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Research Article

DIFFERENTIATED HYPEROSMOLARY THERAPY IN CEREBRAL EDEMA IN PATIENTS WITH CRANIOCEREBRAL INJURY

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ABSTRACT

to study the pathophysiological aspects of cerebral edema and compare the effectiveness of using 15% mannitol solution and hypertonic 3.5%, 7%, 10% sodium chloride solution in the complex treatment of patients with head injury. **Material and methods:** 90 patients from 18 years old to 68 years old with various traumatic brain injuries and inhibition of consciousness level from 4 to 13 points on the Glasgow coma scale were examined.

Results: infusion of mannitol at the indicated dosage reduced ICP after 30 minutes by 42, 3%, and after 120 minutes it remained below the initial data by 23.9%. Infusion of a 3.5% NaCl solution already by the 30th minute led to a decrease of ICP by 48.6%, and by the end of 120 minutes the ICP remained below the initial data by 35.9%. Infusion of a 7% NaCl solution already by the 30th minute led to a decrease in ICP by 55.4%, and by the end of 120 minutes the ICP remained below the initial data by 39.9%. Infusion of a 10% NaCl solution already by the 30th minute led to a decrease in ICP by 58.4%, and by the end of 120 minutes the ICP remained below the initial data by 45.9%.

Conclusions: the decrease in ICP within 30 and 120 minutes after the introduction of hyperosmolar solutions is more pronounced with iv administration of 3.5%, 7%, 10% NaCl solution relative to 15% Mannitol in calculated dosages, which should be borne in mind in patients with concomitant cardiac and renal pathology.

KEYWORDS

Traumatic brain injury, hypertonic saline, mannitol, intracranial pressure, cerebral edema, CPP.

INTRODUCTION

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Traumatic brain injury (TBI) is a clinical condition characterized by brain dysfunction resulting from damage by an external mechanical force, causing the brain to quickly change its position inside the skull, while the structure and functions of the brain change dramatically [1]. TBI is a growing public health problem that has caused high mortality and long-term disability, especially among children and young people [12] in middle-income countries. More than 50 million people around the world receive TBI with a high economic value of about 400 billion US dollars [8]. A large population of patients receive brain injuries with serious physical and emotional consequences for patients and their relatives, as well as to a large extent for society as a whole [7]. In connection with urbanization, as well as with the growth of road accidents, the number of TBI cases is growing rapidly every year [2]. Finding a way to treat TBI patients has become a serious public health problem in many countries, which has led to the emergence of many monotherapies that have shown promising results in animal models with TBI but have not yet shown any significant efficacy in clinical trials.

People with TBI may develop cognitive and sensorimotor impairments, such as reduced information processing time, memory loss, and difficulties associated with fine coordination of movement [6].

In addition, people with a history of TBI are subsequently more likely to suffer from neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease [9,10]. When damaged, the brain undergoes structural and functional changes, pathological cellular and biochemical dysfunctions with a serious loss of neurons and glial [3,4]. According to clinical indications, a brain injury can go from mild to severe due to pathological lesions that usually occur sometime after the injury, such as edema, bruising, and cerebral hemorrhage [5]. The processing and transmission of neural signals largely depends on the ionic and osmotic balance of the brain tissue. In order to discover new therapeutic methods, it is necessary to understand the complex pathophysiology of TBI and to study the molecular mechanisms involved in the process of the onset of the disease.

Research has shown the participation in the pathogenesis of cerebral edema (CE) associated with brain injury, such proteins as aquaporin-4 (AQP4), matrix metalloproteinases (MMP), cotransporter Na + K (+) - 2Cl (-) (NKCC1) and sulfonylurea receptor (Sur1) is a member of the 4 cation channel with transient receptor potential (Trpm4) [13]. These mechanisms affect the blood-brain barrier integrity, cellular volume regulation, oncotic gradients, and inflammatory reactions culminating in various forms of CE - described as concussive compared to diffuse or classified as vasogenic, cytotoxic, or osmotic [14]. Brain edema with head injury is an unfavorable outcome and can lead to mortality up to 50% [15].

