Research Article

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Neuroprotective Effects of Inhaled Xenon for Sedation Compared With Propofol Intravenous Sedation in Severe Ischemic Stroke

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ABSTRACTS Ischemic stroke occupies a leading position among the causes of mortality and disability. Long-lasting motor and cognitive impairments, a decrease in the level of consciousness over time aggravate the course of the disease, leading to immobilization syndrome and comorbidity load, which contributes to the development of life-threatening conditions in this category of patients. In this regard, the search for new neuroprotective strategies used at an early stage and capable of minimizing the severe consequences of stroke for the patient in particular and society as a whole seems extremely relevant. The paper presents the effect of inhaled xenon for sedation in patients with severe ischemic stroke on the level of consciousness and severity of neurological disorders, and also shows its effect on S100B protein, a marker for blood brain barrier damage.

AIM OF STUDY To evaluate the effect of inhaled xenon for sedation in comparison with propofol intravenous sedation on the dynamics of the level of consciousness, the severity of neurological dysfunction and changes in the concentration of astroglial-derived S100B protein in severe ischemic stroke.

MATERIAL AND METHODS The research was conducted on two groups of patients comparable in age, gender, comorbid background, as well as the severity of the underlying disease. In both groups, the condition of patients required the start of mechanical ventilation immediately after admission to the intensive care unit. Group I (control, n=12). After intubation and the start of ventilation, patients were sedated with propofol at a dose of 1-2 mg/ kg / hour for 24–72 hours. Group II (xenon, n=12). After intubation and the start of ventilation, patients underwent xenon inhalation at a concentration of 40 vol. % for the first 6 hours. If it was necessary to continue sedation after the end of xenon inhalation, propofol was used in doses similar to Group I. Neurological status was assessed on days 1, 3 and 8 using the Glasgow Coma Scale (GCS), the Full Outline of UnResponsivness (FOUR) score and the National Institutes of Health Stroke Scale (NIHSS). The critical analysis of the value of S100B as a marker of brain damage was carried out before the start of sedation, on the 3rd and 8th days.

RESULTS Xenon inhalation (40 vol. %) in comparison with propofol intravenous sedation significantly increases the level of consciousness in patients with severe ischemic stroke (p=0,026), reduces neurological disorders assessed using NIHSS (p=0,007) on day 7, and also reduces serum S100B levels on day 3 (p<0,05) after ischemic stroke.

CONCLUSION Our open randomized clinical trial of xenon inhalation versus propofol intravenous sedation revealed the neuroprotective properties of xenon anesthesia in patients with severe ischemic stroke.

Based on the obtained clinical and laboratory data, it can be concluded about the effective implementation of the neuroprotective effects of xenon in the administration scheme used in the research.

Keywords: xenon, neuroprotection, ischemic stroke, consciousness, neurological disorders, S100b protein

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IV - intravenously
MV - mechanical ventilation
IS - ischemic stroke
ABS - acid-base status
ABB - acid-base balance
ACVA - acute cerebrovascular accident
ICU - intensive care unit
ECG – electrocardiography

INTRODUCTION

In the structure of all strokes, ischemic stroke occupies 80% [1], and in general, all cerebrovascular diseases are the second cause of death in the world [2]. According to sociologists' forecasts, with progressing human population ageing, the incidence of stroke will continue to grow, and mortality from stroke may exceed 12% by 2030 [3]. In the Russian Federation, the annual death rate from stroke is 374 cases per 100,000 population [4], and the disability rate among stroke survivors reaches 50% [5]. In this regard, the search for new effective neuroprotective strategies for the treatment of ischemic stroke (IS) seems to be an urgent task.

Most drugs with neuroprotective properties that had passed preclinical trials did not show sufficient efficacy in clinical trials [6, 7]. With the development of IS, a whole cascade of pathological processes is triggered, the main links of which are: oxidative distress, neuronal and glial apoptosis, as well as neuroinflammation, which determine the clinical outcome and recovery after a stroke [8, 9].

