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Effect of Melatonin Supplementation on Serum LH Level and BMI in Women with Polycystic Ovarian Syndrome

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Abstract

Background: Melatonin is a pineal gland secreted hormone and plays a role in circadian rhythms, sleep, reproduction, mood, tumor growth, and aging regulation . It has an inhibitory effect on GnRH secretion. Also, body weight has been shown to be affected by melatonin.

The aim of this study: is to evaluate the effect of supplementation of melatonin on S. LH and body BMI in patients with polycystic ovaries in whom obesity and elevated LH level were important pathological features.

Patients and methods: Three study groups:30 PCOS patients received melatonin 3mg tab at 10 p.m. daily for 2 months, 20 PCOS patients didn't take any treatment and 20 healthy control group.

Results: The s.milatonin level was significantly higher in control group and s. LH was significantly higher in PCOS patients than control group also there was a significant negative correlation between s.melatonin level and both s.LH and BMI and a significant positive correlation betweens.LH and BMI. melatonin treatment resulted in reduced s.LH and BMI. **Conclusion** melatonin treatment has beneficial effects on PCOS patients by affecting s.LH and body weight.

Keywords: BMI; LH; Melatonin; PCOS.

INTRODUCTION

Melatonin (N-acetyl-5-methoxy tryptamine), is a pineal gland- secreted hormone and regulate circadian rhythms, sleep , reproduction, growth, mood, and aging [1]. Melatonin thought to act through activation of melatonin receptors which are G-protein coupled receptors (GPCRs) which have been classified as MT1 and MT2 [2] to produce some of its biological effects while other effects are due to its antioxidant role , especially its role in the nuclear and mitochondrial DNA protection[3]. Melatonin is classified by the US Food and Drug Administration (FDA) as a dietary supplement, and in Canada and USA, it is sold over-the-counter [4]. In humans, an inhibitory influence of nocturnal melatonin secretary pattern on GnRH secretion from the hypothalamus has been suggested [5]. It has been shown that before puberty high melatonin concentrations prevent activation of the hypothalamus. But the decline in the level of melatonin in the serum at age of 9 or 10 years trigger GnRH secretion and the onset of puberty occur [6]. Body weight has been shown to be affected by melatonin. It has been found that women with obesity and those with anorexia nervosa have high melatonin secretion [7]. According to some studies on animals, there was excessive resistance to insulin, more glucose intolerance and weight gain in rats with pinealectomy [8]. Majority of PCOS women have elevated LH levels [9]. and normal or decreased FSH levels. The elevated LH production results in androgens production of from the theca cells of the ovaries as it carries LH receptors [10]. Obesity has been related to hypothalamic-pituitary-ovarian (HPO) axis abnormal function by many mechanisms that result in PCOS also it is accompanied with insulin resistance and hyperinsulinemia as a compensatory mechanism. In culture, insulin has a co-gonadotropin action and stimulate the production of androgen from the ovaries [11]. So the current study was designed to demonstrate the effect of melatonin treatment on serum LH level and on BMI in patients with polycystic ovaries.

PATIENTS AND METHODS

Study Design: prospective a 4-week screening phase and a 2-months treatment phase.

Patient selection: 65 unmarried female patients (mean age 26.43 range from 22 to 29 years) selected at gynecology outpatient clinic – Baghdad teaching hospital, Baghdad-Iraq from July 2017 to November 2017. Informed consent obtained from the patients also an ethical approval obtained. They were diagnosed as PCOS patients according to international criteria of PCOS by 2 of three of oligo or anovulation, increased androgen, radiological evidence of polycystic ovaries. Patients with diabetes mellitus, hyperprolactinemia, androgen-secreting tumors or receiving drugs as steroids, antipsychotic drugs, were excluded. All patients underwent medical screening include history, physical examination, BMI measurement and investigations include serum testosterone, FSH, LH prolactin, and melatonin level (at 8 a.m) by RIA. other normal 20 females act as a control.

Treatment assignment: Three groups: the first group contains 30 patients receive 3mg tablet of melatonin once daily at 10 p.m for 2 months. the second group contains 20 patients not receive any treatment and the 20 healthy controls also not receive any treatment. Serum melatonin level, serum LH level and BMI and were measured at baseline and after 2 months of treatment, patients were also assessed for any side effects. The patients advised not to take any hormonal or other PCOS treatment and to maintain their eating routine the same.

Study parameter: The study parameter is s.melatonin, serum LH level, and BMI which were measured at baseline and BMI ,S.LH was measured after 2 months of treatment.

