Age-Related Changes in Ceruloplasmin Content in W/SSM Rats

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The content of ceruloplasmin was studied in W/SSM rats with hereditary galactosemia. Carbohydrate component constitutes about 40% of the molecule of this antioxidant. The content of ceruloplasmin in 2- and 11-month-old W/SSM rats was elevated compared to the corresponding parameters in Wistar rats.

Key Words: *Ceruloplasmin; age; W/SSM rats*

In W/SSM rats with hereditary galactosemia, disturbed integrity of cell membranes resulting from increased transport of hexoses into cells is one the mechanisms of the pathological process [4]. Excessive transport of hexoses into cells promotes generation of hydroxyl radicals and activation of LPO, which is seen from accumulation of TBA-reactive substances, *e.g*. MDA, in the organism. Age-related peculiarities of MDA content in the myocardium were revealed: its content was increased in 3-month-old rats and decreased in 10-12-month-old rats compared to Wistar rats of the corresponding age. The content of the major lipid-soluble antioxidant α-tocopherol in the myocardium of 3-month-old W/SMM and Wistar rats was similar, while in 10-12-month-old W/SMM rats this parameter was elevated compared to both Wistar rats and 3-month-old W/SMM rats [2]. Another proportion between the content of MDA and α-tocopherol was found in the plasma: no differences in MDA content was found despite low content of α-tocopherol in the plasma of 2-3-month-old W/SSM rats and high content of α-tocopherol in 10-12-month-old W/SSM rats. It cannot be excluded that other factors of the antioxidant defense system are involved in the maintenance of LPO processes in W/SSM rats. It is of particular interest to study the content of serum antioxidant ceruloplasmin (CP), whose synthesis depends on the state of the carbohydrate metabolism and hepatocytes in W/SSM rats.

The aim of this study was to reveal age-related differences in the content of serum antioxidant CP in W/SSM rats.

MATERIALS AND METHODS

Male W/SSM rats bred in the Laboratory of Animal Breeding, Research Center of Clinical and Experimental Medicine, were used in the experiments. The rats (n=17) were divided into 3 age groups: 2, 6, and 11 months. Wistar rats (n=18) of the same ages served as controls. Serum CP (EC 1.16.3.1) was measured as described elsewhere [1]. *p*-Phenylenediamine hydrochloride (Sigma) was used as the substrate. The reaction was stopped by adding sodium fluoride into the incubation medium followed by cooling the samples at 4°C.

The significance of differences was evaluated using Student t test. The differences were significant at $p<0.05$.

RESULTS

The content of CP was minimum in 2-month-old W/SSM rats, in 6-month-old animals this parameter increased and attained maximum values in 11-month-old rats (Table 1).

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In Wistar rats, the content was CP was minimum at the age of 2 month; this parameter increased in 6-month-old animals, but remained practically unchanged in 11-month-old rats. CP content in 2-month-old W/SSM rats was higher than in Wistar rats of the corresponding age. At the age of 6 months, no differences in serum CP content was found between W/SSM and Wistar rats. CP content in 11-month-old W/SSM rats was higher than in Wistar rats of the corresponding age.

It can be hypothesized that increased content of CP in W/SSM rats is a manifestation of the compensatory and adaptive reaction of the organism to activation of free-radical and peroxidation processes. Previous studies demonstrated enhanced generation of hydroxyl radicals (by 1.5 times) in the myocardium of 10-12-month-old W/SSM rats [4] against the background of reduced activities of catalase and SOD [6]; reduced content of α-tocopherol in the plasma of 2-month-old W/SSM rats was also reported [2].

Antiradical role of CP can be realized via inhibition of myeloperoxidase activity of neutrophils [5], which are the main source of oxygen radicals in 3- and 12-month-old W/SSM rats [3]. The content of CP in W/SSM rats in these periods considerably surpassed the corresponding parameters in Wistar rats (Table 1).

Thus, we revealed an increase in CP content in W/SSM rats with genetically determined disturbances in carbohydrate (galactose) metabolism from the 2nd through 11th month of life. In Wistar rats, the increase in CP level was observed from the 2nd through 6th month of life. The increase in CP content is an important mechanism of the antioxidant and antiradical defense at the age of 2 and 11 months.

TABLE 1. Serum CP Content in W/SSM and Wistar Rats of Different Age (mg/liter, $M \pm m$)

Age, months	Wistar rats	W/SSM rats
2	192.46±19.35 (n=7)	246.82±18.6^{+} (n=7)
6	373.3±24.1** (n=6)	357.3±25.1* (n=5)
11	390.2±18.2** (n=6)	502.5±0.1^{*+o} (n=5)

Note. *p<0.01, **p<0.001 compared to 2-month-old rats; ^{o}p<0.01 compared to 6-month-old rats; ^{+}p<0.05, ^{++}p<0.01 compared to Wistar rats.

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