Mannitol

Mannitol is a non-metabolizable sugar alcohol ($C_6H_{14}O_6$), which reduces the reabsorption of water and sodium in the renal tubules and is used for osmotherapy to reduce intracranial pressure or cerebral edema since the 1960s as the main treatment, increased intracranial pressure, and remains the main component of treatment TBI. Mannitol increases cerebral blood flow due to an increase in plasma, reduces the viscosity of the blood, which was caused by deformed red blood cells and stimulate osmotic diuresis. Mannitol reduces intracranial pressure through two different effects in the brain: firstly, the rheological effect, reduces blood viscosity and helps

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increase plasma and oxygen delivery to the brain. In response, cerebral vasoconstriction occurs due to autoregulation, and cerebral blood volume decreases. The second effect occurs through the creation of an osmotic gradient through the blood-brain barrier, which leads to the movement of water from the parenchyma into the intravascular space [17]. The volume of brain tissue is reduced and, therefore, ICP is reduced. The effect on ICP is usually observed 15 minutes after the recommended bolus injection of 0.25 to 1 g / kg [18,19]. Mannitol also acts as an osmotic diuretic, which leads to free clearance of water and an increase in serum osmolality. As a result, water moves from the intracellular to the extracellular space, causing a long-lasting dehydrating effect. Mannitol inhibits sodium resorption in the renal tubules.

Hypertonic saline

Weed and McKibben, 1919, were the first to describe hypertonic saline therapy in TBI [151]. Hypertonic saline has become an alternative over the past 20 years, but there remains a contradiction as to which solution is the best tool and the relatively best method of administration. Hypertonic saline has been used successfully to treat cerebral edema in brain injury. The effect on ICP begins within a few minutes after the introduction of a NaCl solution with concentrations ranging from 3.5% to 23.4% [20,21]. It has osmotic, rheological and metabolic effects. The osmotic property is due to sodium, since it increases the osmotic pressure of the plasma, thus reducing permeability through the blood-brain barrier. The rheological effect is due to its ability to reduce blood viscosity by changing the deformation of red blood cells. This compensates for vasoconstriction to maintain cerebral blood flow and thus reduces cerebral blood volume and intracranial pressure. Hypertonic saline promotes the flow of water through the BBB and improves blood flow by increasing plasma volume.

Cerebral edema is a common consequence of neurological damage and is defined as abnormal fluid accumulation in the brain parenchyma. Hyperosmolar therapy is the basis for the treatment of cerebral edema, creating an osmolar gradient inside the blood-brain barrier [17].

2. The purpose of the study

To study the pathophysiological aspects of cerebral edema and compare the effectiveness of using 15% mannitol solution and hypertonic 3.5%, 7%, 10% sodium chloride solution in the complex treatment of patients with head injury.

3. Materials and research methods.

20 patients with mannitol and 3.5% sodium chloride solution, 10 patients with mannitol and 7% sodium chloride solution, 10 patients with mannitol and 7% sodium chloride solution, 22 patients and 28 patients with mannitol and 10% sodium chloride solution with TBI were examined (archived data) from the age of 18 to 68 years and the inhibition of consciousness from 4 to 13 points on the Glasgow Coma Scale (GCS). All patients underwent invasive monitoring of ICP by lumbar puncture with monometry. Lumbar puncture was performed at the level of L2-L4.

To reduce the ICP to 20 mmHg and less, at the first stage, intravenous administration was used; intravenous administration of 15% mannitol solution at the rate of 1.0 g / kg body weight for 15 min (n = 15) and a 3.5% sodium chloride solution at the rate of 3.5 ml was used kg for 15 min (n = 15). in the second stage, a 15% mannitol solution at a rate of 1.0 g / kg body weight for 15 min (n = 10) and a 7% sodium chloride solution at a rate of 3.5 ml / kg for 15 min (n = 10). in the triturated

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stages, a 15% mannitol solution at a rate of 1.0 g / kg body weight for 15 min (n = 25) and a 10% sodium chloride solution at a rate of 3.5 ml / kg for 15 min (n = 25). The duration and frequency of administration of these drugs was determined by indicators of plasma osmolarity, electrolyte levels, glucose concentration, plasma urea, as well as the dynamics of ICP.

