A Brief Update on Ubiquinone (Coenzyme Q_{10})

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Abstract

Ubiquinone is one of the two most important essential nutrients (the other being ascorbic acid). These two molecules, along with other essential nutrients, have been rejected as unpatentable and unprofitable by certain "authorities" and interests, according to exposés by Pauling and others.[1,2] This has been one of the most lethal errors of modern medicine because no cell, organ, function or remedy can avoid failure unless essential nutrients, especially these two, are optimal. Supplementation of both is mandatory: for ascorbate, lifelong (since humans can't synthesize it); for ubiquinone, increasingly with age. In this update, to facilitate study of ubiquinone, we seek to assemble in one place vital information that is not widely known.

Introduction

Ubiquinone has been listed for years as an essential nutrient in the Physicians' Desk Reference (PDR).[3] The chemistry, history, and the many clinical trials that established the safety and efficacy of ubiquinone were well described in 1995 by one of the leaders in this work, Peter H. Langsjoen, M.D., FACC, in his Introduction to Coenzyme Q_{10}. In the 1997 PDR, Langsjoen's "Intro" is cited but the full text is not in print.[4] With his permission, we placed the entire "Intro" on a web site[5] with much other material in 1996. From his 65 references, we transferred selected reports to the bibliography here and numbered them as follows: nine large scale placebo controlled clinical trials;[6-14] nine additional open-label trials,[15-22] including the 2,664 patient multicenter study in Italy reported by Baggio;[23] and the Proceedings of eight international symposia.[24-31] The web site created in 1996 as a "Physicians' Update on Coenzyme Q_{10}", was made in response to the request from Clinical Chemistry that we determine the demand for blood tests. Clinical Chemistry would need to robot (automate) the complex 14-step HPLC assay (provided to Ely by Karl Folkers) sufficiently to make it efficient to run and affordable. To determine if the demand for the ubiquinone blood test justifies this considerable effort, the web site asks that physicians complete the extremely brief electronic questionnaire linked to the site.

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Ubiquinone Turnover

Naturally, many details concerning the pharmacokinetics and clinical use of ubiquinone have been learned since the 1970s in the cited clinical trials, symposia and in related research. Possibly the most important details are those related to ubiquinone body pool and turnover rate that mandate human supplementation. Adult human body pool has been found to be approximately 2 g[32,33] and requires replacement of about 0.5 g/day based on its average turnover rate of about 4 days in various tissues.[34] This must be supplied either by endogenous synthesis or from exogenous sources. Synthesis decreases progressively in humans above age 21. Furthermore, the average ubiquinone content of the western diet is less than 5 mg/day.[35] Thus, ubiquinone supplementation appears to be the only way for older people, and certainly the ill, to obtain the major proportion of the 0.5 g/day need. Failure to supplement by the aged, ill or stressed, can have tragic consequences in the form of irreversible damage in the brain, other organs and mitochondria everywhere.[36,37] In addition to production of adenosine triphosphate (ATP, molecules for energy), and maintenance of cellular and mitochondrial membrane fluidity, ubiquinone has a possibly even greater value. This is its free radical quenching

ability (50 times greater than vitamin E), that prevents the above mentioned irreversible oxidative damage.

In Professor Littarru's authoritative 91-page book, he devotes 65 pages (71%) to ubiquinone's defense against free radical damage.[38] He points out that knowledge of mitochondrial aging in unsupplemented mammals has been published since 1985.[38] Regarding the aging mechanism, Littarru and others have stated that low values of ubiquinone permit oxidative damage to the DNA of mitochondria, permanently impairing their ability to function. If, by supplementation, the ubiquinone level is restored to its proper value, the rate of oxidative damage will be lessened, but the impairment remains. Doesn't it appear that physicians who tell their patients not to take ubiquinone, are saying: "Age more rapidly, have more health problems including cardiopathy, intellectual impairment (especially strokes) and die early"? Isn't this what is happening in America today?

