EFFECT OF POTASSIUM OROTATE ON THE TRANSPORT OF ORGANIC SUBSTANCES IN THE KIDNEYS

B. Ya. Varshavskii, S. G. Verlinskii, and V. A. Biryulya

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Daily administration of 50-100 mg/kg potassium orotate for 7-10 days in experiments on dogs and rats led to an increase in the renal tubular secretion of diodone and the reabsorption of glucose and, to a lesser degree, an increase in glomerular filtration. The results point to an involvement of the tubular transport systems for the secretion and reabsorption of organic substances with protein synthesis.

The secretion of organic substances and reabsorption of glucose in the proximal tubules of the kidneys are known to be active processes performed by special carriers [12] of presumptive protein nature [2].

To study the role of proteins in the tubular transport of organic acids and glucose, the effect of potassium orotate, an anabolic agent, on these processes was studied.

EXPERIMENTAL METHOD

The effect of orotate on the secretion of diodone and reabsorption of glucose was studied in chronic experiments on dogs and rats. The experiments on dogs were carried out by the classical method [10] adapted for chronic experiments. Dogs with ureters exteriorized by the Pavlov–Tsitovich method received an infusion of a solution containing 20% glucose, 4% diodone, and 2% inulin at the rate of 2-5 ml/min into a subcutaneous vein of the hind limb. After the lapse of 1 h the urine was collected every 10 min (2-3 clearance periods). In the middle of each period blood was taken from a vein of another limb. Inulin [4], diodone [6], and glucose (by the orthotoluidine method) were determined in the blood and urine. Potassium orotate was given to the dogs by mouth for 10 days in a dose of 50 mg/kg.

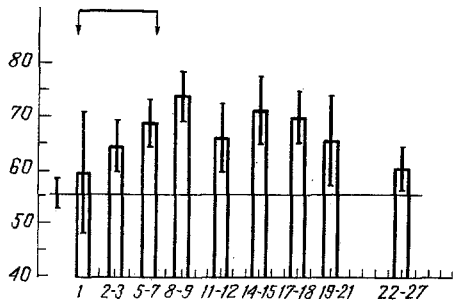

Fig. 1. Effect of potassium orotate (100 mg/kg) on the secretory activity of the rat kidney. Horizontal line represents initial level of diodone excretion. Arrows mark period during which animals received potassium orotate. Abscissa, days of observation (numbers represent days for which the mean data are shown as columns); ordinate, percentage excretion of diodone.

The hourly diuresis was recorded after this time and diodone was determined in the collected urine and its percentage excretion calculated. According to these observations, 80% of the diodone excreted hourly was accounted for by the secretory fraction [1]. Potassium orotate was given to the rats in a dose of 100 mg/kg for 7 days.

EXPERIMENTAL RESULTS AND DISCUSSION

The mean results of 129 experiments on 14 rats are illustrated in Fig. 1. This shows that, starting from the 2nd-3rd day of administration of orotate to the animals there was a gradual increase in the secretory function of the kidneys,

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TABLE 1. Effect of Potassium Orotate on Filtration, Maximal Diodone Secretion, and Maximal Glucose Reabsorption in Dogs (M ± m)

Day of observations	Filtration	Number of clearance periods	Diodone secretion	Glucose reabsorption
Initial level	26	100±1,2	100±1,8	100±2,2
Potassium orotate (50 mg/kg for 10 days)				
9-th	8	106±4,5	149±16,7	118±14,1
P		>0,5	<0,01	>0,5
13-th	8	116±4,5	152±15,6	153±16,1
P		<0,01	<0,001	<0,01
16-th	8	112±2,8	134±3,9	136±8,1
P		<0,001	<0,001	<0,001
20-th	8	109±5,0	119±6,5	133±16,2
P		<0,1	<0,01	<0,05
26-th	8	96±3,1	99±3,2	104±7,8
P		>0,5	>0,5	>0,5

Note. Changes are shown in the Table as percentages of the initial level.

reaching a maximum by the 8th-9th day of observation. On the following days the secretory index fell slowly and the initial level was not reached until the end of a month of observations.

In the chronic experiments on four dogs, the results of which are summarized in Table 1, feeding for 10 days with orotate led to a progressive increase in the maximal diodone secretion and maximal glucose reabsorption, and also in the glomerular filtration with the greatest changes on the 13th day of observation. Later these indices gradually fell, to reach their initial values by the end of 1 month after the experiments began. Quantitatively speaking the changes in diodone secretion and glucose reabsorption were more marked than the changes in glomerular filtration.

These experiments thus showed that under the influence of potassium orotate there is a marked increase in the activity of the tubular secretion of diodone and reabsorption of glucose and, to a lesser degree, in the glomerular filtration. According to data in the literature, after administration of orotic acid to animals the tissue respiration in the kidneys is virtually unchanged [3], but the content of pyridine nucleotides and ATP in the tissues actually falls somewhat [5, 9]. This last observation may indicate activation of the transport ATPases of the cell membranes of the kidneys responsible for active transport of macromolecules through the cells of the proximal tubules. Orotic acid, meanwhile, penetrates readily into the cells of many different organs, where it induces a sharp increase in RNA synthesis [7], especially mRNA [8], and promotes the formation of polysomes [11], thereby activating protein synthesis. This could lead to hypertrophy of the cells of the renal tubules and glomeruli, with a subsequent increase in their function. The possibility cannot be ruled out that the increase in the secretory transport of organic acids and the reabsorption transport of glucose observed in these experiments is due to an increase in the number of protein carriers in the cells and, in particular, of transport ATPases in the cell membranes of the proximal tubules. This link between the observed effects and protein synthesis is also confirmed by the fact that changes in secretion, reabsorption, and filtration developed gradually over a period of several days.

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