Hemorrhagic Stroke in Human Pretreated with Coenzyme Q10: Exceptional Recovery as Seen in Animal Models

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Abstract

Minimizing neurologic injury from stroke is still the elusive goal of large scale controlled clinical trials of new synthetic agents whose efficacy is dependent upon prompt post-insult administration. In 26 years of animal model stroke studies, one substance that afforded a markedly higher degree of protection than all others tested was a normal endogenous molecule, coenzyme Q10 (Q10). Because of increasing worldwide use of Q10, we are able serendipidously to report on possibly the first observation of a human recovering almost completely from an unexpected cerebral hemorrhage following four weeks of pretreatment with Q10 at a pharmacologic dose commonly employed for a wide variety of disorders. Clearly, clinical studies are needed to confirm the significance of our observed result. These would be facilitated by the safety and efficacy of Q10 already proven in nine large scale international trials in cardiomyopathy, etc., and its apparent benefits in numerous disorders, including AIDS and possibly aging itself. However, the confirmation should be done in trials specifically designed for stroke because of detection difficulty arising from the anticipated protection. If confirmed, this result does not diminish the urgent need for development of synthetic stroke agents, but may facilitate their realization by decreasing the protective functions needed from the agent.

Abbreviations: coenzyme Q10, Q10, ; cardiovascular diseases, CVD.

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Introduction

Ischemic reperfusion injury (IRI) in various organs, especially brain, heart and kidney has recently been cited as responsible for the majority of deaths in developed countries.[1] Annual U.S.A. stroke specifics include 150,000 deaths, and only circa one third of the 400,000 survivors have little or no impairment.[2] We report an unexpected favorable recovery from a complicated cerebral hemorrhage that is consistent with the remarkable results obtained for animal models of stroke using coenzyme Q10, reported to be far superior to all other substances tested.[3,4] Gerbil survival to 40 days following carotid ligation induction of ischemic stroke, was 45% on Q10, over twice the 20% on naloxone, the second best agent tested (no deaths occurred after day 4 and the experiments were terminated at day 40). Such recoveries are not implausible since Q10's exceptional antioxidant and free radical quenching properties have been cited as offering "great implications in the treatment of IRI."[5] The first isolation of Q10 was from beef heart mitochondria by Frederick Crane et al at Wisconsin in 1957. After determination of the molecular structure and synthesis of Q10 by Karl Folkers and his coworkers at Merck in 1958, its successful use in cardiovascular diseases and a steadily growing list of other conditions that now include cancer, AIDS and aging in humans and animals have been reported.[5-12] It has been shown to be safe and efficacious in nine large scale international trials, and has no known toxicity or side effects.[5] At least three functions have been demonstrated for Q10 and it must be continually replaced throughout life;[5] it is

necessary for: bioenergetics in the mitochondria; stability of mitochondrial and other cellular membranes; and important antioxidant roles in many tissues (including stronger protection of LDL against oxidation than is provided by vitamin E). Endogenous synthesis of Q10 uses a complex and easily imperiled process requiring many vitamins and other nutrients as substrate. Low levels of Q10 in blood and other tissues have been associated with cardiovascular diseases, cancer and other disorders. Such Q10 deficiency states may result from at least three factors: increased utilization, reduced endogenous synthesis and inadequate dietary intake.[5] Oral supplementation of Q10 between 100 and 400 mg/d has been reported to produce significant dose-dependent enhancement of recovery in these patients.[5] Such amounts of Q10 are unlikely to be provided by dietary intake only.[10]

Patients and Methods

We have been engaged in a program designed to accelerate evaluation of the remarkable efficacy reported in recent years for Q10 in animal and human studies of a wide variety of disorders including CVD, neurological and immunological. We have posted a Q10 update on a University of Washington web site[5] and urged physicians everywhere to consider its relevance to their practices. Incidental to this routine study of symptom and Q10 blood level response in many patients of numerous physicians, we were able to recognize, analyze, and report this surprising recovery from an unanticipated stroke due to accidental trauma in one patient.

