Impact of baseline free serum triiodothyronine on stroke severity and outcome in patients with atherothrombotic ischemic stroke

Abstract. Background. According to recent studies, thyroid hormones may have various effects on stroke severity, course and outcome, but underlying mechanisms of this association are still unclear. The purpose was to determine the relationship of thyroid hormones during stroke onset with stroke severity and outcome in a clinical study. Materials and methods. In this study, 168 adult patients with acute ischemic stroke were enrolled. Concentrations of free triiodothyronine (fT3), free thyroxine (fT4), thyroid-stimulating hormone and basic stroke risk factors were assessed during 24 h from symptoms onset. Neurological deficit was evaluated by Scandinavian Stroke Scale (SSS). Disabling deficit was defined as Modified Rankin Scale score ≥3 points six months after stroke. Results. ANOVA showed that SSS scores were significantly higher in patients with fT3 level in quartile IV (≥5.35 pmol/l) compared to quartiles II–III (SSS median 48 vs. 37, p = 0.0481) and especially to quartile I (≤3.4050 pmol/l, SSS median 48 vs. 30, p = 0.0018). In patients without prior stroke (n = 124), fT3 independently affected baseline SSS score (corrected R² = 0.49, p < 0.0001). The analysis showed that in patients with atherothrombotic stroke subtype (n = 108), fT3 level was an independent risk factor for unfavourable stroke outcome (odds ratio = 0.3498, 95% confidence interval 0.1235–0.9904). According to ROC-analysis, fT3 level < 4.44 pmol/l was a predictor of disabling deficit (AUC = 0.727, specificity — 96.4 %, sensitivity — 66.8 %, p = 0.003). Conclusions. The study showed that a low serum free triiodothyronine level during stroke onset negatively affects the stroke severity in first stroke patients and may be a predictor of its unfavourable outcome. In patients with atherothrombotic stroke, lower baseline fT3 levels were independently associated with poor outcome after 6 months. Beneficial effects of additional fT3 supplement during stroke should be assessed in future studies.

Keywords: ischemic stroke; outcome; thyroid hormones; triiodothyronine

Introduction

According to statistics over the past decade, mortality from cardiovascular diseases invariably ranks first in the world, although in certain countries of Europe and in the United States there is some stabilization of growth dynamics [1]. During recent years, governments of many countries have significantly strengthened preventive measures aimed at reducing the frequency of risk factors for cerebrovascular pathologies. Although the growth in the number of strokes slowed down, this pathology still remains one of the most common causes of death in Europe, North America and Asia.

The results of several controlled randomized trials of treatment in hyperacute stroke phase were published in recent years. All studies have confirmed the obvious advantage of an integrated approach in the treatment of acute ischemic stroke caused by thrombotic occlusion of the intracranial arteries of the carotid system. This approach consists of using a combination of systemic thrombolysis and endovascular thrombectomy in the first few hours after the onset of the first symptoms of acute stroke [2, 3]. However, reperfusion therapy is possible only within a relatively narrow therapeutic window [4]. In cases where thrombolysis or thrombec-
ney hormone (TSH) were determined using enzyme-linked
immunosorbent assay (ChemWell EIA analyzer with DRG
International kits). Blood sampling was performed during 24
hours from stroke onset. Neurological deficit was assessed
using Scandinavian Stroke Scale (SSS). Poor stroke outcome
was assumed as 3 or more points on the modified Rankin
Scale (mRs) 6 months after stroke onset. Thyroid hormones
and TSH levels below 25th and above 75th percentile were
considered low and high, respectively.

Statistical analysis was performed using MedCalc v14
software. Continuous data with non-normal distribution
are presented as median and 95% confidence interval
(CI). Analysis of variation (ANOVA) was used to evalu-
ate the degree of neurological deficit, and patients were
divided to subgroups according to T3 levels: hypothy-
roid (T3 below 25th percentile), euthyroid (T3 in 25–75th
percentile), hyperthyroid (T3 above 75th percentile).
For determining the impact of thyroid hormones on
stroke outcome using logistic regression, patients were
divided into subgroups with good (mRs 0–2) and poor
outcome (mRs 3–6).