All patients underwent standard intensive care, adopted in our clinic. The head end of the bed was raised by 30-40°. Ventilation device Wella and Drager with a respiratory volume of 8-10 ml per kg of ideal body weight in SIMV (Synchronized Intermittent Mandatory Ventilation) mode and PEEP 2-10 cm. Infusion therapy was performed by combining colloidal and crystalloid solutions. They sought to maintain the state of normovolemia (CVP 6-12 cm.). They tried to start enteral probe nutrition from the first day of the patient's stay in the intensive care unit at the rate of 20-25 kcal per kg of body weight per day after stabilization of vital parameters of the body. The daily protein requirement was estimated by calculating the nitrogen balance. If necessary, parenteral nutrition was added. To prevent infectious complications, all patients from the first day after surgery or in the presence of respiratory support were prescribed monotherapy with cephalosporins (ceftriaxone 2-4 g / day) or fluoroquinolones (ciprofloxacin 0.2-0.4 g / day). For the prevention of deep vein thrombosis of the lower extremities (in the absence of signs of external and internal bleeding), clexane was prescribed (0.4 thousand units per day subcutaneously). In patients who did not measure intracranial pressure, with the appearance of clinical signs of a dislocation syndrome (anisocoria, paresis of the gaze upward, Gerdwig Magandie syndrome in combination with bradycardia, arterial hypertension), brain CT was performed. Controlled osmolarity of blood plasma. In order to stop psychomotor agitation, medication sedation was combined with narcotic analgesics with benzodiazepines. With an increase in ICP against the background of hyperthermia, antipyretics were introduced and physical cooling methods were used. With a progressive deterioration in the level of consciousness, despite conservative therapy, CT brain scans were performed.

In the presence of ICP monitoring, they sought to maintain ICP within 20 mmHg. and less. Anesthesia and sedatives were used during invasive procedures (tracheostomy, vascular catheterization) and, if necessary, relief of the patient's psychomotor agitation. To reduce the increased ICP, hyperosmolar solutions were used under the control of the osmolality of blood plasma. With an increase in blood osmolality of more than 320 mosm / l, the introduction of hyperosmolar drugs was stopped. In the presence of persistent intracranial hypertension, which is difficult to correct with conservative methods of treatment (ICP more than 20 mm Hg for 6-12 hours), decompressive craniotomy was performed.

Before the start of the study and 30 and 120 minutes after the introduction of the solutions, ICP, SBP, heart rate, CPP, osmolarity and plasma electrolytes were determined.

4. Results and discussion: the table below shows the dynamics of changes in ICP, CPP and systemic hemodynamics in response to iv administration of mannitol and HTS.

Tab. No. 1 Effect of hyperosmolar solutions on ICP, CPP and hemodynamic parameters.

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Parameters at the research stages						
Solutions	15% mannitol solution			3,5% NaCl solution		
Stages Showings	Beginnig	After 30 mins	After 120 mins	Beginning	After 30 mins	After 120 mins
HR per min.	76,0±4,5	80,2±3,7	82,7±4,5	74,6±2,7	78,0±3,4	75,9±3,1
BP	102,6±9,5	106,7±4,2	104,4±4,0	100,2±3,1	104,6±4,2	104,1±3,5
ICP	31,7±2,6	18,3±4,1*	24,1±3,9*	29,8±1,8	15,3±2.4*	19,1±2,7*
CPP.	70,9±6,9	88,4±2,7*	80,3±2,3*	70,4±1,3	89.3±2,9*	85,8±2,1*

Note: * - significantly relative to the initial values (p <0.05)

The use of hyperosmolar drugs for the correction of intracranial hypertension is a routine practice. The results of our study confirm a significant decrease in ICP when using both 15% mannitol solution and 3.5% sodium chloride solution. Infusion of mannitol at the indicated dosage led to a decrease in ICP after 30 minutes by 42.3%, and after 120 minutes it remained below the baseline by 23.9%. Infusion of a 3.5% NaCl solution already by the 30th minute led to a decrease in ICP by 48.6%, and by the end of 120 minutes the ICP remained below the initial data by 35.9%. The above data clearly indicates a more pronounced decrease in ICP with iv infusion of a hypertonic (3.5%) NaCl solution. Both mannitol and a hypertonic solution of sodium chloride also led to an increase in cerebral perfusion pressure, presumably due to the volemic effect and a decrease in ICP. The decrease in ICP after the infusion of hyperosmolar solutions inversely affected the CPP. So the CPP after mannitol infusion after 30 and 120 minutes increased by 19.7% and 11.7%, respectively, while the infusion of 3.5% NaCl led to an increase in CPP in the indicated stages of the study by 21.2% and 17.9%, testifying to improved blood supply to the brain. As for the indicators of systemic hemodynamics, their changes in response to the introduction of hyperosmolar solutions were unreliable. However, it should be noted that the calculated doses of 15% mannitol led to a more pronounced tachycardia than a 3.5% NaCl solution.

