EVALUATION OF THE EFFICIENCY OF ALPHA-LIPOIC ACID AND IPIDACRINE HYDROCHLORIDE FOR THE PREVENTION OF PACLITAXEL-INDUCED PERIPHERAL NEUROPATHY ACCORDING TO THE TOTAL NEUROPATHY SCORE

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Aim: To evaluate the efficacy of combination of alpha-lipoic acid and acetylcholinesterase inhibitor (ipidacrine hydrochloride) to prevent the development and improve the course of paclitaxel-induced peripheral neuropathy (PIPN) in patients with breast cancer according to the Total Neuropathy Score. Materials and Methods: 32 patients with breast cancer T1-4N0-3M0 received six cycles of polychemotherapy according to the AT scheme (paclitaxel, doxorubicin) or ET scheme (paclitaxel, epirubicin). Patients were randomized into two groups — without (group I) or with (group II) medication for prevention of neuropathy. A comprehensive neurological examination of patients was performed according to all ten parameters of the Total Neuropathy Score before chemotherapy, and after third and sixth cycles of chemotherapy. Each parameter was evaluated from 0 (no deficit) to 4 (no function/the most severe deficit). The scores obtained from the scale were summarized to obtain a total score from 0 to 40. Results: The use of alpha-lipoic acid in combination with an acetylcholinesterase inhibitor (ipidacrine hydrochloride) significantly reduces the symptoms and severity of PIPN. The manifestations of PIPN in patients of the control group were significantly more severe compared to the group in which the study drugs were used. The average severity of neuropathy after 3 and 6 cycles was 1.75 and 2.62 in group I, and 1.12 and 1.62 — in group II, respectively (improvement by 15.75% (p < 0.05) and 25.00% (p < 0.001) after 3 and 6 cycles). Conclusions: Proposed combination of alpha-lipoic acid and ipidacrine hydrochloride led to a statistically significant reduction in the severity of PIPN, and thus to improvement of the functional capacity and quality of life of patients.

Key Words: paclitaxel, chemotherapy, neuropathy, Total Neuropathy Score, alpha-lipoic acid, acetylcholinesterase inhibitors.

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Paclitaxel is widely used to treat a number of solid tumors, including breast, ovarian and lung cancers. The drug is classified as a microtubule binder [1–3]. Its main antitumor effect is mediated by disruption of the dynamics of mitotic spindles and microtubules in malignant cells, which leads to their apoptosis [4–6]. Paclitaxel causes dose-dependent, mostly sensory distal axonopathy. Cumulative doses of paclitaxel exceeding 1000 mg/m² are closely associated with the development of chemotherapy-induced peripheral neuropathy (CIPN) [7]. Typical symptoms of peripheral neuropathy are bilateral numbness, paresthesia, neuropathic pain, and spontaneous pain from mechanical and cold stimuli in the upper and/or lower extremities [8, 9]. Paclitaxel-induced peripheral neuropathy (PIPN) may be persistent and keep on for months or years after cessation of the chemotherapy.

Despite numerous scientific studies, well-known means of prevention and treatment of taxane-induced peripheral neuropathy have not been invented, and all the medicines studied so far have not been effective. None of the 19 studied drugs for the prevention of neuropathy showed stable and systematic clinically significant results compared with the placebo group [10, 11]. Therefore, the development of peripheral neuropathy during paclitaxel therapy often leads to a reduction in chemotherapy dosages or early cessation of successful chemotherapy, thus adversely affecting the quality of life and effectiveness of treatment of patients with malignancies [12–14].

The exact mechanism of PIPN is not fully understood [15, 16]. In recent years, oxidative stress has been considered an important factor responsible for CIPN [17–19]. Neurons are more sensitive to oxidative stress due to low activity of antioxidant enzymes [20]. Experimental studies have confirmed the availability of data on PIPN associated with oxidative stress [21]. Alpha-lipoic acid (ALA) has been mentioned to reduce the symptoms of polyneuropathy caused by polychemotherapy (PCT) with docetaxel and cisplatin. The neuroprotective mechanism of ALA was associated with a decrease in oxidative stress [22, 23]. In addition, ALA protects sensory neurons due to its antioxidant and mitochondrial regulatory functions in the in vitro model of CIPN [24]. As a “universal antioxidant”, ALA can alleviate the course of diabetic neuropathy and CIPN caused by various chemotherapeutics, however, it is still unclear whether ALA may have a neuroprotective effect in PIPN, due to different pathogenetic mechanisms of these complications [25, 26].

