Plasma Melatonin Levels in Psoriasis*

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Melatonin is synthesized and secreted by the pineal gland. A daily rhythm of melatonin secretion, with high plasma values during the dark period, has been found in all vertebrates studied so far. In psoriatics, several hormones, including GH and prolactin, have altered chronobiology, and some studies in humans suggest that melatonin affects the levels of GH and prolactin. We investigated circadian melatonin rhythm in 13 male psoriatics and 13 healthy males with an RIA specific for measuring the hormone in plasma. Samples were taken at 6 a.m., 8 a.m., 12.00, 4 p.m., 8 p.m. and 2 a.m. Differences in (mean ± SD) plasma melatonin levels were analysed by Student's *t*-test. Our results show that psoriatic patients had lost the nocturnal peak and usual circadian rhythm of melatonin secretion. Levels of melatonin were significantly lower than in controls at 2 a.m., and higher at 6 and 8 a.m. and at 12 noon. Further investigations of this disorder of melatonin secretion in psoriasis are needed to understand its significance. (Received September 16, 1987.)

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Melatonin is synthesized and secreted by the pineal gland in all vertebrate species hitherto tested. It circulates in the blood and, in rats, affects the functions of many endocrine organs, especially the neuro-endocrine centres of the central nervous system (1).

A daily rhythm of melatonin secretion has been found in all vertebrates tested so far, with high plasma, cerebrospinal fluid or urinary melatonin values during the dark period, whether the animal is active nocturnally or diurnally (2, 3). In man, prepubertal plasma melatonin concentrations decrease (4) as a function of age. Whether or not menstrual cycle and season of the year affect human serum melatonin is a matter of discussion (5). Environmental light, acting through the eye in adult mammals, has a strong effect on rhythms of melatonin synthesis. In addition, any manipulation causing a major activation of the sympathetic nervous system, at appropriate times of the day, can override the inhibiting effects of light and stimulate melatonin synthesis (1). The rat pineal gland responds to β-adrenergic stimulation, with an increase of melatonin secretion (6, 7).

In mammals it can be considered as well established that the secretion from the pineal gland participates in several neural and neuro-endocrine mechanisms. Among these are the control of gonadal, adrenal and thyroid secretion, sleep and various biological rhythms. There are conflicting data about the influence of melatonin on the endocrine system in humans (8–12), but recent studies suggest that melatonin affects the concentrations of GH (8) and prolactin (8, 12). Previous chronobiological studies have demonstrated that several hormones (ACTH, cortisol, GH, prolactin, melatonin) have a chronobiology in psoriatic patients (13–16) significantly different from that in healthy subjects.

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We have studied the chronobiology of melatonin secretion in a small, very homogeneous group of psoriatic patients over a very short span of the year.

MATERIALS AND METHODS

We have compared melatonin's circadian rhythm in 13 male psoriatic patients, aged 28 to 60 (mean 42) years, versus that of 13 healthy male subjects, aged 20 to 60 (mean 40) years, using an RIA specific for measuring the hormone in plasma.

The patients all have psoriasis vulgaris, with at least 30% of the skin involved. Patients with eruptive, erythrodermic, arthropathic and pustular psoriasis were excluded. Both the patients and the control subjects were hospitalized under standardized conditions. Neither subjects nor patients had taken any drug for at least 10 days prior to the test.

The venous blood samples were taken in March–April 1985 (L : D cycle = 13 : 11) at 6 and 8 a.m., 12 noon, 4 and 8 p.m., and 2 a.m. This last sample was drawn after exposure to total darkness for at least 3 h, and a red light was used for the short time required, since this type of light has been shown to be the least inhibitory to melatonin secretion (17). The blood was collected in EDTA-coated tubes, centrifuged and immediately stored at −30°C until assayed.

Plasma melatonin levels were measured by the RIA method of Wetterberg (18) using commercially available kits (WHB Sweden). The intra-assay variability was 7% and the inter-assay 10%. The assay detection limit was 7.8 pg/ml. The sample volume used was 200 µl. Recovery of melatonin added to calf serum was 96%.

Differences between mean ± SD values were determined by Student's *t*-test.

RESULTS

Our results show that psoriatic patients do not have the nocturnal peak and the circadian rhythm of melatonin secretion and that their mean values of melatonin are higher than those of controls during the day and lower during the night (Table I). Our healthy controls had physiological values of melatonin and normal circadian rhythm, with the nocturnal peak of secretion (Table I).

The statistical analysis (Student *t*-test) showed that plasma melatonin concentrations were significantly lower than those of healthy subjects at 2 a.m. ($p<0.05$) and significantly higher at 6 a.m. ($p<0.025$), 8 a.m. ($p<0.0025$) and 12.00 noon ($p<0.01$). At 4 and 8 p.m. the plasma melatonin concentrations were also higher than those of the controls, but not significantly so.

