INTERNATIONAL JOURNAL OF
INTEGRATIVE AND
MODERN MEDICINE

An Integrated Approach to Diagnosis, Therapy, and Prognosis of Trigeminal Neuralgia

Khodzhieva Dilbar Tajievna, Mukhamadieva Ferangiz Shukhratovna
Bukhara State Medical Institute
xodjiyeva.dilbar@bsmi.uz, fera19941204@gmail.com

Annotation: Positive dynamics in terms of pulse wave types was also observed in the third subgroup of patients who received comprehensive treatment, including the administration of L-arginine. In this subgroup of patients, there was a tendency to decrease the value of pulse curve type A, increase the value of curve type B and curve type C, which, in turn, indicates an improvement in the elasticity of arterial vessels. Using drug therapy according to scheme 3, two months after the treatment, a statistically significant (p=0.003305) change in the structure of the pulse wave was observed: the content of type A decreased from 53.1% to 33.7%, and the presence of type C increased from 22.9% to 44.6%.

Keywords: trigeminal neuralgia, drug therapy.

Introductions: According to the World Health Organization, the frequency of newly diagnosed cases of trigeminal neuralgia ranges from 3 to 5 per 100,000 people per year, with an average of 4.5 per 100,000 (Love S., Coakhman H.B., 2001). The high intensity and frequency of pain attacks in trigeminal neuralgia lead to significant psychophysical exhaustion of patients, disability and a decrease in quality of life, often leading to disability (Zakrzewska J.M. et al., 2017).

To date, there are ongoing disputes regarding the pathogenesis of the classic form of trigeminal neuralgia. A number of researchers (Ray B. et al., 2005; Tubbs R.S. et al., 2009; Shchedrenok V.V. et al., 2014; Konstantinos Natsis et al., 2015; Liu P. et al., 2016) believe that narrowing of the exit openings of the trigeminal nerve may play a pathogenetic role. The development of neurovascular conflict (NVK), characteristic of classical trigeminal neuralgia, involves the trigeminal nerve root (CTN) and an artery, mainly the superior cerebellar (BMA), less often the inferior anterior cerebellar (NPMA) or basilar (BA). The formation of NVK occurs at a critical convergence of these anatomical structures, which leads to a traumatic effect of the artery on CTN. According to the laws of hydrodynamics, the force of pulsating arterial pressure can worsen nerve damage. At the same time, atherosclerotic changes in the vascular wall and its rigidity caused by endothelial dysfunction enhance this effect (Dzau V.J., Gibbon G.N., 1991).

Existing therapies reflect the development of scientific ideas about the etiological and pathogenetic mechanisms of the disease. The lack of a unified concept of pathogenesis contributes to the continued widespread use of destructive surgical interventions and limited effectiveness of drug therapy (Xu M. et al., 2016; Wang Y. et al., 2017; Gagliardi F. et al., 2017; Deng M. et al., 2018).

Antiepileptic drugs remain among the conservative methods of first-line drug therapy, primarily carbamazepine, which has the ability to suppress foci of sensitization in the cerebral cortex and brainstem. However, over time, trigeminal nerve tolerance develops and side effects increase (Garcia J.B. et al., 2010; Techasatian L. et al., 2015; Nasir S.A. et al., 2017).

If pharmacotherapy is not effective enough, surgical methods are resorted to, including microvascular decompression (MVD) CTN is considered the "gold standard" (da Silva O.T. et al., 2016; Arnone G.D. et al., 2017; Otani N. et al., 2017). This method provides complete relief of pain, but the risk of recurrence of the disease remains significant — according to F. Raymond, J.R. Sekula, M.M. Edward et al. (2011), it is up to 28%. The average mortality after the intervention is about 1.4% (Nurmikko T.J., Eldridge P.R., 2001; Tronnier V.M., Rasche D. et al., 2002; Sandell T., Eide P.K., 2010), and the

main cause of deaths is impaired cerebral circulation (Spatz A.L. et al., 2007). There may also be damage to neighboring cranial nerves — IV, VI, VII and VIII.

Given these risks and limitations of current treatment methods, the urgent task remains to develop new, more effective pharmacological approaches to the treatment of classical trigeminal neuralgia aimed at eliminating pain, reducing the incidence of complications and increasing the duration of remission (Donahue J.H. et al., 2017).