Results
Strokes in the carotid territory were the most frequent
(79%), with the atherothrombotic subtype being the most
common (64%). The leading basic risk factors were arte-
rial hypertension (65%), smoking (42%), ischemic heart
disease (29%), atrial fibrillation (27%). Forty-nine patients
(28%) had history of transient ischemic attack (TIA) or
stroke. Nevertheless, the results of the published works are
different in their mechanism of action and effective in pre-
clinical studies, none of them has enough clinical efficacy.
In this regard, the search for new approaches to neuropro-
tection remains one of the most important tasks of modern
neuroparmacology [5].

The survival of the brain tissue under ischemia de-
ends on the intensity of metabolism, oxygen demand,
as well as the ability to maintain the redox potential and
support the synthesis of high-energy compounds (adeno-
sine triphosphate (ATP), etc.). The mechanism of action
of most neuroprotectors is based on the effects on these
processes [6, 7].

Over the past decades, special attention was paid to
the neuroprotective properties of endogenous molecules
such as vascular endothelial growth factor, erythropoi-
etin, brain-derived neurotrophic factor, etc. It is known
that triiodothyronine, an active form of the thyroid hor-
mone thyroxin, separates tissue respiration and oxidative
phosphorylation. This process leads to disruption of the
Krebs cycle, reduced ATP production, hyperthermia,
and has a potentially negative effect in acute cerebral
ischemia [8]. On the other hand, it is known that triodo-
thyronine has several neuroprotective effects: it contrib-
utes to the uptake of neurotoxic glutamate by astrocytes,
stimulation of the Na+/K+ membrane channels in neu-
rons, the restoration of intracellular pH [9]. Thus, selec-
tive therapeutic effect on thyroid metabolism (stimula-
tion or inhibition of the function of thyroid hormones)
may be promising potential target for new approaches to
the treatment of stroke.

In recent years, more publications appeared in the lit-
erature about the possible effect of thyroid hormones on
the risk of development, severity and outcome of acute ischemic
stroke. Nevertheless, the results of the published works are
rather contradictory [10]. Finally, the nature of the influence
of hyper- or hypothyroidism on the course and outcome of a
stroke is still unclear.

The purpose of this study was to determine the relation-
ship between markers of thyroid function and the severity of
neurological and functional deficit in acute ischemic stroke.

Materials and methods
This study was conducted at the single clinical and re-
search center — V.K. Gusak Institute of Urgent and Re-
parative Surgery. One hundred and sixty-eight patients (71
women, 97 men) aged 42 to 78 years with acute ischemic
heterogeneous stroke were enrolled in this study. Patients
with verified autoimmune thyroiditis or a malignancy were
excluded from the study. Within 24 hours from stroke onset,
basic risk stroke factors were analyzed. Serum free triiodo-
thyronine (fT3), free thyroxine (fT4) and thyroid-stimulat-
hormone (TSH) were determined using enzyme-linked

According to the laboratory reference indicators, 112 patients had thyroid hormones levels in the reference range, 36 individuals had laboratory hypothyroidism, and 20 — laboratory hyperthyroidism. Thyroid hormones levels are presented in Table 2.

Correlation analysis using the Spearman rank correlation revealed a positive statistically significant relationship between the level of free triiodothyronine and the severity of neurological deficit according to the SSS. A statistically significant relationship was also found between the level of free thyroxine and the presence of atrial fibrillation. Among other factors, an inverse correlation was observed between the level of C-reactive protein (CRP) and the severity of neurological deficit according to the SSS. A statistically significant relationship was also found between the level of free thyroxine and the presence of atrial fibrillation. Among other factors, an inverse correlation was observed between the level of C-reactive protein (CRP) and the severity of neurological deficit according to the SSS (R = –0.397, p = 0.0004). No other significant correlation was found between thyroid hormones, severity of neurological deficit, and the presence of basic risk factors for stroke. The results of the correlation analysis are presented in Table 3.

