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EFFECTIVENESS OF ALPHA-LIPOIC ACID AND IPIDACRINE HYDROCHLORIDE IN PREVENTION OF PACLITAXEL-INDUCED PERIPHERAL NEUROPATHY ASSESSED BY ELECTRONEUROMYOGRAPHY OF SUPERFICIAL PERONEAL AND SURAL NERVES

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***Aim*: To investigate the neurofunctional parameters in breast cancer (BC) patients with paclitaxel-induced peripheral neuropathy (PIPN) and to clarify the feasibility of using alpha-lipoic acid (ALA) in combination with the acetylcholinesterase inhibitor ipidacrine hydrochloride (IPD) for its prevention. *Materials and Methods*: 100 BC patients ($T_{1-4}N_{0-3}M_{0-1}$) prescribed for polychemotherapy (PCT) by the AT (paclitaxel, doxorubicin) or ET (paclitaxel, epirubicin) regimens in the neoadjuvant, adjuvant or palliative modes, were enrolled. The patients were randomized into two groups (n = 50 per group): group I treated by PCT only; group II treated with PCT plus the studied PIPN prevention scheme (ALA in combination with IPD). An electroneuromyography (ENMG) of the sensory (superficial peroneal and sural) nerves was performed before PCT, and after the 3 and 6 PCT cycles. *Results:* According to ENMG data, the electrophysiological disturbances in the sensory nerves were manifested in the form of axonal sensory peripheral neuropathy of a symmetrical nature, which was reflected in a decrease in the amplitude of the action potential (AP) of the studied nerves. The AP reduction in sensory nerves was dominant, in contrast to the nerve conduction velocity, which in most patients remained within the reference values, thus evidencing on axonal degeneration rather than demyelination as an underlying cause of PIPN. The ENMG testing of the sensory nerve in the groups of BC patients treated by PCT with paclitaxel with or without PIPN prevention treatment established that the use of ALA in combination with IPD significantly improved AP amplitude, duration and area of the response to the stimulation of the superficial peroneal and sural nerves after 3 and 6 PCT cycles. *Conclusion*: The use of ALA in combination with IPD significantly reduced the severity of damage to the superficial peroneal and sural nerves caused by PCT with paclitaxel and could be recommended for PIPN prevention.**

***Key Words*: paclitaxel, chemotherapy, neuropathy, electroneuromyography, alpha-lipoic acid, acetylcholinesterase inhibitors.**

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Since its antitumor activity was established in the early 1990s, paclitaxel has become one of the most frequently used chemotherapy agents for the treatment of breast cancer (BC), ovarian, and lung cancer [1]. Paclitaxel exerts its therapeutic effect by binding to β-tubulin, impeding the dynamics of microtubules, and leading to their stabilization, which causes arrest of mitosis and apoptosis of malignant cells. The consequence of malfunctioning of the microtubular apparatus consists not only in blocking cell division, but also in the damage of cell skeleton, disruption of cell mobility, intracellular transport, and transduction of transmembrane signals. The mechanism of paclitaxel neurotoxicity is related to its effects on the microtubules of neurons and Schwann cells, which causes axonal degeneration and demyelination [2].

The main dose-limiting side effect of paclitaxel is myelosuppression, but in some cases, especially when using high doses of granulocyte colony-stimulating factors, its neurotoxicity comes to the fore, which limits further use of the drug. Neurological disorders, usually without threatening the patient's life, however, significantly worsen its quality.

In most cases, paclitaxel-induced peripheral neuropathy (PIPN) is manifested by polyneuropathy syndrome of varying severities. Typical symptoms of PIPN include bilateral numbness, neuropathic pain, and paresthesias in the distal extremities with a sock-and-glove distribution. Often, patients complain of spontaneous pain from mechanical and cold aggravators in the upper and/or lower extremities[3]. These symptoms occur in 97% of all paclitaxel-treated patients, especially when the cumulative dose exceeds 1400 mg/m^2 [4]. In general, 60% of all paclitaxel-treated patients experience chronic PIPN [5]. The degree of affection directly depends on the length of the nerve, i.e. long nerves of the upper and lower extremities are primarily affected, as a rule, predominantly the lower ones [6].