Stroke Patient Pretreated with Coenzyme Q10

The patient was a 69 year old Caucasian female with marked short term memory deficit associated with recent onset diabetes, poorly controlled by diet. She had entered the care of a local physician (without complete medical records) and elected to supplement Q10 (Nutricom Products, PO Box 3345, Saratoga, CA 95070), 400 mg chewed with circa 5 grams of fat (to enhance absorption) at one meal each day. In our view, her age and diet made it likely that a Q10 deficiency state existed.[5] After four weeks of supplementation she suffered bifrontal cerebral hemorrhage due to a fall on pavement. That trauma resolved quickly and she was released. Two weeks later she was again brought to the hospital in coma following syncope in her residence with (suspected) head trauma. Vitals: T: 99.7, P: 110, R: 18. BP: 136/74.

Her temperature peaked at 102.2 one hour subsequent to presentation. Basilar crackles were heard in the left lung field and a 3/6 systolic murmur was noted at the left sternal border. Her abdomen was nontender and her neurologic examination revealed the absence of deep tendon reflexes. Corneal reflexes were not intact. The patient was unresponsive even to pain. Her white blood count was 12,500 with 92% lymphocytes. Her serum glucose level was 619 and her serum beta oxybutyrate was 13.4. A chest x-ray showed a left lower lobe infiltrate. Her urine culture was positive for both Candida albicans and Group D enterococci. A CT scan of the head was performed and showed resolution of a bifrontal hemorrhage which had been noted after her previous fall. Encephalomalacia was noted in the area of a prior right temporal lobe hemorrhage, and a small epidural hemorrhage was seen in that region, as well. During the course of her hospitalization, the patient was treated using an insulin drip, then graduated to sliding scale insulin. A lumbar puncture was performed and was unremarkable; CSF cultures were negative. Seizures which had been noted at the time of admission were controlled using Dilantin. Intravenous antibiotics were used to treat the pneumonia and urinary tract infections. Gradually, the patient's level of consciousness returned to normal. A right-sided hemiparesis was then evident. This resolved over the next few

days. She was oriented to name and place at the time of discharge but could not identify the year or the president. She was able to feed herself and was eating 100% of her meals prior to discharge. On her tenth hospital day, she was found to be afebrile and euglycemic and was discharged to a skilled nursing facility on antibiotics, anticonvulsants and insulin.

In the course of an examination two days subsequent to discharge, the patient was found to be alert and talkative. She was still unable to name the president, but quite capable of discussing events from the distant past identifying common objects and ambulating without difficulty. Her short-term memory was still very poor. No motor or sensory deficit was noted.

Discussion

Of principal interest, as stated above, is the fact that for several weeks prior to her initial fall and hospitalization discussed here, the patient had been taking Q10, 400 mg daily at one meal with ca 5 g of fat (i.e. peanut butter) to enhance absorption. Despite sustaining numerous significant insults in close temporal proximity, including a bifrontal cerebral hemorr-hage, an epidural hemorrhage, diabetic ketoacidosis and pneumonia with its attendant hypoxemia, this patient was able to return to her premorbid state with no neurologic sequelae.

Pre- and Post-stroke Q10

A neuroprotective effect of coenzyme Q10 given both pre- and post-stroke has been demonstrated by studies in three animal models and reported in the literature.[3,4] The central question of this paper relates to the relevance of those animal results to humans. A variety of animal experiments using Q10 by Bliznakov, Folkers and others[11,13] on immunity and various organ functions have been shown to predict and or duplicate the corresponding effects in humans. Therefore, in view of the number of effects that have been shown to occur in both humans and lower mammalian species, it should not be surprising if the stroke protection reported here proves real. Hence, we suggest that clinicians should inquire if Q10 pretreatment had occurred in those rare cases where recovery from stroke seems far better than appeared possible during the acute phase. In addition, since: [1] the gerbils were treated successfully with Q10 four hours after induction of stroke; and [2] no side effects have been observed in humans from Q10 in large numbers of clinical trials,[5] prompt post stroke administration of Q10 in humans seems indicated. Kandela recently reported a six-hour post-stroke therapeutic window exists in humans also.[14] What harm to put Q10 in hospital formularies?