It has been shown that acetylcholinesterase inhibitors alter neurotransmitters which are responsible for reducing regulation of glutamate transporters, thus alleviating neurotoxicity of the latter, which in turn protects nerve cells. This mechanism opens up a new pathway for neuroprotection, which should be considered for protection of peripheral nerves in CIPN [27, 28]. Scientific studies have reported the involvement...
of acetylcholine signals in oxaliplatin- and paclitaxel-induced lesions of the nervous system [29–34]. Acetylcholinesterase inhibitors, especially such drug as donepezil which is used in Alzheimer’s disease, have shown their effectiveness in preventing neuronal degeneration in in vitro and in vivo models of oxaliplatin-induced CIPN [35].

It should be noted that cholinesterase inhibitors and ALA did not affect the antitumor activity of the studied chemotherapeutics, and therefore they are considered to be safe drugs for use in clinical settings.

**MATERIALS AND METHODS**

The research program was approved by the Bioethics Commission of Ivano-Frankivsk National Medical University. All patients were informed about the examination and specifics of treatment and gave their written consent to participate in the study. 32 patients with breast cancer (BC), T1–4N0–3M0, who have been hospitalized at the Precarpathian Clinical Oncology Center from 2014 to 2021 were included into the study. In all patients, diagnosis of BC was confirmed histologically before the start of special treatment. 13 of patients (40.62%) were at stage II, 19 (59.37%) at stage III. There was no significant difference between the two groups by stage distribution. The mean age of patients was 57.88 ± 2.44 years in group I and 52.88 ± 3.22 years in group II, respectively.

The parameters of patients’ inclusion in the study were the Eastern Cooperative Oncology Group Scale of Performance Status (0–1), the Karnofski Performance Scale (80–100%), and the absence of data on chemotherapy with neurotoxic agents in the anamnesis. All patients enrolled in the study did not previously receive chemotherapy. The criteria for exclusion from the study were the following: diabetes mellitus of any type and severity, patient’s refusal to participate in the study, patient’s poor general condition due to the concomitant somatic diseases in the stage of decompensation, including liver, kidneys, cardiovascular system, etc., individual intolerance to the drugs used in the study, any psychological disorders that impede following the procedures provided by the study, symptoms of pre-existing neuropathy before chemotherapy (hereditary, paraneoplastic, etc.), vertebrogenic pain syndrome, tunnel syndrome (carpal, tarsal, fibular), chronic venous insufficiency of the lower extremities.

All patients received six cycles of chemotherapy in the scheme of paclitaxel at a dose of 175 mg/m² of body surface in the form of 3 h infusion, doxorubicin 60 mg/m² of body surface or epirubicin 90 mg/m² of body surface once in 3 weeks in neoadjuvant regimen. Patients with BC receiving PCT in this regimen were randomized into two groups. All patients received six cycles of PCT according to the scheme AT (paclitaxel, doxorubicin) or ET (paclitaxel, epirubicin) in the neoadjuvant regimen. Group I (n = 16) did not receive additional medication for prevention of neuropathy. Group II (n = 16) received oral medication of ALA 2 capsules (600 mg) once a day in the morning before meals, in combination with acetylcholinesterase inhibitor (ipidacrine hydrochloride) (20 mg) 3 times daily during chemotherapy, except 2 days before chemotherapy and 4 days after it because of taking concomitant medication and standard premedication.

Patients were examined according to ten parameters of the Total Neuropathy Score (TNS) before chemotherapy, after the third and sixth cycles of chemotherapy. The neurological examination was conducted by a neurologist who performed both clinical and electrophysiological studies. TNS is a rating scale developed in 1994 by Johns Hopkins University; it has a wide range of values which allows accurately grade the severity of CIPN and has a high intra-expert and inter-expert reliability [36]. The ten parameters that make up TNS include assessment of clinical symptoms (sensory, motor and autonomic), objective signs of loss of sensitivity (pain, vibration sensitivity and perception), assessment of deep tendon reflexes and neurophysiological parameters (amplitude of sensory action potential of n. suralis and n. peroneus communis).

All parameters are rated from 0 (no deficit) to 4 (no function/the most severe deficit). Scores are summed to obtain a total score that can range from 0 to 40. A score of 0 means no peripheral neuropathy; 1–9 corresponds to mild peripheral neuropathy; 10–19 means moderate degree, and score > 20 corresponds to severe peripheral neuropathy. TNS and its modified versions have been approved as a clinical tool for assessing the severity of systemic neuropathies, such as diabetic neuropathy and CIPN [37–39].