ANOVA showed that patients with fT3 level in quartile IV (≥ 5.35 pmol/l; 95% CI 5.01—5.61) had less severe stroke (higher SSS scores) compared to those with fT3 level in quartile II–III (SSS median is 48 vs 37 points, respectively; p = 0.0481), and especially compared to people whose T3 level was in quartile I (≤ 3.4050 pmol/l, SSS median is 48 vs 30 points; p = 0.0018). The results of the ANOVA are presented in Fig. 1.

The results of ANOVA suggest that low triiodothyronine levels are associated with a more severe neurological deficit, while high levels may have potential neuroprotective effects. There were no statistically significant variations of SSS score in subgroups of patients according to fT4 or TSH levels.

After 6 months, 120 patients were classified as those having stroke with poor outcome and 48 patients had stroke with favourable outcome. Comparative analysis showed that patients with poor outcome were older, had significantly lower fT3, higher CRP levels and lower free T3 to free T4 ratio.

To clarify the relationship between the severity of neurological deficit and the level of free triiodothyronine in serum, a regression analysis was performed. Univariate regression analysis showed that in patients with cardioembolic stroke, fT4 favourably influenced the severity of the stroke according to the SSS (R² = 0.75, p = 0.0005), but this association

| Table 2. Thyroid hormones levels |
|---------------------------------|
| Level                           | Free T3, pmol/l | Free T4, pmol/l | TSH, IU/l |
| Median (95% CI)                 | 4.57 (4.35–4.79) | 16.2 (15.62–16.60) | 1.28 (1.02–1.433) |
| 25th percentile (95% CI)        | 3.545 (3.019–4.22) | 14.65 (13.84–15.38) | 0.86 (0.64–1.01) |
| 75th percentile (95% CI)        | 5.35 (5.01–5.61) | 17.5 (17.0–17.98) | 2.1 (1.59–3.24) |

| Table 3. Correlation between thyroid function indicators, severity of neurological deficit, and stroke risk factors |
|---------------------------------------------------------------|
| Risk factors                  | Free T3 | Free T4 | TSH |
| Arterial hypertension        | NS      | NS      | NS  |
| Diabetes                     | NS      | NS      | NS  |
| Ischemic heart disease       | NS      | NS      | NS  |
| Atrial fibrillation          | NS      | R = 0.297 (p = 0.0071) | NS  |
| Previous stroke or history of TIA | NS      | NS      | NS  |
| Smoking                      | NS      | NS      | NS  |
| Aspirin use                  | NS      | NS      | NS  |
| Stroke severity (SSS score)  | R = 0.316 (p = 0.0043) | NS      | NS  |
| C-reactive protein           | NS      | NS      | NS  |
Table 4. Thyroid hormones, CRP levels and age of patients with different stroke outcomes

| Parameters                  | mRs 0–2 (n = 48) | mRs 3–6 (n = 120) | P-value |
|-----------------------------|------------------|-------------------|---------|
| Age, years                  | 68 (55–70.4)     | 76 (72–77)        | 0.0006  |
| Free T3, pmol/l             | 4.815 (4.57–5.5798) | 4.43 (4.036–4.65) | 0.0173  |
| Free T4, pmol/l             | 16.1 (14.61–17.22) | 16.5 (15.466–16.834) | NS     |
| TSH, IU/l                   | 1.305 (0.779–1.86) | 1.16 (0.99–1.43)  | NS      |
| C-reactive protein, mg/l    | 6.29 (5.26–8.04)  | 16.1 (8.565–24.696) | 0.0140  |
| Free T3 to free T4 ratio    | 0.366 (0.287–0.343) | 0.27 (0.2355–0.304) | 0.0374  |

Table 5. Independent predictors of stroke outcome in patients with atherothrombotic stroke subtype

| Variable        | Odds ratio | 95% CI         | P-value |
|-----------------|------------|----------------|---------|
| Free T3         | 0.3498     | 0.1235–0.9904  | 0.0479  |
| Free T4         | 0.5555     | 0.2951–1.0456  | 0.0685  |
| SSS score       | 0.7978     | 0.6608–0.9633  | 0.0188  | weakened after adjustment for other stroke risk factors (age, hypertension, carotid stenosis, glucose level, C-reactive protein, SSS score).

