EFFECT OF DEHYDROCHOLIC ACID ON DIURESIS

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Dehydrocholic acid, if administered by mouth and subcutaneously, inhibits water diuresis in mice and rats. Creatinine excretion is unchanged, and sodium excretion is decreased. The total 24-h diuresis and sodium excretion in rats are increased. An increase in salt excretion and, in some experiments, in diuresis is also observed after intravenous injection of dehydrocholic acid in a dose of 0.02 g/kg in chronic experiments on dogs.

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Many steroid compounds are known to have a marked and varied action on kidney function [1,2,4,5,7-9].

For this reason our intention was drawn to dehydrocholic acid, a compound closely related to the steroids. Its soluble salt (Decholin), according to clinical observations, possesses diuretic properties [3,6].

The object of the present investigation was to study the effect of dehydrocholic acid on diuresis and sodium and potassium excretion in mice, rats, and dogs.

EXPERIMENTAL METHOD

Water (1 ml) was introduced into the stomach of 44 mice weighing 18-23 g through a tube. Urine was collected during the next 3 h and the concentration of creatinine (by Folin's method) and of sodium and potassium (by flame photometry) were determined in it. In some experiments on rats (21 animals) the diuresis was recorded during the 3 h after water loading (5 ml/100 g body weight), while in other experiments on rats the 24-h diuresis, excretion of creatinine, sodium, and potassium, and the water intake were determined. For this purpose the animals were kept in individual cages. The compound was given either as a single dose or over a long period (7 days).

In three dogs with exteriorized ureters, urine was collected every 15 min for the 2 h before and 4 h after administration of the preparation in a chronic experiment. The excretion of creatinine, sodium, and potassium was determined every 30-60 min.

During the chronic experiments the animals were kept as far as possible on a constant intake of food and water. Dehydrocholic acid was injected as a 2% solution containing an equal amount of sodium bicarbonate; the preparation dissolved more easily with gentle heating. In control experiments the animals received the corresponding dose of 2% sodium bicarbonate.

EXPERIMENTAL RESULTS

After administration of different doses of dehydrocholic acid to the mice through the gastric tube, the antidiuretic effect was proportional to the dose of the preparation (Fig. 1A). In another series of experiments, 0.01 g dehydrocholic acid was injected subcutaneously. Besides the decrease in diuresis, sodium excretion also fell sharply (Fig. 1B). Potassium excretion was not significantly reduced, and the creatinine excretion was practically unchanged. A statistically significant decrease in water diuresis was also observed in experiments on rats receiving the preparation in a dose of 0.2-0.25 g/kg subcutaneously or via gastric tube (Fig. 1C and D). A dose of 0.1 g/kg, when injected into the stomach, proved ineffective.

A marked increase in sodium excretion was observed (from 124±17.2 to 241±27.8 μeq; $P < 0.002$) 24 h after administration of dehydrocholic acid (0.2 g/kg by gastric tube) to the rats; diuresis increased only on the 2nd day (from 5.3±0.29 to 7.1±0.77; $P < 0.05$). The excretion of potassium and creatinine and the water intake were essentially unchanged. After subcutaneous injection of the same dose of the preparation, the diuresis and sodium excretion increased on the 1st day while the creatinine excretion remained

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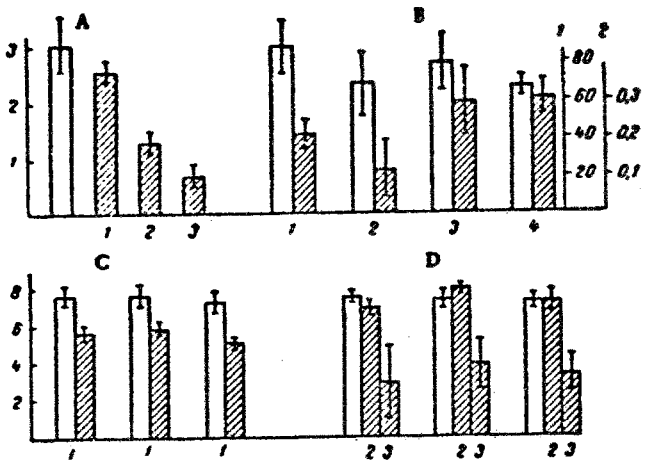

