The role of melatonin in maintenance of immunological internal environment

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Summary

Melatonin hormone secretes from the pineal gland during dark period. This study was designed to investigate the effect of daily melatonin administration to chicks on some physiological parameters .A total of fifty fawbro chicks of one day old were divided into two groups. The first group was given melatonin orally at a dose of 12µg/100g body weight daily for eight weeks and the other group was used as a control. During this experimental work the following parameters were studied. Daily feed and water intake, body temperature before and after melatonin administration with a general observation of chick's behaviour. Blood samples were collected weekly to study some parameters (total red blood cells, hemoglobin content, packed cell volume and differential leukocytic count).

The results showed that, melatonin caused a drop of body temperature with relaxation and sleeping of chicks up to three hours after its administration. This period was accompanied by depression of feed and water intake. Total RBCs count, Hb, PCV, and lymphocytes were significantly increased with a decrease in heterophil / lymphocyte ratio.

In conclusion, results of this investigation indicate that melatonin causes calming and sleeping of chicks and improves their feed conversion ratio.These results appear to be the first indication that melatonin does play an important role in immunity and improvement of blood picture. These effects were suggested to be due to the immuno – enhancing and anti-stress action of melatonin.

دور الميلاتونين في الحفاظ على البيئة الداخلية المناعية

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الخلاصة

هرمون الميلاتونين هو اندول أمين يفرز من الغدة الصنوبرية ليلا و نظرا لقلة الأبحاث عن تأثير هذا الهرمون الفسلجية ، صمم هذا البحث لدراسة تأثير هذا الهرمون عند إعطاءه نهارا كوسيلة

لتشبيه الإفراز الطبيعي له ليلا في فروج اللحم . استخدم 50 فرخ لحم بعمر يوم واحد و بعد تقسيمها إلى مجموعتين متساويتين جرعت الأولى بالميلاتونين و الثانية بالماء الاعتيادي يوميا و لمدة ثمانية أسابيع . تمت مراقبة سلوك الطيور و حالتهم الصحية بالإضافة إلى قياس درجة حرارة الجسم قبل وبعد التجريع كما تم حساب استهلاك العلف و الماء اليومي . تم سحب نماذج من الدم لحساب عدد خلايا الدم الحمراء و كمية الهيموكلوبين و حجم الخلايا المرصوصة و كذلك حساب العدد التفريقي لأنواع كريات الدم البيضاء أسبوعيا طيلة فترة التجربة يعني ثمانية أسابيع .

بينت النتائج أن الطيور تهدأ وتأخذ وضع الراحة و النوم بعد التجريع مع انخفاض درجة حرارة الجسم و معدل استهلاك العلف و الماء . هذا بالإضافة إلى الارتفاع المعنوي في عدد خلايا الدم الحمر و تركيز الهيموكلوبين و حجم الخلايا المرصوصة مع زيادة معنوية في عدد الخلايا اللمفية و انخفاض نسبة الهيتروفيل / اللمفية .

نستدل من هذه النتائج إن إعطاء هرمون الميلاتونين خلال النهار يعمل على تهدئة الطيور و تقليل حركتها مما يؤدي إلى زيادة محسوسة في كفاءة التحويل الغذائي و هذا بالتالي ينعكس بشكل إيجابي على الكفاءة الإنتاجية .

من ناحية أخرى هذه أول دراسة تشير إلى دور الميلاتونين في زيادة مناعة الجسم وتحسين الصورة الدموية و هذا يعود إلى تأثيراته كعامل محفز للمناعة و مضاد للإجهاد و دوره في الحفاظ على البيئة الداخلية للدماغ و تنظيم النسق اليومي .

Introduction

The pineal gland is a small body lies between the cerebral hemispheres and the cerebellum extending dorsally towards the skull .It contains a number of active compounds (norepinephrin, serotonin, histamin, melatonin, dopamin, ectopamin) .The pinealocytes are the chief cells of the gland for melatonin synthesis [1]. These cells can actively take up tryptophan from the blood, hydroxylate it to 5-hydroxytryptophan (5H TP) and decarboxylate it to 5-hydroxytryptamine (5HT) or serotonin. The pineal gland is one of the richest sources of serotonin (5HT) which serves as a precursor for the synthesis of the hormone melatonin whose synthesis is stimulated by darkness and inhibited by light [2]. The inhibitory action of the pineal gland on thyroid function has been studied by several investigators. Pinealectomy had been reported to depress thyroid hormone secretion, which affect the basal metabolic rate [3].