Univariate regression showed no relationship between the severity of neurological deficit and the level of triiodothyronine. However, after exclusion of patients with previous stroke, a regression dependence of the severity of neurological deficit on the level of free triiodothyronine was detected ($F = 15.7920$, $p = 0.0002$, corrected $R^2 = 0.44$).

There were no significant differences in thyroid hormones levels, CRP and SSS score in patients with the first stroke and people with history of stroke or TIA.

To confirm the independent effect of $fT3$ level on the severity of stroke and exclude the influence of co-factors, a multivariate regression analysis was performed. The regression model included basic risk stroke factors (age, arterial hypertension, blood pressure at admission, atrial fibrillation, ischemic heart disease, diabetes, smoking), C-reactive protein, free thyroxine, TSH levels, free T3 to free T4 ratio. Variables were introduced in the regression model using the forward method.

Multivariate regression analysis showed that the independent factors affecting the severity of neurological deficit in patients with no prior stroke were the levels of free triiodothyronine ($p = 0.0035$) and of C-reactive protein ($p = 0.0035$). Model had the coefficient of variation $F = 17.45$ ($p < 0.0001$) and corrected $R^2 = 0.49$. The obtained results confirmed the independent effect of serum free triiodothyronine level on the severity of neurological deficit in newly developed ischemic stroke, while the low levels of triiodothyronine were associated with more severe stroke.

To assess the impact of $fT3$ level on stroke outcome, the multiple logistic regression method was used. Basic stroke risk factors (age, hypertension, blood pressure at admission, atrial fibrillation, coronary artery disease, diabetes mellitus, smoking), C-reactive protein, free thyroxine, TSH levels, $fT3/fT4$ ratio were included in the regression model. Lower $fT3$ levels were independently associated with poor stroke outcome (odds ratio (OR) = 0.3408, 95% CI 0.15–0.77), but this association became insignificant after correction for baseline SSS score.

When multiple logistic regression included only patients with atherothrombotic stroke, the analysis showed that $fT3$ level was an independent risk factor for unfavourable stroke outcome even after correction for baseline SSS score (OR = 0.3498, 95% CI 0.1235–0.9904). Independent factors are demonstrated in Table 5.

In order to determine the critical values of free triiodothyronine associated with the greatest risk of poor stroke outcome, the analysis of receiver operating characteristic (ROC) curves was applied. It was found that $fT3$ level < 4.44 pmol/l is a predictor of poor stroke outcome (area under ROC-curve = 0.727, specificity — 96.4 %, sensitivity — 66.8 %, $p = 0.003$). The results of the analysis of ROC-curves are presented in Fig. 2.
Discussion

The results of this study indicate that low serum free triiodothyronine level during stroke onset is associated with a more severe neurological deficit in a patient with first ischemic stroke. The difference between this and equivalent studies is the identification of independent influence of free triiodothyronine on the stroke severity in multivariate regression analysis. There are several limitations in this study. The main disadvantages are lack of long-term follow-up and inability to use Cox regression method.

This study was underpowered to reveal the independent influence of low free triiodothyronine level on poor stroke outcome in all stroke subtypes. Nevertheless, obtained data showed that in patients with atherothrombotic stroke subtype, lower baseline fT3 levels were independently associated with poor outcome. This association may be attributed to endothelium dysfunction, hyperhomocysteinemia and possibly other mechanisms, which are observed in atherothrombotic stroke subtype.

Our results correlate with the fundamental research carried out in recent years. In experimental models, it has been shown that the administration of L-thyroxin after transient cerebral ischemia contributes to an increase in neuron density and stimulation of angiogenesis in the ischemic brain [11]. The results of another in vitro study revealed that triiodothyronine can restore intracellular concentration of sodium, calcium ions and pH [8]. It was shown that thyroxine stimulates the synthesis of other neurotrophic factors, such as fibroblast growth factor [12].

