ORIGINAL ARTICLE

CONTENTS

Changes in the levels of nerve growth factor and middle molecular mass molecules in patients with post-traumatic neuropathies and plexopathies accompanied by chronic neuropathic pain

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ABSTRACT

Aim: To investigate and compare the levels of the beta-subunit of NGF (Beta-NGF) and middle molecular mass molecules (MMM) in the blood of patients with post-traumatic non-firearm and firearm neuropathies and plexopathies accompanied by chronic neuropathic pain.

Materials and Methods: We examined 93 men aged 21-59 years with compression-ischemic (groupI - comparison), post-traumatic non-firearm (groupII) and firearm (groupIII) neuropathies and plexopathies with and without chronic neuropathic pain syndrome. Quantitative determination of Beta-NGF in serum was performed by enzyme-linked immunosorbent assay. The content of MMM was determined by spectrophotometric method (fractions MMM238, MMM254, MMM260, MMM280). The following integral indices were calculated: peptide-nucleotide ratio, distribution coefficient, aromaticity coefficient.

Results: We revealed an increased level of Beta-NGF in the blood serum of patients with post-traumatic firearm and non-firearm neuropathies and plexopathies accompanied by chronic neuropathic pain (Mann-WhitneyU-test,p=0.0077 and Mann-WhitneyU-test,p=0.04608, respectively). The level of the CR280/254 in patients of groupIII with post-traumatic firearm neuropathies and plexopathies at a statistically significant level depends on the presence of chronic neuropathic pain (Mann-WhitneyU-test,p=0.0113). The accumulation of biologically active molecules involved in the activation of compensatory, protective mechanisms in patients with post-traumatic firearm neuropathies and plexopathies accompanied by chronic neuropathic pain was established.

Conclusions: The results confirm the existing data on the pathophysiological role of Beta-NGF and MMM in the development of chronic neuropathic pain and indicate the potential use of NGF as a therapeutic target, while the CR280/254 ratio may serve as a biomarker reflecting the accumulation of biologically active molecules associated with chronic neuropathic pain in patients with post-traumatic neuropathies and plexopathies.

KEYWORDS: Beta-NGF, molecules of medium mass MMM, post-traumatic non-gunshot and gunshot neuropathies, plexopathies, chronic neuropathic pain

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INTRODUCTION

Nerve Growth Factor (NGF) is a regulatory protein synthesized by neurons, as well as cells in the neuronal environment, such as fibroblasts, smooth muscle cells, keratinocytes, Schwann cells, mast cells, and macrophages. The nerve growth factor was isolated in 1956 by Rita Levi-Montalcini and Stanley Cohen, who received the Nobel Prize for this discovery in 1986 [1,2].

The main physiological effects of nerve growth factor are support of nerve cell proliferation and regeneration, stimulation of axonal growth and sprouting, and NGF is involved in the regulation of the endocrine system and immune processes. Nerve growth factor is synthesized as pro-NGF, a complex of three subunits (α-, β- and γ-NGF), and undergoes post-translational transformation with the release of the active component, β-NGF. Apart from neurons, nerve growth factor receptors are widely expressed on many immunocompetent, endocrine, and stromal cells in the human body. Two major NGF receptors are known: tropomyosin receptor kinase A (TrkA) and the low-affinity receptor NGFR/p75NTR [3-5].

Nerve Growth Factor (Beta-NGF) is involved in the development of central sensitization, the biological basis of which is reversible changes in the neuronal membrane at the level of synapses of the posterior horns of the spinal cord, accompanied by a persistent decrease in pain threshold, hyperalgesia and allodynia. This effect is especially pronounced against the background of an inflammatory reaction accompanied by activation and chemotaxis of macrophages, mastocytes and other lymphohistiocyte cells to the site of injury. At the same time, Beta-NGF can

have a direct effect on nociceptors through TrkA activation of transmembrane channels, which leads to changes in transmembrane potential and increased excitability of nerve endings. Beta-NGF can indirectly affect nociceptors by activating inflammatory response cells and increasing the synthesis of many pain and inflammatory mediators, such as prostaglandins, leukotrienes, bradykinin, histamine, substance P [6-8].