The following table No. 2 reflects the dynamics of osmolarity and plasma electrolytes in response to the iv administration of hyperosmolar solutions.

Table No. 2 Effects of hyperosmolar solutions on electrolytes and plasma osmolarity.

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Parameters at the research stages						
Solutions	15% mannitol solution			3,5% NaCl solution		
Stages / Showings	Beginnig	After 30 mins	After 120 mins	Beginnig	After 30 mins	After 120 mins
Osmolarity of plasma (mOsm/l)	296,1±4,0	315,0±5,4*	313,7±4,1*	304,0±3,9	314,4±4,2*	315,5±4,0*
Na+ of plasma (mmol/l)	151,4±3,1	149,6±2,8	144,0±3,2	149,7±2,1	155,7±3,3	153,1±3,8
K+ of plasma (mmol/l)	5,1±0,3	4,8±0,5	4,3±0,2	5,3±0,2	4,5±0,9	5,0±0,8

Note: * - significantly relative to the initial values (p <0.05)

The data presented in the table indicates a moderate increase in plasma osmolarity in response to the introduction of hyperosmolar solutions. To a lesser extent this applies to 3.5% NaCl solution. So, the calculated doses of mannitol 30 and 120 minutes after administration led to an increase in plasma osmolarity by 6.4% and 5.9%, respectively, while a 3.5% sodium chloride solution at the same time of the study by 3.4% and 3, 8% respectively.

As for the plasma Na concentration, after infusion of 15% mannitol in the calculated dosages after 30 and 120 minutes, it moderately decreased relative to the initial values by 1.2% and 4.9%, while a 3.5% NaCl solution naturally led to an increase in the concentration Na in the indicated periods of the study by 4.0% and 2.2%, respectively. The concentration of plasma K in response to the introduction of hyperosmolarity of solutions of mannitol and 3.5% NaCl very moderately decreased almost equally. It must be assumed that this decrease is associated with the "plasma dilution phenomenon" in response to the injected solutions and their effect. The indicated changes in the osmolarity of plasma electrolytes were insignificant and, as a rule, did not require correction, which was clinically accompanied by positive dynamics in the general neurological status.

In clinical conditions, this difference is significant, since the use of large doses of hyperosmolar drugs can lead to undesirable side effects. So, repeated injections of mannitol may be accompanied by the occurrence of a “recoil phenomenon”, and prolonged use of hyperosmolar drugs leads to an increase in plasma osmolarity and increases the risk of renal failure.

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The table below shows the dynamics of changes in ICP, CPP and systemic hemodynamics in response to iv administration of mannitol and HTS 7% NaCl solution.

Tab. No. 3 Effects of hyperosmolar solutions on ICP, CPP and hemodynamic parameters.

Parameters at the research stages						
Solutions	15% mannitol solution			7% NaCl solution		
Stages / Showings	Beginnig	After 30 mins	After 120 mins	Beginnig	After 30 mins	After 120 mins
HR per min.	76,0±4,5	80,2±3,7	82,7±4,5	73,6±2,7	77,0±3,4	75,9±3,1
BP	102,6±9,5	106,7±4,2	104,4±4,0	100,1±3,1	104,4±4,3	104,2±3,4
ICP	31,7±2,6	18,3±4,1*	24,1±3,9*	29,5±1,8	13,3±3.5*	17,9±3,1 *
CPP.	70,9±6,9	88,4±2,7*	80,3±2,3*	70,6±1,3	91,1.3±2,9*	86,9±1,1*

