Graefe's Arch Clin Exp Ophthalmol (1997)
235: 190–191

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Inhibition of bovine RPE cells by vitamin E succinate

Received: 1 October 1996

Dear editor: We read with great interest the article by Sakamoto et al. [1] reporting an inhibition of proliferation and migration of bovine retinal pigment epithelial (RPE) cells cultured in vitro by vitamin E succinate. In 1994, we reported a dose-dependent inhibitory effect of vitamin E on human RPE cell proliferation with therapeutic implications for proliferative vitreoretinopathy [2]. Unfortunately, Sakamoto et al. [1] did not cite our article. We found inconsistent inhibition at 25 μM vitamin E; more complete inhibition was achieved at 50 μM and 100 μM, doses which can be reached within the eye with oral supplementation. We never observed toxic effects of vitamin E on human cell cultures, even after 8 days of incubation [2, 3].

We did not test the effect of vitamin E *succinate* on human RPE cells since we noticed cytotoxic effects at rather low concentrations. Such a conclusion may be supported by the findings reported by Sakamoto et al. themselves that "after 5 days of incubation in vitamin E succinate (25 μM) RPE cells changed shape from epithelioid to round and started to float into the medium" and "cell viability ... was slightly impaired at 100 μM after 3 days".

Sakamoto et al. used bovine RPE cell cultures and tested only a dose of 25 μM of vitamin E and found a slight stimulation of cell growth. This is an unusual finding that might be interpreted as the removal of lipoperoxide-induced inhibition of growth, occurring at later incubation stages.

References

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Reply

Received: 13 December 1996

Dear editor: We read with interest the comments by Mojon et al. concerning our recent publication in *Graefe's Archive for Clinical and Experimental Ophthalmology* [1]. We apologize for not quoting his recent publication [2]; at the time our paper was submitted, his paper had just been published and was not yet in the Medline database.

While our article studied primarily the effects of vitamin E succinate on retinal pigment epithelium (RPE) cell proliferation and migration, Mojon et al. studied the effects of vitamin E on RPE proliferation. They found that vitamine E inhibited RPE proliferation without toxicity at the doses tested. In our own experience and in the experience of others, low doses of σ-α-tocopherol (vitamin E) do not inhibit cell growth in vitro for RPE cells [1] and a variety of cancer cells [3–6]. Gopalakrishna et al. found in lung cancer cells that only higher doses of vitamin E (250 μM) significantly inhibited thymidine uptake [7]. Some of the differences between our study and that of Mojon et al. may be due to differences in methodology. We perform our studies in log phase of cell growth while they use cells grown to subconfluency, made quiescent by growth in low serum and then tested in the presence of 10% serum.

Mojon et al. indicate that they did not test vitamin E succinate on RPE because of toxicity at rather low concentrations. We do not believe that vitamin E succinate causes acute cytotoxicity because the effects on cell survival occur only after 3 days of incubation, suggesting an active process of cell death, possibly apoptosis. In retrovirus-transformed cells [8] and human breast cancer cells [9] vitamin E succinate inhibits cell proliferation by a cytostatic mechanism which may be mediated by TGF-β.

As indicated by Mojon et al., we found that vitamin E stimulated slightly the proliferation of RPE cells, a finding that has been previously reported in vascular endothelial cells [10] and cancer cells [8]. We agree with their speculation that this may be a result of removal of lipid peroxides.