According to modern research, in the acute period of trauma, endogenous intra- and extracellular molecules specifically formed due to tissue damage are released, which activate immune cells and cause the development of an inflammatory response of excessive intensity with subsequent undesirable consequences for the injured organism. The substances responsible for the development of endogenous intoxication include middle molecular mass molecules - protein toxins that affect various pathophysiological processes, namely, promote hypercoagulation, microcirculatory disorders, functional and structural changes in cell membranes, and hypoxia. On the other hand, low-molecular-weight oligopeptides have a wide range of biological effects and coordinate the performance of biological functions by various organs and tissues, can affect the repair processes in body tissues, and the antioxidant property of medium-molecular peptides has also been proven [9-11].

In patients with post-traumatic neuropathies and plexopathies, an increase in the level of nerve growth factor correlates with the presence of chronic neuropathic pain. This increase is accompanied by an elevated CR 280/254 ratio, indicating the accumulation of biologically active molecules involved in the activation of compensatory and protective mechanisms. Therefore, Beta-NGF and MMM may serve as biomarkers for the development and maintenance of chronic neuropathic pain and represent potential therapeutic targets for its management in patients with post-traumatic neuropathies and plexopathies, which has not been systematically evaluated in peripheral nerve injuries before. By combining quantitative immunological measurements with clinical pain assessment, the study provides a comprehensive approach to understanding the pathophysiology of chronic neuropathic pain in post-traumatic peripheral nerve injuries, contributing new knowledge that can guide future research and therapy.

AIM

The aim of the study is to investigate and compare the levels of the beta subunit of NGF (Beta-NGF) and middle molecular mass molecules (MMM) in the blood of patients with post-traumatic non-firearm and firearm neuropathies and plexopathies accompanied by chronic neuropathic pain.

RESEARCH HYPOTHESIS

We hypothesized that patients with post-traumatic neuropathies and plexopathies accompanied by chronic neuropathic pain would exhibit significantly elevated serum levels of Beta nerve growth factor (β-NGF) and middle molecular mass molecules (MMM) compared with patients without chronic neuropathic pain, and that these alterations would be more pronounced in firearm-related injuries, reflecting greater tissue damage and a more intense and persistent neuroinflammatory response.

MATERIALS AND METHODS

We examined 93 men aged 21 to 59 years with compression (group I - comparison), post-traumatic non-firearm (group II) and firearm (group III) neuropathies and plexopathies with and without chronic neuropathic pain syndrome. Group I included 30 patients with compression neuropathies and plexopathies. Group II included 30 patients with post-traumatic non-firearm neuropathies and plexopathies due to injuries, limb fractures and joint dislocations. Group III included 33 patients with post-traumatic firearm neuropathies and plexopathies due to shrapnel and bullet wounds of the limbs.

The inclusion of Group I (patients with compression neuropathies and plexopathies without chronic neuropathic pain) was necessary to differentiate post-traumatic mechanisms of neurotrophic and metabolic alterations from non-traumatic nerve damage. This group served as a reference model of peripheral nerve pathology without pronounced neuroinflammatory and pain-associated neurotrophic activation, allowing more accurate interpretation of β-NGF and MMM changes specifically related to post-traumatic neuropathies accompanied by chronic neuropathic pain.

Patients with documented chronic viral or bacterial infections, central nervous system disorders, autoimmune, oncological, or hematological conditions were excluded from the study. Patients with compression neuropathies or plexopathies were screened for chronic neuropathic pain using the validated Visual Analog Scale (VAS) and questionnaires PainDETECT, DN4, MPQ and those identified with such pain were also excluded.

To achieve the objectives of the study, we analyzed the following materials and data sources: patients' medical records, including case histories, discharge summaries, clinical examination protocols, and surgical reports; laboratory results, including general and biochemical blood tests; and instrumental examination data, such as radiography (X-ray), computed tomography (CT), ultrasound, and electroneuromyography (ENMG).

