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ORIGINAL ARTICLE

Melatonin circadian rhythm in women with idiopathic hyperprolactinemia

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Abstract

OBJECTIVES: Relationship between melatonin and prolactin has been suggested on the basis of both experimental and clinical studies. However, there are scarce and controversial data concerning melatonin concentrations in hyperprolactinemic patients. Therefore, the aim of the present study was to evaluate the circadian rhythm of melatonin in female patients suffering from hyperprolactinemia.
MATERIAL AND METHODS: The study was performed on 28 women aged 17-58 years (mean±SEM: 30.5±1.8 years) suffering from idiopathic hyperprolactinemia and 14 healthy volunteers aged 20–50 years (mean±SEM: 36.4±3.0 years) with normal prolactin levels. Blood samples for measurements of serum melatonin and prolactin concentrations were collected at 08:00, 12:00, 16:00, 20:00, 24:00, 02:00, 04:00, 06:00, and 08:00 h. Melatonin and prolactin concentrations were measured by enzyme immunoassay.
RESULTS: Significant increase in melatonin serum concentrations was also observed in hyperprolactinemic patients in comparison with healthy volunteers during the night. Similar increase was also observed in the area under curve of melatonin concentrations. However, no correlation was found between prolactin and melatonin concentrations in any examined time points.
CONCLUSION: The results of the present study confirm suggestions of the presence of the relationship between melatonin and prolactin secretion.

Introduction

Although relationship between melatonin and prolactin [6, 10], and regulatory role of melatonin in prolactin secretion [6, 30] has been suggested on the basis of both experimental and clinical studies, there are scarce and controversial data concerning melatonin concentrations in hyperprolactinemic patients. Therefore, the aim of the present study was to evaluate the circadian rhythm of melatonin in female patients suffering from hyperprolactinemia.

Material and Methods

The study was performed on 28 women aged 17–58 years (mean±SEM: 30.4±1.8 years) suffering from idiopathic hyperprolactinemia and 14 healthy volunteers aged 20–50 years (mean±SEM: 36.4±3.0 years) with normal prolactin levels. All subjects were admitted to the hospital at least 48 hours before the study. One day before and during blood sampling the period of darkness in patients' room lasted from 22:00 to 06:00 h. Blood samples for measurements of serum melatonin and prolactin concentrations were collected at 08:00, 12:00, 16:00, 20:00, 24:00, 02:00, 04:00, 06:00, and 08:00 h; the nighttime samples were taken under dim red light. All blood samples were allowed to clot for 45 min, serum was removed after centrifugation, and stored at –20°C until assayed. Melatonin and prolactin concentrations were measured by enzyme immunoassay.

The data were statistically analyzed using Mann-Whitney U-test.

The study was approved by the Regional Committee for Studies with Human Subjects. The experimental protocol was explained to each patient, and informed consent was obtained.

Results

The circadian profiles of prolactin and melatonin as well as area under curve of both hormones are presented in Figures 1 and 2. The concentrations of prolactin in hyperprolactinemic patients were significantly higher in all studied time points in comparison to those of healthy volunteers (Fig. 1A). The area under curve of prolactin levels was also significantly higher in women with hyperprolactinemia (Fig. 1B).

Significant increase in melatonin serum concentrations was also observed in hyperprolacinemic patients in comparison with healthy volunteers during the night (Fig. 2A). Similar increase was also observed in the area under curve of melatonin concentrations (Fig. 2B).

However, no correlation was found between prolactin and melatonin concentrations in any examined time points (data not shown).

Discussion

The studies on relationship between melatonin and prolactin secretion in humans brought about not uniform results. Prolactin concentrations increased following administration of melatonin in healthy subjects of both sexes [13, 30], as well as after acute administration of very high pharmacological doses (80 or 240 mg) in healthy males [29]. Melatonin administration had a stimulatory effect on prolactin release without affecting the temporal pattern of its pulsatile secretion in normal women [25]. Melatonin also caused a significant upward resetting of the pulsatile pattern in healthy women but not in men [20]. Moreover, melatonin administered during daytime raised prolactin levels to those observed at night [16]. Prolactin concentration increased also in healthy males following administration of melatonin for 4 days [9]. Lissoni et al. [11] demonstrated that prolactin response to melatonin may depend on maturation stage. They shave shown that the rise in prolactin concentrations following melatonin acute injection was observed in pubertal subjects of both sexes (mean age 17 years), whereas no effect was seen in prepubertal ones (mean age 10 years).

