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Abstract

Anti-angiogenic activity of melatonin in advanced cancer patients

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Objectives. The anticancer activity of the indole melatonin has been explained to be due to its immunomodulatory, anti-proliferative and anti-oxidant effects, whereas at present no data are available about its possible influence on the angiogenesis, which has been shown to be one of the main biological mechanisms responsible for tumor dissemination. Vascular endothelial growth factor (VEGF) is the most active angiogenic factor, and the evidence of abnormally high blood levels of VEGF has been proven to be associated with poor prognosis in cancer patients. To investigate the influence of melatonin on angiogenesis, in this preliminary study we have evaluated the effects of melatonin therapy on VEGF blood levels in advanced cancer patients.

Material and Methods. The study included 20 metastatic patients, who progressed on previous conventional antitumor therapies and for whom no other effective treatment was available. Melatonin was given orally at 20 mg/day in the evening for at least 2 months. Serum levels of VEGF were measured by an enzyme immunoassay on venous blood samples collected at 15-day intervals.

Results. The clinical response consisted of minor response (MR) in 2, stable disease (SD) in 6 and progressive disease (PD) in the remaining 12 patients. VEGF mean levels decreased on therapy, without, however, statistical differences with respect to the pre-treatment values. In contrast, by evaluating changes in VEGF levels in relation to the clinical response, non-progressing patients (MR + SD) showed a significant decline in VEGF mean concentrations, whereas no effect was achieved in progressing patients.

Conclusions. This study, by showing that melatonin-induced control of the neoplastic growth is associated with a decline in VEGF secretion, would suggest that the pineal hormone may control tumor growth at least in part by acting as a natural anti-angiogenic molecule, with a following opposition of angiogenesis-dependent cancer proliferation.

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