REVIEW

Effects of Coenzyme Q10 in New Indications with Antioxidant Vitamin Deficiency

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Three cases diagnosed as acute glomerulonephritis with renal failure, amyotrophic lateral sclerosis and polymyositis exhibited antioxidant vitamin deficiency and free radical stress. Treatment with coenzyme Q10 was associated with significant improvement for the first time in the published literature.

Keywords: glomerulonephritis, renal failure, polymyositis, motor neurone disease, ubiquinone, antioxidant, vitamin.

INTRODUCTION

Coenzyme Q10 (CoQ) deficiency has been described in apparently healthy subjects as well as in patients with cardiovascular disease, diabetes, cancer and muscular diseases [1–3]. CoQ is normally present in all body cells. It is particularly prevalent in the heart, kidneys, liver, muscles, pancreas, thyroid and brain, and varies between 13.4 μg g⁻¹ tissue in the brain to 114 μg g⁻¹ tissue in the heart [4]. CoQ is a powerful antioxidant and bioenergetic agent and enhances the availability of adenosinetriphosphatase (ATP) in the cells [1–3]. Treatment with CoQ has been beneficial in congestive heart failure, cardiomyopathy, coronary artery disease, diabetes, cancer, muscular dystrophies, myopathies and degenerative diseases [5, 6]. Since CoQ is essential to the optimal function of all cell types, it is not surprising to find a seemingly diverse number of disease states which respond to CoQ supplementation [6–10].

In fact, all metabolically active tissues are highly sensitive to a deficiency of CoQ. Until recently, most of the research was directed at the requirements of CoQ in energy conversion in the mitochondrial compartments of cells or on the antioxidant properties of CoQ. New evidence [6] shows that CoQ is present in other cell membranes. In the outer membrane, it may contribute to the control of cell growth, especially in lymphocytes, indicating its universality in the disease process. It is reasonable to believe that the entire field of medicine should be re-evaluated in light of this growing knowledge and treatment with CoQ should be tried in all so-called polygenic diseases.

CASE STUDIES

Case 1: Acute Renal Failure

A 50-year-old man presented with fever, weakness, sweating and burning in the urine of about 15 days' duration. His pulse was 100 per minute and regular, blood pressure, 110/80
mmHg without any other abnormality. Microscopic examination of his urine showed plenty (+ + +) of pus cells and the urine was positive (+ +) for albumin. Urine output was < 700 ml per 24 h. Twenty-four hour urinary albumin excretion was 5.2 g. His haemoglobin was 13.2 g %, polymorph 75%, lymphocyte 20% and eosinophil 4%. His blood urea was 223 mg dl⁻¹ and serum creatinine 7.7 mg dl⁻¹ suggestive of uraemia. Other laboratory data were: fasting blood glucose 108 mg dl⁻¹, sodium 141 mmol l⁻¹, potassium 4.1 mmol l⁻¹, and urine was sterile in culture after 48 h of incubation. He was given 10% dextrose solution, 1500–2000 ml daily intravenously, and cephotoxine 1 g intravenously twice daily for 10 days without any benefit while under the treatment of concerned doctors.

Repeated examination of blood urea and creatinine every third day and the presence of albumin and pus cells and were indicative of acute renal failure with acute glomerulonephritis. Since there was no improvement and the patient refused to go for hemodialysis, he was admitted under our care. He continued with the same treatment for another week; however, his blood urea remained > 200 mg dl⁻¹ and serum creatinine > 7.5 mg dl⁻¹ on repeated examinations. His plasma levels of vitamin C, vitamin E and beta-carotene were suggestive of antioxidant deficiency. Lipid peroxides (thiobarbituric acid reactive substances, TBARS), malondialdehyde and diene conjugates were higher compared to normal values in our laboratory (see Table 1).

In view of the suspicion of antioxidant deficiency and the presence of oxidative stress, he was given hydrosoluble CoQ (60 mg twice daily). After a week of treatment with CoQ (60 mg twice daily), his urine output increased to 1500 ml daily, blood urea was 150 mg dl⁻¹ and serum creatinine 5.8 mg dl⁻¹. After 14 days of treatment with CoQ, his blood urea was 50 mg dl⁻¹ and serum creatinine 2.2 mg dl⁻¹, serum sodium 144 mmol l⁻¹ and serum potassium 3.6 mmol l⁻¹. Intravenous dextrose, furosemide and antibiotics were stopped; however, he was asked to continue CoQ for another week. After 21 days of treatment, his blood urea was 38 mg dl⁻¹ and serum creatinine 1.4 mg dl⁻¹. Plasma levels of vitamin C, vitamin E and beta-carotene increased to normal limits. Lipid peroxides, malondialdehyde and diene conjugates were within the normal range (see Table 1). Urine examination showed neither pus cells nor albumin. Twenty-four hour urinary albumin excretion was 0.12 g and urine output was > 1400 ml per 24 h. The findings suggested that the patient had acute glomerulonephritis with acute renal failure which may have reversed owing to CoQ supplementation.