Sensory symptoms were first assessed, and patients were asked if they experienced numbness, tingling, or pain in their extremities. If the patient responded positively, a score in the range of 0–4 was established based on the extent to which these symptoms spread proximally: in the phalanges of the hands and/or feet — 1 point, up to ankles and/or wrists — 2 points, up to knees and/or elbows — 3 points, above the knees and/or elbows — 4 points. To assess motor symptoms, patients were asked if they experienced limb weakness. If the patient felt muscle weakness, this symptom was evaluated from 0 to 4, based on the difficulties experienced by the patient: insignificant — 1 point, moderate — 2 points, need for assistance — 3 points, paralysis — 4 points.

Autonomic symptoms that occur as a result of damage to the autonomic nerve fibers are divided into visceral and autonomic-vasomotor ones. Visceral symptoms due to autonomic neuropathy can be represented by cardiovascular (resting tachycardia, orthostatic hypotension), gastrointestinal (motility disorders), urogenital (difficult urination) forms, respiratory disorders, sweating disorders (unexplained increased sweating), abnormal pupillary responses. Vegetative-vasomotor symptoms are characterized by changes in the temperature of the skin of the feet, marble color, increased dermographism. Autonomic symptoms, depending
on the patient’s number of autonomic dysfunctions, were evaluated from 0 to 4 points.

Pain sensitivity was assessed by conventional methods using a sterile needle with a diameter of 18 G (sharp stimulus) and a sterile paper clip, with one tip bent at 90° relative to the base, to form a probe (blunt stimulus). Pain sensitivity was assessed in the big toe, gradually moving proximally to the knees and elbows until the patient reported that the object was sharp. Pain sensitivity was graded similarly to sensory symptoms.

A 128 Hz vibrating tuning fork was used to assess vibration sensitivity. It was determined by the conventional method in the big toe, middle part of the foot and medial malleolus of the ankle joint, and then in the middle third of the fibula and patella. Vibration sensitivity of the upper limb was tested first on the distal interphalangeal joint of the index finger, and then on the styloid process of the ulna and the lateral epicondyle of the elbow joint. Vibration sensitivity was graded similarly to sensory symptoms and pain sensitivity.

The strength of muscle contraction was assessed by manual muscle testing during ankle dorsiflexion of the talocrural joint. Mild weakness corresponds to 1 point, moderate weakness — to 2 points, severe weakness — to 3 points, and paralysis — to 4 points.

Assessment of deep tendon reflexes was performed first in the ankle (Achilles reflex), and then in the knee (knee reflex) according to conventional methods. If the induction of the Achilles reflex required reinforcement, this corresponded to a score of 1 point; if the Achilles reflex was absent — 2 points. If reinforcement was required for induction of the knee reflex, this corresponded to a score of 3 points, if the knee reflex was not determined — 4 points.

To determine the threshold of vibration perception in quantitative sensory testing, the Rydel — Seiffer tuning fork (Fig. 1) was used. The vibration thresholds obtained with the Rydel — Seiffer tuning fork showed a strong correlation with the data of an electronic device for measuring vibration perception, such as the Vibrameter (Somedic, Stockholm, Sweden) [40–42]. The upper limit of the norm of vibration perception for the distal interphalangeal joint of the index finger and for the first metatarsal joint of the foot was such as follows: for patients aged below 40 years — 6 points and for patients aged over 60 — 4 points [43–45]. The gradation of vibration perception for the upper and lower extremities is the following: 0 degree — from normal to 125% of the upper limit of the norm; 1st degree — from 126 to 150% of the upper limit of the norm; 2nd degree — from 151 to 200% of the upper limit of the norm; 3rd degree — from 201 to 300% of the upper limit of the norm; 4th degree — more than 300% of the upper limit of the norm.

Electroneuromyographic examination of peripheral nerves of the lower and upper extremities was performed on a computerized, dual-channel electromyograph “Neuro-EMG-Micro” (“Neurosoft”, Russian Federation). In the case of TNS, only the amplitude of the action potential of motor fibers of the peroneal nerve (n. peroneus communis) and the sensory fibers of the sural nerve (n. suralis) in both extremities is taken into account followed by averaging of the data. According to the TNS rating scale, a score from 0 to 4 was assigned depending on the extent to which the amplitude of the action potential fell below the lower limit of normal according to age. For example, a score of 0 corresponds to an amplitude of nerve conduction of 96% or more than the expected norm for the patient’s age; a score of 1 corresponds to an amplitude from 76 to 95% of the lower limit of norm; 2 points — from 51 to 75% of the lower limit of norm; 3 points — from 26 to 50% of the lower limit of norm; 4 points — from 0 to 25% of the lower limit of norm. The lower limit of the range of normal amplitude of the action potential for the sural nerve according to the age is the following: 0–20 years — 12 μV, 21–40 years — 9 μV, 41–60 years — 7 μV, 61–80 years — 6 μV. The lower limit of the range of normal amplitude of the compound action potential for the peroneal nerve during stimulation in the area of the tarsus and the head of the fibula is 2.0 μV.

