EFFECT OF OVARIAN TRANSPLANTATION ON ZINC METABOLISM OF MALE RATS

A. A. Gaibullaev, N. A. Lopatkin, L. P. Evseev, and E. A. Sevryukov

UDC 612.015.31:546.47].06:[612.661.1+612.621.31].019:599.323.4

KEY WORDS: zinc; transplantation; ovary.

Zinc ions are actively concentrated in the prostate gland of many species of animals and man and they are a specific component of the secretion of this gland [1]. Zinc is found in the secretory granules and in the endoplasmic reticulum of prostate gland cells [4]. Zinc has been shown to bind with prostate gland proteins, which are not the same as androgen-binding proteins [5]. The role of zinc in the function of the male accessory glands has not been precisely established. However, it is known that the concentration of zinc ions in prostate gland tissue is functionally closely related to metabolism of androgens, which determine its metabolic and secretory activity [2]. Injection of estrogens into male rats and castration lead to a decrease in the zinc content in the prostate gland, whereas under the influence of testosterone, its concentration in castrated animals rises significantly [3, 5].

In the present investigation the zinc ion concentration was studied in various biological fluids and organs during continuous estrogenization of the animal after free heterotopic ovarian transplantation into castrated male rats.

EXPERIMENTAL METHOD

The test material consisted of 90 male "August" rats weighing 180-200 g, kept on a standard laboratory diet. Free heterotopic isotransplantation of one-third of a native ovary into the greater omentum was performed on 40 rats after preliminary bilateral orchidectomy (group 1). Another 40 animals underwent bilateral orchidectomy only. Ten intact rats served as the control group. The animals were killed by decapitation 3, 7, 14, and 30 days after the operation. The zinc concentration in the blood serum, 24-hourly urine, and prostate gland homogenate was determined at these times on an atomic-adsorption spectrophotometer. The serum testosterone and estradiol concentrations were determined by radioimmunoassay, using standard "Sterone-T-1251" and "Sterone-E-1251" kits (Minsk). The viability of the transplant was assessed morphologically by light microscopy. The results were subjected to statistical analysis by Student's t test.

EXPERIMENTAL RESULTS

It will be clear from Fig. 1. that the 24-hourly zinc excretion with the urine of the control group of rats was 2.32 ± 0.39 μmoles. In rats after isotransplantation of the ovary (group 1) zinc excretion with the urine 3 days after the operation fell to 1.0 ± 0.21 μmole/day. After 7 and 14 days some tendency was noted for this parameter to rise (1.2 and 1.1 μmoles/day, respectively), but after 30 days zinc excretion was just below that observed 3 days after the operation (0.93 ± 0.14 μmole/day). In the castrated rats (group 2), a decrease in the 24-hourly zinc excretion also was detected by the 3rd day (0.87 ± 0.18 μmoles), by the 7th day it reached 0.72 ± 0.15 μmole/day, and it remained virtually at the same level until the 30th day. Comparison of the data for the three groups showed that the decrease in zinc excretion in rats of groups 1 and 2 compared with the control was significant ($p < 0.05$) at all times, whereas differences between groups 1 and 2 were not significant, except on the 7th day after the operation ($p < 0.05$).

Research Institute of Urology, Ministry of Health of the RSFSR, Moscow. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 112, No. 11, pp. 536-538, November, 1991. Original article submitted November 26, 1990.

0007-4888/91/0011-1653$12.50

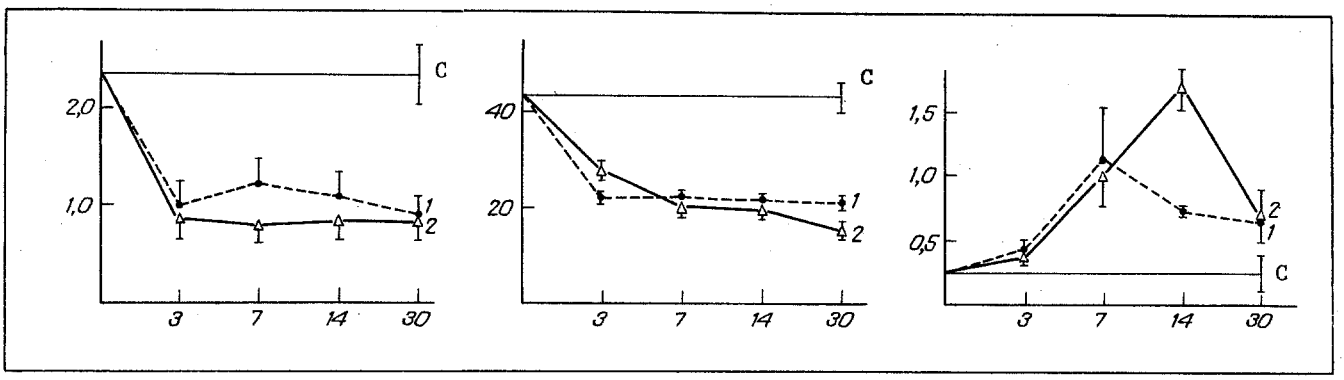

Fig. 1 Fig. 2 Fig. 3

Fig. 1. 24-Hourly excretion of zinc with urine (in μmoles/day) in castrated rats after (1) and without (2) ovarian transplantation. C) Control. Abscissa, time (in days); ordinate, zinc excretion with urine.

Fig. 2. Serum zinc concentration (in μmoles/liter) in castrated rats after (1) and without (2) ovarian transplantation. Here and in Fig. 3: ordinate, zinc concentration. Remainder of legend as in Fig. 1.

