GENERAL PATHOLOGY AND PATHOLOGICAL PHYSIOLOGY

Effect of Polyosm on Viscoelastic Properties of the Craniospinal System in the Model of Acute Hypertensive Encephalopathy

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The effects of Polyosm (polyethylene oxide 400 solution) on viscoelastic properties of the craniospinal system in cats and parameters of systemic hemodynamics were studied on the model of acute hypertensive encephalopathy, induced by intravenous injection of norepinephrine hydrotartrate and intracarotid infusion of papaverine hydrochloride. In control series, a sustained increase in the central venous and intracranial pressure, enhancement of resistance to liquor drainage, and pronounced increase in rigidity of the craniospinal system were observed. Intravenous infusion of Polyosm moderated these disturbances of the blood and liquor dynamics and restored viscoelastic properties of the craniospinal system to an almost initial level.

Key Words: *Polyosm; hypertensive encephalopathy; viscoelastic properties of the craniospinal system*

Osmotic diuretics (mannitol, carbamide) are often used in the complex therapy of brain edema and swelling in acute hypertensive encephalopathy [2]. However, these drugs had a number of side effects, which limit their application: risk of pulmonary edema, elevation of systemic arterial pressure (SAP), excessive increase of the volume of circulating blood, heart and kidneys dysfunction [5]. New preparation Polyosm is prepared on the basis of polyethylene oxide 400 and has a pronounced dehydrating effect on cerebral tissue [1]. This drug demonstrated clear antiedemic effect in experiments on alert rats with acute hypertensive encephalopathy.

In the present study we investigate the effects of Polyosm on viscoelastic properties of the craniospinal system (CSS), intracranial pressure (ICP), central venous pressure (CVP) and SAP on a model of acute hypertensive encephalopathy.

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MATERIALS AND METHODS

The viscoelastic properties of the CSS were experimentally studied on 9 cats weighing 2.5-3.5 kg narcotized intravenously with Nembutal (40 mg/kg). Infiltration anesthesia during surgery was performed with 0.5% Procaine.

Evaluation of viscoelastic properties of the CSS was based on the study of P-V relations, *i.e.*, the dynamics of ICP after infusion of an additional volume of cerebrospinal liquid [12]. To perform the infusion test, a hollow needle was implanted into the right lateral ventricle of the brain under stereotaxic control. Simultaneously, the skull was trepanized above the left hemisphere and a cannula was implanted for direct measurement of ICP during the infusion test. An addi-

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tional volume of artificial liquor was infused at a constant rate of 0.2 ml/min after passing a thermostat, which heated the infused solution to 37.5°C. This procedure increased ICP to 30-40 mm Hg.

The values of CVP and SAP were measured directly in the abdominal part of the inferior vena cava and in the right femoral artery, respectively.

Acute hypertensive encephalopathy was modeled according to previously described method with modifications [2]. Intracarotid infusion of 2% papaverine hydrochloride (0.25 mg/kg) via a catheter inserted into the lingual artery produced a pronounced dilation of cerebral blood vessels without concomitant hypotensive reaction [4]. Simultaneously, 0.2% norepinephrine hydrotartrate was infused into the left femoral vein (1.4 mg/kg), which provoked an acute hypertensive reaction disturbing autoregulation of cerebral blood flow and causing acute hypertensive encephalopathy [2].

Polyosm (a solution containing 1 g/kg polyethylene oxide-400) was infused intravenously 15 min after norepinephrine hydrotartrate. Viscoelastic properties of the CSS and liquor dynamics were quantitatively evaluated by formulas [3,8,11,12]. The following indices were used: PVI, which characterizes volume compliance of the CSS and is equal to the volume that should be added to the craniospinal reservoir to produce a 10-fold pressure increase in the CSS; PEI_1, which reflects the increment of the CSS elasticity as a function of ICP. The current values of CSS elasticity E(P) were calculated, which characterize resistance to displacement of venous and arterial blood, liquor, and interstitial fluid from the cranial cavity. To evaluate the state of liquor dynamics from the data of infusion test, an index was calculated that characterized the state of liquor outflow, *i.e.*, resistance to liquor resorption or drainage.

The cats were euthanized by Nembutal overdose. The data were statistically analyzed using the method of direct differences and Student's *t* test.