Objective: To improve the results of treatment of classical trigeminal neuralgia by optimizing pathogenetically based pharmacotherapy.

A comprehensive examination of 110 patients with a diagnosis of classic trigeminal neuralgia was conducted. There were 83 women and 27 men among them. The average age was 57.2 ± 1.17 years. All patients were divided into two groups: the first group consisted of 89 patients who received conservative therapy, and the second group consisted of 21 patients who received surgical treatment.

The patients who received conservative treatment, in turn, were divided into three subgroups:

- the first subgroup consisted of 29 (32.6%) patients (control group) who received therapy from the first day of inpatient treatment, including the appointment of antioxidants, B vitamins, anticonvulsants, and blockades in the area of the outlets of the trigeminal nerve branches;
- the second subgroup consisted of 33 (37.1%) patients who received therapy from the first day of inpatient treatment, including the appointment of antioxidants, B vitamins, anticonvulsants, blockades in the area of the outlets of the trigeminal nerve branches, as well as intravenous administration of L-lysine escinate.
- the third subgroup consisted of 27 (30.3%) patients who received therapy from the first day of inpatient treatment, including antioxidants, B vitamins, anticonvulsants, blockades in the area of the outlet openings of the trigeminal nerve branches, intravenous L-lysine escinate, as well as L-arginine.

Female patients predominated in all groups of patients.

Among the patients of both groups, older age groups prevailed (the average age of conservative patients was 55.6 ± 1.7 years, surgical patients - 59.8 ± 2.3 years).

According to the frequency of lesions of the TN branches in conservative patients, most often

Branches II and III suffered both together and separately, involving branches I (87.75%), branches I and II (5.8%), and branches I (1.46%). In surgical patients, pain localization prevailed in the zones of the II and III branches both together and

separately and involving the I branch (94.23%), I and II branches (4.75%).

The right-sided localization of pain paroxysms in both groups prevailed over the left-sided one: in conservative 64.5% and 35.6%, respectively, and in surgical 576.1% and 43.9%, respectively.

In the majority of patients, 62.4% who received conservative treatment and 61.9% who received surgical treatment, the duration of the attack was several seconds. The maximum frequency of pain attacks in 39.8% of patients receiving conservative treatment ranged from 11 to 50 times per 10 days, and in 52.4% of surgical patients it was more than 50 attacks. The analysis of daily fluctuations of pain paroxysms in both groups showed the prevalence of daytime.

Research methods: Neurological examination was performed according to the standard method of neurological status examination. When assessing the neurological status, the intensity, frequency, duration and nature of pain paroxysms, the time of day with pain, and the presence of trigger zones were specified. Also, all patients were tested before and after treatment on a ten-point visual analog scale (VAS), on the BNI trigeminal pain syndrome severity scale (Barrow Neurological Institute), night sleep assessment questionnaires were filled out, the Hamilton depression scale was evaluated,

and the dose of Finlepsin (Carbamazepine) was recorded. A general somatic examination of patients was also conducted.

Statistical analysis of the material was performed using the STATISTICA 10.0 "forWindows" software package (StatSoft, USA) and the Microsoft Office Excel 2007 statistical analysis program.

Results: In the examined patients with classical trigeminal nerve neurolgia in a clinical study in the group of patients receiving conservative therapy before treatment, the average frequency of pain attacks during the day in the first (control) subgroup of patients was 42.55±8.53, in the second 42.70±5.69, in the third subgroup 45.91±7.11; in the group of surgical patients before The average frequency of a pain attack was 48.35 ± 8.63. The average VAS pain intensity in the first (control) subgroup of patients was 8.66 ± 0.34, in the second 8.97 ± 0.26, in the third subgroup 8.31 ± 0.39; in surgical patients, this indicator was 9.48 ± 0.25.

VMA injures the upper surface of the CTN without crossing the nerve in the vertical direction, the average pain intensity on the BNI scale in the first subgroup of patients receiving drug treatment was 4.24±0.19, in the second subgroup 4.47 ± 0.13, in the third subgroup 4.31 ± 0.18; in the surgical group patients 4.81 ± 0.09. The results obtained on the VAS and BNI scale indicate the presence of severe pain syndrome in all patients.

