ACTION OF UNITHIOL AND CYSTEINE ON THE RENAL EFFECT OF STROPHANTHIN

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It has recently been shown [2, 7-10] that the cardiac glycosides, by their direct action on the renal tubules, may decrease the reabsorption of sodium and water and, thereby, increase the diuresis and the sodium excretion. Since the thiol enzymes play an important role in the processes of reabsorption [1, 3, 5, 11, 12], it is possible that the renal effect of this group of preparations is the result of blocking of SH groups. In experiments on the isolated heart, unithiol considerably reduced the toxic action of digitalis [6]. V. P. Govorov and A. A. Rogov [4] showed that the prolonged adminstration of strophanthin in experiments on cats was accompanied by a decrease in activity of the SH groups in various organs including the kidneys.

EXPERIMENTAL METHOD

Experiments were carried out on 22 dogs weighing 14-17 kg under hexobarbital anesthesia. The urine was collected every 10-20 min separately from each kidney by means of ureteric catheters. To maintain a constant level of diuresis throughout the experiment, 0.9% sodium chloride solution was injected (3 ml/min) into a leg vein. During the control period (60 min) physiological saline was injected through a fine needle into the left renal artery at the rate of 1 ml min, and the saline was then replaced by strophanthin solution (10 μg/min, in 1 ml in the course of 80 min). These experiments acted as the controls for the next series, in which unithiol or cysteine (0.5 mg/kg in the course of 1 min) was injected into the leg vein 20 min before the beginning of the strophanthin injection. The injection of the SH group donors continued for 100 min. In some experiments unithiol was injected along with the strophanthin into the renal artery directly.

The filtration-reabsorption function of the kidneys was determined by the endogenous creatinine method. The sodium and potassium in the urine were investigated by the flame photometry method.

EXPERIMENTAL RESULTS

Strophanthin caused considerable changes in the diuresis and sodium excretion on the side of perfusion as a result of a decrease in the reabsorption of sodium and water in the tubules (see Table 1). Because the levels of diuresis, filtration, and reabsorption differed from dog to dog, to assess the effect quantitatively the ratio between these indices in the two kidneys was determined, taking the index for the right (control) kidney as 100. In the control periods before injection of the test preparations the right and left kidneys functioned in general on the same level. The diuresis and sodium excretion on the side of injection of strophanthin rose sharply compared with their values on the opposite side. The polyuria and increased sodium excretion were the result of depression of tubular reabsorption (a sharp rise in the amount of unabsorbed water and sodium). The glomerular filtration diminished under the influence of strophanthin, preventing the increase in diuresis and sodium excretion. The excretion of potassium on the side of injection of strophanthin was essentially indistinguishable from that by the intact kidney, and these results are therefore not included in Table 1.

Initially in the experiments in which unithiol or cysteine was injected into the general blood stream (intravenously) or directly into the renal artery a slight diuretic action of these substances was observed, resulting from the decrease in reabsorption of water with a slight increase in filtration, in agreement with observations reported in the literature [3, 5, 11, 12].

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TABLE 1. Action of Unithiol and Cysteine on the Renal Effect of Strophanthin

Experimental conditions	No. of exprs.	Diuresis R	Diuresis L	Na excretion R	Na excretion L	Unreabsorbed filtrate R	Unreabsorbed filtrate L	Unreabsorbed sodium R	Unreabsorbed sodium L	Filtration R	Filtration L	Appearance of an effect	Maximum of effect
Control periods	54	100	105±3,5	100	101±9,3	100	108±3,8	100	103±1,8	100	99±0,9	—	—
Strophanthin	7	100	400±31,9	100	483±33,1	100	474±37,1	100	608±49,3	100	84±2,9	40±4,0	70±7,3
Unithiol + strophanth	7	100	287±20,6	100	287±26,8	100	338±31,6	100	336±31,3	100	84±1,9	55±5,0	110±7,5
			$P<0,02$		$P<0,001$		$P<0,02$		$P<0,001$			$P<0,05$	$P<0,01$
Cysteine + strophanthin	4	100	318±11,6	100	274±36,0	100	361±14,1	100	344±32,0	100	82±0,6	75±10,0	120±8,1
			$P<0,1$		$P<0,01$		$P=0,05$		$P<0,01$			$P<0,01$	$P<0,001$

Note: P — Index of significance of differences between the results of the experiments of that group and the experiments; R — right and L — left kidney.

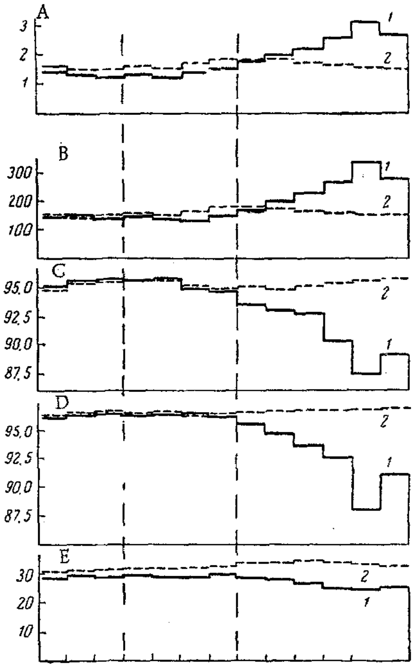

Fig. 1. Action of unithiol on the renal effect of strophanthin. Dog weighing 15 kg. Experiment on February 4, 1964. 1) Left (perfused) kidney; 2) right kidney; A — diuresis (in ml/min); B — sodium excretion (in μeq/min); C — reabsorption of water (in % of filtration); D — reabsorption of sodium (in % of filtration); E — filtration; the vertical broken lines demarcate the period of injection of strophanthin (10 μg/min) into the left renal artery together with unithiol (20 mg per kg/min); abscissa — time in intervals of 20 min.

Unithiol, like cysteine, diminished the renal effect of strophanthin: the increased sodium excretion and polyuria were not so marked. The antistrophanthin action of the SH group donors was due to the less marked depression of sodium and water reabsorption, whereas the effect of strophanthin on glomerular filtration persisted. The time of onset of the strophanthin effect and the time taken for it to reach its maximum were prolonged by the previous administration of unithiol and cysteine (see Table 1).

It should be noted that in none of the experiments was the strophanthin effect completely prevented by unithiol or cysteine. In subsequent experiments unithiol was used in much larger doses (20 mg per kg/min) and was injected together with the strophanthin directly into the renal artery. In these experiments, the results of one of which are given in Fig. 1, unithiol likewise did not completely abolish the action of strophanthin on the kidney.

It is evident that a definite role in the mechanism of action of strophanthin on tubular reabsorption is played by its action on SH groups. However, this mechanism is not decisive.

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