The risk of neurotoxicity increases in patients with diabetes and alcohol abuse who have previously received neurotoxic drugs, especially vinca alkaloids and platinum derivatives. Also, it should be noted that PIPN can have a persistent course for months or years after stopping chemotherapy [7].

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Abbreviations used: ALA – alpha-lipoic acid; AP – action potential; BC – breast cancer; CIPN – chemotherapy-induced peripheral neuropathy; ENMG – electroneuromyography; IPD – ipidacrine hydrochloride; NCV – nerve conduction velocity; PCT – polychemotherapy; PHI – practically healthy individuals; PIPN – paclitaxel-induced peripheral neuropathy; SN – sural nerve; SPN – superficial peroneal nerve; TL – terminal latency.

In practice, the treatment of chemotherapy-induced peripheral neuropathy (CIPN) is empirical, mostly unsuccessful, and is usually carried out already at the second (moderate) degree of neuropathy. A typical way to prevent peripheral neuropathy is to reduce the pre-planned dose of paclitaxel or to avoid taxanes, which definitely affects the treatment potential.

It should be noted that of more than 20 drugs studied so far for the prevention of neuropathy, none has shown stable and systematic clinically significant effects in comparison with the placebo group. Unfortunately, there are currently no established clear strategies for the prevention or treatment of CIPN [8–10].

Therefore, we aimed to investigate the features of neurofunctional parameters in BC patients with PIPN and to clarify the feasibility of using alpha-lipoic acid (ALA) in combination with the acetylcholinesterase inhibitor ipidacrine hydrochloride (IPD) for its prevention.

MATERIALS AND METHODS

The research program was approved by the Bioethics Commission of the Ivano-Frankivsk National Medical University. All patients provided informed written consent to participate in the study. The diagnosis of breast cancer (ICD 10: C50) before the start of special treatment was established on the basis of histological confirmation of carcinoma in tumor biopsy. Only patients with no history of chemotherapy with neurotoxic agents, general functional status according to the Eastern Cooperative Oncology Group scale not higher than 1, and an activity index according to the Karnofsky scale not lower than 80 were included in the study.

The criteria for not including patients in the study were: diabetes of any type and severity, the patient's refusal to participate in the study, the general serious condition of the patient due to the presence of concomitant somatic diseases in the stage of decompensation, individual intolerance of the drugs used in the study, the presence of symptoms of pre-existing neuropathy before the start of chemotherapy, spinal pain syndrome, the presence of tunnel syndrome, chronic venous insufficiency of the lower extremities, the presence of distant metastases in the bones of the skeleton or the brain according to the data of the initial examination.

100 patients with BC $T_{1-4}N_{0-3}M_{0-1}$ who were undergoing inpatient treatment at the CNE "Prykarpathian Clinical Oncology Center of the Ivano-Frankivsk Regional Council" in 2014–2022 were enrolled to the study. All patients received from three to six cycles of polychemotherapy (PCT) according to AT or ET regimens: paclitaxel at a dose of 175 mg/m^2 of body surface as a 3-h infusion + doxorubicin 60 mg/m^2 (AT scheme), or paclitaxel at a similar dose + epirubicin 90 mg/m^2 (ET scheme) once every 3 weeks in neoadjuvant, adjuvant or palliative modes. The patients were randomized into two groups (n = 50 per group) who received PCT in combination with the investigated neuropathy prevention scheme (group II) or without neuropathy prevention treatment (group I). There were no statistically significant differences between the two groups in terms of stage of the disease, age, concomitant diseases, composition and regimens of PCT.

In order to determine the normal ranges for the studied electroneuromyography (ENMG) parameters, a group of conventionally healthy women (practically healthy individuals — PHI, n = 30) was examined. This group included those examined individuals who did not complain about their health, were actively involved in work, had no history of chronic somatic and neurological diseases, and during the examination, no deviations from the neurological status were found.

Our scheme for PIPN prevention was the following one: 2 capsules (600 mg) of ALA orally once a day in the morning before meal in combination with IPD — 1 tablet (20 mg) 3 times a day during chemotherapy, except for 2 days before and 4 days after the administration of chemotherapy because of treatment with accompanying drugs and standard premedication these days.

