BIOENERGETICS IN CLINICAL MEDICINE. VI. ADJUNCTIVE TREATMENT OF PERIODONTAL DISEASE WITH COENZYME Q_{10}

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ABSTRACT

Eighteen patients with periodontal disease and measurable pockets were treated on a double-blind basis with coenzyme Q_{10} and a matching placebo. The treatment was significant (P < 0.01). Before decoding, all 8 patients receiving coenzyme Q_{10} and 7/10 patients receiving placebo were correctly assigned. Of the remaining 3 placebo patients, the status of one was borderline and could have been assigned to either group, and two improved due to better hygiene. Crevicular fluid flow as a measure of inflammation was newly monitored. Pocket-depth, periodontal health, calculus, and plaque scores provided the most valuable data for evaluation.

INTRODUCTION

Nakamura et al. (1973) cooperatively with Wilkinson reviewed previous literature on coenzyme Q (CoQ) and periodontal disease, and reported for the first time the specific activities of the succinate dehydrogenase-coenzyme Q_{10} reductase of gingival tissue of 22 patients with advanced periodontal disease. The diseased gingival biopsies showed a significant (P < 0.001) deficiency of coenzyme Q_{10} (CoQ_{10}) as based upon the analytical data of enzyme activities in comparison with those of normal gingival tissue. These same investigators (Nakamura et al., 1974) extended this study on the CoQ_{10}-enzyme on normal periodontal tissues from 24 individuals and on diseased periodontal tissues from 40 individuals. They found that about 60% of the 40 diseased gingival tissues showed a deficiency of CoQ_{10} at its site in this succinate-CoQ_{10} enzyme. As a group, the control tissues showed no deficiency of CoQ_{10}, but there was a 26% incidence of deficiency.

The mean value of the deficiency of CoQ_{10}, expressed as enzyme activity, was 36% for the 40 patients with this oral disease.

Coenzyme Q. 200.
On the basis of the extensive enzyme data showing that the prevalence of a deficiency of CoQ₁₀ in the diseased gingival tissues of patients with periodontitis, a cooperative study by Wilkinson and Folkers (1975) and their respective coworkers was made of the oral administration of CoQ to 8 patients under routine care for periodontitis. Seven patients received CoQ₁₀ and one received hexahydrocoenzyme Q₄ (H₆CoQ₄). The patients cooperated and were under plaque control. The periodontal score decreased (P<0.01) on CoQ treatment, and unexpectedly, the periodontal pocket depth decreased (P<0.05) on treatment since all patients had been considered as candidates for surgical intervention. Healing was so excellent 5-7 days post-biopsy that biopsy sites were difficult to discern, and the overall healing was viewed as extraordinarily effective. An increase (P<0.05) of the mean value of the specific activities of the CoQ₁₀-enzyme of the diseased biopsies indicated possible correlation with the extraordinary healing.

On the basis of the favorable oral administration (Wilkinson et al., 1975) of CoQ₁₀ to 7 patients under routine care for periodontitis, a sequence of double-blind studies with CoQ was planned, and the first double-blind data on CoQ₁₀ are herein summarized.

METHODS

Ten bottles of capsules of CoQ₁₀ (25 mg each) and ten bottles of matching placebo were randomly coded by consecutive numbers, 1 through 20. The code was known only to Karl Folkers at The University of Texas, and the double-blind administration was conducted at Travis Air Force Base, California. The dosage was two capsules per day for three weeks, and the dosage of CoQ₁₀ was 25 mg twice daily.

Patients selected for study had to have measurable periodontal pockets either because of the enlargement of gingiva due to inflammation, pseudo-pocketing, or as the result of loss of alveolar bone. Pocket depths were measured on the distal, mid-line facial, mesial and lingual of each tooth using a Merriott probe. Gingival temperatures were taken, with a Tele-Thermometer (Yellow Springs Instrument Co., Yellow Springs, Ohio), and crevicular fluid was measured using a Periotron (Harcor Electronics, Winnipeg, Canada) in the six most involved areas. Periodontal health was evaluated, as before by Wilkinson et al. (1975) by scoring purulent exudate,
tooth mobility, gingival swelling, bleeding, redness, pain and itching. Calculus was scored as was bacterial plaque which was stained with a disclosing solution. A score of 1 to 5 was used, 1 being none and 5 being severe. The patient's health was self-evaluated and evaluated by taking a written and oral medical history. Patient's sex, age, weight and height were recorded, and three intra-oral photographs were taken at each visit. Data were collected on days 1, 7, 14 and 21 of the study. Two clinicians, who calibrated each other prior to initiating the study, collected the data and took the photographs.