Note: * - significantly relative to the initial values in the subgroups (p <0.05)

The results of our study confirm a significant decrease in ICP when using both 15% mannitol solution and 7% sodium chloride solution. Infusion of mannitol at the indicated dosage led to a decrease in ICP after 30 minutes by 42.3%, and after 120 minutes it remained below the baseline by 23.9%. Infusion of a 7% NaCl solution already by the 30th minute led to a decrease in ICP by 55.4%, and by the end of 120 minutes the ICP remained below the initial data by 39.9%. The data presented clearly indicate a more pronounced and prolonged decrease in ICP with iv infusion of a hypertonic 7% NaCl solution, which does not contradict the Mangat data. Both mannitol and a hypertonic solution of sodium chloride led to an increase in cerebral perfusion pressure, presumably due to their volemic effect and a decrease in ICP. The decrease in ICP after the infusion of hyperosmolar solutions inversely affected the CPP. So, the CPP after mannitol infusion after 30 and 120 minutes increased by 19.7% and 11.7%, respectively, while the infusion of 7% NaCl led to an increase in CPP in the indicated stages of the study by 22.5% and 18.7%, indicating improving blood supply to the brain. As for the indicators of systemic hemodynamics, their changes in response to the administration of the studied hyperosmolar solutions were unreliable. However, it should be noted that the calculated doses of 15% mannitol led to a more pronounced tachycardia than a 7% NaCl solution.

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The following table No. 4 shows the dynamics of osmolarity and plasma electrolytes in response to the iv administration of hyperosmolar solutions.

Table No. 4 Effects of hyperosmolar solutions on electrolytes and plasma osmolarity.

Parameters at the research stages						
Solutions	15% mannitol solution			7% NaCl solution		
Stages / Showings	Beginnig	After 30 mins	After 120 mins	Beginnig	After 30 mins	After 120 mins
Osmolarity of plasma (mOsm/l)	296,1±4,0	315,0±5,4*	313,7±4,1*	300,4±3,9	316,2±3,1*	315,8±5,2*
Na+ of plasma (mmol/l)	151,4±3,1	149,6±2,8	144,0±3,2	149,7±2,1	157,2±3,3	154,1±3,5
K+ of plasma (mmol/l)	5,1±0,3	4,8±0,5	4,3±0,2	5,3±0,2	4,5±0,9	5,0±0,8

Note: * - significantly relative to the initial values in the subgroups (p <0.05)

The data presented in the table indicate a moderate increase in plasma osmolality in response to the introduction of hyperosmolar solutions. To a lesser extent, this applies to a 7% NaCl solution. So, the calculated doses of mannitol 30 and 120 minutes after administration led to an increase in plasma osmolality by 6.4% and 5.9%, respectively, while a 7% sodium chloride solution at the same time of the study led to an increase in plasma osmolality by 4.9% and 4.8%, respectively.

As for the plasma Na + concentration, after infusion of 15% mannitol in the calculated dosages after 30 and 120 minutes, it moderately decreased relative to the initial values by 1.2% and 4.9%, while the 7% NaCl solution naturally led to an increase in the concentration Na + in the indicated periods of the study by 4.7% and 2.8%, respectively, which must be borne in mind with initial hypernatremia in patients. The concentration of K + plasma in response to the introduction of hyperosmolar solutions of mannitol and 7% NaCl very moderately decreased almost equally. It must be assumed that this decrease is associated with the "plasma dilution phenomenon" in response to the injected solutions and their diuretic effect.

As for changes in the concentration of sugar and nitrogenous slag in the blood after the introduction of

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HTS, in the "plasma dilution phenomenon" there was only a tendency to decrease them relative to the initial values, which is reflected in the table below.

Tab. No. 5 Effects of hyperosmolar solutions of the level of sugar and plasma urea.

Parameters at the research stages						
Solutions	15% mannitol solution			7% NaCl solution		
Stages / Showings	Beginning	3rd day	5th day	Beginning	3rd day	5th day
Sugar levels (mmol/l)	7,1±1,8	6,5±0,7	5,1±1,2	7,3±1,5	6,1±0,4	4,8±1,7
Plasma urea levels (mmol/l)	9,3±1,4	7,8±2,3	6,1±1,9	9,1±1,7	7,5±2,5	6,7±1,6

The table below shows the dynamics of changes in the values of ICP, CPP and systemic hemodynamics in response to iv administration of mannitol and HTS 10% NaCl solution.