Absence of the nocturnal increase in prolactin concentrations has been demonstrated in woman with surgically excised pineal gland who had no nocturnal increase in melatonin [4]. Moreover, melatonin administration caused robust nocturnal peaks in serum prolactin immediately following its ingestion in the male patient who lacked detectable circulating levels of endogenous melatonin [19].

It has been also demonstrated that prolactin response to TRH stimulation was higher 1 hour after oral intake of melatonin in young women in the follicular phase of the menstrual cycle than that observed after placebo [23].

On the other hand, acute administration of melatonin did not influence prolactin secretion in young healthy men [5]. Long-term (two months) treatment with melatonin did not influenced either concentrations or circadian rhythm of prolactin in healthy men [23]. No changes in prolactin concentrations were observed also after six months melatonin treatment in middle-aged and elderly subjects [22]

Bispink et al. [1] observed decrease in both prolactin and melatonin concentrations after bright light at night with subsequent rise after switching off the lights. However, there was a time delay of about 30 min between the melatonin and prolactin decline and rise. On the basis of this study the authors concluded that melatonin is associated with an endogenous circadian component of prolactin secretion. However, although bright light exposure at night caused decline in melatonin levels, no obvious modification in prolactin patters was observed by McIntyre et al. [14] and Touitou et al. [26].

Like in reports of Vaughan et al. [27, 28], in the present study we did not observe correlation between melatonin and prolactin concentrations at any of stud-

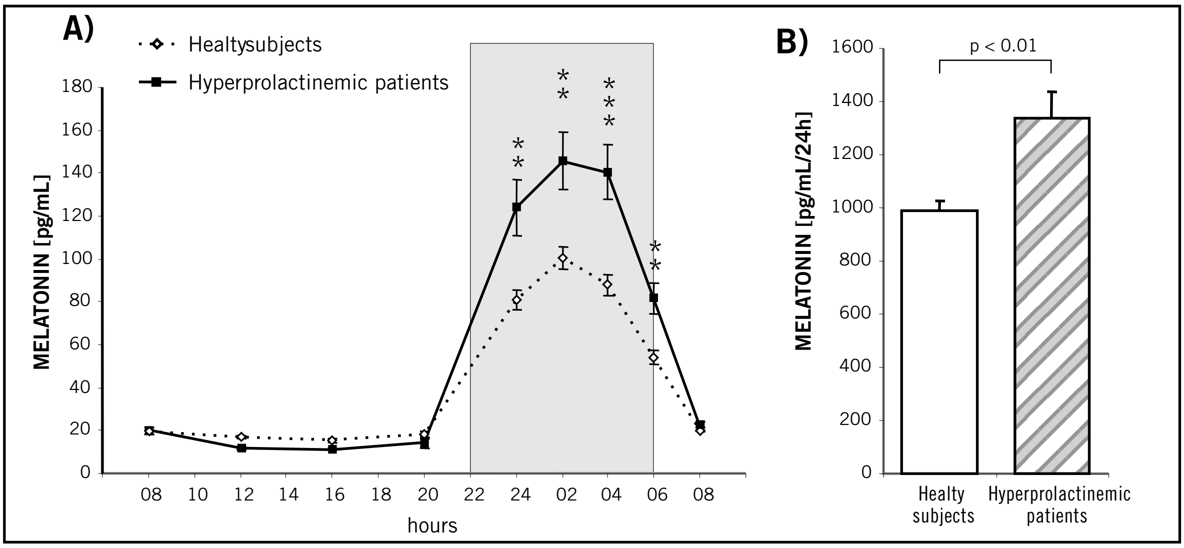

Figure 1. Circadian prolactin profiles (A) and area under curve (B) in healthy individuals and in women with idiopathic hyperprolactinemia; gray area – period of darkness. * p < 0.05, ** p < 0.01 vs. healthy subjects.

