EFFECT OF PROCAINE ON SECRETION OF THE HORMONE OF THE HYPOTHALAMUS-PITUITARY SYSTEM AND THE REDISTRIBUTION OF THE BODY FLUID

N. N. Pronina

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The author has previously shown [5,6] that the intravenous injection of procaine causes inhibition of water diuresis by stimulating the processes of reabsorption of water in the kidney tubules. Hypophysectomy temporarily (for 2-4 months) abolishes the action of procaine on diuresis. Consequently, the inhibition of diuresis after injection of procaine takes place with the participation of the hypothalamo-pituitary system.

The object of this investigation was to determine the effect of procaine on the blood concentration of hormones of the posterior lobe of the pituitary and on the redistribution of the body fluid.

EXPERIMENTAL METHOD

The concentration of antidiuretic hormone (ADH) in the blood serum of dogs 15-30 min after intravenous injection of procaine (15 mg/kg) was determined by Heller's biological method [12]. The concentration of oxytocin in the blood was studied on the isolated rat's uterus. The serum protein concentration was investigated refractometrically and the osmotic pressure of the blood serum determined cryoscopically by means of a semiconductor thermistor. The pressor properties of the blood were estimated from recordings of the blood pressure by a clinical oscillograph. In two dogs the common carotid arteries were exteriorized in skin flaps, and the internal carotid artery was ligated on one side. Procaine (3.5-6.5 mg/kg) was injected into the common carotid artery of these animals on the intact side and on the side with the ligated internal carotid artery.

EXPERIMENTAL RESULTS

The antidiuretic activity of the blood serum of the dogs rose considerably 30 min after the injection of procaine. The ADH concentration in the blood reached 240 microunits pituitrin per ml blood. In the control animals the ADH concentration did not exceed 5 microunits/ml blood.

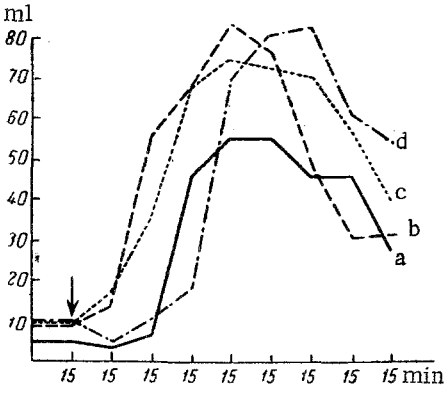

Fig. 1. Effect of various doses of procaine, administered in various ways, on the water diuresis in the dog Kudryava. a) 3.3 mg/kg into the common carotid artery; b) 5.3 mg/kg into the common carotid artery after ligation of the internal carotid artery; c) 6.6 mg/kg into the great saphenous vein. The arrow indicates the time of injection of procaine and of introduction of water into the stomach.

The increased production of ADH under the influence of the intravenous injection of procaine was not the result of its anesthetic effect on the peripheral osmoceptors. Injection of procaine (3.5 mg/kg) into the common carotid artery of two dogs 5 min before water loading (introduction of water into the stomach) gave an antidiuretic effect with high values of the tubular reabsorption of water. Injection of procaine (5.0-6.5 mg/kg) into the great saphenous vein or the common carotid artery after the preliminary ligation of the internal carotid artery did not cause inhibition of the water diuresis. To obtain a diuretic effect in these conditions, doses of procaine were required which were roughly four times larger than when injected into the common carotid artery after ligation of the internal, i.e., 15 mg/kg (Fig. 1). Evidently stimulation of ADH production by the action of procaine was effected by zones of the central nervous system supplied with blood by the internal carotid artery.

After intravenous injection of procaine a pressor effect also was observed. Data in the literature concerning the effect of procaine on the blood pressure are conflicting. A pressor action in experimental [2, 14] and clinical [3, 10, 11] conditions has been reported, but some investigators recommend procaine in hypertension [1, 9]. In acute experimental conditions T. V. Pravdich-Neminskaya [4] injected procaine into the blood stream in cats and obtained a pressor or a combined pressor-depressor reaction depending on the dosage. In the present experi-

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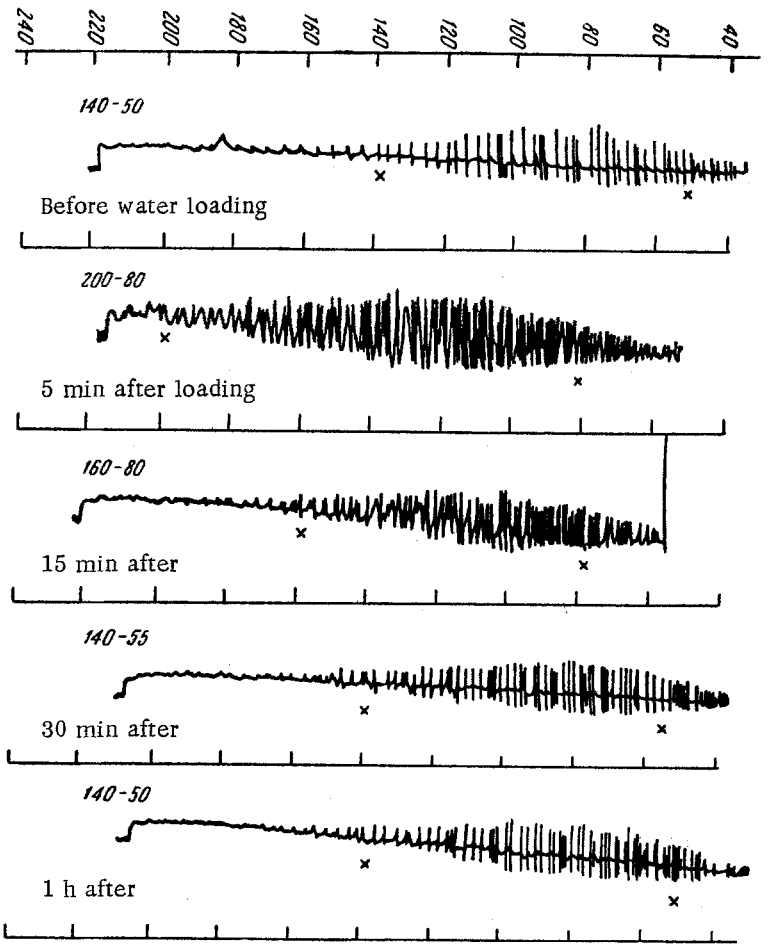

