EXPERIMENTAL DETERMINATION OF THE EFFECTIVENESS OF HEMODIALYSIS OF CERTAIN DRUGS AND TOXINS

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During hemodialysis with the Soviet artificial kidney apparatus, the clearance of methyl alcohol was 150 ml/min. The clearance of ethyl alcohol was 100 ml/min, and of dichloroethane 40 ml/min. The clearance of barbital was 35 ml/min, of phenobarbital 22 ml/min, and of nembutal 15 ml/min.

The use of hemodialysis in the treatment of acute clinical poisoning is increasing year by year [1-6, 8]. However, the value of this method of treatment is mainly assessed by its clinical effect. The clearance of most drugs and toxic substances by the Soviet artificial kidney is not known, and it is difficult to predict the required duration of dialysis or to estimate its effectiveness correctly.

The object of the investigation described below was to determine the effectiveness of hemodialysis of barbiturates, dichloroethane, and methyl and ethyl alcohols and to establish the clearance of these substances under experimental conditions as close to clinical as possible.

EXPERIMENTAL METHOD AND RESULTS

The substance for testing was dissolved in 2.5-5 liters blood taken from a cadaver, or in blood obtained during exchange transfusion. The dialyzing solution was prepared by the usual formula. Blood with the substance dissolved in it was perfused through the Soviet artificial kidney apparatus at the rate of between 50 and 200 ml/min. In experiments with volatile substances (methyl and ethyl alcohols, dichloroethane) the reservoir was made airtight. During dialysis a check was kept on the pH, osmotic pressure, temperature, and electrolyte composition both of the blood and of the dialyzing solution. Periodically the concentration of the test substance in the blood was determined, and at the end of the experiment a curve of the change in concentration in the dialyzed blood volume was plotted. The concentration of barbiturates was determined by ultraviolet spectrophotometry, and that of the other substances by gas chromatography.

Since dialysis is diffusion of a substance through a capillary system, and obeys Fick's law,

$$j = L(C_b - C_d),$$

the general rule governing the change in concentration of the substance during dialysis is exponential in form:

$$C_b = C_0 \exp\left(-\frac{L}{V}t\right), \quad (1)$$

where C_b is the concentration of the substance in the blood, L the clearance, V the volume of solution undergoing dialysis, t the time, C_d the concentration of the substance in the dialyzing solution, and C_0

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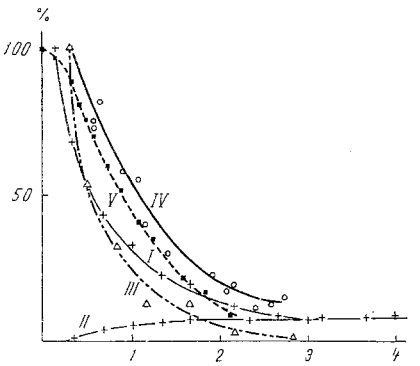

Fig. 1. Results of hemodialysis experiments: I) concentration of ethyl alcohol in blood; II) concentration of ethyl alcohol in dialyzing solution; III) concentration of methyl alcohol in blood; IV) concentration of dichloroethane in blood; V) concentration of aqueous solution of sodium amytal during dialysis. Abscissa, time (in h); ordinate, changes in concentration (in percent of initial value). Rate of fall of concentration curve corresponds to clearance of the particular substance.

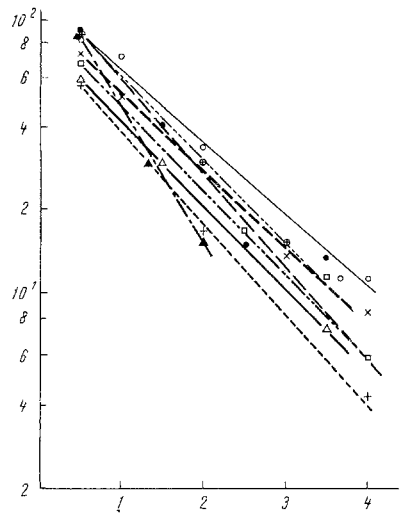

Fig. 2. Changes in barbital concentration during hemodialysis. Concentration graphs on logarithmic scale. Abscissa, duration of dialysis (in h); ordinate, concentration of barbital (in percent of initial value).

the initial concentration of the substance in the dialyzed solution (or blood). These formula for determining the clearance of the test substance has the form

$$L = \frac{V}{t} \ln \frac{C_0}{C_b}.$$

Curves of hemodialysis of methyl and ethyl alcohols and dichloroethane and the curve of dialysis of an aqueous solution of sodium amytal are given in Fig. 1. All the curves are clearly exponential in character, in accordance with formula (1). The clearance of methyl alcohol has the highest value (150 ml/min). The clearance of ethyl alcohol was 100 ml/min, and that of dichloroethane about 40 ml/min. The difference is evidently due to differences in the molecular weight of the tested substances.

Experiments were also carried out to determine the clearance of nembutal, phenobarbital, and barbital as the most widely used barbiturates. Graphs showing the change in barbital concentration in semilogarithmic coordinates are given in Fig. 2. Nearly all measurements lie on straight lines forming different angles with the time axis. Barbital had the highest mean clearance (35 ml/min). The clearance of phenobarbital was 22 ml/min, and of nembutal 15 ml/min. Comparison of these clearance results with the data obtained by Edwards [7] for the degree of binding of barbiturates with the blood proteins shows a high level of correlation. The quantity of barbital bound by proteins is not more than 5%, compared with 15% for phenobarbital and 55% for nembutal. This determines the quantity of the free form of the compound capable of diffusing in the blood plasma.

No correlation was found between the volume velocity (between 50 and 200 ml/min) of perfusion of blood through the dialyzer and the clearance of the barbiturates.

LITERATURE CITED

1. M. M. Mendel'son and G. P. Kulakov, Klin. Med., No. 8, 129 (1964).
2. M. F. Sakaeva and R. M. Urazaev, in: Collected Scientific Investigations of the Bashkir Republic Hospital [in Russian], No. 5, Ufa (1966), p. 147.
3. P. L. Sukhinin, I. I. Shimanko, and A. A. Yaroslavskii, in: Proceedings of the First All-Russian Scientific and Practical Conference on the Theme: Diagnosis, Clinical Picture, and Treatment of Acute Poisoning [in Russian], Moscow (1968), p. 25.
4. A. A. Yaroslavskii, in: Proceedings of the First All-Russian Scientific and Practical Conference on the Theme: Diagnosis, Clinical Picture, and Treatment of Acute Poisoning [in Russian], Moscow (1968), p. 25.
5. N. Alwall and A. Lunderquist, Acta Med. Scand., 147, 119 (1953).
6. M. De Myttenaere, L. Schoenfeld, and J. F. Maker, J. Am. Med. Assn., 203, 885 (1968).
7. K. D. Edwards, Bull. Postgrad. Comm. Med. Univ. Sydney, 20, 89 (1964).
8. G. E. Schreiner, Arch. Intern. Med., 102, 896 (1958).