ENMG studies of the sensory nerves of the lower extremities were performed on a computerized two-channel electroneuromyograph "Neuro-EMG-Micro" (Neurosoft, RF) before the beginning, after the 3rd and 6th cycles of PCT with paclitaxel. The function of the superficial peroneal (*nervus peroneus superficialis*) and sural (*nervus suralis*) nerves was studied according to generally accepted methods on both lower limbs, and the average values were calculated.

Electrical stimulation of sensory nerves was performed antidromically. Single rectangular unipolar direct current pulses with variable amplitude were used. The duration of the stimulus was 0.2 ms, the frequency was 3/s, and the intensity of the current was selected individually according to the intensity of the action potential (AP) of the nerve, on average up to 25 μA. The following indicators were studied: amplitude of AP (μV), duration of AP (ms) and area of AP of the nerve (mV · ms), terminal latency (TL) (ms), speed of conduction of excitation (nerve conduction velocity — NCV) by afferent fibers (m/s).

For statistical processing of the data, licensed Microsoft Excel statistical analysis packages were used, in particular, descriptive statistics and graphic image programs. Taking into account the large number of observations and the resulting closeness to the normal distribution, the statistical significance of the data differences in the compared groups was assessed based on the calculation of the Student's *t*-test, and the use of the error-free forecast accuracy table (*p*).

RESULTS

During the ENMG study, 10% of the patients showed signs of a lack of response from sensory nerves before the start and during PCT with paclitaxel, which, according to literature data, is normal in 10–20% of healthy people of various ages, and, in most cases, represents a physiological feature [11–13]. Absence of response from sural nerves (SNs) before the beginning and during PCT with paclitaxel was observed in 2 patients of group I and in 1 patient of group II. Absence of response from the superficial peroneal nerves (SPN) was found in 3 patients of group I and 4 patients of group II.

Examination of the SNs. AP amplitude, duration and area of response to SN stimulation in patients of groups I and II before the start of PCT with paclitaxel did not differ significantly from these indicators in the PHI group ($p > 0.05$) (Table 1). The comparison of the ENMG SN data in group I before PCT with paclitaxel and after 3 PCT cycles revealed a sharp decrease in AP amplitude, duration and area of the response to SN stimulation by 145.36% ($p < 0.001$), 56.99% ($p < 0.001$) and 115.30% ($p < 0.001$) respectively, *vs* 85.18% ($p < 0.001$), 52.76% ($p < 0.001$) and 80.66% ($p < 0.001$) in group II, respectively. This evidenced clinically significant damage to the axon already after 3 cycles of PCT with paclitaxel. The treatment with ALA and IPD in group II led to a significant improvement of the average value of AP amplitude, duration and area of the response to SN stimulation after 3 cycles of PCT with paclitaxel by 28.04% ($p < 0.01$), 12.43% ($p < 0.05$) and 16.73% ($p < 0.05$), respectively.

After 6 cycles of PCT with paclitaxel, the axons of the SN became progressively affected, which was evidenced by a decrease in AP amplitude, duration and area of the response to their stimulation. When compared with the average values after 3 cycles of PCT with paclitaxel, these values decreased in group I by 47.86% ($p < 0.001$), 40.87% ($p < 0.001$) and 67.97% ($p < 0.001$), respectively *vs* 28.04% ($p < 0.05$), 23.29% ($p < 0.001$) and 47.54% ($p < 0.001$) in group II. The use of the studied scheme for PIPN prevention in group II led to a significant improvement of the average values of the AP amplitude, duration and area of the response to stimulation after 6 cycles of PCT with paclitaxel by 47.86% ($p < 0.01$), 28.46% ($p < 0.001$) and 32.89% ($p < 0.01$), respectively.

In order to study the NCV on the distal parts of the nerve, the latent period, or TL is analyzed, that is, the time between the application of irritation to the nerve and the AP occurrence, when the nerve is stimulated at the most distal point available for stimulation. Indicators of TL and NCV reflect the state of myelin and the functional state of fast-conducting fibers, in particular. The average value of TL and NCV of the SN in groups I and II before the start of PCT with paclitaxel did not differ significantly from that in the PHI group ($p > 0.05$). When comparing the results of the ENMG study of the SN before PCT with paclitaxel and after 3 PCT cycles, an increase in TL by 22.44% ($p < 0.001$) was observed in group I, as opposed to 15.05% ($p < 0.001$) in group II. Therefore, the use of ALA and IPD improved the TL index in group II after 3 cycles of PCT by 4.36% ($p < 0.05$). After 6 cycles of PCT compared with 3 cycles of PCT, TL progressively increased in group I by 15.11% ($p < 0.001$), in contrast to 13.08% ($p < 0.001$) in group II. After 6 PCT cycles in group II the TL index improved by 6.23% ($p < 0.05$).