Several clinical studies also confirm experimental data. L.M. O’Keefe et al. in a study of 868 patients with heterogeneous ischemic stroke found that a low triiodothyronine level was associated with greater functional deficiency 3 months after a stroke and with higher nosocomial mortality [13]. Results of another study of 833 patients with acute ischemic stroke indicate that low levels of total triiodothyronine (even within the reference range) were associated with poor stroke outcome [14].

In the first hours after disturbance of cerebral blood flow in neurons in the affected area, ATP pool depletion, inhibition of protein synthesis, and an intracellular pH shift to the acidic side are observed. Excessive release of excitatory and inhibitory neurotransmitters, especially glutamate, leads to the development of the excitotoxicity. Activation of ionotropic and metabotropic glutamate receptors increases the cytosolic level of calcium ions. In turn, an excess of calcium ions disrupts the function of ion pumps and simultaneously activates many catabolic enzymes, resulting in depolarization and disintegration of the intracellular membranes. The destruction of mitochondrial membranes involves apoptosis by the release of proapoptotic proteins.

Some experimental studies demonstrated that after the addition of T3 in in vivo astrocyte culture, the number of glutamate transporters (glutamate transporter-1 and glutamate aspartate transporter) increased. Activation of glutamate uptake by astrocytes significantly reduced the gliotoxic effect of this neurotransmitter for neurons [23]. In another experiment, it was revealed that triiodothyronine reduced the activity of N-methyl-D-aspartate receptors in hippocampal neurons, which, according to the authors, prevented glutamate-induced cell death [24].

The key role of iodothyronines in the synthesis and stimulation of ion exchange pumps has been proved. So, T3 activates the expression of the sodium/hydrogen exchanger gene, which, in turn, is responsible for removing excess protons and normalizing intracellular pH. Under the action of T3, the number of Na/K-ATPases integrated into the membranes increases, the functioning of Ca2+-ATPases increases, which ultimately contributes to the normalization of the ion balance of neurons [25].

Normal work of ion pumps is not possible under conditions of ATP pool depletion in cells against ischemia. When studying the effect of T3 on astrocyte cultures, an increase in the expression of palmitate beta-oxidation enzymes in mitochondria: beta-hydroxyacyl-CoA dehydrogenase, beta-thiolase, and enoyl-CoA hydratase was recorded [26]. As a result, the amount of ATP in astrocytes increased. Since the protective role of these cells in stroke is considered to be proven, the authors of the study concluded that there was the normalization of energy exchange under the action of triiodothyronine in astrocytes that significantly reduced the lesion area in experimental models of transient cerebral ischemia and stroke.

A comparison of two experimental models of ischemic stroke, with transient and permanent occlusion, revealed another important feature of the neuroprotective effect of T3 — inhibition of protein aquaporin-4 synthesis in transient occlusion [27]. As a result of treatment of experimental animals with triiodothyronine preparations, a marked decrease in swelling and the area of brain damage was observed, the probability of a favourable outcome increased, but only in the model of transient ischemia.

Nevertheless, the biological basis of the association of hypothyroidism with the stroke course and outcome has not been finally studied. In this context, researches of new class of thyroid hormones — thyronamines (decarboxylated triiodothyronine derivatives) seems promising. These substances are a new class of endogenous signaling hormones that exhibit significant in vivo effects, such as:

1) decrease in the rate of basal metabolism, decrease in respiratory rate [15];
2) fast, deep and reversible hypothermia [16];
3) weight loss [17];
4) negative inotropic and chronotropic effects without changing the absorption of glucose and oxygen [18];
5) decrease in Ca2+ level in the endoplasmic reticulum [19];
6) ischemia resistance [20];
7) increase in high-energy compounds level in target cells [21].