Quantitative determination of the beta subunit of human nerve growth factor (β-NGF) in serum was performed by enzyme-linked immunosorbent assay using the Ray Bio Human Beta-NGF ELISA Kit. The study was performed on a STATFAX

3200 enzyme-linked immunosorbent assay analyzer (USA). Non-heparinized peripheral blood (5 ml) was collected from the antecubital vein under sterile conditions. The samples were centrifuged at 3000 rpm at room temperature to obtain serum, which was subsequently frozen at –20 °C or lower and stored for 3 to 6 months.

The content of middle molecular mass molecules (MMM) was determined on a Shimadzu UV-2600 spectrophotometer (Japan) by extinction at wavelengths of 238 nm, 254 nm, 260 nm and 280 nm according to the method of Gabrielyan N.I. The concentration of MMM was expressed in optical units of the optical density of the centrifugate obtained after precipitation of plasma proteins with 10% trichloroacetic acid solution. At a wavelength of 238 nm, the fraction containing biologically active oligopeptides was determined, at a wavelength of 254 nm - the MMM254 fraction, which reflects the level of intermediate products of intensive proteolysis, the nucleotide fraction at a wavelength of 280 nm - the MMM280 fraction, which contains aromatic chromatophores. The following integral indices were calculated: peptide-nucleotide ratio, distribution ratio, and aromaticity ratio.

Assessment of pain severity and characteristics was performed using the Visual Analog Scale (VAS) and neuropathic pain questionnaires, including DN4, PainDETECT, and the McGill Pain Questionnaire (MPQ).

The data obtained were statistically processed using the STATISTICA 6.0 program. Quantitative indicators are presented in the form Me [LQ; UQ], where Me is the median, LQ is the lower quartile, and UQ is the upper quartile. The statistical significance of differences was tested using the Mann-Whitney U-test (MWU). Differences were considered statistically significant at $p<0.05$.

ETHICS

This work complies with the principles of the Declaration of Helsinki.

AI STATEMENT

The author states that no AI tools were used in writing this article.

RESULTS

Fig. 1 shows the quantitative content of nerve growth factor (Beta-NGF) in patients of group II with post-traumatic non-firearm neuropathies and plexopathies with chronic neuropathic pain and without chronic neuropathic pain.

The level of Beta-NGF in patients of group II with post-traumatic non-firearm neuropathies and plexopathies was significantly associated with the presence of chronic neuropathic pain (Mann-Whitney U-test, p=0.04608). Thus, in patients with post-traumatic non-firearm neuropathies and plexopathies in the presence of chronic neuropathic pain, the level of Beta-NGF is 165.8 [69.3;510] pg/ml, which is significantly higher than in patients with post-traumatic non-firearm neuropathies and plexopathies without chronic neuropathic pain, in whom the level of Beta-NGF is 47.9 [25;93] pg/ml.

Fig. 2 shows the quantitative content of nerve growth factor (Beta-NGF) in patients with post-traumatic firearm neuropathies and plexopathies with and without chronic neuropathic pain.

The level of Beta-NGF in patients of group III with post-traumatic firearm neuropathies and plexopathies at a statistically significant level depends on the presence of chronic neuropathic pain (Mann-Whitney U-test, p=0.0077). Thus, in patients with post-traumatic firearm neuropathy and plexopathy in the presence of chronic neuropathic pain, the level of Beta-NGF is 337.1 [39.2; 579.25] pg/ml, which is significantly higher than in patients with post-traumatic firearm neuropathy and plexopathy without chronic neuropathic pain, in whom the level of Beta-NGF is 25.9 [25; 35.3] pg/ml.

Fig. 3 demonstrates the CR level of 280/254 in patients with post-traumatic firearm neuropathy and plexopathy with chronic neuropathic pain and in patients with post-traumatic firearm neuropathy and plexopathy without chronic neuropathic pain.