Safety of Ubiquinone

In many large-scale clinical trials, oral ubiquinone has been shown to be safe and efficacious at blood levels of about 4 ppm (considered pharmacologic and attained by 800 mg/day). In addition, even at levels of 80 ppm measured by the Japanese in 1984 with an IV ubiquinone preparation, only beneficial effects were reported. A new injectable liposomal ubiquinone is available from Eisai. A caveat: in patients with alkalinized stomachs, oral Candida can colonize upper gut (potentially lethal); before prescribing ubiquinone, their physicians should study Marshall et al.[39] Our studies show that ubiquinone enhances growth of Candida albicans.[40]

Stroke

Since 1972, in studies of stroke in three animal models (dog, rat, gerbil) ubiquinone was the only agent giving complete protection and this was over two times more often than the next best agent (naloxone) of the many tested to date. Some of the animals were pretreated and some post-stroke (less than 12 hrs). None of the 50+ synthetic stroke agents tested in humans has yet proven successful as of February 2000. If mainstream medicine has any humanistic motivation, why doesn't it use ubiquinone in the interim?

The first human observation using ubiquinone was in a patient predicted by the very experienced stroke specialists in a large California facility to remain permanently comatose. She recovered completely after about 10 days in coma.[41] She had been in treatment for a memory problem with oral ubiquinone 400 mg/day for a month prior to an accidental head trauma with massive hemorrhage. In a second case (unpublished), a woman in her sixties, the mother of Dr Fudenberg's former secretary, had a similar stroke with the same prognosis of permanently vegetative; he traveled from South Carolina to Oklahoma, got the patient out of hospital and gave her 400 mg ubiquinone b.i.d. (starting four days post-stroke, which we felt would be too late) and she recovered to much better than her pre-stroke condition (i.e., mental acuity, speech, agility, equal to what she had experienced in her 40s). There has been a third case which we do not "advertise" because it is extremely important to elevate ubiquinone as rapidly as possible to minimize the ischemic reperfusion injury. This is a 70-year old male professional dancer in Seattle who was given ubiquinone in similar oral dosing starting on the eleventh day and made progress much above predicted; he regained speech and ability to do dance steps but had difficulty with names and his recovery plateaued after a few weeks; his stroke was not comatose and his recovery was not complete to his pre-stroke condition. Can't the medical (and lay) readers of this journal help stimulate a grass-roots evaluation of this simple innocuous treatment? We emphasize that we are not ad-

vising people to self-treat. However, everyone must realize that, each year in the U.S.A. alone, over 650,000 families have a loved one hospitalized for stroke. Only 1/4 of these escape death or permanent disability. The families have a right to know that ubiquinone exists at their health food stores, has the properties described above and appears likely to avert the tragic prognoses. If you readers pass this information to such families, many, in their desperation, may elect ubiquinone. We request the readers suggest: (1) this be done with the best open-minded preventive medicine supervision available; and (2) the supervising physician report by email (apresi@aol.com) the patient identification, date of stroke, treating stroke center, prognosis, time delay before ubiquinone (swallowed or intubation), dosage including other agents, and progress up to four weeks post-stroke.

Ubiquinone in Cardiology

Negative "Studies": A very few negative studies from the early 1990s up to present have reported lack of beneficial effects of ubiquinone for congestive heart failure (CHF). Fundamentally, these negative studies have been criticized as cases of too little ubiquinone, for too short a time and too late in the course of CHF in the trial patients. Correct treatment should include the essential nutrients (ubiquinone, vitamin E, and ascorbic acid) and no statins. Self-appointed "experts" who have no experience in treating CHF correctly have praised these few negative "studies" while ignoring the vastly greater literature cited above including the large scale trials demonstrating the positive aspects of ubiquinone. Could the negative studies have been "designed" to produce failures? Is this action designed to oppose acceptance of the low cost (unprofitable), non-toxic (endogenous), versatile ubiquinone modality? Certainly the investigators and extollers of these negative "trials" appear to be totally oblivious of the fundamental physiology of ubiquinone requiring its constant replacement at 500 mg/day by synthesis from exogenous substrate or by supplementation.