Tab. No. 6 Effect of hyperosmolar solutions on ICP, CPP and hemodynamic parameters.

Parameters at the research stages						
Solutions	15% p-p маннитола			10% p-p NaCl		
Stages / Showings	Beginnig	After 30 mins	After 120 mins	Beginnig	After 30 mins	After 120 mins
HR per min.	76,1±4,6	81,1±3,5	83,2±4,3	73,7±2,4	77,4±3,6	76,1±3,3
BP	101,7±9,5	106,5±5,2	105,1±5,7	100,2±2,9	104,3±6,5	104,1±5,1
ICP	29,9±3,2	17,9±4,1*	23,9±2,9*	29,4±1,9	12,1±3.4*	15,9±3,9 *
CPP.	71,8±6,3	88,6±1,1*	81,3±2,8*	70,8±1,0	92,2±3,1*	88,2±1,2*

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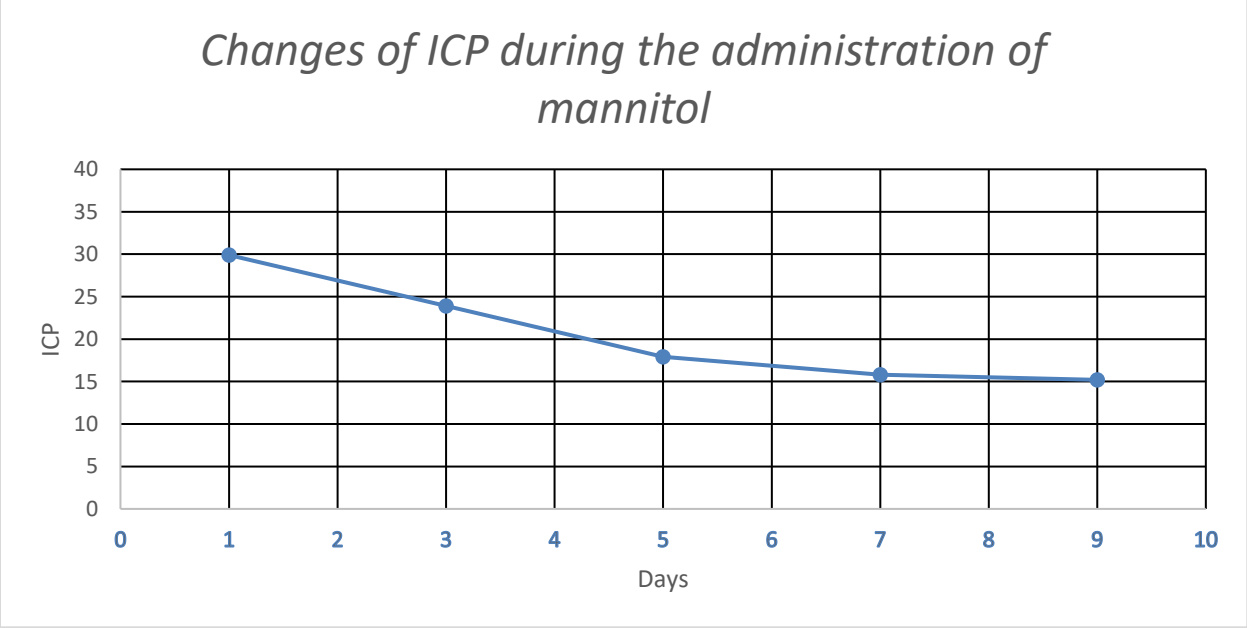
The results of our study confirm a significant decrease in ICP when using both 15% mannitol solution and 10% sodium chloride solution. Infusion of mannitol at the indicated dosage led to a decrease in ICP after 30 minutes by 40.1%, and after 120 minutes it remained below the baseline by 20.1%. Infusion of a 10% NaCl solution already by the 30th minute led to a decrease in ICP by 58.4%, and by the end of 120 minutes the ICP remained below the initial data by 45.9%. The data presented clearly indicate a more pronounced and prolonged decrease in ICP with iv infusion of a hypertonic 10% NaCl solution. Both mannitol and a hypertonic solution of sodium chloride led to an increase in cerebral perfusion pressure, presumably due to their volemic effect and a decrease in ICP. The decrease in ICP after the infusion of hyperosmolar solutions inversely affected the CPP. So the CPP after mannitol infusion after 30 and 120 minutes increased by 23.3% and 13.2%, respectively, while the infusion of 10% NaCl led to an increase in CPP in the indicated stages of the study by 30.2% and 24.5%, indicating improving blood supply to the brain. As for the indicators of systemic hemodynamics, their changes in response to the administration of the studied hyperosmolar solutions were unreliable. However, it should be noted that the calculated doses of 15% mannitol led to a more pronounced tachycardia than 10% NaCl solution.