The level of the distribution coefficient of CR 280/254 in patients of group III with post-traumatic firearm neuropathies and plexopathies at a statistically significant level depends on the presence of chronic neuropathic pain (MWU, p=0.0113). Thus, in patients with post-traumatic firearm neuropathies and plexopathies accompanied by chronic neuropathic pain, the CR 280/254 was found to be significantly higher and equal to 1.17 [1.15; 1.21] than in patients with post-traumatic firearm neuropathies and plexopathies without chronic neuropathic pain, the CR 280/254 was 1.13 [1.12; 1.14]. The data obtained indicate the accumulation of biologically active substances involved in the activation of compensatory and protective mechanisms in patients with post-traumatic firearm neuropathy and plexopathy accompanied by chronic neuropathic pain.

Table 1 presents the levels of β-NGF and the CR 280/254 ratio in patients with compression, post-traumatic non-firearm and firearm neuropathies and plexopathies depending on the presence of chronic neuropathic pain. The inclusion of Group I (compression neuropathies without chronic pain) as a reference allows us to differentiate post-traumatic neurotrophic and neuroinflammatory responses from non-traumatic nerve alterations. In Group II patients with post-traumatic non-firearm neuropathies and plexopathies, the presence of chronic neuropathic pain was associated with a statistically significantly higher β-NGF level compared with patients without pain 165.8 [69.3; 510] vs. 47.9 [25; 93] pg/mL, p = 0.04608. At the same time, for the CR 280/254

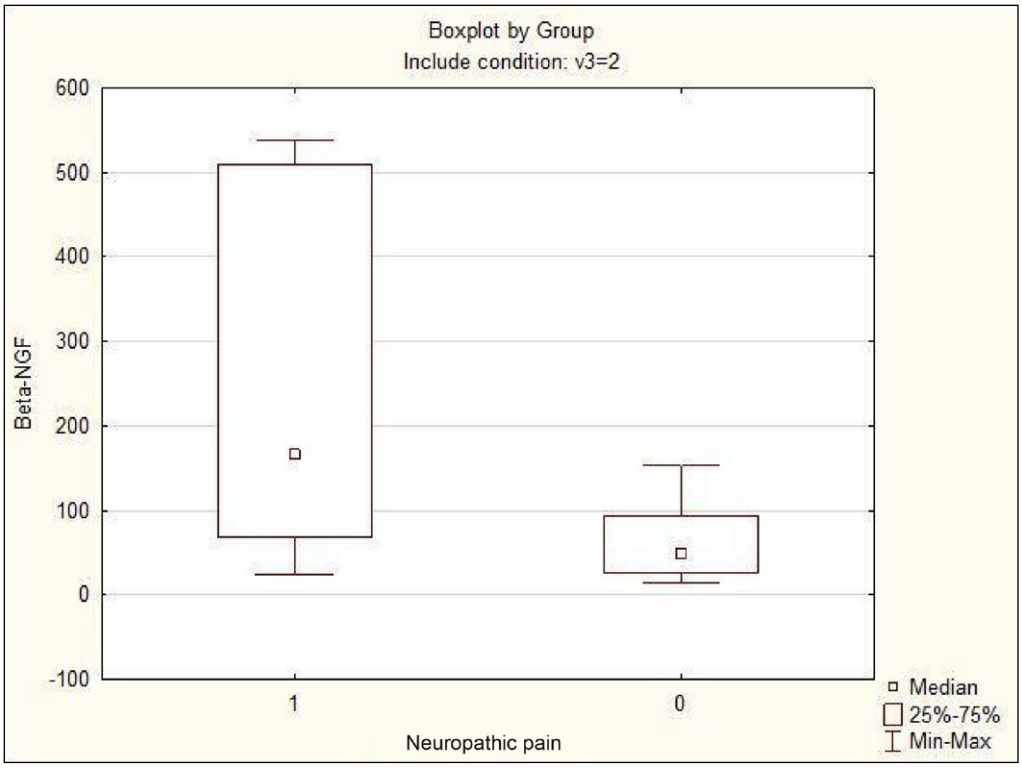

Fig. 1. Quantitative content of nerve growth factor (Beta-NGF) in patients with post-traumatic non-firearm neuropathies and plexopathies with chronic neuropathic pain and without chronic neuropathic pain (pg/ml)
Picture taken by the authors

