THE EFFECT OF SUBSTANCES STIMULATING AND DEPRESSING THE CENTRAL NERVOUS SYSTEM ON THE QUANTITY AND QUALITY OF CORTICOSTEROIDS IN THE BLOOD OF DOGS AND GUINEA PIGS

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This work was carried out to study the effect of the neurotropic substances Dibazol and Diphenin on the hypophysis – adrenal cortex system.

Dibazol stimulates the central nervous system [1]. Diphenin, on the other hand, depresses certain centers of the brain (anticonvulsive, inhibits calomel secretion, decreases the amount of gastric juice during the reflex phase of secretion) [4, 8].

EXPERIMENTAL METHODS

We studied the effect of these substances on the adrenocortical function of male dogs weighing 20-25 kg each.

Our first undertaking was to determine the effect of Dibazol and Diphenin on the concentration of 17-hydroxycorticosteroids in the plasma of peripheral blood taken from the lateral vein of the dog's leg. The Silver and Porter method as modified by N. A. Yudaev and Yu. A. Pankov [10] was used to determine the content of 17-hydroxycorticosteroids. The low level of 17-hydroxycorticosteroids in these dogs (less than 0.5 γ% in two dogs and 1γ% in one) made it impossible to determine any authentic pattern of change in the 17-hydroxycorticosteroid content of the peripheral blood plasma.

We used the following method in order to obtain blood with a higher content of 17-hydroxycorticosteroids in the plasma: the dog was put under ether-oxygen endotracheal anesthesia, and an incision was made along the middle line of the abdomen. The section of the caudal vena cava with the renal and lumboadrenal veins was dissected out. Through an incision in the femoral vein, a polyethylene catheter was inserted somewhat craniad to the mouths of the lumboadrenal veins. When the catheter inserted was ascertained to have reached the required level, the vena cava was ligated caudad to the renal veins.

This method permits determination of 17-hydroxycorticosteroids in higher concentrations than are found in the peripheral blood.

At the mouths of the lumboadrenal veins, the 17-hydroxycorticosteroid content was four times that in the peripheral blood. The catheter was filled with heparin when no blood was being taken. Three to four days after the operation, when the increased 17-hydroxycorticosteroid content induced by the operation had returned to the normal level, we began taking blood samples from the mouths of the lumboadrenal veins.

We first determined the control level of the 17-hydroxycorticosteroid content in the dogs. Over a period of 30-50 days, 20 ml of blood for two parallel determinations was taken 5-6 times from each dog at intervals of 1-2 days. We next determined the 17-hydroxycorticosteroid content under the influence of Dibazol or Diphenin, the latter being introduced into the polyethylene catheter in a dose of 20 mg/kg each. Blood samples were taken 90 min after the administration of the experimental substance. The 17-hydroxycorticosteroids were determined by the method mentioned above.

EXPERIMENTAL RESULTS

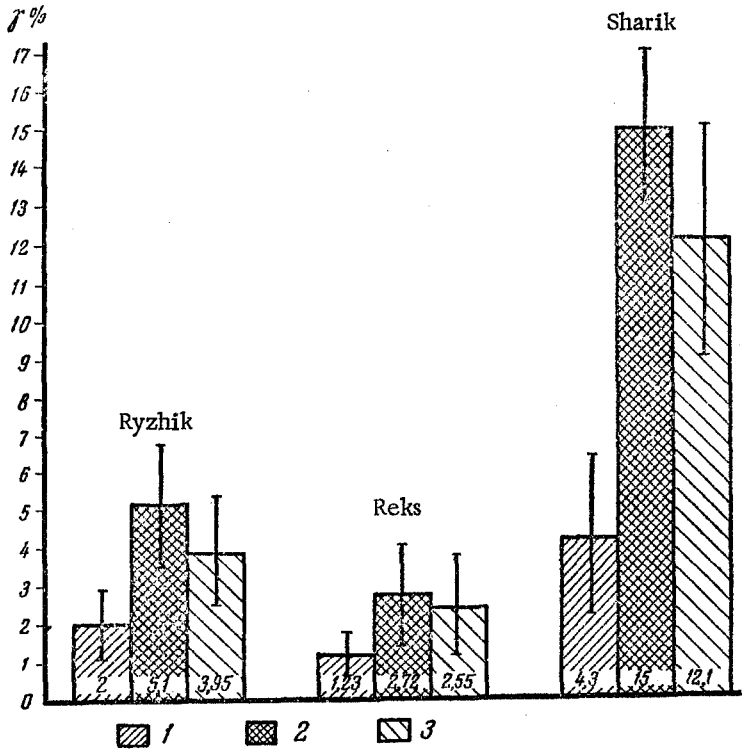
As the figure shows, the 17-hydroxycorticosteroid content of the blood plasma doubled under the influence of Diphenin and increased 2½ times under that of Dibazol. Statistical processing of the experimental results proved the effect observed to be significant.