Case 2: amyotrophic lateral sclerosis (motor neurone disease)

A 40-year-old man presented with insidious onset of gradually progressive weakness in the left upper limb followed by the right upper limb after a bout of 6–8 weeks, accompanied by thinning of both limbs. He had developed difficulty in walking and getting up from a squatting position over the last 2 years. He also had slurring of speech and dysphagia for solids over the last year. He had developed generalized fasciculation over the last 6 months. He also had a fever for 1–2 weeks about 2 years ago, after which the illness started.

Physical examination revealed pulse 80 per min, regular, blood pressure 128/80 mmHg, and systemic examination showed no abnormality except in the nervous system. He had wasting of the supraspinatus, deltoid, tongue and the small muscles of the hands in both upper limbs. Jaw jerk and muscular tone were within normal limits. His reflexes were exaggerated in all four limbs and planters were extensors. Fasciculations were observed in the tongue and limbs. There was no sensory deficit and power was grade III–IVN in all the four limbs and 0 to 1 in the thumbs and little fingers, which also had contractures owing to muscle wasting. Higher centres and sensory centres were within normal limits.

Laboratory data analysed on 10 February 1998 at SGPGI, Lucknow were: haemoglobin 13.6 g %, total leucocyte count 43000%, polymorph 42%, lymphocyte 58%, ESR 11 mm h⁻¹, serum creatinine 1.1 mg dl⁻¹, blood urea nitrogen 10 mg dl⁻¹, fasting blood glucose 81 mg dl⁻¹, total protein 7.4 g dl⁻¹, albumin 4.5 mg dl⁻¹. Urine examination for Bence-Jones
<table>
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<tr>
<th>Cases</th>
<th>Vitamin C (μmol L⁻¹)</th>
<th>Vitamin E (μmol L⁻¹)</th>
<th>Beta-carotene (μmol L⁻¹)</th>
<th>TBARS (pmol L⁻¹)</th>
<th>Malondialdehyde (pmol L⁻¹)</th>
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<td>Acute glomerulonephritis with acute renal failure</td>
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<td>Before treatment</td>
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<td>After coenzyme Q10</td>
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<td>Polymyositis</td>
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<td>Before treatment</td>
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proteins was negative. Radiological examination of the cervical spine was within normal limits. While an electromyogram was suggestive of a chronic denervation, nerve conduction velocity was within normal limits. Vitamin E 400 mg day⁻¹, in conjunction with vitamin B complex given for 90 days showed no benefit.

Laboratory data analysed on 10 May 1998 at our centre were: serum calcium 9 mg dl⁻¹, potassium 4.9 mEq l⁻¹, phosphorus 4.9 mg dl⁻¹, magnesium 1.7 mg dl⁻¹, zinc 120 μg dl⁻¹, and copper 96 μg dl⁻¹. Antioxidant vitamin C, vitamin E and beta-carotene were lower and lipid peroxides, malondialdehyde and diene conjugates (see Table 1) higher compared to normal values in our laboratory. Cerebrospinal fluid showed no biochemical abnormality in glucose, proteins and cells. Cerebrospinal fluid: vitamin C was 0.8 μmol l⁻¹, vitamin E 0.03 μmol l⁻¹, lipid peroxides 0.7 μmol ml⁻¹, malondialdehyde 1.9 nmol ml⁻¹ and diene conjugates 42.00 units. Creatine phosphokinase was 22 units l⁻¹.

In view of the above findings, a diagnosis of amyotrophic lateral sclerosis, a variety of motor neurone disease was made. Since the patient had oxidative stress, he was administered CoQ, two capsules three times daily (180 mg/day). After 1 week's treatment, there was a symptomatic improvement in weakness and an increase in power in the lower and upper limbs. After 4 weeks, there was a substantial decrease in lipid peroxides, malondialdehyde and diene conjugates and an improvement in vitamin status (see Table 1), in association with an improvement in speech, swallowing and walking as well as in general well-being. There was an improvement in the power of the hand muscles from 0 to 1 grade and 3 to 4 grade after treatment. The patient is on 4 weekly follow-up.

Case 3: Polymyositis

A 38-year-old man presented with sudden onset of pain in the legs and thighs and difficulty in walking, mild cough and a fever of 48 h duration. There was no headache or vomiting. He was unable to get up after squatting and there was no history of such an illness in the past. Initially, he had painless weakness in the muscles of the hips and thighs on the first day.

Physical examination revealed: pulse 98 per min, regular, blood pressure 120/82 mmHg, without any evidence of neck rigidity, pain in the neck, with no sign of trauma in the spine. Tenderness of mild intensity was noted in the hip, thigh and calf muscles. Anterior and posterior neck muscles were normal. Knee and ankle joint reflexes were diminished. Joint pain and tenderness were absent and an examination of the central nervous system showed no abnormality.