It appears that a therapeutic approach that aims at a single event in the ischemic cascade may be ineffective despite successful inhibition of a specific target. Therefore, it is especially important to search for drugs with pleiotropic mechanisms of action on all the links in the chain of the ischemic cascade to ensure neuroprotection. These conditions are met by inhaled xenon whose neuroprotective properties have been convincingly demonstrated both in experimental [10–12] and clinical trials [13, 14]. It is important to note that recent experimental studies have shown new molecular mechanisms of xenon's protective properties that level apoptosis, neuroinflammation, and enhance antioxidant protection [15–17]. All of the above made it possible to initiate a pilot randomized controlled trial, the purpose of which was: a) to study the effect of inhaled xenon anaesthesia versus intravenous propofol sedation on the dynamics of the level of consciousness; b) the severity of neurological dysfunction and the dynamics of the level of the astroglial protein S100B in severe IS.

MATERIAL AND METHODS

After the approval of the Local Ethical Committee (LEC) of the Federal Research and Clinical Center of Intensive Care Medicine and Rehabilitology (protocol No. 4/21/2, dated 04.10.2021), a prospective open randomized clinical pilot trial of the effect of inhaled xenon for sedation in comparison with propofol intravenous sedation on the level of consciousness recovery, the severity of neurological dysfunctions and dynamics of the astroglial protein S100B in patients after severe IS requiring mechanical ventilation (MV).

Group I (control, n=12): 7 men and 5 women; intravenous sedation based on propofol (1–2 mg/kg/hour for 24–72 hours). The beginning of sedation was due to the severity of the condition, the need for airway prosthesis against the background of depression of consciousness as a result of a stroke. The mean age was 45.8±10.1 years.

Group II (main, n=12): 6 men and 6 women; xenon inhalation (40 vol.%) for 6 hours. Criteria for sedation and mechanical ventilation were comparable to Group I. The mean age was 45.0±10, 2 years.

The scheme for patient enrollment in the research is shown in Fig. 1.

Inclusion Criteria:

- men and women aged 18 to 75;
- acute phase of cerebral infarction;
- severe neurological disorders (the Glasgow Coma Scale - GCS<12 points, the National Institutes of Health Stroke Scale - NIHSS>15 points, the Full Outline of UnResponsiveness - FOUR Score <13 points);
- need for MV;
- no cerebral infarction in the previous 6 months;
- absence of infectious diseases for the last month.

Exclusion Criteria:

- myocardial infarction or stroke in the previous 6 months;
- victims transferred from other hospitals more than 24 hours after confirmation of cerebral infarction diagnosis;
- morbid obesity with a body mass index of more than 45 kg/m2;
- need for inotropic and vasopressor support assessed on the Vasoactive Inotropic Score - VIS>10 points;
- severe renal failure requiring renal replacement therapy;
- malignant tumors of the central nervous system;
- atonic coma;
- burdened allergic anamnesis.

After inclusion in the study, patients were divided into groups using the sealed envelope method to exclude the influence of investigator preferences on the choice of therapy. Patients from the comparison group underwent intravenous sedation using propofol against the background of ongoing mechanical ventilation. Patients from the main group underwent inhalation anesthesia with xenon (40% vol.) for 6 hours.

