The Protection of Coenzyme Q₁₀ against Experimental Viral Myocarditis in Mice

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We studied the effects of Coenzyme Q₁₀ (CoQ₁₀) on DBA/2 mice inoculated with the M variant of encephalomyocarditis virus. The mice were treated as follows: 1) CoQ group (n = 49); CoQ₁₀ 1.0 mg (0.1 ml) x 2/day (0.1 mg/g/day), 2) control group (n = 55); sham-liquid 0.1 ml x 2/day. These treatments were intraperitoneally performed every day on days −1 to 12. In both groups, we determined the heart and serum contents of CoQ₉ and CoQ₁₀, which are the biologically active forms of CoQ in mice, in the mice killed on days 3–4 and 7. There was no significant change in the cumulative incidence of myocarditis in both groups. The survival rate was significantly higher on days 5–12 in the CoQ group than in the control group. There were significant increases of CoQ₉ content on days 3–4, and CoQ₁₀ content on days 3–4 and 7, in the heart in the CoQ group as compared with the control group. There was no significant change in the serum content of CoQ₉ in both groups. The marked increase of the serum CoQ₁₀ content seen in the CoQ group was due to the results of the exogenous administration of CoQ₁₀. Thus, it may be concluded that CoQ₁₀ may have a protective effect against viral myocarditis in man, in whom CoQ₁₀ is only an active form of CoQ.

MYOCARDITIS is an inflammatory disease of the myocardium caused by viruses, bacteria and other cardiototoxic agents.¹⁻² Cardiac lesions of myocarditis include inflammatory cell infiltrations, myocardial cell necrosis and residual myocardial fibrosis.¹⁻⁶ However, the initial phenomenon occurring in the myocardium of myocarditis is considered to be myocardial ischemia.

Ubiquinones (coenzymes Q = CoQ) have long been known to be constituents of mitochondria and their role as electron and proton carriers in respiration has been noted. In some clinical and experimental studies, CoQ₁₀ has protective effects against adriamycin induced myocardial damage and myocardial ischemia.⁵⁻¹⁰

The purpose of this study was to establish whether CoQ₁₀ could have a protective effect against viral myocarditis in mice.

METHODS

Our methods were similar to those reported previously:⁵⁻⁶; inbred strain of DBA/2 mice at 4–6 weeks of age were inoculated intraperitoneally with the M variant of encephalomyocarditis (EMC) virus with a titer of 100 TCID₅₀ per 0.1 ml and were observed up to the 12th day. The mice were divided and treated as follows: 1) CoQ group (n = 49); CoQ₁₀ 1.0 mg (0.1 ml) x
2/day (0.1 mg/g/day), 2) control group (n = 55); sham-liquid 0.1 ml x 2/day. These treatments were intraperitoneally performed every day on days -1 to 12. Their hearts were fixed in a 10% formalin solution, sectioned longitudinally through the four chambers.

In both groups, we determined the heart and serum contents of CoQ9 and CoQ10, which are the biologically active forms of CoQ in mice, in the mice killed on days 3-4 and 7, using the high performance liquid chromatography method. We also determined the heart and serum contents of CoQ9 and CoQ10 in normal DBA/2 mice at 4-6 weeks old.

RESULTS
There were no significant changes in the cumulative incidence of myocarditis in both groups; CoQ group = 85.7% (42/49), control group = 92.7% (51/55). However, the survival rate was significantly higher on days 5-12 in the CoQ group than in the control group (Fig. 1: 12th day; CoQ group = 45.5% (15/33), control group = 17.5% (7/40)). Table I shows normal heart and serum contents of CoQ9 and CoQ10 in the mouse.

There was a significant increase (p < 0.05) in the heart content of CoQ9 on days 3-4 in the CoQ group (237.5 ± 15.3 μg/g, n = 8) as compared with the control group (213.9 ± 25.5 μg/g, n = 10) (Fig. 2). There was no significant change in the heart content of CoQ9 on day 7 in both groups (CoQ group = 204.7 ± 24.7, n = 8, control group = 215.3 ± 33.5, n = 5) (Fig. 2).

There were significant increases (p < 0.001) in the heart content of CoQ10 on days 3-4 and on day 7 in the CoQ group (3-4 day; 95.0 ± 26.9
Table 1: Normal values of CoQ9 and CoQ10 determined from normal DBA/2 mice at 4–6 weeks of age

<table>
<thead>
<tr>
<th>Sample</th>
<th>Co-Q9 (μg/ml)</th>
<th>Co-Q10 (μg/ml)</th>
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<tbody>
<tr>
<td>Heart</td>
<td>317.7 ± 29.5  (n = 15)</td>
<td>32.7 ± 3.9  (n = 15)</td>
</tr>
<tr>
<td>Serum</td>
<td>0.32 ± 0.09  (n = 8)</td>
<td>. . .  (n = 12)</td>
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--- = not detected.

**Discussion**

Coenzyme Q10 is a physiologically essential substance in man as one of the respiratory chain members in mitochondria, and has been known to exist abundantly in the heart, which repeats the contraction and relaxation cycle continuously. CoQ10 deficiency in ischemic heart tissue and the amelioration of cardiac function by CoQ10 replenishment have been previously demonstrated.

In this experimental study, we found a significantly higher survival rate in the CoQ group as compared with the control group. We also found higher contents of CoQ9 and CoQ10 in the myocardium of the CoQ group as compared with the control group. In addition, the values of CoQ9 and CoQ10 contents in the hearts of the mice with myocarditis were demonstrated to be lower than those of the normal mice (Table I and Figs. 2, 3). Thus, CoQ9 and CoQ10 may play some role against viral myocarditis in mice.

Although further studies may be necessary to determine the precise mechanism of CoQ10 against viral myocarditis in mice, it may be suggested that CoQ10 could have a protective effect against viral myocarditis in man, in whom CoQ10 is only an active form of CoQ11.

**References**

2. Kawai C, Matsumori A, Kitauro Y, Takatsu T: Viruses and the heart: viral myocarditis and cardiomyopathy. Prog Cardiol 7: 141,

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