The licensed Microsoft Excel statistical analysis packages, including descriptive statistics and graphical imaging programs, were used for statistical processing of the material. Statistical significance of the difference was determined using non-parametric criteria. A pairwise factor correlation analysis was performed by calculating the Pearson correlation coefficient (r).

RESULTS

According to the TNS, the PIPN in patients from the control group was significantly more severe compared to the group in which the studied drugs were used (Fig. 2). The average severity of neuropathy after 3 and 6 cycles was 1.75 and 2.62 in group I, and 1.12 and 1.62 in group II, respectively (improvement by 15.75% (p < 0.05) and 25.00% (p < 0.001) after 3 and 6 cycles).

Sensory symptoms presented on the TNS scale include numbness, paresthesia, and neuropathic pain. Sensory symptoms are very common among patients with PIPN. Injuries in PIPN directly depend on the length of the nerve, i.e. long nerves of the upper and

Fig. 1. The graduated Rydel — Seiffer tuning fork
lower extremities are affected in the first turn. Most patients were diagnosed with asymmetric lesions, usually in the tips of the toes and then, with increasing cumulative dose of paclitaxel — in the fingers, although sensory symptoms often appeared simultaneously in the upper and lower extremities. Subsequently, the symptoms spread in the proximal direction to the lower surface of the feet and palms. The symmetrical nature of sensory symptoms with a predominance of “gloves and stockings” distribution was observed after the third cycle of PCT with paclitaxel. The average severity of sensory symptoms after 3 and 6 cycles of PCT with paclitaxel was 1.75 and 2.62 in group I as compared to 1.12 and 1.62 in group II (improvement by 15.75% ($p < 0.01$) and 25% ($p < 0.01$), respectively).

In most cases, the neurotoxicity of paclitaxel is manifested by polyneuropathy syndrome of varying severity. Paclitaxel mainly causes sensory neuropathy, however, in our study, there were cases of sensorimotor neuropathy with moderate heaviness in muscles, both distal and proximal, or more generalized character. Weakness of idiosyncratic nature occurred at different stages of treatment and had a variable course. The most common symptoms were difficulty in climbing up stairs and getting up from a chair or toilet seat. There was no statistically significant improvement in motor symptoms of patients of study group II. The average severity of motor symptoms after 3 and 6 cycles of PCT with paclitaxel was 1.68 and 1.62 for group I patients compared with 0.56 and 1.18 for group II ($p > 0.05$). Also, there was no statistically significant improvement in muscle contraction in patients of study group II. The average severity of muscle weakness after 3 and 6 cycles of PCT with paclitaxel is 0.62 and 1.31 in group I as opposed to 0.43 and 1.0 in group II ($p > 0.05$). In most cases, the symptoms of motor neuropathy and decreased muscle contraction preceded a decrease in the amplitude of the compound action potential in the peroneal nerve (n. peroneus communis); the latter mostly occurred after 6 cycles of PCT with paclitaxel. The average degree of decrease in the amplitude of the compound action potential in the peroneal nerve after 3 and 6 cycles of PCT is 0.18 and 0.81 in group I as opposed to 0.12 and 0.43 in group II ($p > 0.05$). Symptoms associated with changes in autonomic nervous system function were rare in our study. Symptoms of autonomic dysfunction in patients in the study groups were manifested by orthostatic hypotension and/or constipation. The average severity of autonomic symptoms after 3 and 6 cycles of PCT with paclitaxel was 0.12 and 0.25 in group I as opposed to 0.0 and 0.12 in group II (improvement by 3.0% and 3.25%, $p > 0.05$).

