EFFECT OF FUROSEMIDE ON TRANSPORT OF ORGANIC SUBSTANCES IN THE KIDNEYS

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UDC 615.254.1.015.45:612.46

The effect of furosemide on maximal reabsorption of glucose on the secretion of diodone, and on the excretion of urates was investigated in chronic experiments. After a single injection of furosemide the maximal reabsorption of glucose was found to be increased in dogs. The substance was found to have no effect on the secretory transport of diodone. Furosemide has an uricosuric action in rats and dogs.

KEY WORDS: *furosemide; glucose reabsorption; tubular secretion; excretion of urates.*

Some organic compounds (glucose, amino acids) are known to be reabsorbed in the proximal segments of the kidney tubules, whereas others are actively secreted (diodone), and a third group are transported in two directions (uric acid). Considering the ability of furosemide to inhibit proximal reabsorption of sodium [2, 9, 12], it was interesting to discover whether it also effects other transport processes located in this part of the kidney.

The object of this investigation was to study the effect of furosemide on the transport of glucose, diodone, and urates in chronic experiments on animals.

EXPERIMENTAL METHOD

Experiments were carried out on nine mongrel dogs weighing 15-20 kg and on 20 rats weighing 150-200 g. Dogs with their ureters exteriorized by the Pablov—Tsitovich method were given an intravenous injection of a solution containing 35% glucose, 2.5% diodone, and 0.5% inulin at the rate of 3.5 ml/min over a period of 1.5-2 h, so that their plasma glucose concentration was maintained at 350-500 mg% and their cardiotrast and inulin concentrations at 20-30 mg%. After establishment of a constant initial background the urine was collected during three or four 10-min clearance periods, in the middle of which blood was taken for analysis. Furosemide was injected intravenously as a single dose of 5 mg/kg. In the experiments with prolonged administration (10 days) the drug was given in the same dose by mouth, and the determinations described above were carried out every 3 days; the glucose and uric acid concentrations in the plasma also were investigated. The rats were given furosemide in a dose of 20 mg/kg subcutaneously, after which the excretion of cardiotrast was investigated by the method described previously [3] and the hourly excretion of urates determined. During prolonged administration of furosemide (14 days) the rats were kept in individual cages on a constant diet with free access to water. Every 3-4 days the 24-h excretion of urates and creatinine and the hourly excretion of diodone were determined. Inulin in the plasma and urine was determined by the resorcin method, glucose with the aid of orthotoluidine reagent, diodone by the method of White and Rolf in the modification of Bak et al. [7], urates by Sullo's method [5], and creatinine by Folin's method.

EXPERIMENTAL RESULTS

The results given in Table 1 show that a single injection of furosemide into the dogs led to the development of a marked diuretic reaction. The rate of glomerular filtration remained virtually unchanged under these circumstances. Maximal glucose reabsorption was increased considerably in all the animals. In the writer's opinion, this fact is associated with the considerable loss of fluid by the animal, for in the opinion of several workers [8,

Department of Pharmacology, Altai Medical Institute, Barnaul. (Presented by Academician of the Academy of Medical Sciences of the USSR V. V. Zakusov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 84, No. 10, pp. 436-438, October, 1977. Original article submitted April 15, 1977.

 0007-4888/77/8410-1436$07.50

TABLE 1. Effect of Single Injection of Furosemide on Maximal Reabsorption of Glucose, Maximal Secretion of Diodone, and Excretion of Urates in Dogs

Index studied	Control		During 35 min after injection		P
	n	M±m	n	M±n	
Diuresis, ml/min	11	4,3±0,6	11	11,6±1,4	<0,001
Filtration, ml/min	11	57,3±3,7	11	54,3±2,9	>0,5
Reabsorption of glucose, mg/min	11	132,0±11,0	11	196,0±14,5	<0,01
Secretion of diodone, mg/min	9	29,4±2,2	8	31,0±2,9	>0,5
Excretion of urates, mg/min	7	0,23±0,03	7	0,32±0,03	<0,05

Legend. Results of experiments on five dogs are shown; each experiment is mean of three clearance periods; n) number of experiments.

