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

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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.

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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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 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 gallbladder reflex appeared in dogs with a fistula of the common bile duct, as was always observed after injection of pituitrin containing 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.