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Effect of Intravenous Infusion of Polyosm on Diuresis and Parameters of Systemic and Cerebral Hemodynamics

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The effect of 30-min infusion of Polyosm (a polyethylene oxide 400 solution) is studied on anesthetized cats. The preparation stimulates diuresis and has no effect on arterial and venous pressure and cardiac and stroke indices. By the 30th min of infusion, the total peripheral and cerebral vascular resistance significantly decrease, while cerebral blood flow increases.

Key Words: *polyethylene oxide; systemic and cerebral hemodynamics; diuresis*

Intravenous administration of osmotically active diuretics modifies the hemodynamics parameters associated with distribution of intra- and extracellular fluids [2]. Polyosm, a preparation for intravenous infusions, was developed on the basis of the osmotically active compound polyethylene oxide 400. This preparation produces a rapid and stable antiedematous effect on brain tissue in models of acute ischemia and hypertonic encephalopathy.

In the present study we examined the effects of intravenous infusion of Polyosm on the major hemodynamic parameters in intact anesthetized cats.

MATERIALS AND METHODS

Experiments were performed on 14 cats of both sexes weighing 2.5-4 kg. The animals were anesthetized with sodium pentobarbital (40 mg/kg intravenously). After intravenous administration of heparin (500 units/kg), catheters were implanted in the left femoral artery for measuring systemic arterial pressure (SAP), in the left femoral vein for infusion of Polyosm, in the caudal vena cava (via the right femoral vein to the heart level) for measuring central venous pressure (CVP), and in the right heart (via the right external jugular vein) for infusion of normal saline. The branches of the right external carotid artery were ligated up to the maxillary internal artery, and a sensor of an MFV-1100 flowmeter (Nihon Kohden) was placed in it to measure cerebral blood flow. A catheter with a thermistor was inserted into the aorta via the carotid artery to record the thermodilution curve upon determination of minute volume. The volume of circulating blood was measured using the evans blue method [3]. Total peripheral vascular resistance (TPVR), cardiac and stroke indices, and cerebral vascular resistance were calculated using conventional formulas [7].

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Polyosm was infused into the left femoral vein during a 30-min period to attain the total dose of polyethylene oxide 400 of 1 g/kg (therapeutic dose for osmotic diuretics [4]). An equal volume of physiological saline was infused into control cats.

RESULTS

In the control group, intravenous infusion of normal saline was accompanied by statistically insignificant changes in diuresis (Table 1) and induced no significant changes in SAP and cerebral blood flow. The tendency toward a decrease in CVP and in cardiac and stoke indices was statistically insignificant. A slight increase in the volume of circulating blood on the 30th min of experiment was probably caused by infusion of normal saline. Total peripheral vascular resistance slightly decreased by the 30th min of infusion and significantly increased by the end of experiment (by 28% compared with the initial level). Cerebral vascular resistance increased throughout the entire experimental period: by 9% on the 30th min of infusion and by 18% at the end of experiment in comparison with the initial level (Table 1).

Intravenous infusion of Polyosm markedly stimulated diuresis: the volume of excreted urine increased by 188% at the end of infusion and by 115% 30 min after it in comparison with the initial value; the differences were significant compared with the control. However, changes in SAP and cardiac and stroke indices were statistically insignificant. Central venous pressure remained at a stable and higher level than in the control. The preparation increased the volume of circulating blood: a 18% statistically significant increase in this parameter was observed at the end of experiment. Presumably, this provided a higher CVP (Table 1). By the 30th min of infusion, TPVR decreased by 10% compared with the initial level and returned to normal by the end of experiment, remaining lower than in the control. In contrast to the systemic hemodynamics parameters, cerebral blood flow was significantly increased on the 30th min of infusion (by 19%) and normalized on the 60th min of experiment. An increase in cerebral blood flow was associated with a decrease in cerebral vascular resistance (by 20% compared with the initial value, being significantly different from the control). Cerebral vascular resistance normalized by the end of experiment. By the 30th min of infusion, TPVR decreased by 10% compared with the initial level; by the end of experiment it increased, remaining at a lower level compared with the control (Table 1). The dynamics of cerebral vascular resistance reflected changes in TPVR, therefore, cerebral blood flow increased by the end of Polyosm infusion.

