INHIBITION OF SULFATE REABSORPTION IN THE KIDNEY AFTER INJECTION OF SODIUM SULFATE SOLUTION INTO RATS

O. A. Goncharevskaya and Yu. V. Natochin

UDC 615.31:546.33'226].015.45:612.46.015.31:546.22

Rats were injected intravenously with 2% sodium sulfate solution (35 μeq/100 g body weight) under conditions of a high and stable water-alcohol diuresis. The concentration of sulfate in the blood serum and the quantity of sulfates filtered in the glomeruli 20 min after the injection were not significantly different from the initial values. Meanwhile, the reabsorption of sulfates was reduced from 1.82 ± 1.09 to 0.99 ± 0.22 μeq/min · 100 g, while their excretion rose from 0.17 ± 0.01 to 1.06 ± 0.13 μeq/min · 100 g. The reabsorption of sulfates still remained low 1 h after the injection. During this time all the injected dose of sulfates was completely excreted.

With an increase in the concentration of sulfate in the blood, the system of its reabsorption in the kidneys quickly becomes saturated, and excretion of sulfate can be increased only by an increase in the quantity of it which is filtered.

The stability of the blood plasma sulfate level suggests the existence of a system regulating the content of this anion in the fluids of the internal medium.

The object of this investigation was to study tubular transport of sulfates when their level in the blood plasma is slightly raised.

EXPERIMENTAL METHOD

Experiments were carried out on female Wistar albino rats weighing about 200 g. The animals were provided with food and water ad lib.; on the day of the experiment were deprived of food. A 12% solution of alcohol body weight was introduced into the stomach through a tube at the rate of 5 ml/100 g to induce anesthesia, and it was followed by infusion of a 1-2% solution of alcohol during the experiment in a volume equal to that of the urine excreted. In this way a uniform water diuresis was obtained. Urine was collected every 10 min through a catheter introduced into the bladder. The first four portions acted as the control, after which 0.125 ml of 2% sodium sulfate solution (35 μeq/100 g body weight) was injected into the caudal vein and six samples of urine were collected. The quantity of sulfate injected was approximately equal to the total content of sulfates in the whole extracellular fluids. Blood was taken for analysis (0.5-0.6 ml) from the jugular vein in the control period and at the end of the experiment. To measure the rate of glomerular filtration in the 45 min before collection of the urine began, 0.72 ml of 7% inulin solution/100 g body weight was injected intramuscularly.

The concentration of sulfates [1], of phosphates [5], of chlorides (by potentiometric titration with $AgNO_3$), of sodium and potassium (with the Zeiss III flame photometer), of magnesium (with the "Spektr-1" atomic absorptiometer), and of inulin (by Cole's method using resorcin with $FeCl_3$ as catalyst) was deter-

Laboratory of Development of Excretory Function, I. M. Sechenov Institute of Evolutionary Physiology and Biochemistry, Academy of Sciences of the USSR, Leningrad. (Presented by Academician V. N. Chernigovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 75, No. 6, pp. 63-65, June, 1973. Original article submitted June 8, 1972.

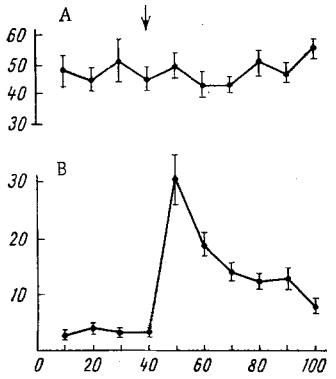

Fig. 1

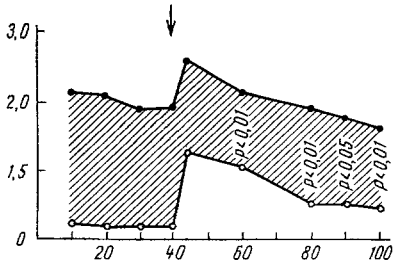

Fig. 2

Fig. 1. Effect of intravenous injection of sodium sulfate on diuresis (A) and concentration (M ± m) of sulfate (B) in urine (from results of 11 experiments). Arrow indicates time of injection of sodium sulfate. Abscissa: time (in min); ordinate: in A) diuresis (in μl/min · 100 g), in B) concentration of sulfate (in meq/liter).

Fig. 2. Dynamics of filtration and reabsorption of inorganic sulfate in kidney after intravenous injection of sodium sulfate solution. Each point is mean value of experiments on 10 animals; P) criterion of significance of change in reabsorption relative to control level. Abscissa: time (in min); ordinate: quantity of sulfate (in μeq/min · 100 g) filtered in glomeruli ($C_{in} \cdot P_{SO_4}$) (top line) quantity excreted with urine ($U_{SO_4} \cdot V$) (bottom line), and quantity reabsorbed by tubule cells ($T^R_{SO_4}$) (shaded part).

