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The Use of Vitamin E in Mitochondrial Antioxidant Cocktails

The inclusion of pharmacological amounts of vitamin E in mitochondrial antioxidant cocktails suddenly became controversial in 2004 with the publication of a meta-analysis of 19 published trials of vitamin E treatment of subjects with, or at risk for, adult-onset medical conditions, including cardiovascular artery disease, precancerous lesions, and smokers, together with three large non-disease cohorts of healthy adults [Miller et al, 2004]. The study endpoint assessed in the meta-analysis was mortality. Unfortunately, because the study concluded that vitamin E in excess of 400 IU/day increased mortality, vitamin E has since been removed from or its dose substantially reduced in the treatment of many children and adults with mitochondrial disorders, sometimes followed by deterioration of mitochondrial function and neurological damage. However, as pointed out 2 years later by Robinson et al. [2006], there were many design flaws in the studies included in the 2004 meta-analysis, such as the lack or inadequate amounts of vitamin C and the failure to adjust treatment based on measures of oxidative stress and levels of vitamin E. Moreover, the trial contributing the greatest statistical weight to increased mortality involved adults with high-risk cardiovascular disease, which has doubtful relevance to the treatment of children and most adults with mitochondrial diseases. In addition, the omission of supplemental CoQ10 from the studies prevented adequate neutralization of higher levels of vitamin E chromanoxyl radicals accumulating in the inner mitochondrial membrane. In contrast, when patients with mitochondrial disorders are given high-dose vitamin E together with vitamin C and CoQ10, there usually is coincident clinical improvement and amelioration or normalization of systemic markers of mitochondrial function, such as plasma levels of CAC intermediates (R. Kelley, unpublished data). Clinical evidence for the importance of giving enough vitamin E to reach a level of at least 150% of the upper limit of normal comes from the author's experience with several treated, clinically stable patients with historically progressive mitochondrial diseases who suddenly worsened after many years of stability. In each case, the transient deterioration was traced to an unexpected fall into the normal range of a previously therapeutic level of vitamin E, due to corrupted vitamin E, technical problems in the preparation of mitochondrial cocktails, and, in one patient, use of desflurane, an inhalational anesthetic that causes oxidative stress and inactivates vitamin E [Eroglu et al., 2010]. All patients improved and have since remained stable after their vitamin E levels were restored to the target therapeutic range of 150 to 200% of the upper limit of normal.

References

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