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SEASONAL DYNAMICS OF ADRENAL MINERALOCORTICOID FUNCTION IN RATS

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UDC 612.453.018-06:613.3

KEY WORDS: aldosterone, mineralocorticoid activity, zona glomerulosa of adrenal cortex, melatonin, pineal gland, plasma clearance

Ever-increasing attention is currently being paid to the study of seasonal changes in function of the endocrine glands as an important factor in adaptation of the living organism to changing external environmental conditions. An important role in the chain of these adaptive mechanisms is played by the adrenals. The problem of circadian and circannual fluctuations of glucocorticoid secretion both in man and in various species of animals has been discussed sufficiently fully in the literature; as regards rhythms of mineralocorticoid activity of the adrenal cortex, however, only fragmentary information is available, pointing to considerable seasonal fluctuations [4, 10]. Accordingly it was decided to investigate seasonal rhythms of aldosterone metabolism in albino rats and to compare them with the time course of the concentration of pineal melatonin, a central regulator of adaptation of the organism to changing conditions of illumination.

EXPERIMENTAL METHOD

Male Wistar rats (10 to 15 individuals) weighing 150-180 g were used in the experiments, which were carried out in January, March, July, and October. Values of the plasma aldosterone level and its daily excretion with the urine were determined by radioimmunoassay, using standard test kits from CEA-IRE-Sörin (France), and the plasma metabolic clearance was determined by calculation by Van Slyke's formula. The melatonin content in the pineal gland was determined fluorometrically [3]. The animals were kept on an ordinary diet and water intake, under natural conditions of illumination. To collect the 24-hour urine and subsequently to determine its aldosterone concentration, the rats were kept under conditions of relative hypokinesia, by being confined to metabolic cages of small size. The diuresis and level of excretion of the hormone were determined separately on the 1st and 2nd days of the experiment.

Laboratory of Biochemistry of Endocrine Diseases, Khar'kov Research Institute of Endocrinology and Hormone Chemistry. (Presented by Academician of the Academy of Medical Sciences of the USSR L. T. Malaya.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 105, No. 2, pp. 221-224, February, 1988. Original article submitted September 24, 1986.

TABLE 1. Seasonal Dynamics of Parameters of Mineralocorticoid Function of Rat Adrenal Cortex

Season	Diuresis, ml/24 h		Urinary aldosterone, nmoles/24 h		Plasma aldosterone, pmoles/ml	Plasma metabolic clearance, liters/24 h
	1st day	2nd day	1st day	2nd day		
Winter	23,0±1,16	42,7±2,31	0,20±0,016	0,36±0,03	1019±75	14,7±0,62
Spring	7,5±0,54 (<0,05)	40,3±2,30 —	0,42±0,017 (<0,05)	0,60<0,043 (<0,01)	1875±108 (<0,01)	12,4±0,51 —
Summer	10,7±0,83 (<0,05)	29,6±1,26 (<0,05)	0,11±0,016 (<0,05)	0,25±0,016 —	1055±61 —	6,8±0,26 (<0,01)
Fall	7,6±0,62 (<0,05)	26,5±1,37 (<0,05)	0,09±0,001 (<0,05)	0,29±0,018 —	908±52 —	8,2±0,30 (<0,05)

Legend. Significance of difference compared with values in winter shown in parentheses.

Plasma renin activity (PRA) was determined by radioimmunoassay using commercial kits. In a special series of experiments the rats were given intramuscular injections of melatonin in a dose of 50 μg/100 g body weight for 5 days and 100 μg/100 g body weight for 10 days. Intact rats served as the control.

EXPERIMENTAL RESUTLS

It will be clear from the data given in Fig. 1 and Table 1 that the 24-hour excretion of urine in the spring and winter period was significantly higher than in the summer and fall; within these periods, however, there were virtually no differences.

At all stages of the experiment the diuresis during the 1st day was much lower than during the 2nd day; this must evidently be interpreted as the response of the animals to hypodynamia and subsequent adaptation. Diuresis during the 1st day of the investigation in the spring and fall was virtually identical (on average 7.6 ml), it was increased a little in summer (up to 10.8 ml), and gave a marked upward jump in winter (up to 23 ml). A clear line could be drawn between values for the spring-winter (40.3-42.7 ml) and the summer-fall (92.6-26.5 ml) periods without any significant differences within these groups of parameters. Thus irrespective of the day of measurement, maximal values of diuresis were found in the spring and winter. A definite role in this situation may be played by involvement of a factor such as loss of fluid by the animal (perspiration) in the hot season of the year.

The blood aldosterone level also showed considerable seasonal variations. By contrast with the data given above on diuresis, peak values of the plasma aldosterone concentration were observed in the spring (1875 ± 108 nM), and at all the other times of the year fluctuations of the values of this parameter were not significant; the lowest blood aldosterone levels were observed in October (908 ± 52 nM).

The dynamics of the values of aldosterone excretion with the urine repeated to a certain extent the curve of plasma aldosterone concentrations, but values of excretion of aldosterone were nevertheless significantly higher in winter than in summer, whereas the 24-hour excretion of the hormone was identical in summer and the fall. Aldosterone excretion with the urine during the 1st day, like the value of diuresis, was significantly lower than on the 2nd day at all stages of the investigation; a particularly wide gap in the parameters compared was observed in the spring-summer period (from 0.09-0.11 to 0.25-0.29 nmole/24 h).