According to the results of the evaluation of nighttime sleep questionnaires, both patients receiving conservative treatment and surgical patients had sleep disorders: in the first subgroup, its average value was 20.48±0.44, in the second 20.90±0.39, in the third subgroup 20.77±0.45; in the group of surgical patients, 19.71±0.71. When assessing the condition of patients on the Hamilton depression scale, depression was detected in all the patients studied: the average in the first (control) subgroup of patients was 7.55±0.69, in the second 7.71± 0.90, in the third subgroup 6.26±0.79; in the surgical group 11.67± 1.32. Comparing the obtained results of the frequency of pain attacks, intensity of pain, sleep disorders, severity of depression, etc. before treatment, statistically insignificant differences were obtained between the subgroups of patients receiving drug treatment and the surgical group, which indicates the comparability of the studied groups.

Deviations from the norm in indicators of the marker of endothelial dysfunction endothelin-1 (Table 1) and total cholesterol were detected in all examined patients before treatment. At the same time, no significant differences have been established between the studied groups. The highest levels of endothelin-1 in the surgical group indicate a significant decrease in the elastic properties of the arterial wall, and as a result, the ineffectiveness of the traditional conservative therapy performed at the stages.

Table 1. Average values of endothelin 1 before treatment in the group of conservative and surgical patients

Groups of patients	Indicator		
	Endothelin-1 (norm 0.26 ± 0.066 fmol/ml)		
	trigeminal neuralgia (M±m)	trigeminal neuralgia +connective tissue. pathology (M±m)	p
1 subgroup with conservative treatment (control)	0,52±0,10	0,52±0,03	0,983966
2 subgroup with conservative treatment	0,70±0,18	0,69±0,11	0,095029
3 subgroup with conservative treatment	0,81±0,31	0,92±0,35	0,833029

The differences in the average values of total cholesterol before treatment between the groups of patients studied turned out to be statistically insignificant, which underlines their comparability in these indicators (Table 2).

Table 2. Average total cholesterol levels before treatment in the group of conservative and surgical patients

Groups of patients	Indicator		
	Total cholesterol (norm 3.2 - 5.6 mmol/l)		
	trigeminal neuralgia (M±m)	trigeminal neuralgia +connective tissue. pathology (M±m)	p
1 subgroup with conservative treatment (control)	6,66±0,42	6,77±0,29	0,368066
2 subgroup with conservative treatment	6,55±0,17	6,48±0,21	0,789383
3 subgroup with conservative treatment	6,30±0,26	6,42±0,34	0,771417

An increase in the average value of total cholesterol, as one of the factors damaging the endothelium, in patients with classical trigeminal neuralgia also indicates a decrease in the elastic properties of the arterial wall.

The average values of homocysteine and cytokines before treatment in patients receiving conservative therapy and surgical patients turned out to be within normal values, and the differences in average values between the studied groups turned out to be statistically insignificant ($p>0.05$). The average values of homocysteine and cytokines before treatment were within the normal range both in the group of patients suffering from classical trigeminal neuralgia in isolation and in the group of patients with classical trigeminal neuralgia and concomitant pathology. The absence of abnormalities in homocysteine and cytokine levels indicates that these laboratory parameters have no effect on the development of endothelial dysfunction in patients suffering from classical trigeminal neuralgia.

Prior to treatment, patients receiving drug therapy had deviations from the norm in angioscanning parameters in the form of an increase in vascular stiffness (a negative value of the numbers indicates the normal state of the elastic properties of the vessel), which indicates a loss of elastic properties of the arterial wall, as well as the predominance of A type of pulse wave, indicating an unsatisfactory condition of the vessels. The average value of vascular stiffness before treatment in patients receiving pharmacotherapy was: in the first subgroup 3.32%±1.22%, in the second 7.10%±1.43%, in the third subgroup 4.51%±2.31%. The differences in the average values in the studied groups before treatment turned out to be statistically insignificant, which also confirms the comparability of changes in vascular wall elasticity in these patients.

As for the types of pulse waves, it prevailed both in patients receiving conservative therapy and in surgical patients before treatment. And the type of pulse wave, indicating an unsatisfactory vascular condition. In patients receiving drug treatment, the pulse wave before treatment in the first subgroup type A averaged 46.9%, type B 24.2%, type C 28.9%, in the second subgroup type A averaged 45.3%, type B 31.1%, type C 23.6%, in the third subgroup type A B The average was 53.1%, type B 23.9%, type C 22.9%. In the group of surgical patients, the pulse wave before treatment averaged 57.8% type Ab, 17.6% type B, and 24.3% type C. Deviations in the types of pulse waves were observed both in the group of patients suffering from classical trigeminal neuralgia in isolation and in the group with

classical trigeminal neuralgia and concomitant pathology, and differences in the average values in these groups before treatment turned out to be statistically insignificant ($p>0.05$).

