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 hypothesized 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
of the present study was to investigate the effect of CoQ10 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 CoQ10 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, HbA1c, total cholesterol, HDL-cholesterol, triglycerides, vitamin E and CoQ10 were obtained.

The total amount of CoQ10 and vitamin E was determined by means of HPLC with electrochemical detection [4].

Coenzyme Q10 (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 CoQ10.

<table>
<thead>
<tr>
<th></th>
<th>Q10</th>
<th>Placebo</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>12</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Age (year)</td>
<td>65 ± 5</td>
<td>64 ± 7</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.0 ± 4.2</td>
<td>29.8 ± 3.4</td>
<td>29.3 ± 3.5</td>
</tr>
<tr>
<td>Blood glucose (mmol/l)</td>
<td>11.7 ± 2.8</td>
<td>11.3 ± 1.9</td>
<td>10.6 ± 2.1</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>8.7 ± 1.5</td>
<td>7.9 ± 0.9</td>
<td>8.1 ± 0.8</td>
</tr>
<tr>
<td>Cholesterol (mmol/l)</td>
<td>5.6 ± 0.8</td>
<td>5.4 ± 0.8</td>
<td>5.7 ± 1.1</td>
</tr>
<tr>
<td>HDL-cholesterol (mmol/l)</td>
<td>1.07 ± 0.26</td>
<td>1.18 ± 0.28</td>
<td>1.27 ± 0.27</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>1.9 ± 1.1</td>
<td>2.6 ± 2.0</td>
<td>1.9 ± 0.7</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>142 ± 14</td>
<td>155 ± 27</td>
<td>151 ± 32</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>80 ± 8</td>
<td>81 ± 13</td>
<td>83 ± 12</td>
</tr>
<tr>
<td>P-CoQ10 (µg/ml)</td>
<td>1.20 ± 0.21</td>
<td>1.38 ± 0.41</td>
<td>1.29 ± 0.39</td>
</tr>
<tr>
<td>P-vitamin E (µg/ml)</td>
<td>16.5 ± 4.3</td>
<td>14.8 ± 4.5</td>
<td>16.1 ± 4.3</td>
</tr>
</tbody>
</table>

***p < 0.001 vs. baseline.
The glycemic control (fasting blood glucose and HbA1c) was similar – and unsatisfactory – in both groups at baseline.

Treatment with CoQ10 caused a more than three-fold rise in serum Q10 concentration (Table 1) ($p < 0.001$). No associations were found between plasma level of CoQ10 and the parameters used to assess the glycemic control, i.e., fasting blood glucose and HbA1c ($r = 0.13–0.20; p = 0.36–0.53$).

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 CoQ10 has primarily been advocated in the treatment of cardiovascular diseases, muscular disorders and periodontal disease [6]. CoQ10 is closely associated with energetic and oxidative processes. Therefore theoretically CoQ10 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 CoQ10 could be of importance [5,7]. Muscle tissue is rich in mitochondria – mitochondrias again contain CoQ10. A decrease in the amount of CoQ10 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 CoQ10 in diabetes is on the pancreatic insulin secretion. A deficiency of CoQ10 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 CoQ10. A Medline search covering the years 1966–1998 (June) for diabetes and coenzyme Q10/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 CoQ10 supplementation on glycemic control and insulin requirement in type 1 diabetic patients [1].

For certain subgroups of diabetes the role of CoQ10 seem to be more obvious and of potential significance. These are primarily diabetes caused by mutations in mitochondrial DNA while the role of CoQ10 in type 2 diabetes remains unsettled [12,13].

The activity and concentration of CoQ10 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 CoQ10 concentration. The deficiency of CoQ10 observed in many diabetics may even be enhanced by certain antidiabetic drugs [8]. We were able to show that exogenous administration of CoQ10 leads to increased serum levels of CoQ10, also in the presence of sulphonylureas. However, no correlation between plasma level of CoQ10 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 CoQ10 concentration/bioavailability 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 consistent with the results published by Andersen et al. on type 1 diabetic patients, i.e., that no major effect of CoQ10 on metabolic parameters in diabetics was found [1].

We conclude from our study that treatment with CoQ10 is well tolerated among type 2 diabetics and that CoQ10 does not interfere with the glycemic control, i.e., CoQ10 is neutral with respect to diabetes control. Therefore, CoQ10 may be used safely in type 2 diabetes, and especially in association with arterial hypertension, coronary artery disease or heart failure CoQ10 may contribute to potential long term benefits in the treatment of type 2 diabetic patients.

References