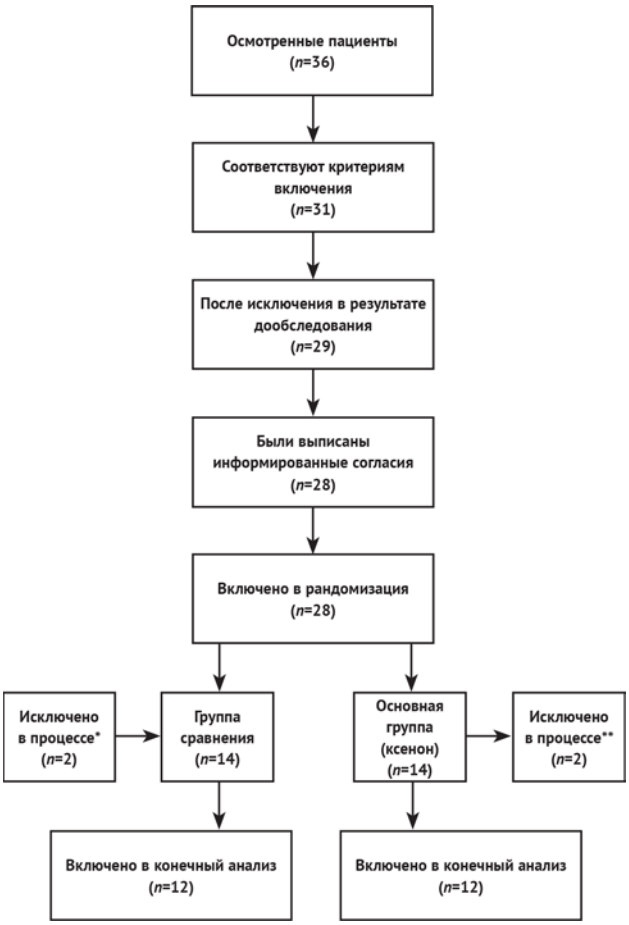


Fig. 1. Scheme of patient enrollment in the research
Notes: * - patients excluded from the comparison group - one developed a recurrent stroke, the other was diagnosed with COVID-19; ** — patients excluded from the study group. One developed massive pulmonary embolism, the other developed duodenal ulcer bleeding

The method of intravenous sedation of patients from the comparison group:

1. Beginning of sedation: within the first 6 hours from the moment of admission to the intensive care unit (ICU) or confirmation of the acute cerebrovascular accident diagnosis;

2. Anaesthetic induction - intravenous (IV) administration of the following drugs: propofol 1.5-2 mg/kg of body weight, rocuronium 0.6 mg/kg, tramadol 100 mg.

3. MV - by a Drager device in the BIPAP mode.

4. Intravenous sedation with propofol (2–3 mg/kg/h) via a perfusor.

5. Bedside monitor, assessment of heart rate, blood pressure, respiratory rate, saturation, capnometry and capnography.

6. Acid-base status (ABS) of arterial blood.

7. Electrocardiography (ECG) and chest X-ray.

The method of inhaled xenon sedation in patients in the xenon study group:

1. Beginning of remedial anesthesia with xenon - within the first 6 hours from the moment of admission to the ICU or confirmation of the diagnosis of stroke.

2. Anaesthetic induction - intravenous administration of the following drugs: propofol 1.5–2 mg/kg of body weight, rocuronium - 0.6 mg/kg, tramadol - 100 mg.

3. MV - by a Drager device in the BIPAP mode.

4. Inhalation sedation with XeMed xenon (International Nonproprietary Names – INN - Xenon) - for 6 hours at a concentration of 40 vol.% using XeMed xenon therapeutic circuit KNP-01 (Fig. 2).

Fig. 2. Xenon therapeutic circuit KNP-01 (XeMed®) designed to supply a respiratory mixture using oxygen, xenon or a combination of these gases

5. If necessary, during the first day, after xenon inhalation, sedation with propofol (at a dose of 2–3 mg/kg per hour) was performed for 6 hours.

6. Bedside monitor, assessment of heart rate, blood pressure, respiratory rate, saturation, capnometry and capnography.

7. ABS of arterial blood.

8. ECG, chest X-ray.

Assessment of neurological status of the patients from the main and comparison groups was performed on admission on the 1st, 3rd and 8th days from the start of therapy. For this, the GCS [18], the FOUR score [19], and the NIHSS [20] were used.

To assess the damage to the nervous tissue of the brain, the level of the S100β protein was evaluated before the start of sedation, as well as on the 3rd and 8th days.

Preparation for biochemical analysis was carried out according to the following scheme:

— venous blood was taken to perform general and biochemical analyzes; to monitor the state of the hemostasis system, coagulograms were taken; and the acid-base balance (ABB) was monitored. Puncture of the radial artery to assess ABB was performed; blood samples (two K2-EDTA tubes) were centrifuged for 30 min. Plasma was dispensed into five 1 ml Eppendorf tubes, followed by freezing;

— venous blood was taken from the internal jugular vein after 72 hours and on the 8th day. Blood samples (two K2-EDTA tubes) were centrifuged for 30 min. Plasma was poured into five 1 ml Eppendorf tubes, followed by freezing.