The diagram below shows the dynamics of changes in ICP during the administration of mannitol



The chart below №2 shows the dynamics of changes in ICP during the administration of 10% NaCl

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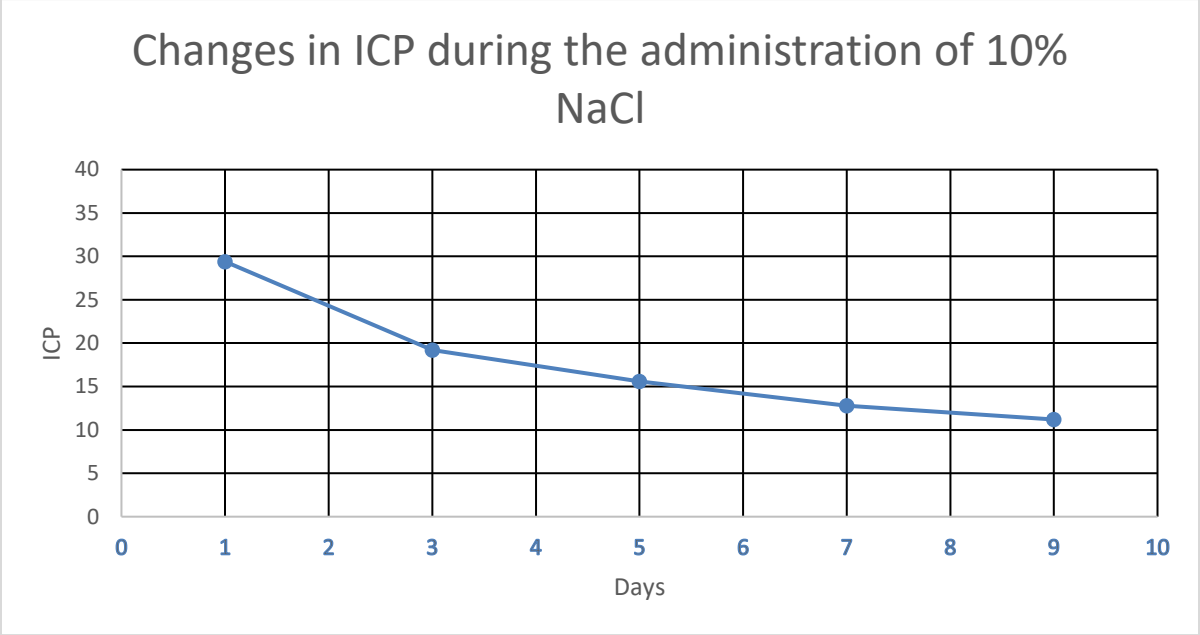

As can be seen from the above diagrams, 10% NaCl had a faster and better drop in intracranial pressure during treatment days than mannitol.

The following table No. 7 reflects the dynamics of osmolarity and plasma electrolytes in response to the iv administration of hyperosmolar solutions.

Table No. 7 Effect of hyperosmolar solutions on electrolytes and plasma osmolarity.