RESULTS AND DISCUSSION

Two of the 20 patients reported side-effects, but it was considered that these effects were not due to the treatment. On the advent of these side-effects, the code for these two individuals was broken, and the administration of CoQ=10 was terminated at 4 and 7 days, respectively. The incomplete data for these two patients are not included in the final results. The first patient complained during the initial four days of a slight dizziness. It appeared that this dizziness was coincidental with previously undiagnosed cardiac disease which became clearly evident several weeks later. The second terminated patient developed classic symptoms of influenza, and the administration of capsules was terminated upon request of the family.

Eighteen patients completed the study, and the data are in Table 1. All 8 patients receiving CoQ=10 were correctly assigned before breaking the code. Seven out of the 10 patients receiving the placebo were also correctly assigned before breaking the code, and 3 placebo patients were incorrectly assigned to having received CoQ=10. The number of patients receiving CoQ=10 and those receiving placebo were also unknown within the coding procedure. On a statistical basis alone, the administration of CoQ=10 and a matching placebo to these eighteen patients having periodontal disease was significant (P<0.01).

Before decoding, it was noted that one of the three patients receiving placebo, who had incorrectly been assigned to the CoQ=10 group, was clinically marginal that assignment to the placebo or CoQ=10 group was difficult. All three patients had extremely inadequate oral hygiene and had visited the dentist infrequently. It is frequently observed that such
patients will attempt to improve their oral hygiene when they have frequent dental appointments, and two of these three patients who had improved periodontal health were wrongly assigned to the CoQ₁₀-group.

This is the third double-blind study made of the administration of a form of coenzyme Q to groups of patients having periodontal disease, but it is the first double-blind study conducted with CoQ₁₀, which is that form of CoQ existing naturally in all cells of the human body having mitochondrial, including the gingival tissue. The first double-blind study was by Tsunemitsu et al. (1970) and it was with CoQ₇ and placebo. The second such study was with H₄CoQ₄ and placebo as conducted cooperatively by Matsumura and Folkers and their colleagues (1973). The recording clinicians for each of these three double-blind studies were different individuals.

In the interpretation of all these clinical results over several years on coenzyme Q₁₀ in periodontitis, CoQ₁₀ should not be considered as a drug, but rather as the administration of a vitamin-like substance in pure form by the oral route to patients having a deficiency of this substance in their diseased gingival tissue and to correct such deficiency. The administration of coenzyme Q₁₀, as an adjunctive treatment, is clinically beneficial and presumably by correctly of an existing deficiency which is demonstrable.

Coenzyme Q₁₀ is an indispensable vitamin-like substance in cellular energy formation, and is essential for the health of tissue. It is to be expected that increased availability of CoQ₁₀ to deficient gingival tissue should improve the bioenergetics of such tissue, facilitate healing, and response to oral hygiene. Lehninger (1970) in his "Biochemistry" positioned CoQ in respiration, applicable to gingival tissue, as in Scheme 1.

### Scheme 1

\[
\begin{align*}
\text{NAD} & \rightarrow \text{FAD} \rightarrow \text{ATP} \\
\text{Succ.} & \rightarrow \text{FAD} \rightarrow \text{ATP} \\
\text{Fatty acyl CoA} & \rightarrow \text{CoQ} \rightarrow \text{Cyt.b} \rightarrow \text{Cyt.c₁} \rightarrow \text{Cyt.c} \rightarrow \text{Cyt.a} + a_3 \rightarrow \text{O}_2 \\
\text{Gly PO₄} & \rightarrow \text{FAD} \\
\end{align*}
\]

Using crevicular fluid flow as a measure of inflammation has been proven, but the Periotron is still being evaluated for this purpose. Measuring gingival temperature as an indicator of health vs. disease is
Table 1. Data from Double-Blind Administration to Patients Having Severe Periodontal Disease

<table>
<thead>
<tr>
<th></th>
<th>Clinically Improved</th>
<th>Clinically Unimproved</th>
<th>Total Number</th>
<th>% of Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>COG16 (a)</td>
<td>6</td>
<td>0</td>
<td>8</td>
<td>100</td>
</tr>
<tr>
<td>Placebo</td>
<td>3</td>
<td>7</td>
<td>10</td>
<td>30</td>
</tr>
</tbody>
</table>

(a) versus (b) \( \chi^2, 9.164; \quad P < 0.01 \).

an unproven technique, but may be considered as offering interesting observations and a degree of assistance in final evaluation. Pocket depth evaluation, periodontal health, calculus, and plaque scores offered the most valuable data for evaluation. Decreased pocket depth with plaque score remaining constantly high, coupled with photographic evidence of improved health, was considered as strong evidence of improved periodontal health due to administration of coenzyme Q10.

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REFERENCES