Reduction of Stroke Incidence

Decreasing incidence is also clearly vital to reducing stroke morbidity and mortality. In spite of the exceptional protection that may prove to result from Q10 (and stroke drugs in development), the physician faces the task of identifying and reducing several classes of stroke risk in essentially all people consuming the developed nations' diets. These individuals will have varying degrees of arteriosclerosis and other lesions due to elevated levels of xanthurenic acid and homocysteine intermittent or persistent since childhood. To reduce the incidence, we suggest physicians must educate the public in simple modalities that utilize certain inexpensive substances (notably pyridoxine, other B vitamins, magnesium and trivalent Cr), previously demonstrated in animal and human studies to prevent vascular disease including stroke. Those studies by Kotake, Ellis, McCully, Mertz, etc., and the methods, published and known for some decades (since Karl Folkers and his coworkers determined the structure and function of pyridoxine), have recently been reviewed.[15]

Additional Reasons for Large Scale Supplementation beyond Middle Age

In addition to protection against stroke, the findings of numerous scientific studies mandate supplementation of Q10 by all humans past middle age to optimize quality of life and minimize cost of health care.[5,7] These include the critical dependence of Q10 synthesis upon diet, its decline after age 20, and the acceleration of all types of disease risk and aging changes associated with that decline.[5] It is of great importance to note that: human brain Q10 concentration at age 80 is decreased to roughly half the value at age 40[7] In both animal and human investigations, diseases of every body system are increased when Q10 deficiency states afflict those systems.[5] In very old mice (aged 16 to 18 months)[11] Q10 has been reported to reverse the immune senescence associated with thymic involution, restoring youthful immune response and resistance to infections and neoplasia.[9,12] The same studies reported that aging itself was markedly slowed in terms of the Q10-treated animals' appearance and agility, and their mean survival time after treatment was 56% longer than in controls, 218 vs 140 days; the ages at death were ca 104 weeks for the last control mouse and ca 150 weeks for the last treated mouse.[11,13] From human clinical trials in cardiology, cancer and infectious disease alone it appears that significant improvements in health and major decreases in cost of health care are associated with Q10 supplementation.[5] The rationale for Q10 in AIDS and a striking clinical response in human AIDS patients treated with Q10 have been reported by Folkers, Langsjoen, et al.[5,16]

Recommendations to the Clinical Community

Hence, oral supplementation of Q10 to compensate for age impaired synthesis and inadequate food content should provide many clinically established benefits. In addition to these, if the present paper does truly reflect a human equivalence of the impressive animal stroke model findings, widespread Q10 intake by those above middle age can produce a marked reduction in the incidence and severity of stroke. These results suggest it is urgent that the need for Q10 supplementation be evaluated for people above middle age, and especially for those considered at risk for cardiovascular disease including stroke. At the present time, far less than 1% of the US population may be supplementing Q10 at or above the 100 mg/day level. Three major reasons for this are: high cost; lack of physician exposure to information; and dearth of clinical laboratories that offer the Q10 blood test at a low cost (ca US$50). Solutions to these three obstacles may be at hand: [1] The retail cost of a 100 mg chewable Q10 tablet emulsified with lecithin has recently been reduced 62% by one California company; hopefully, increased use will result in lower costs from Japan for all distributors; [2] A physician's update written by Langsjoen is available on the web;[5] and [3] With that update, there is an extremely brief electronic questionnaire to assess demand for the blood-test as a function of price. If demand is sufficiently high, clinical labs at the University of Washington hope to automate the research assay (provided to us by Folkers) and be able to offer a low cost test to facilitate the clinical evaluation of Q10 supplementation in every medical specialty. Meanwhile, all physicians could benefit from 40 years of clinical experience by the well-known Canadian investigator, Wilfrid E. Shute, MD, using vitamin antioxidants in cardiovascular disease and stroke in the "early days" before Q10.[17]

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