After drug treatment, the frequency of pain attacks decreased, differences in frequency distribution before and after conservative

The therapy proved to be statistically significant with a confidence level of $p<0.001$.

The average values of homocysteine and cytokines two months

after treatment in all groups of patients were within normal values. The differences in the mean values between the groups turned out to be statistically insignificant ($p>0.05$).

According to the results of angioscanning, the differences in the average values of vascular stiffness before and two months after treatment using scheme 3, which included taking L-arginine, turned out to be statistically significant ($p=0.001474$). At the same time, a statistically significant improvement in stiffness using scheme 3 was observed both in the group of patients suffering from classical trigeminal neuralgia in isolation ($p=0.007661$) and in the group of patients with trigeminal neuralgia and concomitant pathology ($p=0.027709$).

In terms of vascular stiffness, two months after therapy, according to schemes 1 and 2, statistically insignificant changes in the average values were revealed ($p=0.850619$ and $p=0.818295$, respectively), since these methods of drug treatment do not affect the elastic properties of the arteries.

Positive dynamics in terms of pulse wave types was also observed in the third subgroup of patients who received comprehensive treatment, including the administration of L-arginine. In this subgroup of patients

There was a tendency to decrease the value of pulse curve type A, increase the value of curve type B and curve type C, which, in turn, indicates an improvement in the elasticity of arterial vessels. Using drug therapy according to scheme 3, two months after the treatment, a statistically significant ($p=0.003305$) change in the structure of the pulse wave was observed: the content of type A decreased from 53.1% to 33.7%, and the presence of type C increased from 22.9% to 44.6%. Statistically significant differences in the average composition of the pulse wave before and two months after treatment according to scheme 3 were noted both in the group of patients suffering from classical trigeminal neuralgia in isolation ($p=0.003872$) and in the group of patients with trigeminal neuralgia and concomitant diseases ($p=0.00009$). In the control subgroup of patients after treatment, type A in the pulse wave averaged 46.3%, type B 25.6%, type C 26.9%. The difference in the average composition of the pulse wave in this group of patients before and two months after treatment was statistically insignificant ($p=0.95090$). In the second subgroup of patients (who did not receive L-arginine), the pulse wave after treatment averaged 38.5% type A, 29.2% type B, and 32.3% type C. The difference in the average composition of the pulse wave before treatment and two months after therapy in this subgroup turned out to be statistically insignificant ($p=0.37331$). The absence of a positive trend in the pulse wave graph using schemes 1 and 2 also indicates the absence of an effect of these treatment methods on elastic properties of arteries. A decrease in the average vascular stiffness index, as well as a change in the structure of the pulse wave towards an increase in the percentage of trigeminal neuralgia of type C using scheme 3, indicates a decrease in the severity of endothelial dysfunction in patients with classical trigeminal neuralgia and an increase in the elasticity of arterial vessels.

Conclusions: In the formation of neurovascular conflict and the occurrence of classical trigeminal neuralgia, it is not the size of the cranial exit openings that is significant, but a decrease or loss of elasticity of the artery wall involved in the conflict, which is confirmed by an increase in the level of endothelin-1 (on average 0.95±0.19fmol/ml), total cholesterol (on average 6.21±0.16mmol/l) and the results of angioscanning (increased arterial stiffness (on average 5.44% ± 1.09%), the predominance of type A pulse wave (on average 59.75%±4.53%)) in patients with classical trigeminal neuralgia. Before treatment, patients with classical trigeminal neuralgia showed no abnormalities in homocysteine (on

average 9.29±0.38mmol/L) and cytokines (IL-1b (on average 3.27±0.11pg/ml), IL-8 (on average 13.91±0.47pg/ml), TNF-α (on average an average of 5.30±0.18pg/ml)). The differences in their mean values before and after treatment turned out to be statistically insignificant (p>0.05).

Drug therapy for classical trigeminal neuralgia should be aimed at three components of the pathogenesis: reducing CTN volume, stimulating the remyelination process at the site of neurovascular conflict, and improving the elastic properties of the arterial wall.