Positive Studies: Clinical observations of cardiologists who have had extensive experience with the use of ubiquinone (such as Peter Langsjoen) find dramatic improvements in heart function in CHF patients treated with ubiquinone prior to the development of irreversible damage. While the optimal dose of ubiquinone in the treatment of congestive heart failure is not established, it has become clear over the past 15 years, that 100 mg per day (the dose used in some of the negative studies) is suboptimal for the majority of patients. A higher dose of ubiquinone for a longer period of time has demonstrated highly significant benefit in many previously published trials. An extensive review of ubiquinone use for cardiovascular disease (CVD) in 34 controlled clinical trials and several open-label and long-term studies has recently been published.[42]

Statins: Toxic Misuse: Karl Folkers, the frequently honored chemist who first determined the structure of ubiquinone in 1958 and was Director of Research for Merck for 20 years, warned in 1990[43] that heart disease is caused or worsened by the depression of ubiquinone that is associated with statin use and that ubiquinone must be supplemented adequately in patients given statins. Others have also documented this high level mandate for use of ubiquinone with statins.[32,42] Theoretically curable CVD patients on statins will progressively decompensate and decrease ejection fraction if given only 100mg ubiquinone/day or less. They can reverse these losses and recover if given sufficiently greater than 200mg ubiquinone/day. If the lethal effects of violating this higher need for ubiquinone created by statins are overlooked, CVD patients are trapped in an expensive downward spiral to death and vastly more dollars are spent on their care

than if given adequate ubiquinone. Ironically, statins may only be needed in the truly rare familial hypercholesterolemias. It is well known that: (1) cholesterol is not a risk factor for CVD unless LDL is oxidized; and (2) this is simply prevented by supplementation of vitamin E in nearly all humans.[44,45]

Ubiquinone and Ascorbic Acid (AA)

There can be little expectation for significant improvement in ejection fraction or any other parameter of cardiovascular function without high AA levels. These levels are necessary for hydroxylation reactions in the constant restoration of the structural proteins, collagen and elastin.[46] Virtually all unstressed mammals need roughly 50 mg AA/kg body weight daily, or ~3.5 g/70kg in humans. Of course, CVD patients may not be exactly "unstressed". If AA intake is only 60 mg or 200 mg (the current and proposed RDAs for AA), patients would likely not have frank clinical scurvy. However, at these low intakes, it is extremely unlikely that they could restore or maintain youthful elasticity of blood vessels to increase ejection fraction, even though ubiquinone is supplied. Moreover, glycemic level must be controlled; AA cannot enter cells of hyperglycemic tissues because glucose competitively inhibits its insulin-medicated active transport (Ely, 1972, unpublished). Thus, modest hyperglycemia can cause scorbutic conditions to exist in the intimal surface of blood vessels even when plasma AA levels are reasonable.

Glycation and Aging

Ely discovered in animal model work (and confirmed with Warner et al in a study of 300 human patients) that elevated plasma AA levels antagonize glycation of hemoglobin and all other proteins, which improves health and slows aging.[47] Unfortunately, we are then faced with the nuisance that glycated hemoglobin reads falsely low when used as a measure of average blood glucose level for purposes of glycemic control. Bliznakov demonstrated restoration of youthful thymic response against viruses and tumors and major increases in lifespan of very old mice given ubiquinone.[48] There is ample evidence that high levels of ubiquinone, and AA, slow the detrimental biochemical, structural and other changes that occur with aging in all mammals. Ubiquinone may reverse some age-related bioenergetic degradation that acutely affects the systems with the highest energy demand (cardiovascular and immune). Failure in these systems is a major cause of morbidity and mortality in the elderly. However, it has been known since 1985 that mitochondrial aging (in all systems) that accumulates in intervals when ubiquinone is low, especially the brain, is not reversible. Supplementation of ubiquinone and AA with glycemic control should be considered by all adults, especially the elderly, ill and stressed. Amounts of AA needed in health and disease have been discussed previously.[2]

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