EFFECT OF TACTIVIN ON DIURESIS AND TUBULAR SECRETION OF DIODONE IN THE KIDNEY

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UDC 615.275.4.015.4:612.46].076.9

KEY WORDS: tactivin; xenobiotics; renal transport.

A number of preparations with high immunobiologial activity have now been obtained from the thymus [1, 9, 11]. One of them is tactivin (or T-activin), which has been well characterized from both physicochemical and biological aspects [3, 4]. Tactivin has found widespread application in clinical practice [2].

In view of reports that the thymus influences the endocrine system and processes of protein biosynthesis and energy metabolism [10], it was decided to study the action of tactivin on renal function, including tubular secretion of foreign substances, more especially because other preparations with an influence on the immune system (levamisole, prodigiosan, 5-hydroxymethyluracil) also accelerate renal transport of xenobiotics [6, 7].

EXPERIMENTAL METHOD

Experiments were carried out on noninbred rats kept on a constant diet with water ad lib. The effects on diuresis were studied in chronic experiments, for which purpose the animals were kept in individual metabolism cages. Diuresis, excretion of sodium, potassium, uric acid, and creatinine (the last of these serving as a measure of glomerular filtration) were determined daily. Mean parameters were calculated for each animal in the initial period, after which tactivin was injected subcutaneously in a dose of 20 μg/kg daily for 6 days. Tubular secretion was studied in intact animals on the basis of diodone excretion [8]. The determination was carried out twice or three times in the initial period and four or five times at various times after the beginning of administration of tactivin. In addition, maximal transport of diodone was investigated in acute experiments under pentobarbital anesthesia by the classical method, with simultaneous determination of glomerular filtration by the inulin method. A solution of electrolytes with inulin and diodone was injected intravenously at the rate of 0.1 ml/min by means of a perfusion pump. In this series of experiments tactivin was injected on six consecutive days in a dose of 7 μg/kg. The results were compared with data for the control group of animals, not receiving tactivin.

EXPERIMENTAL RESULTS

It will be clear from Table 1 that the 24-hour diuresis increased significantly (on average by 70%) after the first injection of tactivin, but later returned to its initial level. The first injection of tactivin was also accompanied by stimulation of natriuresis (on average by 73%). Starting with the 2nd day, sodium excretion did not differ from the control. Potassium excretion showed no significant changes. Excretion of creatinine likewise was virtually unchanged, evidence of the relative stability of glomerular filtration. Excretion of uric acid showed a weak tendency to rise during the first days, but later it did not differ from the background value. Thus a course of tactivin injections had no adverse effect on diuresis. A brief increase in the diuresis and natriuresis was observed.

Table 2 gives results of a study of tubular secretion in the kidneys. Diodone excretion was significantly increased throughout the period of tactivin administration (at most by 21% of the initial level). This parameter 3 days after the end of the injections was already within the limits of the control values. Since diodone excretion depends partly on

Research Institute of Physicochemical Medicine, Ministry of Health of the RSFSR, Moscow. Department of Pharmacology, Altai Medical Institute, Barnaul. (Presented by Academician of the Academy of Medical Sciences of the USSR Yu. M. Lopukhin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 107, No. 3, pp. 264-266, March, 1989. Original article submitted March 25, 1988.

0007-4888/89/0003-0283$12.50

TABLE 1. Effect of Tactivin (20 μg/kg, 6 days) on Renal Function in Rats (M ± m, n = 11)

Period of observation	Diuresis, ml/day	Sodium excretion, μeq/day	Potassium excretion, μeq/day	Creatinine excretion, μmoles/day	Uric acid, mg/day
Control (background)	5,6±0,4	14,8±1,5	548,0±35,7	30,3±2,6	1,1±0,1
After 1st injection	9,6±1,3*	25,6±3,8*	662,0±66,3	35,6±3,0	1,5±0,2
After 2nd injection	7,5±1,0	19,6±5,3	535,0±46,1	29,6±2,5	1,4±0,2
After 4th injection	7,8±1,4	15,9±4,2	540,0±74,6	26,9±3,2	1,1±0,3
After 6th injection	6,3±0,6	12,1±2,8	519,0±54,3	25,6±1,4	1,1±0,2
3 days after end	5,9±0,9	14,2±1,6	575,0±54,5	33,1±5,6	1,2±0,1

Legend. Here and in Table 2: *p < 0.05.

TABLE 2. Effect of Tactivin (20 μg/kg, 6 days) on Diodone Excretion in Rats (M ± m)

Period of observation	n	Diuresis, ml/h	Diodone excretion, %/h
Control	12	4,8±0,2	60,6±1,0
After 1st injection	11	6,0±0,2*	67,1±2,6*
After 4th injection	9	5,6±0,4	67,7±2,9*
After 6th injection	10	5,3±0,2	73,1±4,1*
3 days after end	9	5,3±0,3	63,7±4,9
7 days after end	8	4,9±0,8	59,8±4,7

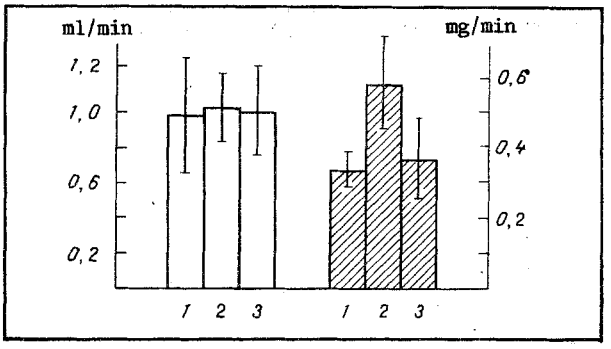

Fig. 1. Effect of tactivin (7 μg/kg subcutaneously daily for 6 days) on glomerular filtration and maximal diodone transport (shaded columns, ordinate on right) in rats. Abscissa: 1) control group, 2) after course of treatment with tactivin, 3) 6 days after end of course; ordinate: on left, glomerular filtration (in ml/min); on right, maximal diodone transport.

changes in glomerular filtration, the result was tested in experiments to determine maximal diodone transport. In this case the effect of filtration was ruled out, and secretion was expressed in absolute amounts of substrate transported in unit time. The results (Fig. 1) show that six daily injections of tactivin led to a considerable increase in transport of the xenobiotic (on average by 73%), whereas glomerular filtration remained stable. Diodone secretion did not differ from the control 6 days after the end of tactivin injections.

The results show that a course of treatment with tactivin does not disturb renal function as regards excretion of water, electrolytes, and products of nitrogen metabolism, and does not change glomerular filtration, but causes a significant increase in secretory transport of xenobiotics and, in particular, of diodone. The mechanism of increased secretion may be connected with the influence of the thymus on protein synthesis, of which there are indications in the literature [10]. Meanwhile we know that anabolic agents have a stimulating effect on tubular secretion in the kidneys [5]. Since tubular transport of xenobiotics is an active, energy-dependent process, attention must also be paid to data on the stimulating

effect of tactivin on energy metabolism obtained in rats in response to doses similar to those used in the present study [10]. Finally, the possibility cannot be ruled out that certain mechanisms of the effect of tactivin and other immunostimulants on the macrophagal-lymphocytic system are involved in activation of the secretory-transport system of the kidneys, which protects the body against low-molecular-weight xenobiotics. This view is supported by the analogous effect of other immunostimulating agents on the tubular system [6, 7].

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