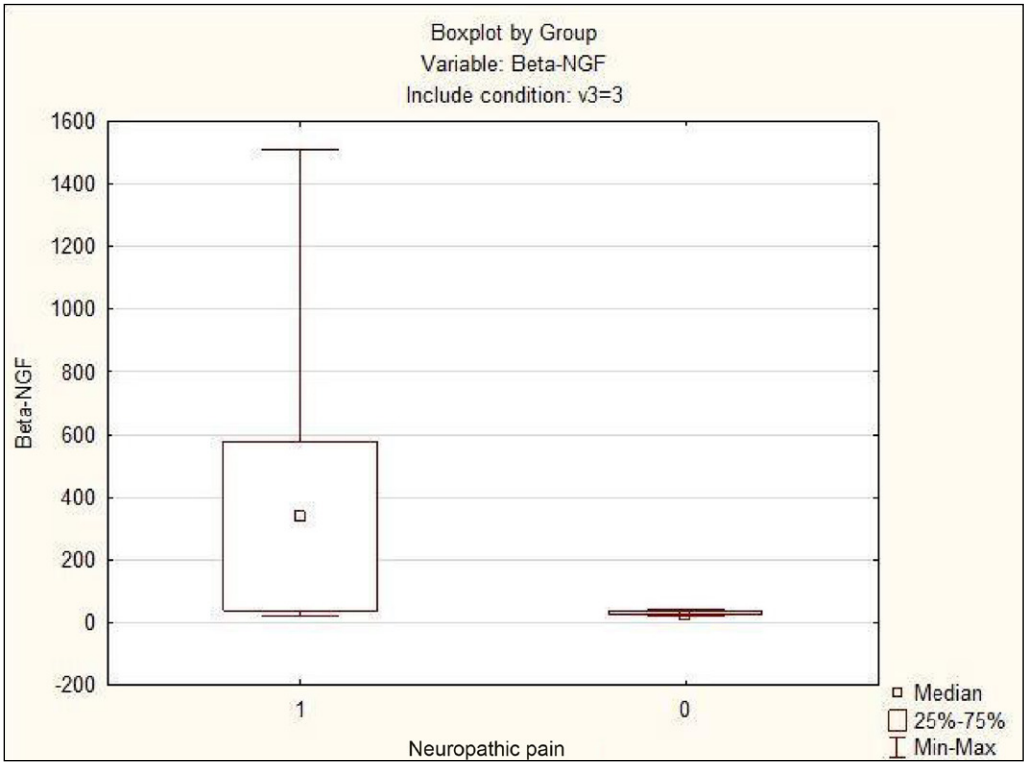

Fig. 2. Quantitative content of nerve growth factor (Beta-NGF) in patients with post-traumatic firearm neuropathies and plexopathies with chronic neuropathic pain and without chronic neuropathic pain (pg/ml)
Picture taken by the authors

ratio in this group, a borderline level of association with chronic neuropathic pain was observed: values were higher in patients with pain 1.213 [1.141; 1.263] than in those without pain 1.137 [1.0795; 1.2025], corresponding to a trend toward differences at p = 0.1006. In Group III patients with post-traumatic firearm neuropathies and plexopathies, both β-NGF levels and the CR 280/254 ratio were statistically significantly higher in the presence of chronic neuropathic pain. Specifically, β-NGF concentrations were markedly higher in patients with pain than in those without pain 337.1 [39.2; 579.25] vs. 25.9 [25; 35.3] pg/mL, p = 0.0077. Similarly, the CR 280/254 ratio was significantly elevated in patients with chronic neuropathic pain 1.17 [1.15; 1.21] compared with pain-free patients 1.13 [1.12; 1.14], p = 0.0113.