The content of S100b protein in blood serum was determined by immunoenzyme technique using CanAg kits (Sweden).

Statistical analysis was performed using the Statistica 10 software package (StatSoft, Inc., USA). Descriptive statistics of quantitative traits are presented as medians and quartiles in Me format (LQ; UQ). The study groups were compared using the Mann–Whitney U test and the Wilcoxon signed-rank test. Differences were considered statistically significant at $p<0.05$.

RESULTS

EVALUATION OF THE LEVEL OF CONSCIOUSNESS DYNAMICS USING THE GLASGOW COMA SCALE (GCS).

The final evaluation included 12 patients receiving propofol sedation (Table 1) and 12 patients receiving xenon sedation (Table 2). The data are presented by median and interquartile range. Intergroup comparison of the initial level of consciousness, as well as on the 1st, 3rd and 8th days are presented in Table. 3.

Table 1

GCS level of consciousness in the Propofol Group

Patient code, age (years)	Diagnosis	Level of Consciousness (GCS)			
		Before sedation	1st day	3rd day	8th day
# 1, 29	ACVA [1]	9	10	11	8
# 2, 33	ACVA [3]	9	11	9	8
# 3, 38	ACVA [1, 4, 5]	12	11	10	8
# 4, 40	ACVA [1, 3]	11	12	10	8
# 5, 49	ACVA [2, 4, 5]	10	10	8	6
# 6, 41	ACVA [2, 4]	10	12	8	7
# 7, 44	ACVA [1, 2]	9	11	12	7
# 8, 47	ACVA [2]	12	11	12	8
# 9, 56	ACVA [2, 5]	11	12	9	7
# 10, 53	ACVA [2, 3]	9	10	11	6
# 11, 59	ACVA [2, 3, 6]	10	10	11	6
# 12, 60	ACVA [2, 4, 5]	9	12	12	8
Me [*Q*1; *Q*3]		10 [9; 12]	11 [10; 12]	10 [8; 12]	7 [6; 8]*

Notes: * — when compared with the baseline, the consciousness of patients on the 8th day was significantly lower (p=0.037). The comorbid background is represented by the following pathologies: 1 — type 1 or 2 diabetes mellitus; 2 — hypertension in the stage of subcompensation or decompensation; 3 — obesity; 4 — thyroid disorders; 5 — obliterative bronchiolitis, bronchial asthma; 6 — chronic kidney disease. ACVA — acute cerebrovascular accident; GCS — Glasgow Coma Scale

Table 2

GCS level of consciousness in the Xenon Group

Patient code, age (years)	Diagnosis	Level of Consciousness (GCS)			
		Before sedation	1st day	3rd day	8th day
# 1, 29	ACVA [3]	10	11	13	15
# 2, 31	ACVA [3]	11	11	14	15
# 3, 37	ACVA [2, 4]	11	11	11	11
# 4, 40	ACVA [2, 5]	10	11	12	14
# 5, 45	ACVA [2, 3]	11	12	13	13
# 6, 41	ACVA [4]	11	14	14	14
# 7, 48	ACVA [2, 3]	10	12	12	14
# 8, 43	ACVA [4]	11	13	13	14
# 9, 59	ACVA [2, 6]	11	14	14	15
# 10, 55	ACVA [2, 3, 6]	10	12	13	15
# 11, 52	ACVA [1, 2, 3]	10	13	14	13
# 12, 60	ACVA [2, 3, 5]	10	12	13	14
Me [*Q*1; *Q*3]		10 [10; 11]	11 [11; 14]	13 [10; 14]	13* [11; 15]