Thus, in contrast to urea and mannitol, Polyosm produces a moderate effect on systemic hemodynamics. It does not change cardiac activity and SAP. An increase in the circulating blood volume is probably compensated by increased diuresis, as evidenced by low CVP values. This is an advantage over the osmotic diuretics mannitol and urea [1,2]. Mannitol markedly increases SAP, the circulating blood volume and heart rate, which restricts its use in some diseases (pulmonary edema and renal and cardiac disorders) and may lead to circulatory insufficiency [2]. A decrease in TPVR and cerebral vascular resistance can be regarded as a positive effect of Polyosm.

The absence of pronounced hemodynamic changes after intravenous infusion of Polyosm may be as-

TABLE 1. Changes in Systemic and Cerebral Hemodynamics Under the Action of Polyosm

Parameter	Control			Experiment		
	initial value	30 min	60 min	initial value	30 min	60 min
Systemic arterial pressure, mm Hg	98±8	95±3	101±5	107±9	102±9	103±10
Central venous pressure, mm H_2O	8±3	4±3	2±3	6±2	8±2**	6±1**
Cardiac index, liter/min×m	1.92±0.27	1.83±0.35	1.77±0.49	1.80±0.22	1.87±0.23	1.81±0.25
Cerebral index, ml/m	11.53±1.48	9.75±1.57	8.42±2.28	10.54±1.51	10.88±1.81	9.42±1.28
Cerebral blood flow, ml/min	23.2±4.5	23.7±5.0	23.2±4.5	26.5±1.5	31.6±2.9*,**	24.8±4.2
Total peripheral vascular resistance, $\times 10^4 \times dyn \times sec \times cm^{-5}$	1.74±0.12	1.66±0.21	2.28±0.20*	1.90±3.87	1.72±0.10*	1.87±0.26**
Cerebral vascular resistance, $\times 10^4 \times dyn \times sec \times cm^{-5}$	32.58±1.87	35.54±5.58	38.36±2.69*	34.90±2.87	28.14±2.32*,**	38.97±5.98
Circulating blood volume, ml/kg	57.3±4.2	61.7±5.9	55.6±5.7	58.1±4.5	60.9±7.4	71.6±11.3**
Volume of excreted urine, ml	3.7±1.0	3.9±1.2	3.1±1.0	4.4±0.9	12.7±3.2*,**	9.5±1.7*,**

Note. $p<0.05$: *compared with the initial value, **between the groups.

sociated with its partial deposition in the intracellular space with subsequent release into circulation [6]. This is consistent with our observation that osmotic activity of Polyosm increases gradually, reaching the maximum 10-15 min after injection [8]. The finding that Polyosm induces no abrupt changes in SAP and CVP agrees with the data of others on the effects of polyethylene oxide 400 in glaucoma [5,9].

Our results indicate that Polyosm is a prospective preparation producing no side effects typical of osmotic diuretics.

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Postnatal Stress Impairs the Learning of Two-Way Avoidance Task in Prenatally Alcoholized Adult Rats

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Mild stress (handling and subcutaneous injection of 0.9% NaCl from postnatal day 8 through day 20) normally improves acquisition of a shuttle-box avoidance task in mature male rats. In the offspring of rats given intragastral injections of 25% ethanol (5 g/kg) from day 1 till day 20 of pregnancy, both handling and injections impair learning.

Key Words: *prenatal alcoholization; postnatal stress; bilateral avoidance; rats*

Environmental enrichment during early postnatal ontogeny, in particular handling, usually improves learning and increases the mass of the brain and especially of brain cortex in healthy mature animals, while environmental depletion during this period impairs behavioral capacity of the offspring [3,9]. On the other hand, in some cases mild stress caused by handling and injections impairs the higher nervous activity, for instance, the retrieval of passive avoidance task [6]. In light of this two questions arise: how stressful environental enrichment during early postnatal ontogeny affects the offspring with various disturbances of the central nervous system (CNS), for example, induced by prenatal alcoholization [4], and whether such environmental enrichment acts as therapeutic or pathogenic factor.

The aim of the present study was to examine the effect of environmental enrichment in the form of handling and injections in early postnatal ontogeny on learning in health and after prenatal alcoholization.

MATERIALS AND METHODS

The study was carried out on 16 random-bred albino rats. Each group comprised 4 litters. The rats of

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