 ± 32
Diastolic BP (mm Hg)	80 ± 8	79 ± 9	81 ± 13	83 ± 12
P-CoQ_{10} (μg/ml)	1.20 ± 0.21	4.00 ± 1.64***	1.38 ± 0.41	1.29 ± 0.39
P-vitamin E (μg/ml)	16.5 ± 4.3	18.4 ± 6.1	14.8 ± 4.5	16.1 ± 4.3

***$p <$ 0.001 vs. baseline.

The glycemic control (fasting blood glucose and HbA_{1c}) was similar – and unsatisfactory – in both groups at baseline.

Treatment with CoQ_{10} caused a more than three-fold rise in serum Q_{10} concentration (Table 1) ($p < 0.001$). No associations were found between plasma level of CoQ_{10} and the parameters used to assess the glycemic control, i.e., fasting blood glucose and HbA_{1c} ($r = 0.13$–0.20; $p = 0.36$–0.53).

Overall no improvement in glycemic control during the treatment period was observed (Table 1).

Blood pressure and lipids remained unchanged during the study.

The treatment was well tolerated and no adverse effects were observed during the follow-up period.

The results of the variables assessed are given in Table 1.

4. Discussion

The therapeutical use of CoQ_{10} has primarily been advocated in the treatment of cardiovascular diseases, muscular disorders and periodontal disease [6]. CoQ_{10} is closely associated with energetic and oxidative processes. Therefore theoretically CoQ_{10} substitution could contribute to correction of the impaired energy metabolism in type 2 diabetes. Since the underlying metabolic disorder in type 2 diabetes is located in the muscle tissue a role for CoQ_{10} could be of importance [5,7]. Muscle tissue is rich in mitochondria – mitochondrias again contain CoQ_{10}. A decrease in the amount of CoQ_{10} might lead to impaired function of the muscle tissue and consequently insulin resistance. The main tissue responsible for glucose disposal in humans is muscle tissue, consequently the most important site of insulin resistance is at the level of muscle tissue [5,7].

Another interesting hypothetical mode of action of CoQ_{10} in diabetes is on the pancreatic insulin secretion. A deficiency of CoQ_{10} in the pancreas could impair bioenergetics, the generation of ATP and the synthesis of insulin [8,9].

Despite the very interesting theoretical background extremely little is known about diabetes and CoQ_{10}. A Medline search covering the years 1966–1998 (June) for diabetes and coenzyme Q_{10}/ubiquinone gave only 17 references – and none specifically focusing on treatment of type 2 diabetes. There is only one Danish study focusing on the impact of CoQ_{10} supplemention on glycemic control and insulin requirement in type 1 diabetic patients [1].

For certain subgroups of diabetes the role of CoQ_{10} seem to be more obvious and of potential significance. These are primarily diabetes caused by mutations in mitochondrial DNA while the role of CoQ_{10} in type 2 diabetes remains unsettled [12,13].

The activity and concentration of CoQ_{10} in diabetics is lower than compared to controls [8]. The level in our patients was not low compared to the level in healthy individuals, i.e., 0.75–1.00 μg/ml (10). Quite interestingly antidiabetic medication seems to affect CoQ_{10} concentration. The deficiency of CoQ_{10} observed in many diabetics may even be enhanced by certain antidiabetic drugs [8]. We were able to show that exogenous administration of CoQ_{10} leads to increased serum levels of CoQ_{10}, also in the presence of sulphonylureas. However, no correlation between plasma level of CoQ_{10} and glycemic control was seen in the type 2 diabetic subjects studied. In order to avoid the confounding effect of different anti-diabetic drugs on CoQ_{10} concentration/bioavailablity only diabetics on diet or diet combined with sulphonylurea-treatment were included in the present study.

An improved insulin sensitivity would lead to improvement of diabetes control, which was however not found in the present study. Likewise improvement in insulin secretion would be reflected as an overall better glycemic control.

Our results are quite consistant with the results published by Andersen et al. on type 1 diabetic patients, i.e., that no major effect of CoQ_{10} on metabolic parameters in diabetics was found [1].

We conclude from our study that treatment with CoQ_{10} is well tolerated among type 2 diabetics and that CoQ_{10} does not interfere with the glycemic control, i.e., CoQ_{10} is neutral with respect to diabetes control. Therefore, CoQ_{10} may be used safely in type 2 diabetes, and especially in association with arterial hypertension, coronary artery disease or heart failure CoQ_{10} may contribute to potential long term benefits in the treatment of type 2 diabetic patients.

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