When comparing the ENMG SN data before PCT and after 3 PCT cycles, a decrease in NCV by 20.92% ($p < 0.001$) in group I *vs* 12.88% ($p < 0.001$) in group II was registered. Treatment of patients of group II with ALA and IPD led to a significant improvement in the average NCV values after 3 cycles of PCT with paclitaxel by 5.69% ($p < 0.05$). After 6 cycles of PCT, the average NCV value in group I decreased by 15.74% ($p < 0.001$) compared to that after 3 PCT cycles *vs* 11.32% ($p < 0.01$) in group II. At the same time, in group I, the average NCV value was slightly lower than the lower limit of the norm and amounted to 37.61 ± 0.69 m/s. On the other hand, in group II, the average NCV value of SN remained within the reference range and was 41.33 ± 1.12 m/s. Despite the slightly expressed electrophysiological changes in the myelin of the SNs, the use of the studied scheme of PIPN prevention led to a statistically significant

Table 1. Indicators of ENMG examination of sural nerves in BC patients

ENMG indicators	ENMG values in the BC patients						
	PHI, n = 30	Group I before PCT, n = 48	Group II before PCT, n = 49	Group I , 3 PCT cycles, n = 48	Group II, 3 PCT cycles, n = 49	Group I , 6 PCT cycles, n = 37	Group II , 6 PCT cycles, n = 35
Nerve action potential, μV	11.76 ± 0.40	11.90 ± 0.44	11.50 ± 0.38	4.85 ± 0.18[a]	6.21 ± 0.42[b, c]	3.28 ± 0.13[a, c]	4.85 ± 0.51[b, d, e]
Duration of response to nerve stimulation, ms	6.31 ± 0.16	6.06 ± 0.25	6.63 ± 0.23	3.86 ± 0.17[a]	4.34 ± 0.15[b, c]	2.74 ± 0.14[a, c]	3.52 ± 0.17[b, d, e]
Area of response to nerve stimulation, mV·ms	16.10 ± 0.48	16.60 ± 0.48	16.26 ± 0.63	7.71 ± 0.28[a]	9.00 ± 0.43[b, c]	4.59 ± 0.25[a, c]	6.10 ± 0.49[b, d, e]
Terminal latency, ms	2.55 ± 0.02	2.54 ± 0.02	2.59 ± 0.02	3.11 ± 0.03[a]	2.98 ± 0.05[b, c]	3.58 ± 0.05[a, c]	3.37 ± 0.09[b, d, e]
NCV by sensitive fibers, m/s	53.27 ± 0.52	52.64 ± 0.60	51.94 ± 0.58	43.53 ± 0.65[a]	46.01 ± 0.78[b, c]	37.61 ± 0.69[a, c]	41.33 ± 1.12[b, d, e]

Notes: [a] – the difference is significant compared to the indicators in group I before chemotherapy ($p < 0.05$); [b] – the difference is significant compared to the indicators in group II before chemotherapy ($p < 0.05$); [c] – the difference is significant compared to the indicators in group I after 3 PCT cycles ($p < 0.05$); [d] – the difference is significant compared to the indicators in group II after 3 PCT cycles ($p < 0.05$); [e] – the difference is significant compared to the indicators in group I after 6 PCT cycles ($p < 0.05$).

improvement in the NCV index after 6 cycles of PCT with paclitaxel by 9.89% ($p < 0.01$).