Parameters at the research stages						
Solutions	15% mannitol solution			10% NaCl solution		
Stages / Showings	Beginnig	After 30 mins	After 120 mins	Beginnig	After 30 mins	After 120 mins
Osmolarity of plasma (mOsm/l)	296,1±4,0	315,0±5,4*	311,7±4,1*	297,4±3,9	316,2±3,7*	315,8±5,2*
Na+ of plasma (mmol/l)	145,4±3,1	143,6±2,8	141,0±3,2	144,7±2,1	158,2±2,1	155,3±3,6

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K+ of plasma (mmol/l)	5,1±0,3	4,7±0,6	4,4±0,3	5,3±0,2	4,9±0,9	4,5±0,7

Note: * - significantly relative to the initial values in the subgroups (p <0.05)

The data presented in the table indicate a moderate increase in plasma osmolality in response to the introduction of hyperosmolar solutions. So, the calculated doses of mannitol 30 and 120 minutes after administration led to an increase in plasma osmolality by 6.4% and 5.2%, respectively, while a 10% sodium chloride solution at the same time of the study led to an increase in plasma osmolarity by 6.3% and 6.2%, respectively.

As for the plasma Na + concentration, after infusion of 15% mannitol in the calculated dosages after 30 and 120 minutes it moderately decreased relative to the initial values by 1.2% and 3.0%, while a 10% NaCl solution naturally led to an increase in the concentration Na + in the indicated periods of the study by 9.3% and 7.3%, respectively. The concentration of K + plasma in response to the introduction of hyperosmolar solutions of mannitol and 10% NaCl very moderately decreased almost equally. It must be assumed that this decrease is associated with the "plasma dilution phenomenon" in response to the injected solutions and their diuretic effect.

Mannitol effectively reduces the water content in the brain, but osmotherapy performed with mannitol increased the content of Na + in the brain as well. HTS did not cause abnormal accumulation of Na + in brain tissue [27]. The content of Cl - in the brain, on the contrary, increases to the same extent during treatment with both mannitol and 10% NaCl solution [16]. The accumulation of ions in the brain occurs through transcellular pathways, one of which may well be the hyperosmolar-induced activity of Na + / K + - ATPase, and not due to hyperosmolar disturbance of the brain barriers. The use of GSR in TBI suppresses apoptosis and inflammation in the brain is reduced, due to a decrease in the level of inflammatory cytokines. HTS plays a key role in inhibiting the expression of AQP4, IL-1b, and TNF-a and prevents neuronal damage after head injury [23]. The function of microglia protects the nerve parenchyma, removing cellular debris not only under normal conditions, but also in pathological conditions; in addition to the purification function, activated microglia has a strong inflammatory response [26]. Notch signaling is activated after TBI and is involved in the release of neuroinflammatory mediators from activated microglia [22,24,25]. HTS suppresses inflammatory mediators after head injury through Notch signaling (Notch is a family of transmembrane proteins. The notch signaling pathway is an evolutionarily conserved intracellular signaling pathway and regulates interactions between neighboring cells), which act synergistically with the NF-kB pathway in activated microglia [2]. In the central nervous system (CNS) neutrophils are rarely found in the brain parenchyma due to the existence of the BBB [28,29]. In TBI, the number of neutrophils in the brain tissue increases [28,30]. HTS also acts as an anti-inflammatory agent, decreasing leukocyte adhesion [31]. It was shown that HTS has an effect on the interaction of leukocytes and endothelium in the injured brain of rabbits by reducing the adhesion of leukocytes in the microcirculation of the brain. [32].

CONCLUSIONS

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1. Hyperosmolar solutions (15% Mannitol and 3.5%, 7%, 10% NaCl solution) cause a decrease in intracranial pressure within 55-40% in patients with head injury.
2. The decrease in ICP within 30 and 120 minutes after the administration of hyperosmolar solutions is more pronounced with iv introduction of 3.5%, 7%, 10% NaCl solution relative to 15% Mannitol in calculated dosages.
3. The use of infusion of 15% Mannitolum solution and 3.5%, 7%, 10% sodium chloride solution is an effective method for the correction of intracranial hypertension in patients with head injury.
4. NaCl reduces the inflammation of neurons and has a positive effect on the integrity of the BBB in TBI.
5. Traumatic brain injury is a very complex and heterogeneous condition with a complex pathophysiological mechanism and with the correct use of treatment, it significantly improves functional results.
6. The use of 3.5%, 7%, 10% NaCl leads to a more prolonged significant increase in the CPP and a prolonged decrease in ICP relative to a 15% mannitol solution.

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