

EFFECT OF THE PITUITARY - ADRENAL SYSTEM AND INJECTIONS OF PHYSIOLOGICAL SALINE ON UROPEPSINOGEN EXCRETION

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Removal of the pituitary or adrenals does not affect the 24-hourly excretion of uropepsinogen, whereas administration of physiological saline in a volume equivalent to the diuresis increases pepsinogen clearance from the blood and thus increases its excretion in the urine.

Investigations have shown that the quantity of uropepsinogen excreted is a constant proportion of the total mass of pepsinogen produced. According to the calculations of Gottlieb [3, 4], for instance, 1/500 of the pepsinogen is excreted by the kidneys in the form of uropepsinogen, while the ratio between the pepsinogen concentration in the gastric juice and urine is 500:1. According to Strehler [5], this ratio varies between 400:1 and 600:1.

Since the mechanisms regulating uropepsinogen excretion have not been studied, the investigation described below was carried out to examine the role of the pituitary-adrenal system and the effect of loading with physiological saline on the excretion of this proteolytic enzyme.

EXPERIMENTAL METHOD

All the experimental animals received the same diet except the adrenalectomized rats which received 1.5% NaCl solution instead of water after the operation. The uropepsinogen concentration under normal conditions and at different times (up to 40 days) after the operation was determined in hypophysectomized and adrenalectomized rats (males weighing 180-200 g). In the intact animals the uropepsinogen concentration was determined under normal conditions and after loading with physiological saline. Uropepsinogen was determined by Tugolukov's method [2]. The 24-hourly sample of urine was collected in a receiver. Altogether 370 rats were used. Because of changes observed in the 24-hourly diuresis after the operations, uropepsinogen estimations were made soon (2nd-4th days) after the operation, on the 8th-12th day, i.e., when the normal 24-hourly diuresis was restored, and also later.

EXPERIMENTAL RESULTS

The 24-hourly diuresis of the rats averaged 9.52 ± 0.3 ml, the uropepsinogen concentration was 0.035 ± 0.005 mg/ml, and the excretion of uropepsinogen in the urine was 0.34 ± 0.01 mg/day. From figures

TABLE 1. Effect of Hypophysectomy and Adrenalectomy on Uropepsinogen Excretion

Operation	Hypophysectomy				Adrenalectomy	
	number of animals	before operation	10-40 days after operation	P	8-36 days after operation	P
Hypophysectomy	9	0.331 ± 0.057	0.422 ± 0.05	>0.1	0.367 ± 0.041	>0.1
Adrenalectomy	11	0.376 ± 0.0367				

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TABLE 2. 24-Hourly Diuresis and Concentration and Excretion of Uropepsinogen under Normal Conditions and after Injection of Physiological Saline (volumes of fluid injected corresponded to volume of urine excreted in 24 h)

	Normal	After injection of physiological saline	P
No. of animals	15	15	
Mean volume of urine excreted in 24 h (in ml)	11,3±0,56	18,6±0,76	<0,001
Uropepsinogen concentration (in mg/ml)	0,032±0,001 (100%)	0,026±0,001 (81,2%)	<0,01
Uropepsinogen excretion in 24 h (in ml)	0,36±0,026 (100%)	0,47±0,025 (130,6%)	<0,01

TABLE 3. 24-Hourly Diuresis and Concentration and Excretion of Uropepsinogen under Normal Conditions and after Injection of Physiological Saline (volume of solution injected equal to half of the volume of urine excreted in 24 h)

	Normal	After injection of physiological saline	P
No. of animals	10	10	
Mean volume of urine excreted in 24 h (in ml)	8,6±0,63 (100%)	10,7±0,6 124%	<0,02
Uropepsinogen concentration (in mg/ml)	0,037±0,002 100%	0,037±0,002 100%	>0,1
Uropepsinogen excretion in 24 h (in ml)	0,357±0,025 100%	0,419±0,037 117%	>0,1

for the concentration of the enzyme in gastric juice [1], it can be calculated that the ratio between the uropepsinogen concentration and the pepsinogen concentration is 1:514, and that the 24-hourly excretion of uropepsinogen with the urine is 0.4% of the quantity of pepsinogen secreted into the lumen of the stomach.

Neither hypophysectomy nor adrenalectomy produced any significant changes in the uropepsinogen excretion (Table 1). During the first few days after hypophysectomy or adrenalectomy there was a slight increase in the 24-hourly diuresis, leading to a decrease in the uropepsinogen concentration, but the net effect was that the 24-hourly excretion of uropepsinogen was unchanged.

Experiments were accordingly carried out to determine the effect of loading with water (physiological saline) on the uropepsinogen excretion. The animals received 2 intramuscular injections (at intervals of 8 h) of physiological saline corresponding in volume to the 24-hourly diuresis.

The results given in Table 2 show that the introduction of an excess of fluid into the body, causing an increase in the 24-hourly diuresis, was accompanied by a decrease in the uropepsinogen concentration, although the total quantity of the proteolytic enzyme excreted was increased (by 30.6%). If the volume of solution injected was reduced (Table 3), the uropepsinogen concentration was almost unchanged but the quantity of proteolytic enzyme excreted in the urine showed a tendency to rise.

Removal of the pituitary or adrenals thus did not disturb the excretion of uropepsinogen. Injection of physiological saline, on the other hand, increased the excretion of uropepsinogen as a result of an increase in diuresis, promoting the clearance of pepsinogen from the blood.

Uropepsinogen excretion is used sometimes in clinical practice as a test of gastric secretory function. This investigation with physiological saline loading suggests that when uropepsinogen levels are determined in patients allowance must evidently be made for their 24-hourly fluid intake, for the quantity of the proteolytic enzyme excreted and its concentration in the urine are dependent to some extent on the volume of fluid consumed.

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