Examination of SPNs. It should be noted that during the ENMG examination of the SPNs the changes found are similar to those of the SNs. AP amplitude, duration and area of the response to SPN stimulation in groups I and II before the start of PCT with paclitaxel did not significantly differ from the average values in the PHI group ($p > 0.05$) (Table 2). When comparing the ENMG indicators before PCT and after 3 PCT cycles, a sharp decrease in AP amplitude, duration and area of response to SPN stimulation was observed — by 143.81% ($p < 0.001$), 110.37% ($p < 0.001$) and 118.20% ($p < 0.001$), respectively, in group I *vs* 100.20% ($p < 0.001$), 79.90% ($p < 0.001$) and 82.08% ($p < 0.001$), respectively, in group II. So, the use of ALA and IPD in group II led to a significant improvement in the average values of AP amplitude, duration and area of the response to SPN stimulation after 3 cycles of PCT with paclitaxel by 21.03% ($p < 0.01$), 16.13% ($p < 0.05$) and 15.56% ($p < 0.05$), respectively.

After 6 cycles of PCT with paclitaxel, the axons of the SPN became progressively affected, which was evidenced by a decrease in AP amplitude, duration and area of the response to their stimulation; compared with corresponding indicators after 3 cycles of PCT the average values in group I decreased by 54.78% ($p < 0.001$), 79.79% ($p < 0.001$) and 56.19% ($p < 0.001$), respectively *vs* 46.40% ($p < 0.001$), 66.52% ($p < 0.001$) and 46.28% ($p < 0.001$) in group II, respectively.

The use of the studied scheme for the PIPN prevention led to a significant improvement of the average values of the AP amplitude, duration and area of the response to the SPN stimulation in group II after 6 cycles of PCT by 27.96% ($p < 0.05$), 25.38% ($p < 0.05$) and 23.39% ($p < 0.01$), respectively.

The average values of TL and NCV of the SPN in groups I and II before the start of PCT with paclitaxel did not differ significantly from the indicators in the PHI group ($p > 0.05$). When comparing the ENMG data before PCT and after 3 PCT cycles, an increase in TL by 23.82% ($p < 0.001$) was observed in group I, as opposed to 13.75% ($p < 0.001$) in group II. Thus, the use of ALA and IPD in group II resulted in the improvement of TL index by 6.59% ($p < 0.01$) after 3 PCT cycles and its further improvement by 8.96% ($p < 0.01$) after 6 cycles of PCT. In group I the TL indicator progressively increased after 6 cycles of PCT compared with that after 3 cycles of PCT by 8.59% ($p < 0.05$), as opposed to 6.22% ($p < 0.01$) in group II.

The average NCV values of the SPN in groups I and II before the start of PCT with paclitaxel did not differ significantly from the indicators in the PHI group ($p > 0.05$). The NCV values before and after 3 PCT cycles decreased by 20.79% ($p < 0.001$) in group I, as opposed to 12.14% ($p < 0.001$) in group II. It should be noted that the use of ALA and IPD in group II led to a significant improvement in the average NCV value of the SPN after 3 cycles of PCT by 8.08% ($p < 0.01$). After 6 PCT cycles, the average NCV value of the SPN in group I decreased by 10.02% ($p < 0.01$) compared to 3 cycles of PCT *vs* 9.52% ($p < 0.01$) in group II. At the same time, in group I the average NCV index of the SPN was slightly lower than the lower limit of the norm and was 38.02 ± 0.99 m/s. In group II this indicator remained within the reference range and was 41.28 ± 1.05 m/s. Despite the slightly expressed electrophysiological changes in the myelin of the SPN, the use of the studied scheme of PIPN prevention in group II led to significant improvement of the NCV by 8.57% ($p < 0.05$).

DISCUSSION

The "gold standard" of the objective evaluation of CIPN is ENMG, which allows measuring the amplitude and conduction velocity of total sensory and motor APs. Nerve conduction studies provide valuable information about the degree and extent of axonal degeneration in patients with CIPN. A decrease in the amplitude of the total sensory AP is a frequent finding in CIPN, which in turn confirms the presence of axonal sensory neuropathy in patients [14–17].