Notes: * — when compared with the baseline, the consciousness of patients on the 8th day was significantly better (p=0.023) in the Xenon Group. The comorbid background is represented by the following pathologies: 1 — type 1 or 2 diabetes mellitus; 2 — hypertension in the stage of subcompensation or decompensation; 3 — obesity; 4 — thyroid disorders; 5 — obliterative bronchiolitis, bronchial asthma; 6 — chronic kidney disease. ACVA — acute cerebrovascular accident; GCS — Glasgow Coma Scale

Table 3

Dynamics of the level of consciousness in the comparison groups Me [Q1; Q3]

Group	Before the procedure	1st day	2nd day	3rd day	8th day
Xenon	10 (10; 11)	11,5 (11; 14)	13 (11; 14)	13,5 (10; 14)	13 (11; 15)
Propofol	10,5 (9; 12)	11,5 (10; 12)	11 (9; 12)	10,5 (8; 12)	7 (6; 8)
p-value (Mann–Whitney U test)	0,721	0,382	0,065	0,050	0,026*

Notes: * — differences are statistically significant. Data are presented as median and quartiles

EVALUATION OF THE LEVEL OF CONSCIOUSNESS DYNAMICS USING A GLASGOW COMA SCALE MODIFICATION FOR NEUROLOGICAL PATIENTS - THE FULL OUTLINE OF UNRESPONSIVNESS (FOUR) SCORE

The final evaluation included 12 patients who received propofol sedation (Table 4) and 12 patients who received xenon sedation (Table 5). The data are presented by median and interquartile range. Intergroup comparison of the initial level of consciousness, as well as the level of consciousness of patients on the 1st, 3rd and 8th days are presented in Table 6.

Table 4

The level of consciousness assessed by the FOUR Score in the Propofol Group with the diagnosis of "Acute cerebrovascular accident"

Patient code, age (years)	Level of consciousness (FOUR Score)			
	Before sedation	1st day	3rd day	After sedation
# 1, 29	9	10	11	8
# 2, 33	9	11	9	8
# 3, 38	14	11	10	8
# 4, 40	11	13	10	8
# 5, 49	10	10	12	6
# 6, 41	10	12	11	7
# 7, 44	9	11	15	7
м 8, 47	12	11	12	8
# 9, 56	11	12	9	7
# 10, 53	14	13	14	6
# 11, 59	10	10	11	6
# 12, 60	9	12	12	8
Me [*Q*1; *Q*3]	13 [10; 14]	13 [11; 13]	12 [9; 15]	8 [7; 8]*

Note: * — in case of intragroup comparison of changes in the level of consciousness on the 8th day, the level was significantly lower relative to the baseline (p=0.035)

Table 5

The level of consciousness assessed by the FOUR Score in the Xenon Group with the diagnosis of "Acute cerebrovascular accident"

Patient code, age (years)	Level of consciousness (FOUR Score)			
	Before sedation	1st day	3rd day	8th day
# 1, 29	10	11	12	14
# 2, 31	10	11	12	14
# 3, 37	13	11	14	15
# 4, 40	11	13	14	14
# 5, 45	11	14	12	13
# 6, 41	11	13	15	15
# 7, 48	10	11	14	15
# 8, 43	12	11	12	14
# 9, 59	11	12	12	13
# 10, 55	13	15	15	15
# 11, 52	10	11	12	13
# 12, 60	11	12	13	14
Me [*Q*1; *Q*3]	12 [10; 13]	13 [11; 15]	15 [12; 15]	14 [13; 15]*

Note: * — in case of intragroup comparison of changes in the level of consciousness on the 8th day, the level was significantly higher relative to the baseline (p=0.037) in the Xenon Group

Table 6

Dynamics of the level of consciousness in the comparison groups Me [Q1; Q3]

Group	Before the procedure	1st day	2nd day	3rd day	8th day
Xenon	12 (10; 13)	13 (11; 15)	14 (12; 15)	15 (12; 15)	14 (13; 15)
Propofol	13 (10; 14)	13 (11; 13)	12 (10; 13)	13 (9; 15)	8 (7; 8)
p-value	0,382	0,505	0,038*	0,195	0,026*

Note: * — differences are statistically significant

ASSESSMENT OF NEUROLOGIC DEFICIT USING THE NATIONAL INSTITUTES OF HEALTH STROKE SCALE (NIHSS)

The final evaluation included 12 patients receiving propofol sedation (Table 7) and 12 patients receiving xenon sedation (Table 8). The data are presented by median and interquartile range. Intergroup comparison of the initial level of consciousness, as well as on the 1st, 3rd and 8th days are presented in Table 9.