Laboratory data were: haemoglobin 14.1 %, total leucocyte count 11 500 per cumm, polymorph 75% and lymphocyte 25%, ESR 38 mm, first hour. Creatine phosphokinase (CPK) (256 IU l⁻¹) and lactic dehydrogenase (LDH) (550 IU l⁻¹) were raised, suggestive of muscle damage. An electromyogram revealed a typical myopathic pattern characterized by several abnormal brief action potentials and salvos of pseudomyotonic activity. The electrocardiogram was within normal limits. Plasma levels of lipid peroxides or TBARs, malondialdehyde and diene conjugates were raised; however, antioxidant vitamins were within normal limits (see Table 1). He was administered prednisolone 40 mg/day and CoQ, 2 capsules twice daily (120 mg/day). The weakness and pain in the thigh and calf muscles disappeared on the 5th day and both CPK (50 IU l⁻¹) and LDH (156 IU l⁻¹) decreased to normal levels by the 7th day of treatment. He was discharged from hospital on lower doses of prednisolone (10 mg/day) and CoQ (60 mg/day). However, he stopped the treatment and after about another two weeks he presented with similar pain in proximal muscles and weakness. He was administered CoQ (120 mg/day) without cortisone for 10 days, which was associated with complete remission. He continued taking CoQ (60 mg/day) for another 20 days without any recurrence. Plasma levels of lipid peroxides, malondialdehyde and diene conjugates showed a marked decrease after 4 weeks of treatment with CoQ.
DISCUSSION

These case reports indicate that treatment with CoQ in three completely different complaints, which are apparently linked by one common factor, a deficiency of certain antioxidants, may be beneficial. Acute glomerulonephritis and amyotrophic lateral sclerosis have no specific medical treatment at present, while the third, polymyositis, usually responds to corticosteroid therapy or, in the case of non-response, to immunosuppressive agents. Beneficial results in all three cases are expected in view of the possible aetiology of all three residing in an autoimmune reaction.

At an international congress on vitamin E held in Venice in 1955, O'Connor reported that normal kidney function was restored in both acute and chronic nephritis with massive doses of vitamin E and Butturini claimed benefits in nephrotic syndrome using similar therapy. About the same time, Mervyn observed low tissue levels of vitamin E and CoQ in postmortem kidneys from patients with nephritis compared to healthy kidneys (personal communication, Len Mervyn, Lamberts, Kent, UK). The response of our patient with acute glomerulonephritis to CoQ alone indicates that it is useful. What is of interest is the fact that when renal function was restored to normal, all antioxidants increased in blood plasma, although only CoQ was given (see Table 1).

The second case diagnosed as motor neurone disease appeared to respond well to treatment with CoQ alone, with increased antioxidant status and decreased free radical stress. Lack of response to vitamin E and the B complex suggests a more specific antioxidant deficiency of CoQ. However, in the absence of measured plasma levels in these cases, it is difficult to assess any degree of deficiency.

Our patient with polymyositis did not respond to conventional corticosteroid treatment. Antioxidant vitamin status was within the normal range but free radical damage criteria showed increases. These were reversed after CoQ therapy combined with that of prednisolone, although complete remission of symptoms occurred with the CoQ alone. Improvement in clinical status paralleled decreased free radical damage, indicating the response to antioxidant activity of CoQ.

Free radical stress has been implicated in the pathogenesis of tissue damage in all three diseases [7]. The brain and spinal cord tissue have certain attributes which make these organs exceptionally vulnerable to free radical attack [7]. The brain is a highly oxygenated structure and it contains large amounts of iron (with poor binding capacity) and polyunsaturated fatty acids, and it is relatively poor in antioxidant enzyme systems. Motor neurone disease is a disease causing degeneration of motor neurons in the Betz cells in the motor areas of the cerebral cortex, brain stem and spinal cord. Most cases are sporadic but occasionally it may occur in families owing to the interaction of genetic and environmental factors. In nephropathy and muscle disease, CoQ deficiency can occur owing to its poor synthesis and increased utilization to fight the disease process. Treatment with CoQ may repair the deficiency and be beneficial.

In the three patients under study, a clinical response was obtained with CoQ therapy alone. These results should be sufficient to stimulate interest in CoQ as the sole therapy in the idiopathic conditions described. However, until more patients at different centres have been treated successfully with this agent, it cannot be claimed to be a worthwhile therapeutic approach. Nevertheless, CoQ is safe and the daily doses used are not excessive. The substance is now readily available and, compared to some drugs, it is inexpensive. It is also possible that CoQ deficiency may be a risk factor for these diseases, which should be diagnosed by assay of plasma levels.

REFERENCES