Reduction of the urinary aldosterone excretion under conditions of hypodynamia and adaptation to the new conditions may be regarded as the result of switching of steroid production in the adrenals toward the formation of glucocorticoids, which are stress hormones. Data were obtained previously [1] to show that glucocorticoid synthesis in rabbits in a state of stress was discovered even in the gonads.

Interesting data have been obtained by evaluating the trend of the plasma metabolic clearance of aldosterone in different groups of rats. Unlike the other parameters of mineralocorticoid metabolism studied, its highest value was recorded in the winter months. This may perhaps be connected with the fact that, as many workers have noted [3, 4, 10, 11], this is the time of year when maximal values of parameters of the circulatory system are observed, and we know that this has a marked effect on aldosterone clearance. The fact that with high values of plasma metabolic clearance for hormones, low blood and urinary aldosterone levels

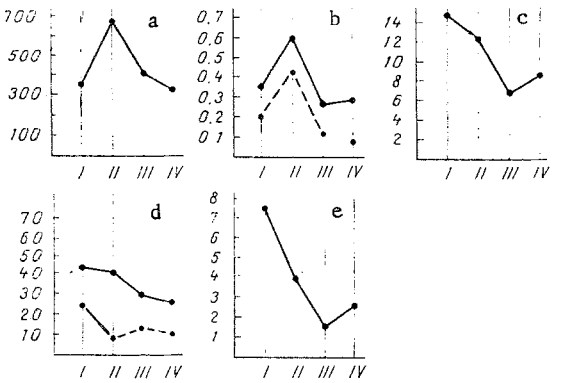

Fig. 1. Seasonal dynamics of parameters of mineralocorticoid function of rat adrenals and melatonin content in pineal gland. a and b) Aldosterone content in plasma (in pM) and urine (in nmoles/24 h), respectively, c) plasma metabolic clearance (in liters/24 h), d) diuresis (in ml), e) melatonin concentration (in ng per organ). I-IV) Winter, spring, summer, and fall, respectively. Continuous and broken lines indicate 1st and 2nd days of tests.

are observed, as also is evidence of a generally low level of aldosterone production in the winter, as is evident from the numerical values and their graphic interpretation. Increased aldosterone excretion in the spring corresponds to a reduction of the clearance values. High blood levels of aldosterone at this time are evidently due not only to increased functional activity of the zona glomerulosa of the adrenal cortex, but also to some delay in elimination of the hormone from the plasma.

In the next stage (spring-summer) changes in all three parameters were in the same direction, but the sharp fall in the plasma and urinary aldosterone levels, despite reduction of the plasma metabolic clearance, pointed unequivocally to a decrease in production of the hormone in the summer.

According to data in the literature [2-4, 7], the plasma cortisol concentration (and, correspondingly, urinary excretion of glucocorticoids) fell distinctly in the summer; the authors cited interpret this finding as the result of reduction of ACTH secretion. This explanation evidently also can be used in the present case, for ACTH is one of the principal regulators of aldosterone secretion.

When these data are compared with the results of determination of PRA in the winter and summer, it must be remembered that minimal mineralocorticoid activity in summer is accompanied by the highest values of PRA at this time of the year (3116 pg/ml/h compared with 1828 pg/ml/h in winter). Increased activity of the renin–angiotensin system in summer seems natural in view of the increased loss of fluid and the development of relative hypovolemia. The absence of a parallel between the PRA values and the blood and urinary aldosterone concentrations in rats suggests that the regulatory role of the renin–angiotensin system in relation to aldosterone production is virtually not realized in summer under normal conditions. This conclusion is in agreement with data obtained by several workers on the species-specificity of rats in this respect.

A central place in the mechanism of the "biological clock" of the living organism is assigned to the pineal gland, which synchronizes rhythms of endogenous functions. Comparison of curves for changes in the blood and urinary aldosterone levels with the time course of the melatonin content in the pineal gland (Fig. 1) showed significant disparity between them. Maximal values of melatonin concentration are observed in winter, i.e., the dark time of the year, in agreement with data in the literature [5, 6, 8, 12, 13]. Later a sharp fall in the melatonin concentration was observed, and its minimal values, like those of the mineralocorticoid function of the adrenal cortex, were observed in July.

The data described above indicate that no direct connection exists between the rhythm of mineralocorticoid activity and aldosterone metabolism which is subjected to pineal (usually inhibitory) influences. This conclusion is also confirmed by the results of the

next series of experiments, which showed no definite trend in the blood aldosterone levels in rats receiving daily injections of melatonin for 5 and 10 days: in both cases the parammeters analyzed (1265 ± 99 and 1351 ± 193 nmoles/liter respectively) were indistinguishable from the control (1288 ± 146 pM). The results agree with data in the literature [6], according to which the influence of pineal hormones on the adrenal cortex is manifested mainly under extremal conditions.

Thus under normal conditions the mineralocorticoid activity of the adrenals of intact rats exhibits a marked seasonal rhythm, which is stable as regards exposure to stress and also to the regulatory influence of melatonin.

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