EFFECT OF RETABOLIL ON TUBULAR SECRETION OF THE KIDNEYS

V. A. Kuvshinnikova

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The anabolic steroid retabolil, in chronic experiments on dogs (2 mg/kg for 7 days) and rats (5 mg/kg for 7 days) increased the renal tubular secretion of diodone. At the same time the concentration of protein and RNA in the renal cortex was increased, which could indicate the protein nature of the carrier taking part in renal secretory transport.
KEY WORDS: *anabolic steroids; renal tubular secretion; synthesis of protein and RNA.*

The secretion of organic substances in the proximal tubules of the kidneys is known to be an active process performed with the aid of special carriers [4, 10]. It is considered that one such carrier is a special protein complex [1].

It was accordingly decided to study changes in secretion under the influence of anabolid substances and, in particular, of retabolil.

EXPERIMENTAL METHOD

Experiments were carried out on dogs by the classical method [9] adapted for chronic conditions. A solution containing 4% diodone and 2% inulin was injected intravenously at the rate of 2-5 ml/min into dogs with exteriorized ureters. After 1 h, urine began to be collected every 10 min (2-3 clearance periods). In the middle of the periods blood was taken and inulin [3] and diodone [6] were determined in the blood and urine. Retabolil was injected subcutaneously in a dose of 2 mg/kg daily for 7 days.

TABLE 1. Effect of Retabolil (2 mg/kg daily for 7 days) on Maximal Secretion of Diodone and Glomerular Filtration in Dogs

Index studied	Initial data	Days after beginning of injection of retabolil					
		3	7	10	15	20	30
Secretion of diodone (in mg/min)	22,3 25,1 25,3	32,2	36,1	40,9	43,7	34,2	27,0
Filtration (in ml/min)	27,3 27,7 26,2	25,9	30,5	28,1	34,4	26,0	28,8

Experiments on rats were carried out by a method specially developed in the department [2]. Diodone was injected intraperitoneally in a dose of 500 mg/kg, as a 2.5% solution, into the animals 25 min after water loading. The percentage of excreted diodone was determined in urine collected over a period of 1 h. Retabolil was injected in a dose of 5 mg/kg daily for 7 days. On certain days some of the rats were killed, the kidneys were removed, and the concentration of protein [7] and RNA [5, 8] was determined in the cortex.

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TABLE 2. Effect of Retabolil (5 mg/kg daily for 7 days) on Secretory Power of Rat Kidneys

Index studied	Statistical index	Before beginning of retabolil injections	Days after beginning of injection of retabolil					
			3	8	11	16	21	29
Excretion of diodone (in % of injected dose)	n	33	14	13	11	13	10	12
	M	60,2	72,6	70,5	71,5	67,5	57,4	57,5
	$\pm m$	1,46	3,41	3,27	2,30	2,80	4,47	2,81
	P		<0,001	<0,01	<0,001	<0,05	<0,5	<0,5

TABLE 3. Concentration of Protein and RNA in Renal Cortex of Rats Receiving Retabolil

Times of investigation	Protein (in mg/g)			RNA (in mg/g)		
	n	$M \pm m$	P	n	$M \pm m$	P
Before injection of retabolil	10	93±3,5		10	3,5±0,14	
After injection of retabolil:						
3rd day	10	125±4,4	<0,001	10	4,9±0,25	<0,001
11th day	11	132±7,7	<0,001	11	4,5±0,15	<0,001
21st day	6	90±6,9	<0,5	6	3,6±0,19	<0,5

EXPERIMENTAL RESULTS

Experiments on three dogs showed that injection of retabolil led to a rapid increase in the maximal secretion of diodone, which was at almost twice the initial level by the 10th day (Table 1). Later the secretory ability of the kidneys gradually fell to its initial values. The glomerular filtration showed a much smaller increase. The results of the experiments on rats are given in Table 2. Just as in the experiments on dogs, retabolil caused a rapid and considerable increase in the secretory function of the renal tubules, which lasted for more than 2 weeks.

These experiments showed that under the influence of retabolil the renal secretion of diodone was considerably increased whereas only minor changes occurred in the glomerular filtration. This indicates that the tubular system of the kidneys is influenced by retabolil more than the glomerular system. Since retabolil is an anabolic agent, it could be expected that the activation of transport processes in the tubules would depend on increased protein synthesis in the cells responsible for transport. Since the proximal portion of the tubules in the nephron, where secretion processes take place, lies mainly in the cortical tissue of the kidney, the concentration of protein and RNA was determined in that part of the kidney; animals were killed on days when the changes in secretory function were greatest. It will be clear from the results in Table 3 that there is a clear parallel between changes in secretory activity and the concentrations of protein and RNA in the kidney cortex.

These results support the view that stimulation of the secretory transport of organic substances in the proximal tubules of the nephron is brought about through an increase in the synthesis of RNA and protein in the cells of the tubules, with a consequent increase in the number of carriers.

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