References:

1. AngioScan-01P, AngioScan-01M Devices for personal diagnostics of the cardiovascular system: user manual / AngioScan-Electronics LLC. Moscow: AngioScan-Electronics, 2011. 66 p.
2. Balyazin, V.A. Ways to reduce complications and relapses after microvascular decompression in patients with trigeminal neuralgia / V.A. Balyazin, E.V. Balyazina // Journal. Vopr. neuro. named after N.N. Burdenko. - 2003. - No. 2. - pp. 6-9.
3. Balyazina, E.V. Anatomical prerequisites for the emergence of classical trigeminal neuralgia / E.V. Balyazina // Collection of scientific papers dedicated to the 80th anniversary of the neurological service in Ryazan. - Ryazan, 2010. - pp. 13-17.
4. Balyazina, E.V. Classical trigeminal neuralgia / E.V. Balyazina. Novocherkassk: Lik, 2015. 278 p
5. Balyazina, E.V. Features of neurovascular conflict predisposing to the development of neuralgic status // Proceedings of the X All-Russian Congress of Neurologists. - N. Novgorod, 2012. - pp. 601-602.
6. Balyazina, E.V. Method of treatment of trigeminal neuralgia: Pat. 2612936 Russian. Federation / E.V. Balyazina, T.A. Isakhanova; published on 13.03.2017; announced on 19.11.2015; No. 2015149838; Byul. Inventions. Useful models No. 8. 2017. 6 p
7. Balyazina, E.V. Topographic anatomical relationships of the trigeminal nerve trunk with the superior cerebellar artery in patients with trigeminal neuralgia / E.V. Balyazina // Morphology. - 2009. - No. 5. - pp. 27-31.
8. Grigoryan, Yu.A. Trigeminal neuralgia and tumors of the bridge-cerebellar angle / Yu.A. Grigoryan, A.R. Sitnikov // Russian Neurosurgical Journal named after Professor A.L. Polenov. - 2010. - Vol. 2, No. 1. -pp. 28-41.
9. Dymova, N.V. Immune disorders and endothelial dysfunction in the hypertensive variant of chronic glomerulonephritis and their dynamics against the background of therapy: Dissertation of the Candidate of Medical Sciences / N.V. Dymova. - Kursk, 2007. - 176 p.
10. Kalakutsky, L.I. Measuring transducer of arterial pulsations for vascular reactivity assessment systems / L.I. Kalakutsky, P.A. Lebedev, A.P. Gorlov // Actual problems of radio electronics. Samara, 2003. pp. 105-107.
11. Karnilova, L.E. The effect of intraosseous blockades on pain syndrome, memory and cognitive evoked potential of P300 in a patient with exacerbation of trigeminal neuralgia / L.E. Karnilova, E.L. Sokov, M.S. Nurmagamedova // The Russian Journal of Pain. - 2014. - Vol. 42, No. 1. - pp. 110-111.
12. Konovalov, A.N. Microvascular decompression of the trigeminal nerve root in the treatment of trigeminal neuralgia: Proceedings of the 14th Russian scientific and practical conference "Neuropathic pain" / A.N. Konovalov, O.R. Orlova, U.B. Makhmudov et al. // Vertebroneurology. - 2008. - Vol. 15, No. 1/2. - pp. 81-82.
13. Kurapova, M.V. Clinical and diagnostic significance of endothelial dysfunction in patients with chronic kidney disease: Dissertation of the Candidate of Medical Sciences / M.V. Kurapova. Samara, 2015. 145 p.

14. Milyagin, V.A. Modern methods for determining vascular stiffness / V.A. Milyagin, V.B. Komissarov // Arterial hypertension. - 2010. - Vol. 16, No. 2. - pp. 137-138.
15. Ottewa, E.N. Arterial rigidity is a marker of the development of cardiovascular diseases / E.N. Ottewa, E.V. Klinkova, O.G. Garbuzova et al. // Clinical medicine. - 2012. - Vol. 90, No. 1. - pp. 4-12.
16. Rogozina, L.A. Endothelial dysfunction in patients with allogeneic renal transplant / L.A. Rogozina, I.L. Davydkin, E.N. Iskhakov // Proceedings of the Samara Scientific Center of the Russian Academy of Sciences. - 2014. - Vol.16, No. 5(4). - pp. 1305-1308.