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Both zinc deficiency and supplementation affect plasma melatonin levels in rats

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At physiological levels, zinc and various hormones affect each other reciprocally. Reduction in zinc levels in pinealectomized rats suggests the relation between zinc and melatonin. The effect of both zinc deficiency and supplementation on plasma melatonin levels in rats were investigated in this study.

The study was done in Selçuk University, Experimental Medicine Research and Application Center. Twenty-four adult male Sprague Dawley rats were divided into 3 groups. Eight rats were fed with zinc-deficient diet. Zinc supplementation was administered intraperitoneally to 8 rats. The remaining 8 rats were used as controls. All rats sacrificed 3 weeks later. Plasma melatonin and zinc levels were determined.

The plasma zinc levels of the zinc-supplemented group were higher than those of the other groups as expected ($P<0.01$). Similarly, the melatonin levels in the zinc-supplemented group were higher than those in the other groups. A significant decrease was observed in melatonin levels of the zinc-deficient group compared to the control and zinc-supplemented group ($P<0.01$).

The results of this study suggest that zinc deficiency decreases the melatonin levels and zinc supplementation may increase the plasma melatonin levels in rats.

Keywords: zinc, melatonin, zinc deficiency, zinc supplementation

Zinc is one of the metals, which is widely used in individual cells. More than 300 enzymes require zinc for their function. Due to the activity of these enzymes, zinc is essential for nucleic acid, protein, carbohydrate and lipid metabolism (19). Zinc also plays an important role in immune functions (15, 19) as well as on growth and reproduction (13, 17). Long lasting zinc deficiency causes hypogonadism and delay in growth (13). In the light of these studies, it seems that there is a close interrelation between zinc and the endocrine system. However, the effect of hormonal mechanisms on zinc homeostasis is not yet fully understood.

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Zinc mediates the effects of some hormones and enters the structure of some hormone receptors. In this respect, zinc deficiency may disturb some hormonal functions (4, 9, 10). In recent studies, it is suggested that, the product of pineal gland melatonin has an effect on zinc levels in the body (15, 18). Reduction in zinc levels in pinealectomized rats and elevation in melatonin-supplemented rats supports the relation between zinc and melatonin (11, 12). These studies revealed that both melatonin deficiency and melatonin supplementation have affected the zinc levels.

Investigation of specific binding sites of melatonin in small intestines show that melatonin may enhance the absorption of zinc from the digestive system (12).

Although there were some studies investigating the effects of pineal gland and melatonin on plasma zinc level, there is a lack of knowledge about the effects of zinc on plasma melatonin levels. In this study, it was aimed to investigate the effects of zinc deficiency and zinc supplementation on plasma melatonin levels in rats.

Materials and methods

Animals

Twenty four Sprague Dawley adult male rats were used to prevent intersex differences in the study. All animals were fed with uniform pellet food. Ethical Committee of Research Center approved the experimental procedures.

Experimental design

Twenty four rats were divided into three groups.

Group I (n=8):

The animals were fed with standard diet which includes 96.95 mg of Zn in each kilogram of the diet and tap water ad libitum and they acted as controls.

Group II (n=8):

The animals were fed with normal diet plus tap water and were injected intraperitoneally with zinc sulphate (3 mg/kg/day) at 9 p.m. for 3 weeks. This group acted as zinc-supplemented group.

Group III (n=8):

The animals were fed with zinc-deficient pellets (including 0.650 ppm zinc in each gram of the diet) and distilled water for 3 weeks (5, 6) to prevent uncontrolled Zn intake. This group acted as zinc-deficient group.

All animals in all groups were given a diet of 10 g/100 g body weight every day.

In our previous studies we have found that application of zinc of 3 mg/kg/day activates the endocrine system whereas zinc deficiency has negative effects on the endocrine system within three weeks (1, 2). So we preferred the same dose of application.

At the end of 3 weeks all animals were sacrificed and blood samples were obtained into heparinized tubes.

Analyses

The plasma zinc level was measured by atomic absorption spectrophotometer (Shimatsu ASC-600).

