Premature Decline of the Testicular Endocrine Function in Rats with Hereditary Galactosemia

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 122, No. 9, pp. 318-320, September, 1996
Original article submitted February 28, 1996

Testicular endocrine function and morphometric characteristics of the genital system are examined in W/SSM (galactose sensitive) and R (galactose resistant) rats aging 3 and 10 months. Testicular hypertrophy (in comparison with R rats) is found in W/SSM rats of both ages. Basal plasma testosterone levels in young and old rats of both strains did not differ. After *in vivo* stimulation of the testes with chorionic gonadotropin, the increment of plasma testosterone in 10-month-old W/SSM rats was 2-fold lower than in young rats and in age-matching R rats. Premature decrease of testicular endocrine function in W/SSM may reflect a more intense aging of these animals.

Key Words: *testosterone; testes; chorionic gonadotropin; galactosemic rats*

The W/SSM (S) rat strain was obtained by selection and inbreeding of Wistar rats sensitive to the galactosemic effect of galactose [4]. These rats exhibit the signs of hereditary galactosemia. Simultaneously, the R strain characterized by low incidence of spontaneous galactosemia was created. In galactosemic rats, the activity of galactose-1-phosphate uridyl transferase, an enzyme converting galactose into glucose, is lowered, while the intracellular galactose transport is increased [3]. The free-radical processes in these rats are more intense [2], probably due to oxidation of excessive monosaccharides entering the cells. Multiple DNA rearrangements were detected in W/SSM (S) rats [10]. These rats often develop cataracts and tumors and are characterized by low fertility and premature ageing [2]. Ageing of the reproductive system in these rats is not studied. The available data suggest the presence of age-related differences in endocrine activity of testes of S and R rats. The weight of the testes and accessory glands provides additional information regarding functional activity of the reproductive system of S and R rats. As the testes, the accessory glands are androgen-dependent organs [1]. Therefore, their weight is often employed as a morphometric parameter reflecting hormonal activity of the reproductive system.

We compared age-related changes in the testicular endocrine function and morphometric parameters of the reproductive system in rats sensitive and resistant to galactose.

MATERIALS AND METHODS

Experiments were performed on adult male S and R rats aging 3 and 10 months. Hormonal reactivity of the testes was assessed from the increment of blood testosterone (TS) level 1 h after intraperitoneal injection of chorionic gonadotropin (CG) in a dose of 50 U. Control animals of both strains were injected with normal saline. Plasma TS concentration was measured by radioimmunoassay with the use of highly specific anti-TS antiserum. After blood collection, the testes, seminal vesicles, and preputial glands were removed, stripped of fat tissue, and weighed with an accuracy of 0.5 mg.

The results were analyzed using Student's *t* test.

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0007-4888/96/0009-0929$15.00

TABLE 1. Weight of the Body, Testes, and Accessory Glands (g) in Galactosemic (S) and Galactose-Resistant (R) Rats

Organs	Age of animals, months			
	3		10	
	R (*n*=10)	S (*n*=10)	R (*n*=18)	S (*n*=17)
Body weight	215.7±6.8	229.0±4.0	282.0±8.5	306.7±13.7
Testes	2.31±0.11	2.83±0.13*	2.35±0.09	2.82±0.07*
Seminal vesicles	0.83±0.09	0.76±0.06	1.54±0.13**	1.78±0.15**
Preputial glands	0.10±0.01	0.11±0.01	0.16±0.02**	0.15±0.02**

Note. Here and in Table 2: *n* is the number of animals; $p<0.05$: *compared with age-matching R rats; **compared with young rats.

RESULTS

Differences were revealed in the weight of testes and accessory glands (seminal vesicles and preputial glands) of S and R rats (Table 1). The testes of 3-month-old S rats were heavier than those of R rats. These genetically controlled differences were retained in 10-month-old rats. There were no differences in the weight of the accessory glands in age-matching groups of both strains. In contrast to the weight of the testes, which did not change, the weight of accessory glands markedly increased with age in rats of both strains. Since age-matching animals of both strains did not differ significantly in body weight, the higher weight of the testes S rats cannot be attributed to higher body weight. An increase in blood concentration of follicle-stimulating hormone that stimulates Sertoli cells and spermatogenous epithelium of seminiferous tubules [7] may account for hypertrophy of the testes in galactosemic S rats.

Thus, morphometric studies revealed testicular hypertrophy in S rats of both age groups compared with R rats, implying a different endocrine function of the testes in these rats. In order to test this hypothesis, we compared *in vivo* testicular reactions to CG, an agent stimulating steroidogenesis in the interstitial cells of Leydig that are the major producers of TS in mammals [9].

The basal plasma TS levels were virtually the same in young (3 months) and old (10 months) S and R rats (Table 2). After stimulation with CG, plasma TS levels increased 4-fold in young and old R rats. In young S rats, plasma TS also increased 4-fold, while in old S rats testicular response to CG was half that in young rats of the same strain.

Thus, the reactivity of the testes to CG was lowered in 10-month-old S rats, while in R rats of the same age it was the same as in young animals. These findings show a premature decrease in the testicular endocrine function in S rats, which agrees with our previous *in vivo* observations that the sensitivity of the testes to CG of old rats is lower than that of young rats [6,8]. These results are consistent with the shorter life span of S rats: 14-18 months, i.e., 2- to 3-fold shorter than that of Wistar rats [2]. Thus, 10-month-old S rats can be considered as old animals. Presumably, the decline of the testicular endocrine function in S rats is more pronounced than in R rats, which is probably associated with changes in the function of Leydig cells. They do not involve the basal testicular secretion of TS and are detected only after stimulation with gonadotropins.

Hyperproduction of free radicals was revealed in S rats [10], which accelerates the process of aging [5]. Presumably, premature decrease in the testicular endocrine function is associated with hyperproduction of free radicals. It was found that lipid peroxidation products (hydroperoxide) inhibit the luteinizing hormone-stimulated steroidogenesis in MA-10 Leydig cell tumor by inhibiting 3β-hydroxysteroid dehydrogenase and reducing the production of mitochondrial proteins, which are probably responsible for the transport of cholesterol (a substrate for the

TABLE 2. Changes in the TS Level in Galactosemic (S) and Galactose-Resistant Rats One Hour after Injection of CG, ng/ml

Experimental conditions	Age of animals, months			
	3 (*n*=5)		10 (*n*=9)	
	R	S	R	S
Control	1.91±0.54	2.60±1.10	1.71±0.20	1.92±0.57
CG	7.98±1.22	7.44±0.40	7.20±1.26	3.94±0.78*,**

enzymes involved in steroidogenesis) to the internal mitochondrial membrane [11].

Thus, our results show a premature decrease in the testicular endocrine function in rats with hereditary galactosemia, which may be due to hyperproduction of free radicals and reflect a more intense ageing of these rats.

The study was partially supported by the State Research and Technology Program "Priorities of Genetics."

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