TABLE 1. Excretion of Ions before and after Injection of Sodium Sulfate

Ion	n	K	I	$\overline{\Delta} \pm m_{\overline{\Delta}}$	P	II	$\overline{\Delta} \pm m_{\overline{\Delta}}$	P
SO_4	9	4,5	25,6	21,1±1,2	0,001	16,1	11,6±1,3	0,001
PO_4	7	0,17	1,29	1,12±0,44	0,05	4,43	4,25±1,1	0,01
Cl	9	17,3	17,7	0,43±3,0	0,05	20,0	2,72±4,2	0,5
Na	9	8,4	19,6	11,2±2,7	0,01	16,9	8,5±3,6	0,05
K	9	5,3	11,8	6,5±0,9	0,001	9,3	4,0±0,7	0,001
Mg	8	1,4	2,3	0,8±0,2	0,05	2,2	0,8±0,36	0,5

Legend: n) number of animals investigated; quantity of ions (in μeq) excreted in 30 min, calculated per 100 g body weight in the control period (K), in the first 30 min (I) and in the second 30 min (II) after injection of sulfate; P) level of significance of differences when comparing changes due to injection of sulfate with initial values for the same animal. Statistical analysis by the method of comparing variances in two paired samples: $\overline{\Delta}$) mean differences between values after injection of sulfates and initial values; $m_{\overline{\Delta}}$) its standard error.

mined in the samples of blood serum and urine. Statistical analysis was carried out by the method of comparison of variances in two paired samples: changes in sulfate transport by the kidney before and after administration of sodium sulfate were compared for each animal [2]; the calculations were carried out on the Promin'-2 computer.

EXPERIMENTAL RESULTS AND DISCUSSION

By individual choice of dose of alcohol and accurate maintenance of the water balance it was possible to keep the animals' extracellular volume constant and to obtain a uniform, high diuresis throughout the experiment (Fig. 1).

The sulfate concentration in the blood plasma of the rats was 2.72 ± 0.13 meq/liter (n = 18); under these conditions about 90% of the filtered sulfates was reabsorbed. After intravenous injection of sodium sulfate the excretion of sulfate by the kidney during constant diuresis increased sharply and then remained at a high level throughout the experiment (Fig. 1). The plasma sulfate concentration 1 h after its administration no longer differed from the control and was 2.72 ± 0.22 meq/liter (n = 13). The increased excretion of sulfate cannot be explained by an increased load on the nephron but depended on changes in its reabsorption in the tubules.

Since this conclusion is of fundamental importance, several series of experiments were carried out in which the concentration of sulfates in the plasma was determined at various times after injection. The inorganic sulfate of the plasma is known to be completely filtered by the glomeruli of the kidney [3]. For an accurate calculation of the rate of glomerular filtration, blood was taken twice from each animal for determination of the inulin concentration, and the inulin concentration in the blood plasma corresponding to each 10-min sample of urine was determined by extrapolation. The rate of glomerular filtration during the experiment varied only slightly: 646 ± 33.5 μl/min · 100 g in the control period and 674 ± 31.9 μl/min · 100 g after the injection of sulfate. The sulfate concentration in the plasma was still raised 4 min after intravenous injection of the sodium sulfate solution, but its reabsorption was already reduced; 20 min after the injection the quantity of sulfate filtered did not differ significantly from the initial level, but the reabsorption of sulfate was considerable reduced and its excretion was increased (Fig. 2).

It was important to study the reaction of the kidneys to a prolonged increase in the concentration of sulfates in the blood plasma. Experiments on three rats with continuous infusion of 2% sodium sulfate solution at the rate of 0.42 ml/h · 100 g likewise revealed marked inhibition of sulfate reabsorption in the renal tubules.

To study the specificity of the reaction of the kidneys to injection of sulfate, the excretion of various anions and cations by the kidney was investigated (Table 1). The excretion of sulfate was increased in the first 30 min by 21.1 μeq, the excretion of chlorides remained unchanged, and the excretion of phosphates was increased by 1.1 μeq. The excretion of sodium and potassium rose considerably. Consequently, the body possesses a very sensitive system for regulating the balance of sulfates, capable of rapidly restoring the ionic composition of the internal medium not only through an increase in the load on the nephron when the plasma sulfate level is raised, but also through a modification of the activity of the tubular sulfate transport systems. Since the excretion of sulfates remained increased despite the rapid restoration of the initial plasma concentration, and all the injected sulfate was excreted, the existence of nervous or humoral factors regulating sulfate homeostasis may be postulated.

LITERATURE CITED

1. Yu. V. Natochin, G. P. Gusev, O. A. Goncharevskaya, et al., Zh. Évolyuts. Biokhim. i Fiziol., 7, 365 (1971).
2. V. Yu. Urbakh, Biometric Methods [in Russian], Moscow (1964).
3. F. Berglund, Acta Physiol. Scand., 49, Suppl. 172 (1960).
4. F. Berglund, Acta Physiol. Scand., 62, 336 (1964).
5. P. S. Chen, T. Y. Toribara, and H. Warner, Analyt. Chem., 28, 1756 (1956).