EFFECT OF PROLONGED ADMINISTRATION OF PYRAZOLONE DERIVATIVES TOGETHER WITH PREDNISOLONE ON RENAL TUBULAR FUNCTION

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UDC 612.465.2.014.46:615.754.6

Administration of preparations of the pyrazolone series (amidopyrin, butadione) for 45 days led to a statistically significant decrease in the maximal excretion of cardiotrast. This was the result of a decrease in the excretory power of the epithelium of the proximal tubules. Amidopyrin in conjunction with prednisolone, when administered for a long period, causes a less marked disturbance of the maximal cardiotrast excretion.

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Clinical and experimental studies have shown that the use of pyrazolone preparations may disturb renal activity [4-6, 8-10, 18].

For this reason we studied the tubular function of the nephron during prolonged administration of preparations of the pyrazolone series (amidopyrin and butadione) alone and in conjunction with prednisolone.

EXPERIMENTAL METHOD

Experiments were carried out on 18 dogs with ureters exteriorized onto the anterior abdominal wall. The dogs were divided into two groups. Nine dogs in group 1 received amidopyrin (60 mg/kg) by mouth for 45 days and 3 dogs received butadione (12 mg/kg). Six dogs in group 2 received the same dose of amidopyrin together with prednisolone (20 mg/kg throughout the course). In all the animals the glomerular filtration was determined by the inulin method (C_{in}), and the renal plasma flow (C_c), and the secretory power of the tubular epithelium were determined by means of cardiotrast (T_{m_c}).

EXPERIMENTAL RESULTS

The data given in Table 1 show that administration of amidopyrin and butadione for 45 days led to a decrease in glomerular filtration. The plasma flow through the kidneys was decreased towards the end of this period. The decrease in maximal tubular excretion of cardiotrast was particularly marked (35.8%).

The increase in the ratio C_{in}/T_{m_c} under the influence of pyrazolone derivatives indicates disturbance of glomerulo-tubular equilibrium during the prolonged administration of these preparations.

In the opinion of some investigators [2, 17], the ratio C_c/T_{m_c} reflects the intensity of perfusion of the renal parenchyma. As the results given in Table 1 show, in the animals of group 1 this ratio was substantially increased. When amidopyrine was given together with prednisolone, no statistically significant decrease in the glomerular filtration was found. The renal plasma flow was reduced to a lesser degree than when amidopyrin was given alone. The maximal tubular excretion of cardiotrast fell by 24% compared with the control value. According to some investigators, this value may reflect quantitatively the function of the renal tubular apparatus [2, 17].

The increase in the ratio C_{in}/T_{m_c} in the animals of group 2 was less marked than in those of group 1, but the ratio C_c/T_{m_c} was not significantly changed.

The value of T_{m_c} can be used as quantitative index of renal tubular function. From this point of view, the decrease in the secretory power of the tubular epithelium during prolonged administration of preparations of the pyrazolone series could be the results of exclusion of several nephrons as a result of toxic damage. However, as investigations have shown, the exclusion of this number of nephrons (about 40%) would

Department of Pharmacology, Ivanov Medical Institute (Presented by Active Member of the Academy of Medical Sciences of the USSR V. V. Zakusov). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 66, No. 7, pp. 79-81, July, 1968. Original article submitted April 10, 1967.

TABLE 1. Dynamics of Renal Function during Prolonged Administration of Pyrazolone Derivatives Alone and in Conjunction with Prednisolone

Time of investigation	Indices									
	C_{in} in ml/min/m²		Tm_c in mg/min/m²		C_c in ml/min/m²		$\frac{C_{in}}{Tm_c}$		$\frac{C_c}{Tm_c}$	
	1 Group	2 Group	1 Group	2 Group	1 Group	2 Group	1 Group	2 Group	1 Group	2 Group
Initial data	83.56	83.25	14.05	14.18	392	402	5.85	5.88	27.9	28.3
45 days later	73.84	80.2	8.98*	11.3*	296*	356	8.22*	7.11	33.0*	29.77

*$P < 0.05$.

inevitably cause a decrease of equal degree in the renal plasma flow and the glomerular filtration [12, 17]. However, we did not observe such a marked decrease in the values of glomerular filtration and renal plasma flow.

The increase in the ratio C_{in}/Tm_c indicates damage mainly to the tubular apparatus of the kidneys during prolonged administration of preparations of the pyrazolone series and suggests that the decrease in secretion may be attributed to lowering of the functional power of the tubules. We suggest that the increase in C_c/Tm_c is not the result of an improvement in the blood supply to the tubular apparatus of the kidney, but the result of a decrease in the secretory power of the tubular epithelium.

During combined administration of amidopyrin and prednisolone we observed a less marked disturbance of the excretory power of the tubular epithelium. The mechanism of this action of prednisolone is not yet clear. It may be postulated that it has a beneficial action on some as yet undiscovered enzymic processes essential for the active transport of cardiotrast. Some investigators have found an improvment in excretory function during administration of corticosteroid hormones [3, 7, 13, 16], while others have reported the opposite action [1, 11, 14, 15].

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