Thyronamines have a wide range of potential neuroprotective effects, the most significant of which are induction of hypothermia and a decrease in the rate of basal metabolism. According to K.P. Doyle et al.,
intraperitoneal administration of thyronamines to laboratory mice contributes to a decrease in body temperature from 37 to 31 °C, and significantly reduces the infarction zone after transient cerebral ischemia. At the same time, the observed hypothermia is completely reversible, and is not accompanied by any side effects, and its development is not associated with the effects of the known mechanisms of thermoregulation [22].

It is noteworthy that thyronamines, being derivatives of L-thyroxin, have antagonistic properties in relation to it, and the metabolic effects of thyronamines are close to the effects observed in hypothyroidism. It is possible that this phenomenon is the basis for the neuroprotective effects of thyroid hormones.

To confirm the neuroprotective effects of thyronamines, analogue of T0AM (thyronamine) was synthesized by our colleagues from the L.M. Litvinenko Institute of Physical Organic Chemistry and Coal Chemistry (Donetsk, Donbass region) for research in animal experimental model. Preliminary results showed that injection of T0AM at a dose of 50 mg/kg to laboratory rats prevents a reduction in superoxide dismutase levels after brain ischemia and also leads to a significant reversible body temperature decrease of 2.5 °C. Currently, the study of the thyronamine neuroprotective properties in the experimental stroke model is ongoing at our Institute.

Even though in recent years more and more evidence has been obtained on the influence of thyroid hormones on risk, course and outcome of cerebrovascular disease, the nature and biological basis of this relationship have not been finally identified. This was the reason for initiation in our institute of a complex clinical and experimental trial on the study of the possibility of using thyroid hormones and their derivatives as neuroprotective therapy in acute ischemic stroke.

**Conclusions**

The study showed that a low serum free triiodothyronine level during stroke onset negatively affects the stroke severity in patients with the first stroke and may be a predictor of its unfavourable outcome. In patients with atherothrombotic stroke subtype, lower baseline T3 levels were independently associated with poor outcome. The findings suggest that thyroid metabolism is not only a factor affecting the course of ischemic stroke, but also a potential target for therapeutic correction. To confirm the effectiveness of this approach, it is necessary to conduct further clinical and experimental studies. It is reasonable to monitor thyroid hormones levels during stroke, while the analysis of serum free triiodothyronine can be used to predict a high risk of an unfavourable stroke outcome. Researches to determine possible beneficial effects of additional T3 supplement in ischemic stroke patients are ongoing at our Institute.

**Conflicts of interests.** Authors declare the absence of any conflicts of interests and their own financial interest that might be construed to influence the results or interpretation of their manuscript.

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Вплив початкового рівня вільного трийодтироніну в сироватці крові на тяжкість інсульту і його насладки в пацієнтів з атеротромботичним ішемічним інсультом

Резюме. Актуальність. Згідно з останніми дослідженнями, тиреоїдні гормони можуть мати потенційний вплив на ступінь тяжкості, перебіг та насладки інсульту, але основні механізми цього зв'язку досі не визначені. Мета дослідження: визначити вплив тиреоїдних гормонів на тяжкість неврологічного дефіциту при гостром ішемічному інсульту та ризик постінсультної інвалідизації. Матеріали та методи. До клінічного дослідження було включено 168 дорослих пацієнтів із гострим ішемічним інсультом. Концентрація вільного трийодтироніну (ГТ) в сироватці крові під час дебюту інсульту визначали протягом 24 годин з моменту появи симптомів. Неврологічний дефіцит оцінювали за шкалою SSS. Результати. Статистичний аналіз ANOVA виявив, що показники SSS були значно вищими в пацієнтів із рівнем ГТЗ в 4-му квартилі (≥ 3,55 пмоль/л) порівняно з 2-3-му квартилем (медiana 48 балів проти 37, p = 0,0481) і особливо з 1-м квартилем (≤ 3,4050 пмоль/л, медiana 48 балів проти 30, p = 0,0018). У пацієнтів без інсульту в анамнезі (n = 124) рівень вільного трийодтироніну незалежно впливає на тяжкість неврологічного дефіциту з метою SSS (скорочений R² = 0,49, p < 0,0001). Аналогічний результат показав, що в пацієнтів з атеротромботичним підтипом інсульту (n = 108) рівень ГТЗ є незалежним фактором ризику несприятливого результату інсульту (відносний ризик = 0,3498, 95% довірчий інтервал 0,1235–0,9904). Згідно з ROC-аналізом, рівень ГТЗ ≥ 4,44 пмоль/л був бідним фактором постінсультної інвалідизації (AUC = 0,727, специфічність — 96,4%, чутливість — 66,8%, p = 0,003). Висновки. Дослідження показало, що низький рівень трийодтироніну в сироватці крові під час дебюту інсульту негативно впливає на ступінь тяжкості в пацієнтів, які вперше перенесли інсульт, і може бути предиктором його несприятливого результату. У пацієнтів з атеротромботичним інсультом низький рівень вільного трийодтироніну незалежно підвищує ризик постінсультної інвалідизації через 6 місяців. Для визначення можливих корисних ефектів додавання трийодтироніну як засобу нейропротекції при гострому ішемічному інсульту необхідні майбутні дослідження.  