RESULTS

From the first minutes, intravenous infusion of norepinephrine induced a rapid and sustained hypertensive reaction, which lasted for 20-30 min. In the control group, pronounced increase in SAP (by 43%) and CVP (by 84%) persisted 30 min postinfusion. Then SAP monotonously decreased, while CVP remained above the initial level for 2 h (Table 1). After 30 min, ICP attained 220% of the initial value, and remained increased during the entire observation period (Table 1). One hour postinjection PVI decreased by 30% (Table 2). PEI_1 significantly increased by 22% 2 h postinjection. In the control series, persistent aggravation of liquor drainage was observed: 1 and 2 h postinjection the resistance to liquor drainage significantly increased by 119 and 157%, respectively (Table 2). In the control group, the integral index of CSS viscoelastic properties E(P) also progressively increased (Table 2). This phenomenon is probably underlain by changes in the cerebral blood and liquor dynamics: an increase in the brain blood filling (in the arterial and venous parts of the vascular bed) and impairment of liquor outflow, leading to accumulation of interstitial fluid and filtration brain edema [2,6].

Dynamics of SAP in cats treated with Polyosm did not differ from the control (Table 1). Thirty min after infusion of norepinephrine, CVP surpassed the baseline level by 70%, but after 1-1.5 h there was a tendency to a lower level of CVP than in the control, and after 2 h this difference became significant (Table 1). After a transient 58% increase 30 min after infusion of norepinephrine, ICP progressively dropped. After 2 h it surpassed the initial level only by 8% and significantly differed from the control (Table 1). After Polyosm infusion, PVI was close to the initial value (Table 2). After 1 and 2 h, PEI_1 was below the control values (Table 2). Similar dynamics was observed also for liquor drainage resistance. The increase in E(P)

TABLE 1. SAP, CVP, and ICP in Control Group and after Intravenous Infusion of Polyosm (*M±m*)

Indices	Baseline values	Time after norepinephrine infusion, h		
		0.5	1	2
Control				
SAP, mm Hg	105±9	+45±10*	0±7	-2±9
CVP, mm Hg	50±4	+42±4*	+34±5*	+28±2*
ICP, mm Hg	6±2	+8±1*	+5±2	+6±1*
Polyosm				
SAP, mm Hg	96±11	+49±15*	0±8	-8±6
CVP, mm Hg	51±5	+36±5*	+21±7*	+12±5'
ICP, mm Hg	6±1	+4±1*	+2±1	+1±2'

Note. Here and in Table 2: $p<0.05$: *compared with the initial value; 'compared with the control.

TABLE 2. PVI, PEI_1, Liquor Drainage Resistance (LDR) and E(P) in Control Group and after Intravenous Infusion of Polyosm (*M±m*)

Indices	Baseline values	Time after norepinephrine infusion, h	
		1	2
Control			
PVI, ml	0.54±0.09	-0.16±0.05*	-0.13±0.07
PEI_1, ml^{-1}	2.86±0.87	+0.38±0.19	+0.62±0.22*
LDR, mm Hg/ml	122.2±53.4	+145.0±29.5*	+192.4±62.1*
E(P), mm Hg/ml	21.37±8.32	+15.05±4.17*	+23.97±7.35*
Polyosm			
PVI, ml	0.53±0.11	+0.03±0.05+	-0.02±0.02+
PEI_1, ml^{-1}	3.00±1.25	-0.18±0.10+	+0.23±0.14
LDR, mm Hg/ml	132.3±46.8	+68.0±36.9+	+29.0±22.7+
E(P), mm Hg/ml	18.67±3.57	+7.83±5.18	+3.10±1.85+

after 1 h was insignificant, while after 2 h this index was far below the control values (Table 2).

Therefore, intravenous infusion of Polyosm prevented drastic increase in liquor drainage resistance, CVP, and ICP, and to the end of observation period restored the viscoelastic indices of the CSS to almost initial level. These features can be due to a number of effects of the drug.

Intravenous infusion of Polyosm produced rapid and sustained increase in osmotic activity of the plasma by 9-14 and 5-9 mmol/kg 10-30 min and 1-2 h post-infusion, respectively [9]. The increase in the liquor-venous blood osmotic gradient under the effect of osmoactive agents improved drainage of the cerebrospinal fluid [10]. Evidently, the increase in liquor resorption as well as extra volume of artificial liquor infused into the CSS during P-V test contributed to the drop of liquor drainage resistance.

Treatment with osmotic diuretics such as mannitol and carbamide considerably increased the volume of circulating blood and CVP [5]. Infusion of Polyosm possessing pronounced hyperosmotic properties and a potent diuretic effect [1,7] did not induce so drastic increase in the volume of circulating blood and CVP. Such a "relief" of the cerebral venous system can contribute to the decrease of CSS elasticity, which is confirmed by the dynamics of PVI, PEI_1, and E(P). The pressure drop in the venous system also decreased liquor drainage resistance. Finally, Polyosm producing a pronounced antiedemic effect in the brain, reduced the content of interstitial fluid, the major volume of CSS, thus reducing rigidity and improving volume compliance of the CSS.

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