Overall, the summarized data indicate that β-NGF and the CR 280/254 ratio demonstrate statistically significant

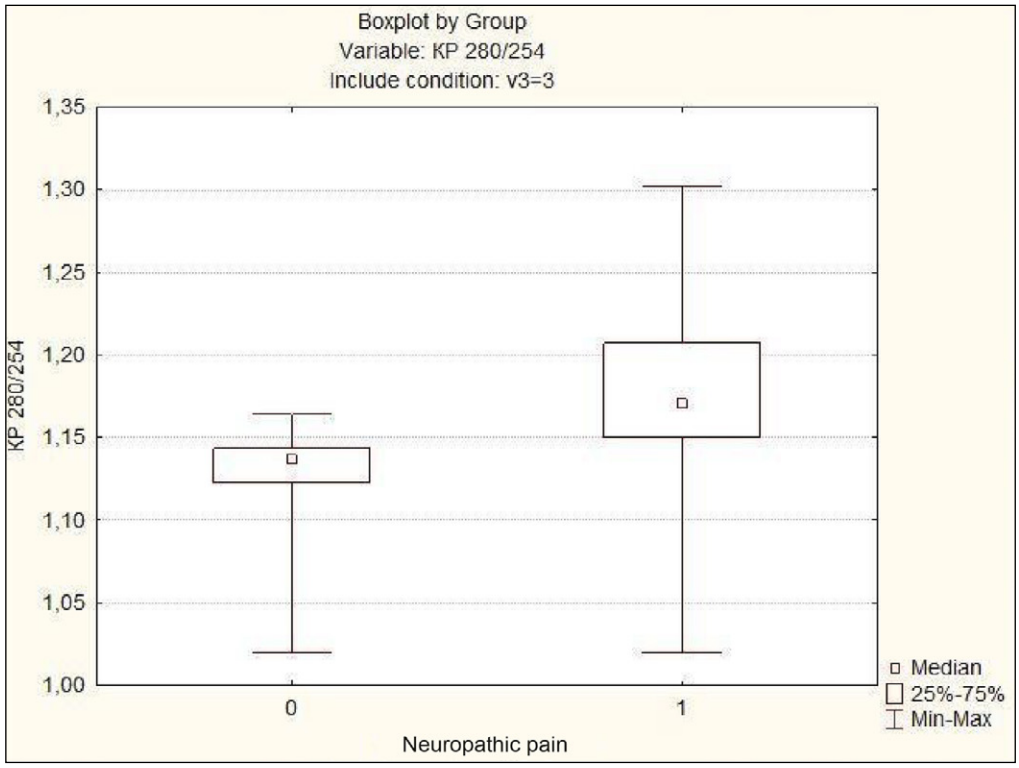

Fig. 3. CR level 280/254 in patients with post-traumatic firearm neuropathy and plexopathy accompanied by chronic neuropathic pain and without chronic neuropathic pain
Picture taken by the authors

Table 1. Content of β-NGF and CR 280/254 in patients with compression, post-traumatic non-firearm and firearm neuropathies and plexopathies depending on the presence of chronic neuropathic pain

Group	Parameter	With chronic neuropathic pain	Without chronic neuropathic pain	p-value
Group I (compression neuropathies and plexopathies)	β-NGF, pg/mL	_	83.6 [42; 335.4]	_
	CR 280/254	_	1.186 [1.137; 1.232]	_
Group II (post-traumatic non-firearm neuropathies and plexopathies)	β-NGF, pg/mL	165.8 [69.3; 510]	47.9 [25; 93]	0.04608
	CR 280/254	1.213 [1.141; 1.263]	1.137 [1.079; 1.202]	0.1006
Group III (post-traumatic firearm neuropathies and plexopathies)	β-NGF, pg/mL	337.1 [39.2; 579.25]	25.9 [25; 35.3]	0.0077
	CR 280/254	1.17 [1.15; 1.21]	1.13 [1.12; 1.14]	0.0113

Source: compiled by the authors of this study

associations at the $p < 0.05$ level in patients with post-traumatic firearm neuropathies and plexopathies, whereas for the CR 280/254 ratio in patients with post-traumatic non-firearm neuropathies and plexopathies, borderline significance at approximately $p \approx 0.1$ was observed, suggesting less robust but potentially clinically meaningful associations. This pattern suggests that the severity and mechanism of nerve injury strongly influence the intensity of neurotrophic and neuroinflammatory activation.

