Light/Dark Rhythm of the Pineal Immunomodulating Hormone Melatonin in Autoimmune Diseases and its Relation to Lymphocyte-to-Monocyte Ratio

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Abstract

It is known that the immune responses are substantially the end-result of interactions between monocytemacrophage and lymphocyte systems, which may be synthetized by the values of lymphocyte-to-monocyte ratio (LMR). The evidence of abnormally low values of LMR values appeared to be the expression of an immunosuppressive status in cancer patients, whereas its significance occurring in the autoimmune diseases is still controversial. Moreover, both lymphocytes and monocytes have appeared to be under a neuroendocrine control. In more detail, lymphocytes are namely stimulated by the pineal hormone melatonin (MLT), and inhibited by cortisol and mu-opioid agonists. On the other hand, the neuroendocrine regulation of macrophage system is more complex, by depending on the subtype of cells macrophage. Cortisol may inhibit M1 and stimulate M2 macrophages, while MLT would inhibit both inflammatory and immunosuppressive actions of macrophages. Moreover, the progressive decline in the pineal function with loss of the physiological light/dark circadian rhythm of MLT represents the main cancer-related endocrine deficiency, while MLT rhythm in autoimmunity has still to be better investigated. This preliminary study was performed to investigate MLT rhythm in autoimmunity. The study included 25 patients with different types of autoimmune pathology, who were investigated during remission phase of their disease. MLT secretion was evaluated by measuring day and night urinary excretion of its main metabolite, the 6-MTS. No patients showed low LMR values. An altered pineal rhythm occurred in 7/25 (28%) patients. LMR mean values were higher in patients with normal MLT rhythm than in those, who showed no MLT rhythm, even though the difference was not statistically significant. These preliminary results study shows the possible occurrence of pineal alterations in autoimmunity, as well as in cancer, whose clinical significance, however, needs to be clarified by monitoring MLT rhythm during the clinical course of the disease. Moreover, this study would seem to exclude the occurrence of low LMR values also in autoimmunity, at least during the remission phase of disease. Therefore, further longitudinal studies, by monitoring patients with autoimmune diseases during both acute and remission phases of their pathology, will be required to establish the clinical and prognostic significance of the alterations of MLT rhythm in relation to the immune status of patients**.**