Statistical analysis Collected data were analyzed using SPSS (statistical package for social sciences, version 20. Descriptive analysis of means and standard deviation (SD) were calculated on all demographic variables, and serum melatonin, serum LH and BMI. Multiple comparisons of paired series of data within groups were done using a paired t-test. Unpaired t-test was then used to evaluate the difference between groups. A p-value <0.05 was considered the minimum for statistical significance.

RESULTS

Mean values parameters at baseline and after 2 months of treatment were compared (table 1) S.milatonin level (pg/ml) was measured only at baseline to be compared between patients and control and it was significantly higher in control 8.09±1.81 than patients6.59±2.46. it was not measured at the end of the study because the patients take it as treatment so serum level will not be significant (figure 1). BMI(kg/m^2) was not significantly different between groups, but there were significant differences between BMI after treatment 26.75±2.34 and that at baseline 27.97±2.43 in the treated group it was lower after treatment (p<0.05). (figure2).

S.LH (MIU/ml) level was significantly lower in control group 5.49±1.28 than in patients at baseline 9.45±1.35 and after treatment 8.45±0.89 (p<0.05). A significant difference between the S.LH level at baseline and after treatment in the treated group and it was lower after treatment 8.45±0.89 vs, 9.45±1.35 (p<0.05) and significant difference between treated and untreated group after treatment and it was lower in the treated group 8.45±0.89 vs 9.34±1.38 (p<0.05) .(figure3).

There was a significant negative correlation between s.melatonin level and both BMI and S.LH level in all groups and a significant positive correlation between BMI and S.LH level in all groups (table 2).

Table (1) Mean value of all study parameters in all study groups at baseline and after 2 months of treatment.

Parameter	Mean ± S.D		
	Treated	Untreated	Control
BMI(baseline)	27.97±2.43	27.38±2.36	28.12±2.65
BMI (after2 months)	26.75±2.34*	27.47±2.05	28.12±2.04
S.LH (baseline)	9.45±1.35	9.64±1.21	5.49±1.28**
S.LH(after2months)	8.45±0.89*	9.34±1.38**	5.45±1.13
S.melatonin (baseline)	6.59±2.46	6.64±2.59	8.09±1.81**
Number	**30**	**20**	**20**

*significant changes (paired t-test) p value<0.05.
** significant changes (paired t-test) p value<0.05

Table (2) Correlation between different study parameters.

Variable	Treated		Untreated		Control	
	r	p	r	p	r	p
S.melatonin-BMI	-0.31	<0.0.5	-0.32	<0.0.5	-0.28	<0.0.5
S.melatonin-S.LH	-0.28	<0.0.5	-0.25	<0.0.5	-0.23	<0.0.5
BMI-S.LH	0.41	<0.0.5	0.25	<0.0.5	0.44	<0.0.5

*Spearman correlation test

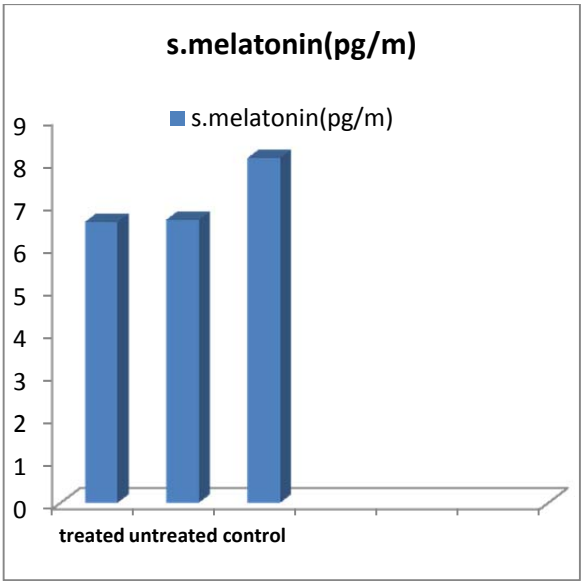

Figure 1: baseline serum melatonin level for all groups.