The electrophysiological disturbances in the sensory nerves that we observed were manifested in the form of axonal sensory peripheral neuropathy of symmetric nature, which was reflected as a decrease in the AP amplitude of the superficial peroneal and SNs. The reduction

Table 2. Indicators of ENMG examination of superficial peroneal nerves in the BC patients

ENMG indicators	ENMG values in the BC patients						
	PHI, n = 30	Group I before PCT, n = 47	Group II before PCT, n = 46	Group I, 3 PCT cycles, n = 47	Group II, 3 PCT cycles, n = 46	Group I, 6 PCT cycles, n = 36	Group II, 6 PCT cycles, n = 32
Nerve action potential, μV	9.56 ± 0.20	9.85 ± 0.19	9.79 ± 0.17	4.04 ± 0.14[a]	4.89 ± 0.25[b, c]	2.61 ± 0.14[a, c]	3.34 ± 0.24[b, d, e]
Duration of response to nerve stimulation, ms	7.01 ± 0.18	7.30 ± 0.23	7.25 ± 0.28	3.47 ± 0.13[a]	4.03 ± 0.18[b, c]	1.93 ± 0.09[a, c]	2.42 ± 0.18[b, d, e]
Area of response to nerve stimulation, mV · ms	14.85 ± 0.47	14.86 ± 0.45	14.33 ± 0.49	6.81 ± 0.25[a]	7.87 ± 0.37[b, c]	4.36 ± 0.24[a, c]	5.38 ± 0.29[b, d, e]
Terminal latency, ms	2.39 ± 0.02	2.35 ± 0.02	2.40 ± 0.02	2.91 ± 0.05[a]	2.73 ± 0.03[b, c]	3.16 ± 0.08[a, c]	2.90 ± 0.05[b, d, e]
NCV by sensitive fibers, m/s	51.24 ± 0.63	50.53 ± 0.79	50.70 ± 0.65	41.83 ± 0.82[a]	45.21 ± 0.76[b, c]	38.02 ± 0.99[a, c]	41.28 ± 1.05[b, d, e]

Notes: [a] – the difference is significant compared to the indicators in group I before chemotherapy ($p < 0.05$); [b] – the difference is significant compared to the indicators in group II before chemotherapy ($p < 0.05$); [c] – the difference is significant compared to the indicators in group I after 3 PCT cycles ($p < 0.05$); [d] – the difference is significant compared to the indicators in group II after 3 PCT cycles ($p < 0.05$); [e] – the difference is significant compared to the indicators in group I after 6 PCT cycles ($p < 0.05$).

of AP in sensory nerves was dominant, in contrast to the NCV, which in most patients remained within the reference values. The AP of a sensory nerve reflects the number of axons conducting impulses, while the NCV reflects the degree of myelination in the axons. In patients with PIPN, the decrease in AP usually precedes the changes in NCV, which reflects the dominant axonopathy [18–20]. Thus, the changes in the AP amplitude and NCV of the sensitive fibers of the superficial peroneal and SNs detected by us indicate deeper disturbances of the axon with a relatively stable functional state of myelin.

In practice, it is impossible to make a clear correlation between the data of the neurological examination of patients and ENMG changes in sensory nerves. However, in our earlier study, we established the effectiveness of ALA and IPD treatment for the PIPN prevention in patients with BC by the Total Neuropathy Score. Our data on clinical and electrophysiological changes in patients who received PCT with paclitaxel indicated the presence of symmetric, axonal, mainly distal sensory neuropathy [21]. Electrophysiological disturbances were reflected in a decrease in the AP amplitude of the SNs and the fading of responses during the neurological examination of patients. Our results did not differ from the clinical and electrophysiological profile of PIPN reported elsewhere, which showed that taxanes cause symmetrical, predominantly sensory, distal axonopathy with episodic motor dysfunction [15, 22].

Currently, the pathophysiological mechanism of PIPN is not completely studied and understood. However, the neurophysiological abnormalities in sensory nerves demonstrated in our study confirm the generally accepted theory of PIPN pathogenesis, which states that the basis is axonal degeneration (not demyelination) caused by damage to dorsal root ganglia, dysfunction of microtubules inside axons, impaired energy production by mitochondria, and the direct damaging effect of chemotherapy on axons in the distal terminals [23–27]. The data of scientific studies suggest that inhibition of tubulin depolarization occurs not only in axons, but also, partially, in Schwann cells [27–36]. According to the results of the ENMG study of the sural and SPNs, we can conclude that damage to the myelin sheaths does occur in PIPN, but it is mild and clinically insignificant.

