lipophilic antioxidant. Although these effects were not very pronounced, vitamin E has been widely used worldwide because of its possible antioxidant effects. Therefore, we believe that the examination of the effect of vitamin E on SOD in this study is of considerable interest. However, the activity and mRNA of SOD in PC-12 cells remained unchanged after supplementation with Vitamin E; this phenomenon can be explained by PC-12 being a tumor cell line which may lose its response to antioxidant stimulation.

In the pathophysiology of atherosclerosis, atherogenesis is initiated by an oxidation of lipids in low-density lipoprotein (LDL)[16] Antioxidants have thus been suggested to be effective in protection from atherosclerosis. Vitamin E is the main naturally occurring lipophilic antioxidant. Similar to the endogenous enzymes, such as catalase, superoxide dismutase (SOD), glutathione peroxidase (GPX), and glutathione-S-transferase, that protect cells through free radical-quenching activity, vitamin E can lower lipid peroxidation at an early stage of OFR attack.[17] Actually, some epidemiologic studies have demonstrated an association between an increase of vitamin E intake and a lowering of morbidity in coronary artery disease.[18-27] The benefit was greatest in subjects taking 100 to 250 IU of supplemental vitamin E per day.[25] Our data show a similar result of direct incubation of vitamin E at a suitable concentration (50 μM) with RBA-1 cells producing an increase in both the activity and mRNA level of SOD within 2 days. The mRNA levels of catalase and GPX, other enzymes in the redox system, also increased in these cells. In this study, short-term treatment with a low dose of vitamin E increased the activity and mRNA level of SOD. Although the underlying mechanism is not clear, it is possible that vitamin E has an effect on cell growth, which can result in an increase of SOD. Also, it is possible that low-dose vitamin E can directly stimulate the genesis of SOD. In the subcellular defense system against oxidative damage, SOD is one of the key enzymes which decrease superoxide radicals.[28] This enzyme, distributed in cytosol and/or mitochondria, is called a free radical scavenger because it can reduce the formation of cytotoxic radicals to prevent tissue damage. Therefore, an increase of SOD in cells seems helpful in the prevention of free radical damage to the brain. However, long-term (7-day) incubation of vitamin E with RBA-1 cells produced a down-regulation in both the activity and mRNA level of SOD. No change of surviving cell numbers in vitamin E-incubated samples ruled out the death of cells. Vitamin E can scavenge free radicals to form tocopherylquinone that may be recycled to vitamin E by glutathione.[29] Therefore, repeated action by vitamin E seems responsible for this down-regulation of SOD. In our laboratory, in order to support this view, the effects of vitamin C was also tested. We found that long-term treatment with a high dose of vitamin C has similar results as the findings in this study (unpubl. observations). Also, long-term (7-day) incubation of vitamin E produced a decrease of mRNA levels of catalase and GPX, other enzymes in the redox system, in a concentration-dependent manner. Down-regulation in the redox system of a cell by repeated stimulation of vitamin E can thus be considered. However, this phenomenon in long-term supplementation of vitamin E to humans needs further evaluation.

In conclusion, the present study shows that supplementation of vitamin E in cultured RBA-1 cells at suitable concentrations may stimulate the expression and activity of the endogenous antioxidant enzyme, SOD, within 2 days. However, long-term supplementation of vitamin E resulted in the down-regulation of SOD; additional evidence is needed to determine whether this phenomenon is deleterious in humans.

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