Fig. 1. Effect of dehydrocholic acid on kidney function in mice and rats. A) Intragastric administration of preparation to mice: 1) 0.005 g, 2) 0.01 g, 3) 0.02 g; B) subcutaneous injection of preparation into mice (0.01 g); 1) diuresis; 2) sodium excretion; 3) potassium excretion; 4) creatinine excretion. On vertical axes: on the left, diureses over 3 h (in ml); on the right: 1) excretion of electrolytes (in μeq), 2) excretion of creatinine (in mg) over 3 h; C) subcutaneous injection of 0.2 g/kg into three rats (1); D) administration of 0.1 g/kg (2) and 0.25 g/kg (3) of preparation via gastric tube to three rats. Along vertical axis, diuresis over 3 h (in ml). Unshaded columns represent control experiments, shaded columns experiments with administration of dehydrocholic acid. Vertical lines show confidence limits.

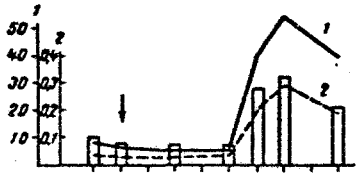

Fig. 2. Effect of dehydrocholic acid on diuresis and excretion of electrolytes. Columns show minute diuresis; 1) sodium excretion; 2) potassium excretion; arrow indicates injection of preparation (0.02 g/kg intraveneously). Abscissa: time (30-min intervals), ordinate: 1) excretion of electrolytes (in μeq); 2) diuresis (in ml/min).

unchanged. After administration of sodium bicarbonate solution to the rats no significant changes were found in the 24-h diuresis or excretion of electrolytes, although in 2 of the 4 animals the sodium excretion rose slightly.

In experiments with prolonged administration of dehydrocholic acid to rats, in the control period for several days sodium bicarbonate was injected subcutaneously (0.2 g/kg). After background levels had been established, administration of dehydrocholic acid to the animals began (0.2 g/kg daily for 7 days, subcutaneously). A small increase in 24-h diuresis was observed (on the average by 29%, $P < 0.05$). The fluid intake and the excretion of creatinine and potassium were essentially unchanged, while the sodium excretion rose slightly.

After intravenous injection of dehydrocholic acid (0.02 g/kg) into dogs the diuresis as a rule was unchanged in the next 4 h, but in some experiments the diuresis was increased after 60 min or more. Sodium and potassium excretion, on the other hand, was more constantly increased and by a considerable degree (Fig. 2).

In experiments in which a diuretic effect was observed, reabsorption was depressed and filtration increased.

The results show that dehydrocholic acid possesses marked activity on the diuretic and salt-excretory functions of the kidneys. However, its action shows certain peculiarities: in dogs and in short-term experiments on rats, an increase in sodium excretion and water diuresis is observed, often with a long latent period, while the water diuresis in mice and rats within a short period of administration of the preparation is reduced. This fact distinguishes dehydrocholic acid from glucocorticoids and cardiac glycosides.

LITERATURE CITED

1. Yu. I. Ivanov, Probl. Éndrokrinol., No. 1, 92 (1965).
2. Yu. I. Ivanov, Farmicol i Toksikol., No. 1, 86 (1966).
3. V. A. Kononyachenko, in: Essential Hypertension [in Russian], No. 2, Moscow (1952), p. 194.
4. B. A. Pakhmurnyi, Farmakol. i Toksikol., No. 3, 362 (1965).
5. B. A. Pakhmurnyi, Byull. Éksperim. Biol. i Med., No. 3, 67 (1965).
6. F. Hauschild, Pharmakologie und Grundlagen der Toxikologie, Leipzig (1960).
7. P. Hempel-Jorgensen and P. Eilersin, Acta Med. Scand., 167, 158 (1960).
8. C. M. Kagawa, J. A. Cella, and C. G. van Arman, Science, 126, 1015 (1957).
9. R. Neher, P. Desaulles, E. Vischer, et al., Helv. Chim. Acta, 48, 1667 (1958).