DOCA-SALT HYPERTENSION IN CATS

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The mineralocorticoid model is one of the experimental models of hypertension which provides a sufficiently stable rise of arterial pressure. The most sensitive animals for the development of hypertensive states caused by injection of mineralocorticoids are rats and pigs [1-3]. Cats are rarely used for producing chronic forms of hypertension [4, 5], and no reports of the production of deoxycorticosterone hypertension in these animals could be traced.

The aim of this investigation was to study the possibility of obtaining stable hypertension in cats by injecting deoxycorticosterone acetate (DOCA) combined with salt loading, and the study of its hemodynamic characteristics.

EXPERIMENTAL METHOD

Experiments were carried out on 19 cats divided into three groups. In the 10 cats of group 1, after the initial pressure had been recorded, a DOCA depot was produced under the skin of the back by implantation of 50-70 mg of the compound in tablets, and in addition, 10 mg DOCA in oily solution was injected on alternate days intramuscularly over a period of 1-1.5 months. The cats were given salted meat and water. The arterial pressure (BP) was recorded in the femoral artery by means of an electromanometer in animals anesthetized with hexobarbital. In groups 2 and 3 (9 animals) DOCA was injected into cats, together with salt loading, after preliminary removal of the kidney through a lumbar approach. In group 2 DOCA was injected intramuscularly for 2 months (total dose 0.44 g). In group 3 the salt loading and dose of DOCA were increased; the latter was given daily for 6 months (total dose 1.8 g).

To assess the state of the cardiovascular system in cats in the initial state and every 2 months during the period of observation the ECG, integral rheogram, and BP curve were recorded under anesthesia. At the end of the investigation the dye (Evans' blue) dilution curve also was recorded (with the RRKM-1 instrument). Simultaneous recording of the dilution curve and integral rheogram enabled the cardiac output (CO) to be calculated retrospectively from the integral rheogram in the initial state and in the course of observation. The animals were killed by intravenous injection of large doses of hexobarbital.

EXPERIMENTAL RESULTS

The results of investigation of the animals of group 1 showed that hypertension developed in five of the 10 cats. The mean pressure in the animals with hypertension was increased from 108 ± 3 to 140 ± 6 mm Hg (Table 1). Marked thirst and increased diuresis were observed in these animals 1 week after the beginning of administration of DOCA and salt. After 1 month these symptoms became weaker or disappeared. The other five cats did not develop hypertension.

In group 2 BP was unchanged after administration of DOCA for 2 months, although some decrease was observed in the stroke volume (SV) and CO. Calculation of the total peripheral resistance (TPR) revealed an increase from 0.24 ± 0.04 to 0.32 ± 0.04 mm Hg.

In group 3, after 2 months BP in all animals was raised, SV and CO were slightly reduced, and TPR was increased (by 30%). After 6 months BP reached a maximum, CO was reduced by 25%, and TRP was sharply increased — by 71% (Table 1). In the nephrectomized cats, just as in the animals of group 1, polydipsia and polyuria were present, to a greater or lesser degree at

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TABLE 1. Changes in Parameters of Systemic Hemodynamics in DOCA-Salt Hypertension

Parameter	Group of animals	Initial value	Change after 1½–2 months	Change after 4 months	Change after 6 months
BP mean mm Hg	1	108±3	140±6	—	—
	2	113±7	115±8	—	—
	3	116±2	138±5	148±6	161±9
BP max, mm Hg	1	125±3	174±6	—	—
	2	126±6	137±10	—	—
	3	128±6	156±9	161±6	190±8
BP min, mm Hg	1	105±6	136±6	—	—
	2	97±8	96±9	—	—
	3	109±1	132±8	140±9	146±7
Pulse rate, beats/min	1	172±1	194±9	—	—
	2	169±2	159±9	—	—
	3	183±10	179±5	182±7	187±5
CO, ml/min	1	—	523±51	—	—
	2	528±75	411±109	—	—
	3	582±45	533±25	638±53	477±45
SV, ml	1	—	2,5±0,2	—	—
	2	3,1±0,7	2,5±0,5	—	—
	3	3,2±0,2	3,0±0,1	3,4±0,3	2,5±0,2
TPR, mm Hg (ml/min)	1	—	0,30±0,02	—	—
	2	0,24±0,04	0,32±0,04	—	—
	3	0,20±0,02	0,26±0,01	0,25±0,03	0,35±0,04

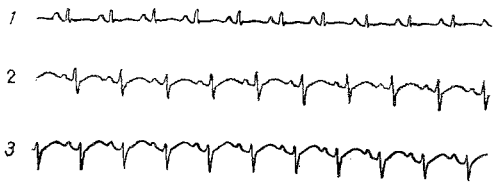

Fig. 1. Changes in ECG during development of DOCA-salt hypertension. 1) Initial ECG, 2) 2 months, 3) 6 months after beginning of DOCA administration.

different times of observation. In animals with increased thirst the increase in pressure was greater. In three cats periods of marked muscular weakness were observed at different times, the animals were unable to raise their head, and most of the time they lay stretched out, their muscles relaxed. The picture thus observed suggested hypokaliemia, manifested as Conn's syndrome. After 2 or 3 days these phenomena usually disappeared. Two cats were found to have ECG changes, namely deepening of the S wave, the appearance of an arched ST segment, and lowering of the amplitude of the R wave after 6 months of observation (Fig. 1).

At autopsy on all animals the residual kidney was enlarged. In the mesentery of the small intestine connective-tissue bands and pinpoint nodules were observed. In one cat an infarct of the wall of the left atrium was found. One cat died after 4 months with disturbance of the cerebral circulation.

As a result of prolonged administration of large quantities of DOCA and salt to unilaterally nephrectomized cats persistent hypertension with a sufficiently high BP level was obtained. In the course of this form of hypertension, changes in CO showed a biphasic tendency. The initial rise of BP was accompanied by a small decrease in CO and an increase in TPR. The subsequent increase in BP was probably the result of the increase in CO. The hypertension which developed was characterized by a sharply increased peripheral resistance and lowered CO.

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