DISCUSSION

The results of the study on changes in the content of nerve growth factor in patients with post-traumatic neuropathies and plexopathies accompanied by chronic neuropathic pain are consistent with the data of other researchers who emphasize the role of NGF in the pathogenesis of chronic neuropathic pain.

According to the study by Schaefer et al, NGF plays an important role in the development of chronic pain syndrome through the activation of signaling pathways, in particular the modulation of sodium channels in neurons, which leads to increased excitability and sensitization to pain [12]. This confirms the correlation between Beta-NGF levels and the presence of chronic neuropathic pain in patients with post-traumatic firearm and non-firearm neuropathies and plexopathies.

Another study conducted by Binshtok et al. showed that NGF activates macrophages and other inflammatory response cells that release biologically active molecules that contribute to nociceptor sensitization [13]. This explains the increase in the levels of middle molecular mass

molecules observed in our study in patients with chronic neuropathic pain, since their accumulation is a marker of the inflammatory response, contributes to homeostasis and the development of endogenous intoxication.

The results are also consistent with the findings of Barker et al. and McMahon et al. who indicate that NGF is a critical regulator of glial cell proliferation and activation that maintains chronic pain by increasing sensitivity to pain stimuli. Studies in animal models have shown that blocking NGF activity leads to a decrease in hyperalgesia and allodynia, which confirms the importance of this factor in maintaining chronic pain in patients [14, 15].

In addition, modern clinical trials confirm the effectiveness of therapy aimed at blocking NGF to reduce chronic pain in patients with nervous system diseases. Thus, a study conducted by Kreiner et al. demonstrated that the use of NGF inhibitors helps to reduce pain scores and improve the functional status of patients with chronic pain [16].

Importantly, most previously published studies have focused on the role of NGF in chronic pain syndromes of inflammatory or degenerative origin, while data regarding its involvement in post-traumatic peripheral nerve injuries, especially in firearm trauma, remain limited. Our study expands existing knowledge by demonstrating that β-NGF elevation is not only associated with the presence of chronic neuropathic pain but also varies depending on the mechanism and severity of nerve injury. The significantly higher β-NGF levels observed in patients with firearm neuropathies and plexopathies compared with non-firearm injuries suggest a more pronounced neurotrophic and neuroinflammatory response, likely reflecting extensive tissue damage, persistent immune activation, and long-term sensitization of nociceptive pathways. Unlike previous studies that evaluated NGF in isolation, our work also assessed middle molecular mass molecules (MMM) and their integral ratios, allowing a more comprehensive characterization of endogenous intoxication and compensatory metabolic processes associated with chronic neuropathic pain. The identified increase in the CR 280/254 ratio in patients with firearm injuries and chronic pain represents a novel finding, indicating the accumulation of biologically active aromatic compounds and peptides that may contribute to sustained neuroinflammation and pain chronification. Thus, the combined assessment of β-NGF and MMM parameters provides new insight into the biochemical and immune mechanisms underlying chronic neuropathic pain following severe peripheral nerve trauma and may serve as a basis for developing targeted neurotrophic or anti-inflammatory therapies. These findings highlight the clinical relevance of β-NGF and CR 280/254 as potential biomarkers for pain severity and for monitoring therapeutic interventions in post-traumatic neuropathies and plexopathies.

CONCLUSIONS

The study revealed elevated levels of Beta-NGF in the serum of patients with post-traumatic firearm and non-firearm neuropathies and plexopathies accompanied by chronic neuropathic pain. Studies of the role of NGF in nerve and plexus injuries indicate the importance of this factor not only in the regulation of neurotrophic activity, but also in the modulation of pain that accompanies most injuries and diseases of the nervous system.

As a result of the study, we found the accumulation of biologically active molecules involved in the activation of compensatory and protective mechanisms in patients with post-traumatic firearm neuropathies and plexopathies accompanied by chronic neuropathic pain.

