THE CARDIAC GLYCOSIDES AND REABSORPTION OF SODIUM IN THE RENAL TUBULES

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The cardiac glycosides, with the structure of steroids, are structurally similar to the hormones of the adrenal cortex. Experiments on erythrocytes [6], nerves [4], and muscles [3, 4] have shown that the cardiac glycosides may influence the transport of electrolytes through cell membranes. According to reports in the literature [2] and to the author's own observations [1], the cardiac glycosides when administered to the intact organism increase the excretion of sodium and water, by depressing their reabsorption in the tubules. This action is not due to the cardiotonic effect of strophanthin, for it is observed after direct injection into the renal artery on the side of perfusion.

The mineralocorticoids (aldosterone, DOCA) are known to stimulate the reabsorption of sodium and to increase the excretion of potassium. It may be postulated that the cardiac glycosides, giving good results in congestive cardiac failure, characterized by secondary hyperaldosteronism, have an antialdosterone action. The present investigation was carried out to study this problem.

EXPERIMENTAL METHOD

Acute experiments were carried out on dogs anesthetized with hexobarbital. Both ureters and the left renal artery were catheterized. The urine was collected separately from both kidneys every 10-20 min. The filtration-reabsorption function of the kidneys was estimated in relation to creatinine. The electrolytes in the urine and blood were investigated by the method of flame photometry. To maintain a constant level of diuresis, a 0.9% solution of sodium chloride was injected intravenously at the rate of 4 ml/min. For a period of 60 min a 0.9% solution of sodium chloride was injected into the renal artery at the rate of 1 ml/min, after which it was changed for a solution of strophanthin injected at the same rate in a dose of 10 μg/min for a period of 80 min.

Four series of experiments were carried out on 28 dogs. In series I (control) only strophanthin was injected by the method described above. In series II, 4-6 h before the experiment, DOCA was injected intramuscularly (2.5 mg/kg, in individual experiments 1 and 5 mg/kg). In series III the effect of strophanthin was studied on the activity of the kidneys after removal of aldosterone from the organism, which was achieved by adrenalectomy. In this case the experiments were carried out on the 4th-5th day after the operation. In the postoperative period the animals received a 1% solution of sodium chloride to drink. In series IV, the previously adrenalectomized dogs received DOCA 4-6 h before the experiment in the same doses as in series II.

EXPERIMENTAL RESULTS

In the control experiments the injection of strophanthin into the kidney caused an increase in the excretion of sodium and in the diuresis 20-40 min after the beginning of the injection as a result of a decrease in reabsorption; in these circumstances the glomerular filtration was slightly reduced (Fig. 1A). The effect described was unilateral and was observed in 7 of 10 experiments, in two experiments the increase in excretory activity affected both kidneys, and in one case no changes were observed in the activity of the kidneys.

In the experiments of series II, despite the preliminary administration of DOCA, in most experiments (in 4 of 7) strophanthin also caused a unilateral increase in sodium excretion as a result of a decrease in its reabsorption in the presence of very slight changes in filtration (Fig. 1B); in two experiments the effect was bilateral, and in one no changes took place in renal activity.

Against the background of DOCA the action of strophanthin developed more slowly. Whereas in the control experiments the excretion of sodium was increased on the average 20-40 min after the beginning of injection of the preparation, and the effect reached its maximum on the average after 80 min, in the experiments with

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Changes in Reabsorption, Filtration, and Excretion of Sodium under the Influence of Strophanthin after Adrenalectomy in a Dog Weighing 12 kg (Experiment on March 15, 1964; Adrenalectomy on March 9, 1964)