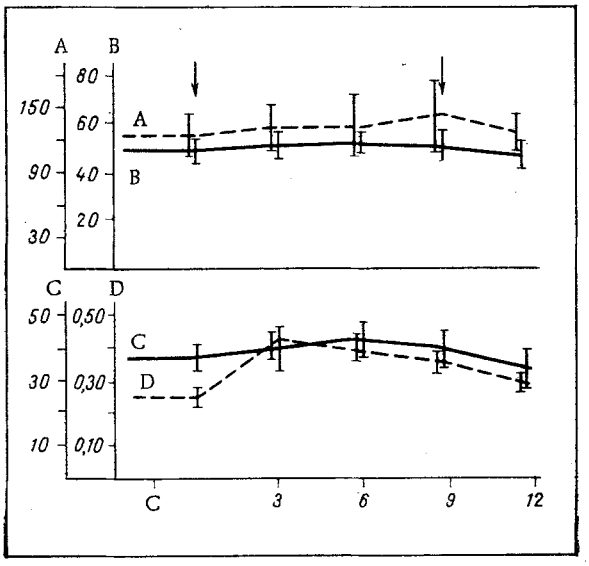

Fig. 1

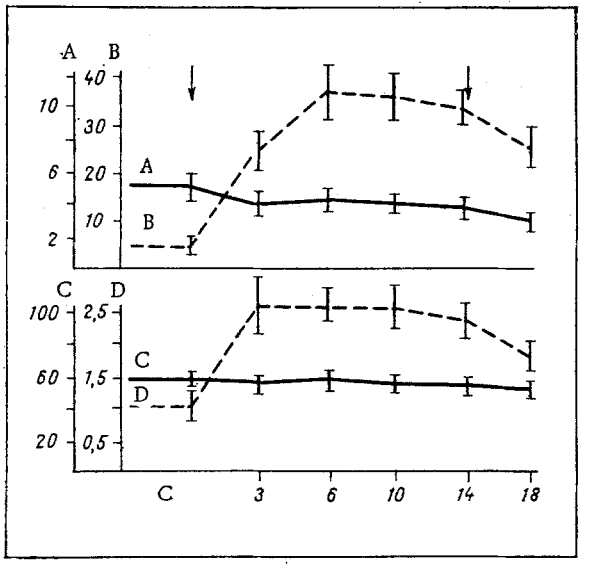

Fig. 2

Fig. 1. Effect of prolonged administration of furosemide on maximal reabsorption of glucose, maximal secretion of diodone, and excretion of urates in dogs. A) Maximal reabsorption of glucose (in mg/min); B) rate of glomerular filtration (in ml/min); C) maximal secretion of dione (in mg/min); D) excretion of urates (in mg/min). Here and in Fig. 2: abscissa, days after injection of furosemide, C) control, arrows mark beginning and end of administration of diuretic.

Fig. 2. Effect of prolonged administration of furosemide on excretion of urates and diodone in rats. A) Excretion of creatinine (in mg/day); B) diuresis (in ml/day); C) hourly excretion of diodone (in % of quantity injected); D) excretion of urates (in mg/day).

10], this may lead to an increase in the maximal reabsorption of glucose. In the only paper published on the study of the effect of furosemide on maximal glucose transport some decrease was found in the maximal reabsorption of glucose following injection of the diuretic in a dose of 10 mg/kg in acute experiments on dogs [6].

Excretion of urates in the experiments in which a single injection of furosemide was given to the dogs was increased (Table 1), in agreement with other observations [11], and probably attributable to a decrease in the reabsorption of uric acid, for its filtration charge was unchanged. Analysis of the effect of a single dose of the diuretic on maximal secretion of diodone shows that it was virtually unchanged. This is in agreement with data in the literature [1], although in experiments on rats furosemide reduced the excretion of penicillins [4].

During prolonged administration of furosemide to the dogs no significant changes were observed in the rate of glomerular filtration, maximal reabsorption of glucose, and maximal secretion of diodone (Fig. 1). The excretion of urates was significantly increased on all

TABLE 2. Effect of Single Dose of Furosemide on Excretion of Diodone and Urates in Rats (M ± m)

Index studied	Control	Experiment	P
Diuresis, ml/h	3,8±0,5	6,9±0,3	<0,001
Excretion of diodone, %	57,0±1,5	56,3±1,9	>0,5
Exretion of urates, mg/h	0,29±0,02	0,43±0,02	<0,01

days of administration, evidently because of inhibition of their reabsorption, for the filtration charge of uric acid was unchanged (the concentration of urates in the plasma was 0.6-0.8 mg% throughout the experiment).

It will be clear from Table 2 that a single injection of furosemide into rats led to an increase in the diuresis and excretion of urates. The excretion of diodone was unchanged under these circumstances. In the experiments with prolonged administration of furosemide to the rats, besides a marked diuretic reaction a considerable increase in the excretion of urates was observed (Fig. 2), in all probability associated with a reduction in their tabular reabsorption, for the excretion of creatinine, a measure of glomerular filtration, was virtually unchanged during the first days of administration, but by the 14th day it was actually significantly reduced. The excretion of diodone during prolonged administration of furosemide, as Fig. 2 shows, was virtually unchanged (57.1 ± 1.2% before administration and 54.6 ± 1.5% by the 14th day).

After administration of a single dose of furosemide the maximal reabsorption of glucose in dogs is thus increased. Administration of furosemide to dogs and rats did not affect diodone secretion. In experiments on dogs and rats furosemide exhibits uricosuric properties.

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