Plasma melatonin analyses were done by RIA (Melatonin J-125 RIA, catologue no.: MEL-180, Marburg Schwanelle 44). This method reliably detects melatonin concentrations as low as 2 pg/ml. Cross reactivity for melatonin is 100 percent.

Statistical analyses

The significance of the differences between means of the groups was assessed using analyses of variance. Statistically significant differences were evaluated by Duncan method. P value less than 0.05 was accepted as significant.

Results

Table I shows the body weights of the rats before and after the experimental period. The change of body weight during 3 weeks is also stated on the table. A statistically significant weight loss was seen in the zinc-deficient group comparing it to the control and zinc-supplemented groups ($P<0.01$).

Table I

Body weights of animals before and after the experiment

Groups	Weights (g) 1st measure	Weights (g) 3 weeks later	Weight change (g)
Controls (n=8)	260.5 ± 30.7	265.4 ± 45.5	6.0 ± 3.2
Zinc-supplemented group (n=8)	262.5 ± 15.5	271.6 ± 27.4	4.6 ± 1.4
Zinc-deficient group (n=8)	263.5 ± 25.5	255.9 ± 32.5	–6.5 ± 4.3*#

The difference, when compared with controls is statistically significant ($P<0.01$)
The difference, when compared with the zinc-supplemented group, is statistically significant ($P<0.01$)

Table II

Plasma zinc and melatonin levels of animals

Groups	Zinc (μg/dl)	Melatonin (pg/dl)
Controls (n=8)	120.5 ± 10.8	19.3 ± 7
Zinc-supplemented group (n=8)	205.2 ± 25.3 ***f***	75.5 ± 10.7 ***f***
Zinc-deficient group (n=8)	48.5 ± 28.5*#	11.63 ± 4.2*#

* Compared with controls the difference is statistically significant ($P<0.01$)
# Compared with the zinc-supplemented group, the difference is statistically significant ($P<0.01$)
f Compared with controls the difference with controls is statistically significant ($P<0.01$)

Plasma zinc and melatonin levels are presented in Table II. Plasma zinc levels in the zinc-supplemented group was significantly higher than those in the other two groups as expected ($P<0.01$). Plasma zinc levels in the zinc-deficient group was lower than those measured in controls ($P<0.01$). Parallel to the zinc levels, plasma melatonin levels of the zinc-supplemented group was significantly higher than those of the others ($P<0.01$), while the zinc-deficient group had lower melatonin levels than the control one ($P<0.01$).

Discussion

Mean weights of the groups were not significantly different during the study. While comparing the weight changes after 3 weeks, a significant loss was seen in the zinc-deficient group. Previous studies concerning zinc deficiency also revealed a weight loss in rats fed with zinc-deficient diet (8, 16).

In the present study, not only the plasma zinc levels but melatonin levels as well were significantly lower in the zinc-deficient group. Unlike to the zinc-deficient group, in the zinc-supplemented group both zinc and melatonin levels were significantly higher than those in the other groups. There are some other studies which investigated the relationships between zinc and various hormones such as growth and thyroid hormones. These studies have suggested that zinc levels directly affect the production or secretion of growth and thyroid hormones or vice versa (4, 10, 13). Studies about the relation between melatonin and zinc mainly focus on effects of them on cellular immunity (7, 11, 12). These studies are about the effects of pineal gland and melatonin on zinc effect. But we could not find any study about the effects of zinc on melatonin. In our previous study plasma zinc levels decreased in parellel to plasma melatonin levels in pinealectomized rats. In contrast presence of significant increase in plasma zinc levels in melatonin-supplemented rats can be thought as an indicator of the relation between melatonin and zinc (3). It is suggested that melatonin increases the absorption of zinc in the gastrointestinal system (12). Also presence of specific binding sites for melatonin in the gastrointestinal system indicates that this hormone plays a basic role in the absorption of zinc (11).

Our previous study (3) and other similar studies (7, 11, 12) have shown that melatonin has effects on zinc. In addition to our previous findings it is seen that zinc exerts important effects on melatonin. But detailed studies about the relationship of zinc and melatonin should be performed to determine other factors playing role in this relation.

The results of this study indicate that zinc deficiency decreases the melatonin levels and zinc supplementation may increase the plasma melatonin levels in rats.

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