Fig. 2. Effect of intravenous injection of procaine (15 mg/kg on the blood pressure.

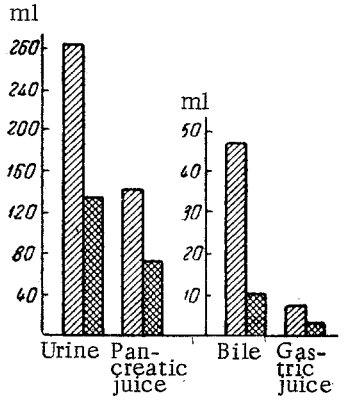

Fig. 3. Effect of intravenous injection of procaine on the function of the kidneys and digestive glands. Obliquely shaded columns – excretion during 2 h without injection of procaine; cross-hatched columns – excretion during 2 h against the background of procaine.

ments the blood pressure always rose, together with the pulse rate, after intravenous injection of procaine, as shown by oscillograms recorded on several occasions in 13 dogs (Fig. 2). The changes gradually disappeared in the course of 30-60 min. Evidently a decisive role in the reaction of the blood pressure to injection of procaine was played by nervous reflex factors, but the possibility of the participation of vasopressin cannot be ruled out.

Experiments conducted by the author jointly with M. D. Kondrakov on the isolated uterus of 22 rats showed that the concentration of oxytocin in the blood taken from the dogs 15-30 min after intravenous injection of procaine did not increase. Consequently, procaine selectively stimulated the secretion of ADH alone, without affecting oxytocin production. The absence of increase in the oxytocin concentration in the blood after injection of procaine was also demonstrated by other observations. After intravenous injection of the drug no gall-bladder reflex appeared in dogs with a fistula of the common bile duct, as was always observed after injection of pituitrin containg oxytocin.

The possibility of the isolated secretion of ADH and oxytocin may be accepted from the point of view of Olivecrona's findings [13]. He concluded that oxytocin is secreted by the paraventricular, and vasopressin by the supraoptic nuclei of the hypothalamic region.

The intravenous injection of procaine, stimulating secretion of ADH, caused inhibition of the excretion of fluid not only via the kidneys, but also by the extrarenal route. It has been shown [7, 8] that the intravenous injection of

procaine into dogs with a Pavlov's gastric pouch delays the secretion of gastric juice in response to the taking of water or food, and lowers its acidity, and also that it inhibits the secretion of bile in dogs with a fistula of the common bile duct by A. N. Bakuradze's method, supplemented by ligation of the cystic duct. The intravenous injection of procaine sharply depressed the secretion of pancreatic juice in response to taking food in dogs with a fistula of the pancreatic duct by A. N. Bakuradze's method. Delay in the excretion of fluid, under the influence of procaine, by different routes is illustrated in Fig. 3.

Where is this water stored? The water does not accumulate in the blood, for after water loading and intravenous injection of procaine in most cases hemoconcentration is actually observed. The results of a refractometric investigation showed that the protein concentration in the blood serum 15 min after introduction of water into the stomach against the background of procaine was 103.09 ± 1.94%, and 30 min after – 104 ± 1.44% in relation to the original value (before injection of procaine). In the experiments without injection of procaine the protein concentration in the dogs 15 min after the water loading was 95.33 ± 0.92%, and 30 min after – 93.15 ± 1.25% in relation to the original value (before loading). The difference between the results of the experiments with and without injection of procaine was statistically significant ($P < 0.001$).

The hemoconcentration was not associated with a disturbance of the absorption of water from the alimentary tract, for injection of procaine at the height of the hydremic reaction also caused an increase in the serum protein concentration.

It has been shown that after an injection of procaine water passes into the tissues. In control rabbits killed by air embolism, the water content of the liver tissues was 23.89 ± 3.1, whereas in rabbits killed 30 min after injection of procaine it was 38.22 ± 2.16% ($P < 0.01$).

As a result of the investigation of the osmotic pressure of the blood serum a significant fall in its level was observed: before injection of procaine the osmotic pressure was 323.4 ± 10.4 mosm/liter, and 25 min after injection it was 272.1 ± 10.8 mosm/liter ($P < 0.01$).

Hence procaine raises the blood level of ADH without affecting the oxytocin concentration. It inhibits the excretion of water from the body via the kidneys and its utilization in secretion formation in the alimentary tract, thus promoting the transfer of water into the tissues.

SUMMARY

Intravenous injection of procaine in a dose of 15 mg/kg stimulates in dogs the activity of the hypothalamo–hypophyseal system and increases the ADH level in the blood without influencing its oxytocic content. Procaine inhibits the discharge of water from the body through the kidneys and its utilization in the secretions of the alimentary tract. Injection of procaine followed by inhibition of secretion of gastric juice, bile, and pancreatic juice. Procaine causes hemoconcentration and facilitates transfer of water into the tissues. It seems that all this should be taken into account when procaine is used under clinical conditions, and in certain cases accounts for its therapeutic effect.

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