Fig. 3. Zinc concentration in prostate homogenate (in mmoles/mg tissue) from castrated rats after (1) and without (2) ovarian transplantation.

The serum zinc concentration in rats of the control group was 43.0 ± 3.05 μmoles/liter (Fig. 2). In rats of group 1, 3 days after the operation the serum zinc concentration was lowered to 22.3 ± 2.18 μmoles/liter, after which it remained virtually unchanged. In rats of group 2 the zinc concentration fell until the 7th day (20.4 ± 1.27 μmoles/liter), after which it also remained virtually unchanged. Significant differences were observed only between parameters for the animals of groups 1 and 2 compared with the control ($p < 0.05$).

The zinc content in the prostatic homogenate was 73.6 ± 1.94 nmoles in rats of the control group. In rats of groups 1 and 2 undergoing the operations a gradual decline was observed in the prostatic zinc level toward the 30th day (to 12.7 ± 1.6 and 14.5 ± 3.9 nmoles, respectively). There was a simultaneous decrease in the mass of the prostate gland. When the zinc content was expressed per milligram prostatic tissue, the curves reflecting its course after the operation were different in character. In both the 1st and the 2nd groups, however, this parameter increased from the 3rd until the 14th day after the operation, and it then declined until the 30th day (Fig. 3).

The serum testosterone and estradiol concentrations in the control amounted to 8.92 ± 0.25 and 0.503 ± 0.86 nmoles/liter, respectively. In the orchidectomized rats the testosterone concentration fell significantly (by 7-90 times), but it was significant higher in group 1 than in group 2. A different pattern was observed in the study of the estradiol concentration. It was significantly raised in the animals of group 1 compared with the control, on average to 0.75 nmole/liter, whereas in group 2 its value fell significantly compared with that in the control and in group 1.

The results of these investigations confirm the interconnection between zinc metabolism and androgens. This is shown by a decrease in the serum zinc and testosterone concentrations in animals undergoing the operation. Starting with the 7th day, the serum zinc concentration was higher (although not significantly) in group 1, which can probably be attributed to the higher serum testosterone level than in group 2. The higher testosterone level in rats with ovarian isotransplantation must be attributed to the functional activity of the transplant, which, together with estrogens, also produces testosterone. In our view, the fall of the blood zinc concentration was due to disturbance of its absorption in the gastrointestinal tract in the presence of androgen deficiency. Reduction of the 24-hourly zinc excretion with the urine can probably be explained by a fall in its serum level.

The increase in the zinc content per milligram prostatic tissue was evidently due to a faster decline in the mass of the prostate gland compared with the decline in its zinc concentration at a certain stage (7th-14th days) of the experiments.

The investigation showed that castration, like free ovarian transplantation after preliminary castration, leads to a decrease in the serum zinc concentration, and reduction of zinc excretion with the urine. The significant differences in the serum estradiol concentration in the animals of these groups do not lead to any significant differences in zinc metabolism, probably due to the lower blood testosterone level than in the control.

LITERATURE CITED

1. W. I. P. Mainwaring, Mechanisms of Action of Androgens [Russian translation], Moscow (1979).
2. A. S. Portnoi and F. L. Grozdovskaya, Carcinoma and Adenoma of the Prostate Gland [in Russian], Leningrad (1984).
3. J. A. Chandler, M. A. Harper, G. K. Blumdell, and M. S. Mortan, J. Endocr., **65**, 34 (1975).
4. S. P. Mettah, A. S. Prasad, E. Du Mouchelle, et al., Nutr. Res., **4**, No. 3, 437 (1984).
5. M. J. Reed and S. R. Stitch, J. Endocr., **58**, 405 (1973).

EFFECT OF CONDITIONED MEDIUM OF NEONATAL RAT HEPATOCYTES ON MIXED CULTURE OF KUPFFER CELLS AND FIBROBLAST-LIKE LIVER CELLS

N. S. Stvolinskaya, S. I. Tabuntsova, and B. F. Korovkin*

UDC 612.35.014.1.086.8.33

KEY WORDS: cell cultures; Kupffer cells.

Kupffer cells (KC) of the liver account for about one-tenth of the cell mass of the liver [9]. The KC are small and occupy about 2% of the volume of the liver [5]. The importance of KC in the body is great. They are unique "cleaners," they play an important role in purification of the circulating fluid from defective and foreign compounds and particles, including aging erythrocytes, liposomes, microorganisms and endotoxins, they remove cholesterol esters [10], and they specifically generate glycoproteins from the blood and utilize them [7]. KC form prostaglandins and thromboxane, and accordingly they play an important role in the regulation of glycogenolysis and of the hemodynamics in the liver [11], and regulate the blood flow through the hepatic sinusoids, working like sphincters [6].

During work with a culture of neonatal rat hepatocytes [2] we paid particular attention to the fact that during culture of these cells for more than 2 weeks, fibroblast-like cells actively proliferate, and small independent colonies of KC and endothelial cells also begin to appear, although the latter usually cannot be cultured without growth factors. The morphological picture observed suggests that during mixed culture the role of growth and differentiation factors is played by cell junctions or by soluble compounds present in the culture medium. We studied the effect of conditioned medium of a neonatal rat hepatocyte culture on a mixed culture of KC and fibroblast-like rat liver cells during culture for 12 days.

EXPERIMENTAL METHOD

The method of obtaining the neonatal rat hepatocyte culture was previously described in detail [2].

*Corresponding Member of the Academy of Medical Sciences of the USSR.

Laboratory of Enzymology of Extremal States, Institute of Biological and Medical Chemistry, Academy of Medical Sciences of the USSR, Moscow.

Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 112, No. 11, pp. 538-541, November, 1991. Original article submitted March 29, 1991.