REDISTRIBUTION OF THE BRAIN FLUIDS WITH AN INCREASE IN BLOOD OSMOLARITY

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With an increase in the concentration of osmotically active substances, not passing through cell membranes or the blood–brain barrier, in the blood, dehydration of the cells takes place. It is claimed that this mechanism lies at the basis of dehydration of the brain during osmotic therapy [1-3, 6]. However, direct experiments have shown that even infusion of concentrated solutions of osmotically active substances into the blood or injection of diuretics, causing rapid excretion of fluid by the kidney, in a volume exceeding total circulating blood volume, had no significant effect on the water content in brain tissue [5].

The present investigation was devoted to an analysis of the mechanism of stabilization of the volume of fluid in the brain during sudden changes in the osmolarity and quantity of extracellular fluid.

EXPERIMENTAL METHOD

Male Wistar albino rats weighing 150-200 g were used. The animals were anesthetized by intraperitoneal injection of 2% pentobarbital solution (0.25 ml/100 g body weight). Polyethylene glycol 400 (PEG) in a dose of 1.5 mmole (0.6 g)/100 g body weight was injected in the course of 30 min into the saphenous vein by means of a perfusion pump. Sodium and potassium concentrations in the blood serum were determined on a "Flapho-4" flame photometer, the protein concentration on an RF-22 refractometer, and the total iron concentration in hemolyzed blood was measured by an AAS-1 atomic absorption spectrophometer in an air–acetylene flame. Brain tissues were place on quartz slides, weighed on VLAO-100 analytical scales, dried for 24 h in a thermostat at 105°C, and reweighed; electrolytes were extracted with concentrated HNO_3 at 100°C in a dry air bath until all the organic matter had completely dissolved. Samples were prepared in 0.1 N HNO_3 (1 g tissue to 30 ml of solution). Corresponding standard solutions of iron were made up in 0.1 N HNO_3 and, besides variable quantities of iron, they contained constant concentrations of sodium and potassium, close to those in the samples taken for analysis.

EXPERIMENTAL RESULTS

To increase the osmolarity of the blood PEG was used; its action resembled that of mannitol, but it can be injected into the blood stream without water because it is in the liquid state at room temperature and it evokes intensive osmotic diuresis [4]. Observations showed that after injection of PEG into a rat the osmolarity of the blood still remained very high after 60 min (316 ± 1.5 milliosmoles/kg H_2O compared with 301 ± 1.0 milliosmoles/kg in the control), whereas the water content was unchanged in both the gray and the white matter of the brain [5], and slight dehydration was observed only in the whole cerebral hemisphere (Table 1). Since PEG does not penetrate into the cells and since an increase in osmolarity ought to have led to marked dehydration of the brain, it was suggested that the absence of adequate dehydration of brain tissue was due to a redistribution of the brain fluid by the entry of blood or CSF into the closed space of the skull, with the result that the water content in the brain tissues remained stable despite dehydration of the cells. Since there are as yet no reliable methods of determining the total volume of extracellular fluid in the brain, it was decided to use a different approach to the analysis of this problem. To test the hypothesis of an increase in cerebral

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TABLE 1. Content of Water and Iron in Tissues of Cerebral Hemisphere in Albino Rats

Experimental conditions	Brain		Blood	
	water cont., kg / kg dry substance	iron cont., mmoles/ kg dry substance	iron content, mmoles kg	water content, g/100 ml
Control (n=7)	3,53±0,01	5,94±0,29	14,5±0,4	8,06±0,23
PEG (n=7)	3,41±0,02†	7,37±0,23*	15,4±0,7	6,73±0,26
Trephining + PEG (n=7)	3,26±0,03†	6,20±0,17	14,6±0,7	—

Legend. Significance of differences calculated relative to control: *) $P < 0.05$; †) $P < 0.01$.

blood volume, the iron content in the brain, which depends on the number of erythrocytes in its blood vessels, mainly in the capillary network, was measured. The results showed that the iron content in the brain increased by 24% after injection of PEG, whereas in the blood there was no significant change. The absence of change in the blood is due to the fact that, besides the increased loss of fluid by the kidney, as a result of its osmotic effect PEG increases the outflow of water from cells of all organs and tissues into the blood. The results thus can be taken as direct proof of an increase in the blood volume of the brain tissue after injection of PEG or, in other words, the decrease in the volume of intracellular water in the closed space of the skull is accompanied by an increase in the volume of extracellular fluid.

This suggestion was confirmed by an increase in the sodium content in the gray matter of the brain from 54 ± 1.1 (n = 10) to 73 ± 2.3 (n = 9) meq/kg wet weight. After disturbance of the airtightness of the skull by trephining, injection of the same volumes of PEG did not cause a statistically significant increase in the cerebral blood volume, and under these conditions the most marked dehydrating effect of PEG was observed: the loss of water was 9% (Table 1). Considering the important role of a rise of venous pressure in the blood volume of the brain [7], and also the role of airtightness of the cranial cavity, it can be concluded that an increase in osmolarity of the blood causes true dehydration of the brain cells, but to compensate for the intracellular water extracted and the fluid draining out from other spaces beyond the blood–brain barrier, the fraction of intravascular fluid and also, perhaps, of CSF, increases. This maintains the fluid level within the cranial cavity relatively stable.

LITERATURE CITED

1. E. Arseni and A. I. Constantinescu, Intracranial Hypertension [in Russian], Bucharest (1978).
2. L. Bakay and D. Lee, Cerebral Edema [Russian translation], Moscow (1969).
3. É. I. Kandel' and N. M. Chebotareva, Zh. Nevropatol. Psikhiat., No. 1, 124 (1972).
4. Yu. V. Natochin and E. I. Shakhmatova, Byull. Éksp. Biol. Med., No. 5, 79 (1970).
5. L. E. Pinegin, L. M. Tibekina, E. I. Shakhmatova, et al., Fiziol. Zh. SSSR, No. 1, 122 (1979).
6. A. Baethman, W. Lanksch, and P. Schmidek, Neurochirurgia, 17, 37 (1974).
7. G. J. Mchedlishvili, L. S. Nicolaischwili, and M. Itkis, Stroke, 10, 52 (1979).