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Involvement of the pineal gland and its principal neurohormone melatonin in controlling various physiological activities.

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Abstract:

Melatonin is a neurohormone essentially produced by the pineal gland at night in all mammals. It is a fascinating molecule as it has been described in many different physio- pathological conditions as a molecule that can reverse or prevent the course of the disease. Melatonin has extraordinary antioxidant and scavenging potential both extra- and intracellularly reducing the level of oxidative stress. Suppression in the synthesis of melatonin resulted in depressed cellular and humoral immune response. Further, the reproductive role of melatonin has also been established. The versatility of melatonin in physiological as well as pathological conditions has opened a new gateway for researchers to explore its importance.

Keywords: Melatonin, antioxidant, cellular and humoral immune response

Introduction:

The endocrine system has a crucial role in coordinating the body homeostasis. The long-held view that homeostatic mechanisms are integrated by the nervous and endocrine systems has recently been expanded by anatomical, physiological, and pharmacological evidence that these systems interact with the immune system. It has recently been shown that endocrine hormones and the immune system have interaction to protect the organism from various microbial attacks by providing strength to the body by augmenting immunity.

The pineal and its principal neurohormone melatonin had been shown to have a well-documented link in controlling the reproductive physiology in photoperiodic rodents. In the last decades, it has been suggested that the pineal gland may act as a neuroendocrine transducer, able to convey environmental information into hormonal signals, mainly through the synthesis and the release of its hormone melatonin.

Melatonin has been identified as a remarkable molecule with diverse physiological actions, signalling not only the time of the day or year but also promoting various immunomodulatory and cytoprotective properties. Secretary nature of melatonin shows a circadian rhythm nocturnal maximum and low concentration in diurnal.

(i) Melatonin is a potent Immunomodulator

The lymphoid organs and the endocrine system have interrelation. There are several pieces of evidence supporting a hormonal control of lymphoid tissues. In recent years it has been shown that the pineal organ and its neurohormone melatonin has an immunomodulatory role. The blockage of melatonin synthesis resulted in the depression of cellular and humoral responses(Maestroni et al.1986). Melatonin treatment has been shown to counteract immunodeficiencies(Maestroni GJ 2001). Melatonin has also been shown to protect hematopoietic precursor cells from the toxic effect of cancer chemotherapeutic agents(Maestroniet al.1994). Melatonin enhances the production of interleukin (IL)- 2 and IL- 6 by cultured mononuclear cells and of IL- 2 and IL- 12 in macrophages. The presence of specific melatonin- binding sites in the lymphoid cells provides evidence for a direct effect of melatonin on the regulation of the immune system. The antioxidant and immuno- enhancing effect depend upon its ability to enhance the production of cytokines. The increase in T- helper cells and nocturnal melatonin levels shows a direct relation. Exogenous melatonin treatment increased the number of CD4+ cells in rats. It has been suggested that melatonin provides a time- related signal to the immune systemEsquifinoet al.2004). In a recent study, melatonin implants were found to enhance a defined T helper 2- based immune response under in vivo conditions (i.e. the increase of antibody titres after aluminium hydroxide), thus demonstrating melatonin's potential as a novel adjuvant immunomodulator.

(ii) Reproductive role of melatonin

Since pineal and its hormone melatonin have a versatile function. Studies in seasonal breeders have shown that melatonin regulates the reproductive function probably by its inhibitory action at various levels of the hypothalamic–pituitary–gonadal axis. GnRH production godown by the influence of melatonin.

The photoperiod in seasonal breeders has shown to regulate reproductive performance. It mediates the influence of photoperiod on luteinizing hormone pulsatile secretion. Removal of the pineal gland disrupts the photoperiod- induced reproductive responses to seasonal changes in the duration of night and day.

Melatonin may mediate the moderate seasonal fluctuations observed in the human reproductive function. The increased conception rate seen in northern countries during the summer season has been reported to be caused by changes in luteinizing hormone and melatonin secretion in these individualsKauppila et al.1987&Aleandriet al.1996).

Melatonin has been implicated in sexual maturation. Melatonin exerts an inhibitory role on the hypothalamus and on pubertal maturation. The inhibitory effects of melatonin on GnRH action gradually decline as a result of decreased expression of functional melatonin receptors.

(iii) Melatonin as a Chrono biotic molecule

Melatonin can entrain free- running rhythms, both in normal individuals and in blind people. As melatonin crosses the placenta, it may play an active role in synchronizing the fetal biological clock Melatonin has been shown to act as an endogenous synchronizer either in stabilizing bodily rhythms or in reinforcing them. Hence, it is called a ‘Chrono biotic’ drug (i.e., a substance that adjusts the timing or reinforces oscillations of the central biological clock)(Dawson & Armstrong1996). The first evidence that exogenous melatonin was effective in this regard was the finding that 2 mg of melatonin was capable of advancing the endogenous circadian rhythm in humans and producing early sleepiness or fatigue.