Table 7

Neurologic deficit assessed by the NIHSS in the Propofol Group with the diagnosis of "Acute cerebrovascular accident"

Patient code, age (years)	Level of Neurological Disorders (NIHSS)			
	Before sedation	1st day	3rd day	8th day
# 1, 29	23	24	25	34
# 2, 33	28	30	31	31
# 3, 38	30	31	32	32
# 4, 40	33	30	30	31
# 5, 49	31	27	22	33
# 6, 41	25	22	23	32
# 7, 44	24	23	25	32
# 8, 47	30	28	25	33
# 9, 56	31	32	30	32
# 10, 53	32	34	31	34
# 11, 59	29	31	30	31
# 12, 60	31	28	29	22
Me [*Q*1; *Q*3]	29 [22; 34]	32 [22; 34]	29 [22; 34]	32 [30; 34]*

Note: * — the level of neurologic deficit on the 8th day was significantly lower than the baseline (p=0.027)

Table 8

Neurologic deficit assessed by the NIHSS in the Xenon Group with the diagnosis of "Acute cerebrovascular accident"

Patient code, age (years)	Level of Neurological Disorders (NIHSS)			
	Before sedation	1st day	3rd day	After sedation
# 1, 29	28	26	25	18
# 2, 31	28	30	27	22
# 3, 37	30	31	32	17
# 4, 40	33	30	30	19
# 5, 45	31	26	16	12
# 6, 41	29	23	21	29
# 7, 48	24	23	25	23
# 8, 43	30	27	25	19
# 9, 59	31	34	25	21
# 10, 55	32	30	31	27
# 11, 52	29	29	28	25
# 12, 60	31	28	19	14
Me [*Q*1; *Q*3]	32 [28; 34]	30 [26; 34]	27 [16; 32]	24 [12; 27]

Note: * — when compared with the baseline, the neurologic deficit in patients on the 8th day after the stroke was significantly lower (p=0.043)

Table 9

Neurologic deficit in the comparison groups Me [Q1; Q3]

Group	Before the procedure	1st day	2nd day	3rd day	8th day
Xenon	34 (34; 34)	30 (26; 34)	27 (16; 33)	21,5 (12; 26)	24 (12; 27)
Propofol	29 (22; 34)	32 (22; 34)	29 (22; 34)	29 (22; 34)	34 (34; 34)
p-value	0,028*	0,721	0,442	0,195	0,007*

Note: * — differences are statistically significant

Despite the fact that the patients in the Propofol Group had better pre-procedure neurological status (29 (22; 34) vs 34 (34; 34), p=0.028) compared to the Xenon Group, neurologic deficit increased on day 8 in the Propofol Group, NIHSS values were significantly higher in the Propofol Group (34 (34; 34) vs 24 (12; 27), p=0.007).

ASSESSMENT OF SERUM S100 PROTEIN - A RELIABLE PREDICTOR OF BRAIN INJURY

The final evaluation included 12 patients who were sedated with propofol and xenon. The S100b protein level was assessed before the start of sedation, as well as on the 3rd and 8th days of sedation. In the comparison group, the initial level was 0.196 [0.158; 0.213] ng/mL. On the 3rd day, the average level was 0.243 [0.199; 0.268] ng/mL, and on the 8th day 0.396 [0.368; 0.418] ng/mL. There was a significant increase in the concentration of this marker on the 8th day in relation to the initial level (Fig. 3). In the Xenon Group, the initial level was 0.188 [0.172; 0.201] ng/mL. On the 3rd day, the average level was 0.126 [0.103; 0.149] ng/mL, and on the 8th day — 0.098 [0.075; 0.116] ng/mL. There was a significant decrease in the concentration of this marker on the 8th day both in relation to the initial level ($p<0.05$) and to the level on the 8th day in the Comparison Group (Fig. 4). The data of intergroup comparison are presented in Fig.5.