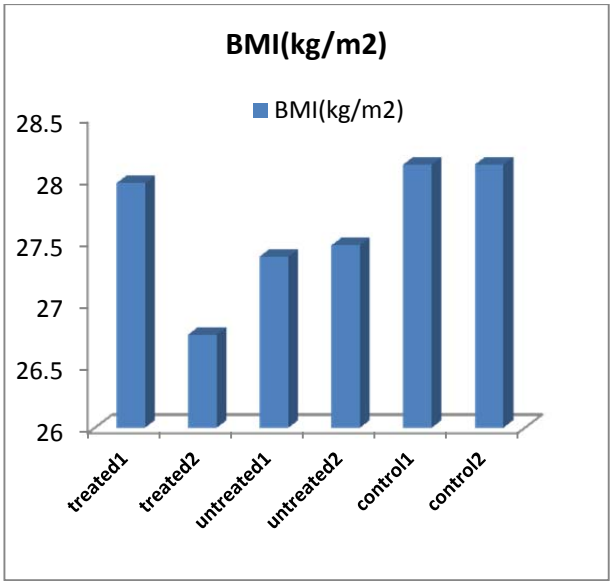

Figure 2: Mean BMI of different groups. (1)at baseline (2) after 2months of treatment.

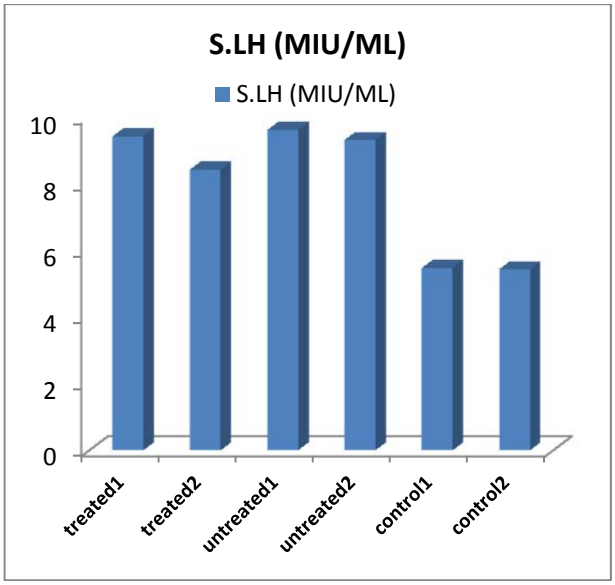

Figure 3: Mean serum LH level of different groups (1) at baseline (2) after 2months of treatment.

DISCUSSION

Melatonin is a diverse molecule and its properties still not well known. Rhythm changes in its secretion were found in certain pathological conditions [12].

Melatonin has an impact on the puberty, ovulation, steroidogenesis, and reproductive behavior. [13]. Pulsatility, 24-h sleep-wake cycle, and circadian rhythmicity are characteristics of the neuroendocrine hypothalamus [13]. Melatonin has been shown to cause down-regulation of the expression of Gn-RH gene in a cell line contains neurons secrete GnRH in a cyclical manner over of 24 h period [14]. The rise in LH secretion is due to increase of the gonadotropin-releasing hormone (GnRH) pulse frequency, which enhance the of the β-subunit production of LH more than the FSH β-subunit, and/or by excessive sensitivity of the pituitary to GnRH stimulation [4]. The current study showed a negative correlation between the s.melatonin level and s.LH level and the melatonin treatment resulted in significant reduction in S.LH level in PCOS patients and many pieces of evidence support these results [1]. Evidence that LH pulsatile secretion may be controlled in part by melatonin [2]. A documented negative correlation between LH concentrations and nocturnal serum melatonin has been found [11,3]. Functional hypothalamic amenorrhea has been shown in women who have increased melatonin blood levels and decreased GnRH /LH pulsatile secretion [12]. Similarly, in athletes with amenorrhea who have irregularities in the function of -pituitary ovarian axis, increased in the duration and peak amplitude of melatonin have been shown [13].

The current study shows a negative correlation between s.melatonin level and BMI and treatment with melatonin resulted in significant reduction of BMI in PCOS patients. It was shown that supplementation with melatonin produces a beneficial effect on leptin and adiponectin secretion and on glucose level, cholesterol and triglycerides in animals with obesity induction [14]. Melatonin has been shown to inhibit the secretion of pepsin and hydrochloric acid and enhance the bicarbonates secretion in the duodenum and its deficiency lower the pH of the duodenum, stimulate the duodenal-pancreatic axis and secretion of insulin and improve appetite [15].

The current study showed a positive correlation between BMI and S. LH level in PCOS patients. Obesity has an effect on the PCOS manifestations [16, 17]. Fatty cells produce estrogen in addition to that produced by the ovaries and adrenals. Estrogen has a positive feedback effect on amplitude and/or pulse frequency causing increased GnRH, LH, and FSH [18-21].

CONCLUSION

Melatonin can give benefits for patients with PCOS by many mechanisms leading to reduced LH level and BMI in overweight patients.

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