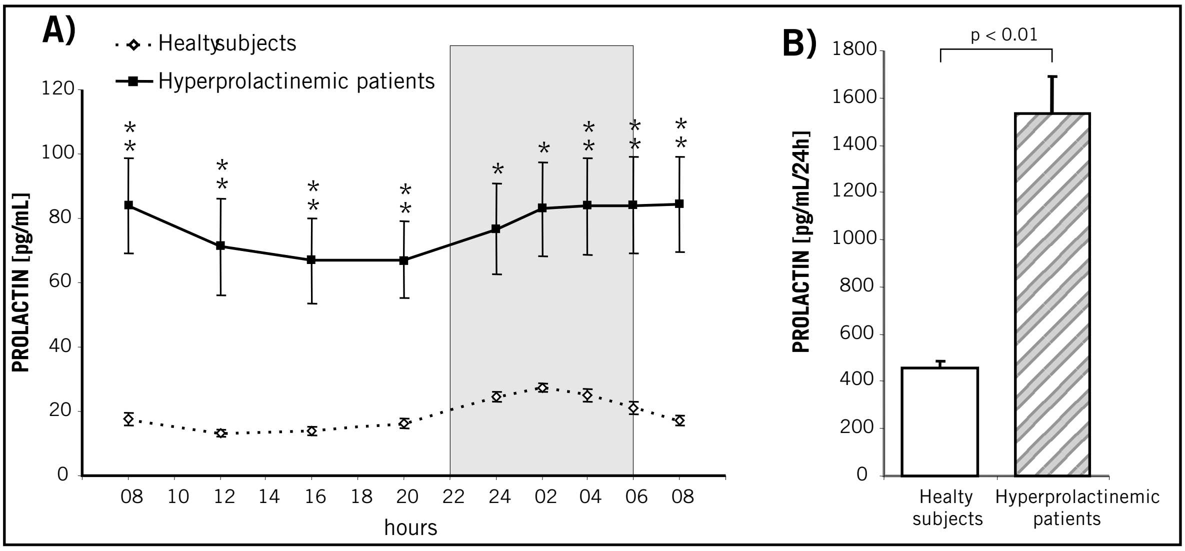

Figure 2. Circadian melatonin profiles (A) and area under curve (B) in healthy individuals and in women with idiopathic hyperprolactinemia; gray area – period of darkness ** p < 0.01, *** p < 0.001 vs. healthy subjects.

ied time points. However, the existence of such correlation has been found in other studies [7, 10, 21, 31].

Also studies on the melatonin secretion in hyperprolactinemic patients brought about not consistent results. Luboshitzky et al. [12] did not find changes in melatonin concentrations in hyperprolactinemic patients. However, the number of both patients and controls was very small (6 vs. 5, respectively). In our initial, preliminary studies using relatively small number of patients suffering from hyperprolactinemia we were not able to demonstrate significant changes in melatonin concentrations [8] but when in the present study we extended the number of patients, the significant increase in nocturnal melatonin concentrations has been found. Moreover, hyperprolactinemia in Luboshitzky et al. [12] study was caused by pituitary adenoma, whereas in our study patients suffered from idiopathic hyperprolactinemia. Similar to our studies, Okatani et al. [17] demonstrated significantly higher nocturnal melatonin levels in 9 hyperprolactinemic women in comparison with 5 healthy subjects. Moreover, the authors observed that administration of 5 mg of melatonin in healthy women resulted in a rapid and prominent prolactin release, similar to that observed at nighttime in patients with hyperprolactinemia [17]. Also, nocturnal urine 6-sulfatoxymelatonin concentrations were significantly higher in patients with hyperprolactinemia compared to their age-matched healthy individuals [2, 3].

The results of the present study confirm suggestions of the presence of the relationship between melatonin and prolactin secretion. The most data accumulated indicate that melatonin may modify secretion of prolactin, though mechanisms involved in the melatonin influence on prolactin are not well understood and seems to be multiple and complex. It is, however, probable that melatonin may exert its effect acting via dopaminergic system because melatonin inhibits the release of dopamine, and a reduction in dopaminergic activity leads to an increase in prolactin secretion [15, 32].Stimulation of prolactin release following melatonin seems not be mediated by opioids [18]. On the other hand, available data, including the results of the present study, suggest that prolactin, in turn, may affect melatonin secretion.

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