Ключові слова: ішемічний інсульт; результат; гормони щитоподібної залози; трийодтиронін

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Original Researches
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Влияние начального уровня свободного трийодтиронина в сыворотке крови на тяжесть инсульта и его последствия у пациентов с атеротромботическим ишемическим инсультом

Резюме. Актуальность. Согласно последним исследованиям, тиреоидные гормоны могут иметь потенциальное влияние на степень тяжести, течение и последствия инсульта, но основные механизмы этой взаимосвязи до сих пор не изучены. Цель исследования: определить влияние тиреоидных гормонов на тяжесть неврологического дефицита при острым ишемическом инсульте и риск постинсультной инвалидизации. Материалы и методы. В клиническое исследование были включены 168 взрослых пациентов с острым ишемическим инсультом. Концентрации свободного трийодтиронина (fT3), свободного тироксина (fT4), тиреотропного гормона и основных факторов риска инсульта определяли в течение 24 часов с момента появления симптомов. Неврологический дефицит оценивали по Скандинавской шкале инсульта (SSS). Неблагоприятный исход инсульта (постинсультная инвалидизация) определяли как показатель модифицированной шкалы Рэнкина ≥3 баллов через 6 месяцев после инсульта.

Результаты. Статистический анализ ANOVA выявил, что показатели SSS были значительно выше у пациентов с уровнем ГТЗ в 4-м квартиле (≥5,35 пмоль/л) по сравнению со 2–3-м квартилем (médiana 48 баллов против 37, p = 0,0481) и особенно с 1-м квартилем (≤3,4050 пмоль/л, médiana 48 баллов против 30, p = 0,0018). У пациентов без инсульта в анамнезе (n = 124) уровень свободного трийодтиронина независимо влиял на тяжесть неврологического дефицита по шкале SSS (скорректированный R² = 0,49, p < 0,0001). Анализ показал, что у пациентов с атеротромботическим подтипом инсульта (n = 108) уровень ГТЗ является независимым фактором риска неблагоприятного исхода инсульта (относительный риск = 0,3498, 95% доверительный интервал 0,1235–0,9904). Согласно ROC-анализу, уровень ГТЗ <4,44 пмоль/л был предиктором постинсультной инвалидизации (AUC = 0,727, специфичность — 96,4 %, чувствительность — 66,8 %, p = 0,003).

Выводы. Исследование показало, что низкий уровень трийодтиронина в сыворотке крови во время дебюта инсульта негативно влияет на степень тяжести у пациентов, впервые перенесших инсульт, и может быть предиктором его неблагоприятного исхода. У пациентов с атеротромботическим инсультом низкий уровень свободного трийодтиронина независимо повышал риск постинсультной инвалидизации через 6 месяцев. Для определения возможных полезных эффектов добавления трийодтиронина как средства нейропротекции во время инсульта необходимы будущие исследования.

Ключевые слова: ишемический инсульт; исход; гормоны щитовидной железы; трийодтиронин