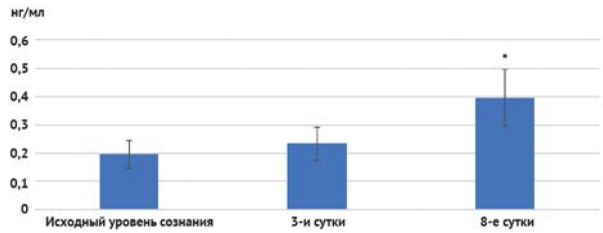


Fig. 3. Dynamics of astroglial-derived S100B protein (a "biomarker" of cerebral damage) concentration in the Propofol Group

Note: * — significant increase in S100B on the 8th day (p=0.028)

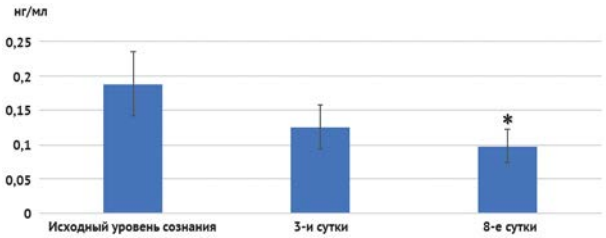
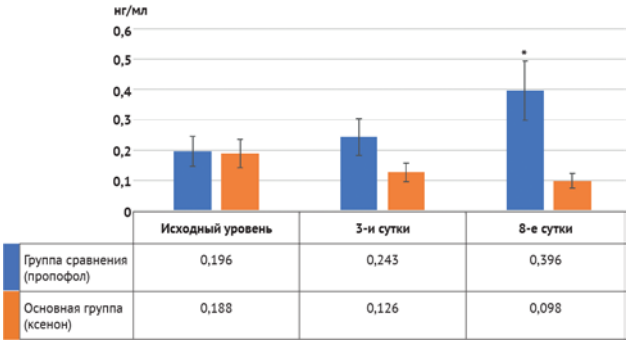


Fig. 4. Dynamics of S100B protein (a "biomarker" of cerebral damage) concentration in the comparison group

Note: * — on the 8th day, the indicators were significantly lower than the initial values (p=0.037)



	Исходный уровень	3-и сутки	8-е сутки
Группа сравнения (пропофол)	0,196	0,243	0,396
Основная группа (ксенон)	0,188	0,126	0,098

Fig. 5. Comparison of S100B concentration between the main and control groups

Note: * — on the 8th day, the marker concentration in the Xenon Group was significantly lower compared to the protein level on the 8th day in the Propofol Group (p=0.018)

DISCUSSION

The search and study of drugs with proven neuroprotective effects is a priority due to both the growing incidence of cerebrovascular diseases and the lack of an effective strategy. Previously, we obtained experimental data convincingly demonstrating the neuroprotective effects of lithium chloride in vivo in an ischemic stroke model [21].

However, at the moment, the drug is presented only in a tablet form, which does not allow realizing its potential in patients with a stroke, where effective therapy is needed already during the first hours. Xenon inhalation can be started immediately after a person enters the intensive care unit, and given the extremely narrow list of contraindications, and intactness in relation to homeostasis systems (the inert gas does not interact and is excreted unchanged), its use in the acute period has a high degree of safety.

In the present research, we decided to use three main scales to determine a) the level of consciousness and b) neurologic deficit, since these indicators are already extremely important predictors in themselves.

If in the case of experimental studies, methods for evaluating the effects of drugs are represented by a very wide range, then, when determining ad aegri lectum effectiveness against the background of an oppressed consciousness, the diagnostic possibilities are quite limited. This was the reason for the choice of three scales at once - two for assessing the level of consciousness and one for evaluating neurologic deficit. The first and most common was the GCS. It was developed in 1974 to objectively assess and predict outcome in patients with brain injury, and then was widely used to evaluate the level of consciousness of patients in the intensive care unit with other causes of impaired consciousness than those considered in this study [22]. Despite its widespread use, GCS has limitations in the form of the impossibility of assessing verbal linguistic output in people with aphasia or in intubated patients [23].