In conclusion, by determining significant differences in the ENMG indicators of sensory nerve parameters between the studied groups, we established that the use of ALA in combination with the inhibitor of acetylcholinesterase IPD significantly reduced the severity of damage to the SPNs and SNs caused by PCT with paclitaxel. The ENMG parameters of the sensory nerves in the patients treated with ALA+IPD were significantly better after 3 and 6 PCT cycles compared to those in the group treated with PCT only. The combination of the ALA and IPD used in our study and substantiated by scientific data on its successful use for the prevention of CIPN and peripheral neuropathies of other genesis [37–42], could be recommended for the prevention of PIPN.

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ОЦІНКА ЕФЕКТИВНОСТІ ЗАСТОСУВАННЯ АЛЬФА-ЛІПОЄВОЇ КИСЛОТИ ТА ІПІДАКРИНУ ГІДРОХЛОРИДУ ДЛЯ ПРОФІЛАКТИКИ ПАКЛІТАКСЕЛ-ІНДУКОВАНОЇ ПЕРИФЕРИЧНОЇ НЕЙРОПАТІЇ ЗА ДАНИМИ ЕЛЕКТРОНЕЙРОМІОГРАФІЧНОГО ДОСЛІДЖЕННЯ ПОВЕРХНЕВИХ МАЛОГОМІЛКОВИХ ТА ЛИТКОВИХ НЕРВІВ

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***Мета*:** дослідити особливості нейрофункціональних параметрів у хворих на рак грудної залози з паклітаксел-індукованою периферичною нейропатією та з'ясувати доцільність застосування альфа-ліпоєвої кислоти в комбінації з іпідакрину гідрохлоридом для її профілактики. ***Матеріали та методи*:** 100 хворих на рак грудної залози $T_{1-4}N_{0-3}M_{0-1}$, яким була показана поліхіміотерапія за схемою АТ (паклітаксел, доксорубіцин) або ЕТ (паклітаксел, епірубіцин), рандомізовано у дві групи. Перша група (n = 50) — хворі на рак грудної залози $T_{1-4}N_{0-3}M_{0-1}$, які отримали від трьох до шести циклів поліхіміотерапії

за схемою АТ або ЕТ у неоад'ювантному, ад'ювантному або паліативному режимі без застосування досліджуваної схеми профілактики нейропатії (альфа-ліпоєва кислота в комбінації з іпідакрину гідрохлоридом). Друга група (n = 50) — хворі на рак грудної залози $T_{1-4}N_{0-3}M_{0-1}$, які отримали від трьох до шести циклів поліхіміотерапії за вказаною схемою із використанням досліджуваної схеми профілактики нейропатії. Проведено електронейроміографічне дослідження сенсорних (поверхневі малогомілкові та литкові) нервів до початку хіміотерапії, після 3-го та 6-го циклів поліхіміотерапії. ***Результати*:** Виявлені нами електрофізіологічні порушення у сенсорних нервах проявлялися у вигляді аксональної сенсорної периферичної нейропатії симетричного характеру, що відображалося у зниженні амплітуди потенціалу дії поверхневих малогомілкових та литкових нервів. Зниження потенціалу дії у сенсорних нервах було домінантним, на відміну від швидкості проведення збудження, яка в більшості пацієнтів залишалася в межах референтних значень. Це підтверджує найбільш поширену теорію патогенезу паклітаксел-індукованої периферичної нейропатії, яка стверджує, що в її основі лежить аксональна дегенерація, а не демієлінізація. Також шляхом визначення статистично значущих відмінностей у показниках електронейроміографічного тестування сенсорних нервів пацієнтів між досліджуваними групами встановлено, що застосування препарату альфа-ліпоєвої кислоти в поєднанні з інгібітором ацетилхолінестерази — іпідакрину гідрохлоридом вагомо зменшує тяжкість ураження поверхневих малогомілкових та литкових нервів при застосуванні поліхіміотерапії з паклітакселом, судячи з показників амплітуди потенціалу дії, тривалості та площі відповіді на стимуляцію. ***Висновки*:** Застосування альфа-ліпоєвої кислоти в поєднанні з іпідакрину гідрохлоридом дозволяє зменшити тяжкість ураження поверхневих малогомілкових та литкових нервів, спричинені поліхіміотерапією з паклітакселом.

***Ключові слова*:** паклітаксел, хіміотерапія, нейропатія, електронейроміографія, альфа-ліпоєва кислота, інгібітори ацетилхолінестерази.