The results obtained are in accord with the literature data [3, 7, 5, 6, 2, 9], which indicate that Dibazol raises the resistance of the organism to different harmful influences, and this effect could easily be the result of a stimulating influence on the hypophyseal-adrenal system.

Diphenin possesses an antidiuretic effect [4] associated with its influence on the secretion of the antidiuretic hormone. It has been established on the basis of much experimental data [12, 13, 14, 15] that ACTH secretion is stimulated by the antidiuretic hormone or by a substance with a polypeptide structure very similar to the latter. One can therefore propose that the antidiuretic hormone participates in the activation of adenohypophysial production of ACTH effected by Diphenin. It has been established that the intravenous injection of 7-10 units of exogenous ACTH induces the same effect.

The regular increase of the 17-hydroxycorticosteroid content in the plasma of the dogs' caudal vena cava being apparent, qualitative determination of the corticosteriods in the peripheral blood plasma following the action of the experimental substances was our next undertaking.

These experiments were performed on 20 male guinea pigs weighing 600-800 g each. Ten of the guinea pigs were injected intraperitoneally with Dibazol (30 mg/kg) or Diphenin (20 mg/kg) prepared in an alkaline solution. The other ten guinea pigs were intraperitoneally injected with distilled water (control for experiments with Dibazol) or an alkaline solution (control for experiments with Diphenin). The alkalinity of the control solution was the same as that of the Diphenin solution. Two hours after the dibazol or Diphenin injection, 8-10 ml of blood was taken from the cardiac cavity of each guinea pig. So that the animals would not die, we put them in a head-down position for 1-2 min immediately after the blood was taken and administered 8-10 ml of a physiological solution intraperitoneally.



Effect of Dibazol and Diphenin on the concentration of 17-hydroxycorticosteroids in the plasma of blood from the caudal vena cava of a dog. 1) Control; 2) Dibazol; 3) Diphenin. Vertical line – significant range of mean.

Content of Corticosteroids in Peripheral Blood Plasma of Guinea Pigs (in μg per 100 ml plasma)

Corticosteroids	Dibazol (30 mg/kg)		Diphenin (20 mg/kg)	
	control	experiment	control	experiment
Hydrocortisone	28.6 + 41.4 + + 37.1 = 35.7	62.8 98.5 + + 91.4 = 84.2	68.5 + 37.1 + + 48.5 = 51.3	131 + 82.8 + + 94.2 = 102.7
Cortisone	–	0 + 11.4 + 5.7 = = 5.7	–	–
Corticosterone	–	22.8 + 13.1 + 0 = = 11.9	11.4 + 0 + 0 = 3.8	24.2 + 22.8 + 14.2 = = 20.4

There were intervals of 8-12 days between the experiments on each animal. The blood taken was centrifuged in order to obtain plasma. In both the control and the experiment, we used the distributive paper chromatography method proposed by N. A. Yudaev, Yu. A. Pankov, and K. V. Druzhinina [9] to determine the corticosteroids in 35 ml plasma. The chromatography was done in Bush's system (benzene : methanol : water). The experimental results are given in the table. Qualitative and quantitative determination of the corticosteroids showed that the increase in the corticosteroid content of guinea pigs' blood plasma which is caused by Dibazol and Diphenin is based on an increase in the hydrocortisone (chiefly) and corticosterone contents.

SUMMARY

A study was made of the action of dibazol and diphenin on the function of adrenal cortex in dogs and guinea pigs. Adrenal cortex function was assessed by 17-hydroxycorticosteroid content in the caudal vena cava of dogs and by the quantity and quality of corticosteroids in the peripheral blood plasma of guinea pigs. 17-corticosteroids were determined by Silber and Porter's method modified by Yudaev and Pankov. Corticosteroids were determined by the paper chromatography method suggested by Yudaev, Pankov and Druzhinina. As shown by experiments, dibazol and diphenin augment the function of adrenal cortex.

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