Further study of the peculiarities of neurotrophic control and changes in the content of biologically active molecules in injuries and diseases of the nervous system accompanied by chronic pain is an urgent and important task of modern medicine. This opens up prospects for the development of new therapies aimed at modulating neurotrophic regulation and correcting pathogenetic mechanisms in patients with chronic neuropathic pain. Thus, the results of our study confirm existing data on the pathophysiological role of NGF and MMM in the development of chronic neuropathic pain and indicate the potential use of NGF as a therapeutic target, while the CR 280/254 ratio may serve as a biomarker reflecting the accumulation of biologically active molecules associated with chronic neuropathic pain in patients with post-traumatic neuropathies and plexopathies.

REFERENCES

1. Levi-Montalcini R. The nerve growth factor and the neuroscience chess board. Prog Brain Res. 2004;146:525-7. doi:10.1016/S0079-6123(03)46034-4. DOI
2. Chao MV, Calissano P. Rita Levi-Montalcini: in memoriam. Neuron. 2013;77(3):385-7. doi:10.1016/j.neuron.2013.01.019. DOI
3. Rocco ML, Soligo M, Manni L, Aloe L. Nerve growth factor: early studies and recent clinical trials. Curr Neuropharmacol. 2018;16(10):1455-65. doi:10.2174/1570159X16666180412092859. DOI
4. Barker PA, Mantyh P, Arendt-Nielsen L et al. Nerve growth factor signaling and its contribution to pain. J Pain Res. 2020;13:1223-41. doi:10.2147/JPR.S247472. DOI
5. Jaffal S, Khalil R. Targeting nerve growth factor for pain relief: pros and cons. Korean J Pain. 2024;37(4):288-98. doi:10.3344/kjp.24235.

DOI
6. Chang DS, Hsu E, Hottinger DG, Cohen SP. Anti-nerve growth factor in pain management: current evidence. J Pain Res. 2016;9:373-83. doi:10.2147/JPR.S89061. DOI
7. Weihrauch T, Limberg MM, Gray N et al. Neurotrophins: neuroimmune interactions in human atopic diseases. Int J Mol Sci. 2023;24(7):6105. doi:10.3390/ijms24076105. DOI
8. Bélanger P, West CR, Brown MT. Development of pain therapies targeting nerve growth factor signal transduction and the strategies used to resolve safety issues. J Toxicol Sci. 2018;43(1):1-10. doi:10.2131/jts.43.1. DOI
9. Aller MA, Arias JI, Alonso-Poza A, Arias J. A review of metabolic staging in severely injured patients. Scand J Trauma Resusc Emerg Med. 2010;18:27. doi:10.1186/1757-7241-18-27. DOI
10. Posti JP, Dickens AM, Orešič M et al. Metabolomics profiling as a diagnostic tool in severe traumatic brain injury. Front Neurol. 2017;8:398. doi:10.3389/fneur.2017.00398. DOI
11. Chmielewski M, Cohen G, Wiecek A, Carrero JJ. The peptidic middle molecules: is molecular weight doing the trick? Semin Nephrol. 2014;34(2):118-34. doi:10.1016/j.semnephrol.2014.02.005. DOI
12. Schaefer I, Prato V, Arcourt A et al. Differential modulation of voltage-gated sodium channels by nerve growth factor in three major subsets of TrkA-expressing nociceptors. Mol Pain. 2018;14:1744806918814640. doi:10.1177/1744806918814640. DOI
13. Binshtok AM, Wang H, Zimmermann K et al. Nociceptors are interleukin-1beta sensors. J Neurosci. 2008;28(52):14062-73. doi:10.1523/JNEUROSCI.3795-08.2008. DOI
14. Barker RA. Parkinson's disease and growth factors - are they the answer? Parkinsonism Relat Disord. 2009;15(3):S181-4. doi:10.1016/S1353-8020(09)70810-7. DOI
15. McMahon SB, Bennett DL, Bevan S et al. Inflammatory mediators and modulators of pain. In: Wall and Melzack's Textbook of Pain. London: Elsevier. 2005, p.49-72.
16. Kreiner DS, Matz P, Bono CM et al. Guideline summary review: an evidence-based clinical guideline for the diagnosis and treatment of low back pain. Spine J. 2020;20(7):998-1024. doi:10.1016/j.spinee.2020.04.006. DOI

CONFLICT OF INTEREST

The Authors declare no conflict of interest

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