Beside that, melatonin is considered as an anti-cancer hormone as it shows a marked elevation in 75% of the patients suffering from cancer after

their recovery [4]. Administration of tryptophan decreases the Heterophil / Lymphocyte ratio and Albumin / Globulin ratio due to the increase in lymphocyte number and globulin amount respectively [5].

The object of this paper is to investigate for the first time the role of pineal gland and melatonin in the immunity of the body.

Materials and Methods

A total of 50 one day old chicks were used. They were divided into two groups .The first group was received melatonin at 12μg/100g body weight daily for eight weeks .The second group was used as a control. During the experimental work, behaviour of the animals was observed and daily anal body temperature before and after melatonin administration was measured. Feed and water intake were also measured every 30 minutes up to 3 hours after administration. Blood samples were collected weekly to study the following parameters of blood picture : -

1- Red blood cell count (RBCs) – The haemocytometer chamber was used for this purpose [6].

2- Packed cell volume (PCV) – The microhaematocrit method was used .

3- Haemoglobin estimation (Hb) – According to the method described by [7], Hb was estimated by using the spectrophotometer.

4-Differential leukocytic count -Blood smears were prepared and then stained with Wright stain to count each type of leukocyte separately. Then H/L ratio was recorded weekly .All data were subjected to analysis of variance and LSD.

Results

Observation of birds shows that melatonin causes relaxation and calming of animals .The sleeping state of birds lasts up to three hours and it was accompanied by a marked depression in body temperature, feed and water intake (table 1). The mean body temperature was 41.6°c for both groups before melatonin administration, compared with 40.5°c and 41.6°c after one houre of administration for melatonin and control groups respectively.

Table (2) shows that melatonin administration produces a significant increase in the total red blood cell count , hemoglobin content and packed cell volume .The H/L reduced significantly in the melatonin group compared with control (table 2).

Table (1) –Body temperature, feed and water, intake before and after melatonin administration for both groups

	Control			Melatonin		
Time (Hours)	Body (°C) Temperature	Feed intake gm/bird	Water intake ml/bird	Body(°C) Temperature	Feed intake gm/bird	Water intake ml/bird
0	41.6 ± 0.1	1.26 ± 0.02	5.0 ± 0.3	41.6 ± 0.2	1.27 ± 0.03	4.8 ± 0.3
½	41.6 ± 0.2	1.10^{a} ± 0.02	4.6^{a} ± 0.4	41.1 ± 0.1	0.80^{b} ± 0.01	3.2^{b} ± 0.2
1	41.6^{a} ± 0.1	0.66^{a} ± 0.03	3.7^{a} ± 0.2	40.5^{b} ± 0.2	0.20^{b} ± 0.01	1.6^{b} ± 0.2
1½	41.6 ± 0.2	1.87^{a} ± 0.01	5.2^{a} ± 0.2	41.1 ± 0.2	0.32^{b} ± 0.02	2.7^{b} ± 0.1
2	41.5 ± 0.1	1.74^{a} ± 0.02	7.7^{a} ± 0.5	41.0 ± 0.2	0.45 ± 0.02	5.3^{b} ± 0.3
2½	41.5 ± 0.2	1.50^{a} ± 0.03	10.2^{a} ± 0.4	41.4 ± 0.1	0.70b ± 0.03	8.0^{b} ± 0.4
3	41.6 ± 0.2	1.29^{a} ±0.01	11.7^{a} ± 0.3	41.6 ± 0.1	0.98b ± 0.03	10.2^{b} ± 0.4

Figures are means ± SEM. Those bearing variable subscripts are significantly different ($P < 0.05$).

Table (2) –Red blood cells, Haemoglobin, packed cell volume and H/L ratio for control and melatonin groups.