DISCUSSION

Recent studies on the chronobiology of psoriatic patients have compared the chronobiology of several hormone secretions, including that of cortisol (14), GH (15) and prolactin (15)

Table I. *Comparison of plasma melatonin concentrations (pg/ml, Means ± SD) in psoriatic patients vs. healthy subjects*

	Plasma melatonin concentration (Means ±SD)		
Time (hours)	Psoriatic patients 13 male subjects mean age: 42 years	Healthy subjects 13 male subjects mean age: 40 years	Statistical probability
6 a.m.	55±37	24±8	$p<0.025$
8 a.m.	66±35	17±6	$p<0.0025$
12.00	33±25	14±4	$p<0.01$
4 p.m.	38±24	19±7	$p<0.10$
8 p.m.	50±39	24±8	$p<0.10$
2 a.m.	62±30	80±10	$p<0.05$

with those of control subjects. Some studies in humans have also indicated that melatonin can affect the levels of GH (8) and prolactin (8, 12). These data suggest there may be a relationship between psoriasis and melatonin secretion and our results confirm the existence of abnormalities in levels and bioperiodicity of plasma melatonin concentrations in psoriatic patients.

In a previous chronobiological study, Birau (16, 19) studied serum melatonin concentrations in adult patients (mean age 28 years) with psoriasis vulgaris, before medical treatment, compared with healthy subjects. This study was performed from July 1978 to June 1980 and the blood samples were taken at 2 and 8 a.m., 2 and 8 p.m. Birau observed that in psoriatic patients, melatonin secretion had lost its circadian rhythmicity and nocturnal peak and that serum melatonin levels were significantly lower than in normal controls at 8 a.m., 8 p.m. and 2 a.m. Our research confirms the loss of the nocturnal peak and the absence of a bioperiodicity in melatonin secretion, but plasma levels of melatonin were lower than those of controls only at night (*h*:2 a.m.), which they were also in Birau's patients, but were significantly higher at 6 and 8 a.m. and 12 noon. It is hard to explain these differences. It is possible that an entire psoriatic population does not have the same pattern of melatonin secretion. In our opinion, it is mandatory in this type of study to obtain highly standardized data for a group as homogeneous as possible for several variables, including activity of the disease, type and extent of the dermatosis, age and season of hospitalization.

In our study, we took only one blood sample during the dark phase, so that a shift in nocturnal peak could have been missed, but our objective was to know whether or not there is a change in bioperiodicity of melatonin secretion in psoriasis and our results confirm that psoriatic patients have lost the 'physiological' increase of melatonin secretion, near the middle of the dark period.

Previous studies in humans have revealed aberrations of serum melatonin levels and/or circadian rhythm in several non-dermatological diseases. There was no circadian rhythm in two chromosomal anomalies, Klinefelter's (19) and Turner's (16) syndrome. In patients with spina bifida (19) and sarcoidosis (16), not only there is no rhythm, but the melatonin levels are also high. Aberrations in melatonin levels and rhythm have been observed in psychiatric disorders, including schizophrenia and manic-depressive disease (20). Recent studies in oncological patients with different types of tumour (21–23) have shown high values of serum melatonin levels, sometimes with an abnormal circadian rhythm of melatonin concentration, sometimes with a decreased nocturnal peak of the hormone. At present the pathophysiological significance of the altered melatonin secretion in all these diseases is not known.

It has been demonstrated that, in rats, melatonin has a well established correlation with the polyamine metabolism: pinealectomy induces a decrease in ornithine decarboxylase (ODC) with a shift in its circadian rhythm (24). ODC is the rate-limiting enzyme in polyamine biosynthesis. Polyamines (putrescine, spermidine, spermine) are polycationics substances that participate in both protein and nucleic acid synthesis and stabilize nucleic acid and ribosome structure, protecting them from several denaturating agents (24). Polyamines also facilitate 'histone' acetylation and RNA synthesis. Since all these metabolic phases are decisive for the cell to pass from the quiescent to the active state, the importance of polyamines for cell function and development is self-evident (25). In fact, it has been extensively proved that the tissue polyamine content is remarkably increased in hypertrophic and hyperplastic tissue (26). Psoriasis is a disease characterized by increased keratinocyte turn-over, with a consequent epidermal hyperplasia and, during recent years, some investigators have demonstrated that both urinary and plasma polyamines are increased in psoriasis (27).

We therefore hypothesize that increased plasma melatonin levels and lack in circadian rhythm observed in psoriasis may be correlated with the increased plasma polyamines and

hyperplastic growth of the epidermis. Further investigations of the polyamine biosynthetic pathway in skin are needed to establish whether the high values of melatonin are correlated with the hyperplastic process in psoriasis.

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