EFFECT OF DIHYDROERGOTAMINE ON PARTIAL FUNCTIONS OF THE KIDNEYS AND WATER AND SALT METABOLISM IN DOGS WITH EXPERIMENTAL HYPERTENSION

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UDC 615.217.24.03:616.12-008,331.1-092.9-07:[616-008.92+616.61]-07

Experimental pituitrin hypertension in dogs was accompanied by elevation of the blood pressure, a reduction in the minute diuresis, glomerular filtration and renal plasma flow, and an increase in the filtered fraction of the plasma and the concentration index. A course of dihydroergotamine treatment lowered the blood pressure and restored the disturbed kidney functions to normal. The water and salt metabolism was not completely restored. In the treatment of hypertension substances promoting salt excretion must be given together with dihydroergotamine in order to restore the water and salt metabolism to normal.

Despite much research into the action of drugs in hypertension, the effect of dihydroergotamine on kidney function and on water and salt metabolism in animals with experimental hypertension has been inadequately studied [1].

The object of this investigation was to study changes in the kidney function and water and salt metabolism in dogs with experimental hypertension before and after a course of dihydroergotamine therapy.

EXPERIMENTAL METHOD

Experiments were carried out on six mongrel dogs with their ureters exteriorized onto the abdominal wall by the method of Orbeli and Tsitovich. Hypertension was induced by subcutaneous injections of pituitrin (1 ml) daily for 10 days [4]. The arterial pressure was measured by Korotkov's method in the carotid artery previously exteriorized in a skin flap. Dihydroergotamine was injected intravenously in a dose of 0.1 mg/kg daily for 7 days. Before and during the experimental hypertension and after dihydroergotamine therapy the following indices of kidney function were studied: the minute diuresis, the filtration and reabsorption of water by the inulin method, the kidney plasma flow and secretion with the aid of diodone. The sodium concentration in the blood plasma and urine was determined by flame photometry, the total water content by the antipyrin method, and the volume of extracellular fluid with the aid of sodium thiocyanate.

EXPERIMENTAL RESULTS

Experimental pituitrin hypertension in these experiments was accompanied by elevation of the maximal and minimal blood pressure from 120/65 to 200/100 mm and also by changes in the partial functions of the kidneys.

The minute diuresis after water loading fell during hypertension from 4.59 ± 0.35 to 3.67 ± 0.1 ml/min/m^2. After a course of dihydroergotamine therapy the minute diuresis rose to 5.0 ± 0.5 ml/min/m^2. Before treatment the glomerular filtration was reduced from 89.61 ± 7.7 to 72.30 ± 9.0 ml/min/m^2 ($P < 0.05$). Injection of dihydroergotamine restored the glomerular filtration (96.6 ± 18.0 ml/min/m^2). Investigation of the dynamics of the renal plasma flow revealed a decrease from 336.11 ± 95.0 to 154.27 ± 32 ml/min/m^2 ($P < 0.05$). After dihydroergotamine therapy the renal plasma flow was increased to 341.2 ± 120.0 ml/min/m^2.

Department of Pharmacology, Ivanovo Medical Institute. (Presented by Academican of the Academy of Medical Sciences of the USSR V. V. Zakusov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 77, No. 2, pp. 23-25, February, 1974. Original article submitted March 26, 1973.

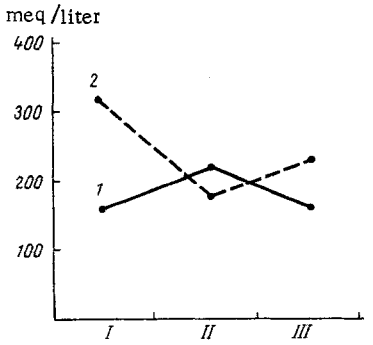

Fig. 1

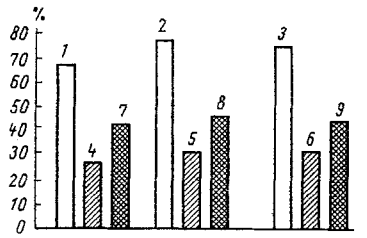

Fig. 2

Fig. 1. Effect of dihydroergotamine on sodium concentration in blood plasma (1) and urine (2) of dogs with experimental hypertension: I) control; II) hypertension; III) after dihydroergotamine treatment.