The difficulty of obtaining a verbal response from intubated patients and patients with aphasia, the lack of assessment of stem functions prompted the creation of a new tool - the FOUR score. This allowed for an improvement in the standardized assessment of the level of consciousness for patients who are intubated or have focal neurologic deficits [19]. Like the GCS, the FOUR score uses the patient's eye reactions and motor response, the verbal component was removed, and the assessments of stem reflexes and respiratory pattern were added. A decrease in the number of points in both scales is associated with deterioration in the level of consciousness [24].

To assess the severity of neurological symptoms in the acute period of stroke, the widely used and well-established NIHSS (National Institutes of Health Stroke Scale), published in 1989, was used [25]. The predictive value of this scale has been shown in many studies [25–29]. This scale is distinguished by the speed of assessment and ease of use.

In addition to clinical diagnostics, the dynamics of the main marker of neuronal damage in the acute period, the S100b protein, was also analyzed, which made it possible to monitor the effectiveness of patient therapy. The astroglial protein S100b has a significant relationship with clinical neurologic deficit, infarct volume, functional disability after ischemic stroke and plays the role of a prognostic marker [30–33], indicating the risk of hemorrhagic transformation after thrombolytic therapy [34]. The level of this protein helps to monitor the disease in a wide range of diseases accompanied by damage to the nervous tissue [35], and shows the level of the

inflammatory response in stroke [36]. An increase in the concentration of S100b after acute IS is recorded starting from 8 hours, and reaches maximum values on days 2–3 [37].

The totality of methods available for ordinary practice of assessing the severity of the condition of this category of patients, as well as the relative ease of using xenon, allows us to hope for a successful implementation of the method into everyday practice. Among other things, one should not forget that the most widely used drug for prolonged sedation, propofol, in case of long-term administration can significantly worsen the prognosis of patients even without brain damage, which potentially makes its use after a stroke undesirable [38].

CONCLUSION

The study showed that the use of xenon as a sedative for patients with severe ischemic stroke, as compared to patients who underwent propofol-based intravenous sedation, significantly raises the level of consciousness and contributes to the regression of neurological disorders, as well as substantially reduces the level of S100b protein.

FINDINGS

1. Xenon inhalation for patients with ischemic stroke can significantly improve the level of consciousness.

a. When comparing the dynamics of the level of consciousness using the Glasgow Coma Scale in patients from Xenon and Propofol groups, we noted a tendency of its improvement in the Xenon group: on the 2nd day — 13 [11; 14] vs 11 [9; 12] (p=0.065); on the 3rd day 13.5 [10; 14] vs 10.5 [8; 12] (p=0.05); and on the 8th day the level of consciousness reaches the level of statistical significance 13 [11; 15] vs 7 [6; 8] (p=0.026), respectively.

b. When comparing the dynamics of the level of consciousness using the FOUR score in patients from Xenon and Propofol groups, we noted a tendency of its improvement in the Xenon group: on the 2nd day — 14 [12; 15] vs 12 [10; 13] (p=0.038); and on the 8th day 14 [13; 15] vs 8 [7; 8] (p=0.026), respectively.

2. Inhaled xenon for sedation of patients with severe ischemic stroke, in comparison with intravenous sedation with propofol, showed a significant improvement in neurological outcome according to the NIHSS: on the eighth day the neurologic deficit increased in the Propofol group, NIHSS values were significantly higher in the Propofol group 34 [34; 34] vs 24 [12; 27] (p=0.007).

3. When assessing the level of protein S100b, a marker of neuronal damage, xenon contributed to a decrease in its level in the patients with both baseline values of the main group (from 0.188 [0.172; 0.201] ng/mL to 0.098 [0.075; 0.116] ng/mL on day 8, p<0.05), and 4 -fold decrease in comparison with the final values of the patients from the comparison group, which amounted to 0.396 ng/mL.

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