Weeks	Control				Melatonin			
	RBCs (cell X 10^{12}/ L)	Hb (gm/dl)	PCV (ratio)	H/L	RBCs (cell X 10^{12}/ L)	Hb (gm/ dl)	PCV (ratio)	H/L
1	1.060± 0.03	7.1^{a}±0.4	22.3^{a} ±0.6	0.90^{a}± 0.001	1.170^{a} ±0.05	7.7^{b} ±0.3	24.3^{b}± 1.0	0.50 ^{b}±0.002
2	1.200^{a}± 0.06	7.3^{a}±0.3	23.2^{a} ±0.5	0.87^{a}± 0.002	1.630^{b} ±0.05	7.9^{b} ±0.4	24.8^{b}± 1.2	0.46^{b}±0 .002
3	2.320^{a}± 0.03	7.5^{a}±0.4	23.5^{a} ±0.8	0.73^{a}± 0.001	2.590^{b} ±0.02	8.2^{b} ±0.3	25.2^{b}± 0.5	0.41^{b}±0 .001
4	2.595^{a}± 0.06	7.7^{a}±0.4	24.3^{a} ±0.6	0.50^{a}± 0.002	3.097^{b} ±0.06	8.4^{b} ±0.5	25.7^{b} ±0.3	0.38^{b}±0 .003
5	2.946 ^{a}±0.08	8.0^{a}±0.5	25.2 ^{a}±0. 6	0.39 ^{a}±0.00 1	3.269 ^{b}±0.05	8.7 ^{b}±0. 4	26.3 ^{b}±0.5	0.30 ^{b}±0.002
6	3.246 ^{a}±0.08	8.3^{a}±0.2	26.1 ^{a}±0. 5	0.35 ^{a}±0.00 3	3.766 ^{b}±0.07	8.9 ^{b}±0. 2	26.9 ^{b}±0.7	0.27 ^{b}±0.002
7	3.316 ^{a}±0.06	8.5^{a}±0.2	26.6 ^{a}±0. 4	0.33 ^{a}±0.00 3	3.840 ^{b}±0.05	9.3 ^{b}±0. 2	27.8 ^{b}±0.3	0.25 ^{b} ±0.001
8	3.468 ^{a}±0.07	8.8^{a}±0.3	27.0 ^{a}±0. 3	0.28 ^{a}±0.00 2	3.948 ^{b}±0.06	9.6 ^{b}±0. 4	28.2 ^{b}±0.4	0.22 ^{b}±0.003

Figures are means ± SEM. Those bearing variable subscripts are significantly different ($P < 0.05$).

Discussion

The calming and sleeping state of birds are mainly due to the central effect of melatonin which produces changes in electroencephalograph pattern and reduces body temperature [8]. The level of melatonin hormone shows a circadian rhythm in both its organ of secretion, the pineal gland and blood. Its peak during the hours of night may be responsible for the suppression of feed and water intake for the same reason mentioned above [9]. Depression of feed intake by melatonin depress the plasma glucose, protein and cholesterol

level[10]. A significant depression of blood glucose during dark period had been reported [11]. On the other hand , low plasma protein level may be attributed to high rate of protein synthesis by cells. Macfarland etal[12] found a significant decrease of total protein level in birds reared in dark places .The significant depression of plasma cholesterol explain the inhibitory role of melatonin hormone either on cholesterol absorption from GIT or its synthesis by cells [13].

Inspite the depression of feed intake by melatonin, [10] reported a marked improvement in body weight and feed conversion ratio of chicks. This result may be attributed to the stimulatory effect of melatonin on nutrient absorption from intestine and their utilization by cells in the body.

Complete blood picture and differential cell count from an individual can provide a thorough evaluation of the health and immunological status of that animal respectively. Melatonin administration produces a significant increase in total red blood cell count, hemoglobin content and packed cell volume. This might be due to the effect of melatonin on thyroid gland function[14]. Thyroid hormones are very well known for their effects on metabolic rate and increasing oxygen demand by tissues [15 and 16].Sturkie [17] reported that more than 30% of blood serotonin is stored in lymphocytes which explains the elevation of lymphocytes after melatonin administration .There is an adverse relation between lymphocytes and heterophils and therefore , the increase of the former one decreases the later one [16].It was concluded that low H/L ratio in chickens can be used as a criterion for selection of high immune response [18].

As tryptophan represents the precursor of melatonin synthesis and its administration causes a marked elevation in lymphocyte number and globulin amount [5]. This provides a good evidence that melatonin does play a very important role in immunity. Moreover, [17] suggested that the pineal may contribute to immuno – component cells by the presence of IgA like substance in it.

Thus, the results of this study and our previous studies on this subject seem to be the first one which indicate the important role of pineal gland and its hormone melatonin in maintaining the internal environment of the body .We conclude that this hormone acts as an immuno – enhancing and stress – suppressor to keep and maintain body environment.

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