Fig. 2. Effect of dihydroergotamine on volume of water compartments in dogs with experimental hypertension: 1, 2, 3) total water; 4, 5, 6) extracellular water; 7, 8, 9) intracellular water.

The decrease in the renal plasma flow led to an increase in the filtered fraction from 27.0 ± 11.0 to 57.5 ± 17.0% ($P < 0.05$). After treatment it was 27.65 ± 6.0%. The decrease in glomerular filtration and in the renal plasma flow indicate changes in the glomerular apparatus of the kidneys [5, 9, 10]. After dihydroergotamine therapy the disturbed functions of the glomerular apparatus of the kidneys were restored, evidently in conjunction with inhibition of vasoconstrictor responses [6]. Restoration of the normal blood pressure was further evidence that this had occurred.

The functions of the tubular apparatus of the kidneys also were studied. Experiments showed an increase in the concentration index during hypertension from 25.16 ±7.0 to 36.6 ± 13.5 ($P < 0.05$), reflecting an increase in the tubular reabsorption of water. After treatment the concentration index was 24.74 ± 6.5. The tubular secretion in experimental hypertension was increased from 19.25 ± 5.0 to 23.41 ± 5.4 mg/min/m^2; this increase was not statistically significant ($P > 0.05$).

The distribution of water in the water compartments of the body depends on the concentration and movements of the electrolytes in the body fluids [7]. In experimental hypertension the sodium concentration in the blood plasma was raised, while in the urine it was lowered (Fig. 1). The sodium reabsorption in hypertension was increased from 99.35 to 99.78%. A course of dihydroergotamine treatment led to an increase in the excretion of sodium in the urine, but the normal situation was not restored.

The results of these experiments showed that the volume of the water compartments is increased in dogs with experimental hypertension (Fig. 2). Dihydroergotamine therapy led to a decrease in the relative percentages of total, extracellular, and intracellular water. However, the normal situation was not completely restored.

In experimental hypertension changes were thus observed in all the functions of the kidneys and in water and salt metabolism, in agreement with observations made by other workers [3, 5, 8, 9]. A course of dihydroergotamine therapy lowered the increased maximal and minimal blood pressure and restored the disturbed partial kidney functions. This was evidently due to blocking by dihydroergotamine of the α-adrenergic receptors of the renal vessels and of the vascular territories receiving vasoconstrictor impulses and playing an important role in the regulation of the arterial pressure [6]. Water and salt metabolism was not fully restored to normal. Retention of sodium in the body was found, with a resulting relative increase in the water compartments. In the treatment of hypertension drugs to promote salt excretion must therefore be given in conjunction with dihydroergotamine in order to promote the excretion of sodium and to prevent the retention of fluid in the tissues [1, 2].

LITERATURE CITED

1. I. Bach, Vengersk. Med., No. 11, 3 (1964).
2. L. Biro, Vengersk. Med., No. 27, 3 (1968).

3. V. M. Bogolyubov, The Pathogenesis and Clinical Picture of Water and Electrolyte Disorders [in Russian], Moscow (1968), p. 193.
4. A. A. Belous, Farmakol. i Toksikol., No. 2, 10 (1954).
5. B. D. Kravchinskii, The Modern Basis of Physiology of the Kidneys [in Russian], Moscow (1958).
6. I. E. Kisin and L. G. Komarova, Farmakol. i Toksikol., No. 1, 45 (1971).
7. A. A. Krokhalev, Water and Electrolyte Metabolism [in Russian], Moscow (1972).
8. M. M. Mendel'son, Ter. Arkh., No. 1, 63 (1961).
9. V. G. Pashinskii, Farmakol. i Toksikol., No. 1, 71 (1967).
10. V. V. Sinyachenko, Ter. Arkh., No. 5, 54 (1964).