Time of collecting urine	Diuresis (in ml/min)		Filtration (in ml/min)		Excretion (in μeq/min)		Filtration (in μeq/min)		Reabsorption (in %)	
	L	R	L	R	L	R	L	R	L	R
11 h 20 min	0,82	0,75	16,0	15,3	121,3	99,0	2097,6	2005,8	94,21	95,06
11 » 40 »	0,86	0,82	16,1	15,7	121,2	102,5	2110,7	2058,3	94,25	95,01
12 »	0,80	0,76	15,7	16,4	120,0	98,8	2058,3	2150,0	94,16	95,40
12 » 20 min	0,61	0,80	12,4	15,6	83,6	102,4	1625,6	2045,1	94,85	94,99
12 » 40 »	0,78	0,84	14,9	15,8	113,1	99,1	1953,4	2071,3	94,21	95,22
13 »	1,05	0,78	12,0	15,4	158,5	95,9	1573,2	2018,9	89,92	95,24
13 » 20 min	1,92	0,75	11,1	15,0	311,0	93,0	1434,1	1938,0	78,31	95,20
13 » 40 »	2,60	0,71	10,6	16,7	364,0	89,5	1369,5	2157,6	73,42	95,85
14 »	2,10	0,67	10,0	16,4	289,8	87,1	1360,0	2118,9	78,69	95,88

Note. From 12 h until 13 h 20 min strophanthin was injected into the left renal artery in a dose of 10 μg/min.

Legend: L—left, R—right renal artery.

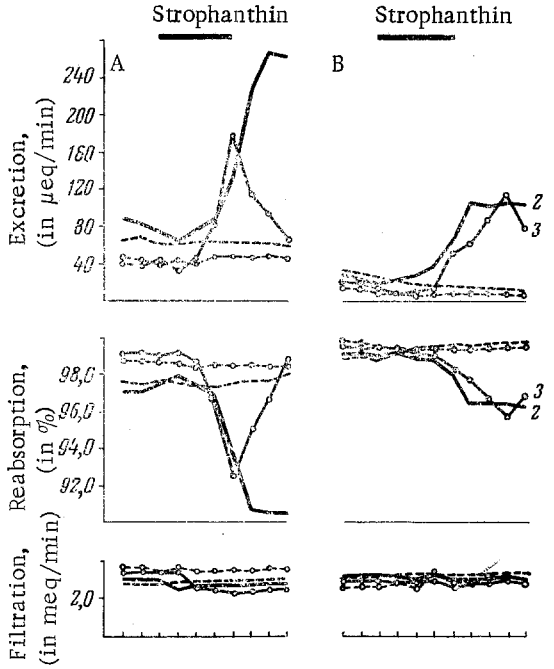

Fig. 1. Effect of strophanthin (10 mg/min) on the excretion, reabsorption, and filtration of sodium in intact dogs (A) and after administration of DOCA (B). Here and in Fig. 2: continuous line—experimental kidney; broken line—control kidney; the thick line denotes the period of excretion of strophanthin; the numbers above the curves show the serial number of the experiments; DOCA was given in doses of 1 mg/kg (Expt. No. 2) and 5 mg/kg (Expt. No. 3); along the horizontal axes—time (marker 20 min).

administration of DOCA the excretion of sodium developed after 60-80 min and reached its maximum on the average after 140 min.

Strophanthin was thus capable of depressing the reabsorption of sodium in the renal tubules even against the background of the action of DOCA, although in the latter case its effect developed later than in the control experiments. No relationship could be found between the dose of DOCA and the depression of the action of strophanthin. In Expt. No. 3 (Fig. 1B), for instance, DOCA was given in a much larger dose (5 mg/kg) than in Expt. No. 2 (1 mg/kg), but strophanthin produced approximately the same sodium-excreting effect. On the basis of these results it is difficult to suggest whether or not there is any direct antagonism between DOCA and strophanthin.

Important results for the solution of this problem may be obtained in experiments on adrenalectomized animals. If strophanthin has an antialdosterone action only, in these conditions it must have no effect on the kidneys.

In 4 of the 5 experiments on adrenalectomized dogs, injection of strophanthin into the renal artery was accompanied, as in the control experiments, by excretion of sodium as a result of depression of the reabsorption of sodium in the tubules (Fig. 2A). The results of one such experiment are given in the table. No effect was found only in one case. The results of these experiments showed that the sodium-excreting action of strophanthin persists after adrenalectomy.