Phase- shifting by melatonin is attributed to its action on MT2 receptors present in the SCN. Melatonin's Chrono biotic effect is caused by its direct influence on the electrical and metabolic activity of the SCN, a finding which has been confirmed both in vivo and in vitro. The application of melatonin directly to the SCN significantly increases the amplitude of the melatonin peak, thereby suggesting that in addition to its phase- shifting effect, melatonin acts directly on the amplitude of the oscillations.

(iv) Melatonin as an Oncotherapeutic Drug

Several experimental studies have proved the oncostatic effect of melatoninBlask et al. 2005). When administered in physiological and pharmacological concentrations, melatonin exhibits a growth inhibitory effect in estrogen- positive, MCF human breast cancer cell lines.

In several studies, melatonin has demonstrated oncostatic effects against a variety of tumour cells, including ovarian carcinoma cell line, endometrial carcinoma, human uveal melanoma cell, prostate tumour cells, and intestinal tumours.

Oxidative stress has been implicated to participate in the initiation, promotion, and progression of carcinogenesis. In terms of reducing mutagenesis, the anticarcinogenic actions of melatonin are primarily attributed to its antioxidative and free radical scavenging activity.

(v) Melatonin's antioxidant action

Free radicals because of their high reactivity can be extremely damaging to macromolecules in cells. Melatonin protects neuronal cells from neurotoxin- induced damage in a variety of neuronal culture media that serve as experimental models for the study of Parkinson's disease(Chen et al. 2005&Dowling et al. 2005).

Conclusions:

Melatonin a principal neurohormone of a pineal organ is reported in unicellular organisms, plants, fungi, other than humans. A wide spectrum of Its actions has been explored today. It acts as a photoperiod messenger molecule, transducing photoperiod changes to reproductive organs, and plays a vital role in the seasonal control of reproduction in certain animals. Melatonin act as a

chemoprotective agent it provides defense against free radicals. melatonin has reported delaying the onset of age-related diseases thus act as a neuroprotective agent. It can be used as a Chrono biotic that is capable of normalizing the disturbed bodily rhythms, including sleep-wake rhythms. Melatonin is implicated in mood disorders. Changes in the amplitude and phasing of the melatonin rhythm have been described in patients with major depressive, bipolar affective, and seasonal affective disorders. Melatonin has been found to be effective in causing clinical remission in patients with major depressive and bipolar disorders. Melatonin synthesis is not restricted to the pineal gland but also takes place in other areas such as the eye, lymphocytes, gut, bone marrow, skin, and gonads where it acts in a paracrine or an autocrine manner. The presence of melatonin in the GI tract suggests that it has a protective role in this organ system. Melatonin therapy reported success in patients with lymphoma, leukaemia, osteosarcoma breast, stomach, and lung cancer thus melatonin has antitumor effects. In humans' circadian rhythms are present in most immune functions, the peak level of circulating lymphocytes is situated close to that of melatonin in a normal (24Hr) environment. Inhibition of melatonin synthesis resulted in depressed cellular and humoral immune response.

The pineal and its principal neurohormone melatonin will be an important matter of future research to investigate the clinical efficacy and safety in detail and melatonin may be used as a miracle drug under different pathological situations.

References:

01 Maestroni GJ, Conti A & Pierpaoli W (1986) Role of the pineal gland in immunity. Circadian synthesis and release of melatonin modulates the antibody response and antagonizes the immunosuppressive effect of corticosterone. *J Neuroimmunol* **13**, 19– 30.

02 Maestroni GJ (2001) The immunotherapeutic potential of melatonin. *Expert Opin Invest Drugs* **10**, 467– 476.

03 Maestroni GJ, Conti A &Lissoni P (1994) Colony- stimulating activity and hematopoietic rescue from cancer chemotherapy compounds are induced by melatonin via endogenous interleukin 4. Cancer Res 54, 4740– 4743.

04 Esquifino AI, Pandi- Perumal SR & Cardinali DP (2004) Circadian organization of the immune response: a role for melatonin. *Clin Appl Immunol Rev* **4**, 423– 433.

05 Kauppila A, Kivela A, Pakarinen A & Vakkuri O (1987) Inverse seasonal relationship between melatonin and ovarian activity in humans in a region with a strong seasonal contrast in luminosity. *J Clin Endocrinol Metab* **65**, 823– 828.
06Aleandri V, Spina V & Morini A (1996) The pineal gland and reproduction. *Hum Reprod Update* **2**, 225– 235.
07Dawson D & Armstrong SM (1996) Chronobiotics – drugs that shift rhythms. *PharmacolTher* **69**, 15– 36.
08 Blask DE, Dauchy RT & Sauer LA (2005) Putting cancer to sleep at night: the neuroendocrine/circadian melatonin signal. *Endocrine* **27**, 179– 188.
09 Chen LJ, Gao YQ, Li XJ, Shen DH & Sun FY (2005) Melatonin protects against MPTP/MPP- induced mitochondrial DNA oxidative damage in vivo and in vitro. *J Pineal Res* **39**, 34– 42.
10 Dowling GA, Mastick J, Colling E, Carter JH, Singer CM & Aminoff MJ (2005) Melatonin for sleep disturbances in Parkinson's disease. *Sleep Med* **6**, 459– 466.