The preliminary injection of DOCA into the adrenalectomized dogs in 5 of 6 cases did not abolish the effect of strophanthin on the tubular processes: the reabsorption of sodium was reduced, resulting in an increase in its excretion. In one of these experiments the effect was bilateral. In one dog injection of strophanthin caused, not a decrease, but an increase in the reabsorption of sodium. The administration of DOCA, without preventing the renal effect of

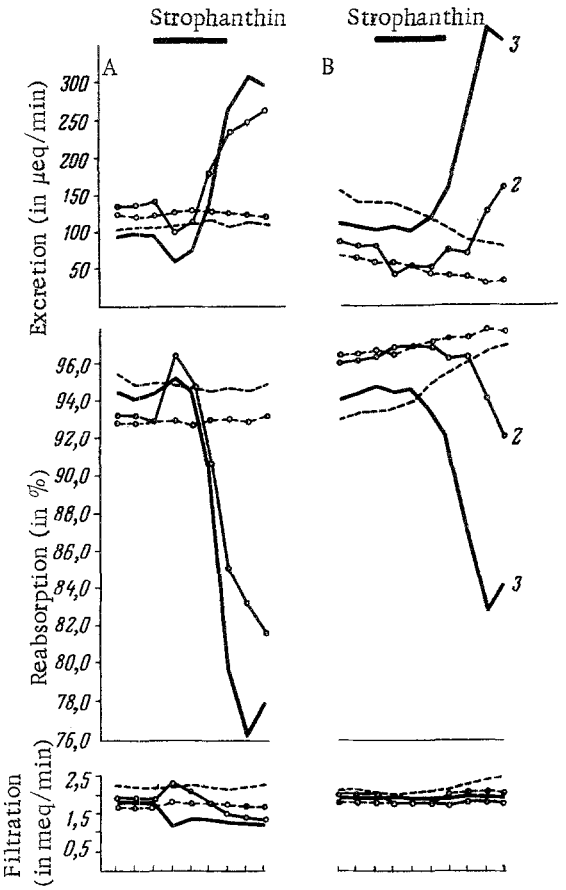

Fig. 2. Effect of strophanthin (10 μg/min) on the excretion, reabsorption, and filtration of sodium in adrenalectomized dogs (A) and in dogs adrenalectomized after administration of DOCA (B).

strophanthin, slightly prolonged the time taken for its development, as in the experiments of series II also. However, as in these earlier experiments, no parallel trend could be observed between the dose of DOCA and the inhibition of the effect of strophanthin on the activity of the kidneys.

When injected into the renal artery, strophanthin thus depresses the reabsorption of sodium in the renal tubules, increasing its excretion. This action of strophanthin persists after adrenalectomy. In experiments on intact and adrenalectomized animals DOCA does not prevent the renal effect of strophanthin, but merely delays its development slightly. The results obtained, although not ruling out the possibility of an antialdosterone action of the cardiac glycosides, demonstrate the direct effect of strophanthin on the tubular reabsorption of sodium.

LITERATURE CITED

1. B. A. Pakhmurnyi, Farmakol. i Toksikol., No. 3, 362 (1965).
2. S. J. Farber, J. D. Alexander, and E. D. Pellegrino et al., Circulation, Vol. 4 (1951), p. 378.
3. S. Hajdu and A. Szent-Gyorgyi, Amer. J. Physiol., Vol. 168 (1952), p. 171.
4. A. L. Hodgkin and R. D. Keynes, Sympos. Soc. Exper. Biol., Vol. 8 (1954), p. 423.
5. J. A. Johnson, Amer. J. Physiol., Vol. 187 (1956), p. 328.
6. H. J. Schatzmann, Helv. physiol. pharmacol. Acta, Vol. 11 (1953), p. 346.