The neurological examination of patients showed progressive loss of reflexes, mainly of the Achilles tendon, which was often the first manifestation of PIPN. We found a direct and strong correlation between the degree of reduction of deep tendon reflexes and the severity of sensory symptoms in patients of group I after 3 cycles of PCT with paclitaxel ($r_{xy} = 0.83 \pm 0.15$); in patients of group I — after 6 cycles of PCT with paclitaxel ($r_{xy} = 0.78 \pm 0.17$); in group II — after 6 cycles of PCT with paclitaxel ($r_{xy} = 0.83 \pm 0.15$) and direct correlation of the average strength in group II after 3 cycles of PCT with paclitaxel ($r_{xy} = 0.53 \pm 0.23$) with the probability of error-free prediction $p < 0.05$. The average severity of decreased deep tendon reflexes after 3 and 6 cycles of PCT with paclitaxel

Fig. 2. The difference in the severity of chemotherapy-induced neuropathy between the control (group I) and the study (group II) groups according to the TNS scale. *A score of 0 indicates the absence of peripheral neuropathy, a score of 1–9 corresponds to mild degree (grade I), a score of 10–19 — moderate degree (grade II), and a score > 20 — severe degree (grade III) of CIPN.
was 1.37 and 2.37 in group I as opposed to 0.56 and 1.25 in group II (improvement by 20.25% \( p < 0.01 \)) and 28.00% \( p < 0.01 \), respectively.

The amplitude of the sensory potential of the sural nerve \( (n. \text{suralis}) \) was determined on both lower extremities followed by averaging of the data. The average severity of the decrease in the amplitude of the sensory potential of the sural nerve after 3 and 6 cycles of PCT with paclitaxel is 2.18 and 3.25 in group I as opposed to 1.37 and 2.18 in group II (improvement by 20.25% \( p < 0.05 \)) and 26.75% \( p < 0.05 \) after 3 and 6 cycles (Fig. 3).

There was a progressive decrease in pain sensitivity of symmetrical nature with a predominant localization in the distal part of the lower extremities. The average reduction in pain sensitivity after 3 and 6 cycles of PCT with paclitaxel is 0.68 and 1.37 in group I as opposed to 0.18 and 0.62 in group II (improvement by 12.5% \( p < 0.05 \)) and 18.75% \( p < 0.05 \), respectively).

In patients of both groups, there was a progressive loss of vibration sensitivity of symmetrical nature with a predominant localization in the distal parts of the lower extremities. Patients in the control group suffered from significantly more severe degrees of reduction of vibration sensitivity compared with the group, in which the studied drugs were used, namely: the average assessment of the severity of reduced vibration sensitivity after 3 and 6 cycles was 1.62 and 2.62 in the first group as opposed to 0.87 and 1.5 in the second group (improvement by 18.75% \( p < 0.05 \)) and 28% \( p < 0.001 \), respectively).

When determining the threshold of vibration perception, a decrease in the average vibration perception after 3 and 6 cycles of PCT with paclitaxel is 1.68 and 2.5 in group I as opposed to 1.12 and 1.75 in group II (improvement by 14% \( p = 0.054 \)) and 18.75% \( p = 0.05 \), respectively.

**DISCUSSION**

The obtained data on clinical and electrophysiological changes in patients receiving PCT with paclitaxel indicated the signs of symmetrical, axonal, mostly distal sensory neuropathy. There were no signs of demyelination, indirectly suggesting Schwann cell injury rather than axon damage. The data that we received did not differ from the clinical and electrophysiological profile of PIPN, which was reported in previous studies that showed that taxanes cause symmetrical, predominantly sensory, distal axonopathy with episodic motor dysfunction [46, 47]. However, small or often no changes in the amplitude of the compound action potential of the peroneal nerve \( (n. \text{peroneus communis}) \) in combination with pronounced variable symptoms of motor dysfunction and muscle weakness indicate the idiosyncratic nature of the latter. Insufficiency of the blood-encephalic barrier in the dorsal root sensory ganglia may be the cause of selective sensory toxicity of paclitaxel compared to motor neurons in the anterior horns of the spinal cord, which justifies the lack of motor conduction in our study [48, 49]. Electrophysiological disorders were manifested in the form of axonal sensory peripheral neuropathy, which was reflected in a decrease in the amplitude of the action potential of sensory nerves

![Fig. 3](image-url)
or attenuation of responses in the study of sensory conduction in patients. The revealed changes in the peripheral nervous system are a reflection of generally accepted theories of the mechanism of peripheral neuropathy as a result of paclitaxel usage, namely: axonal degeneration, in contrast to demyelination, which is caused by the injury of the dorsal spinal root ganglia and, as a consequence, dysfunctional disorders of the microtubules of axons with inhibition of both anterograde and retrograde axonal transport, mitochondrial neurotoxic damage, which in turn leads to chronic energy deficiency in axons and the direct effect of chemotherapy on distal nerve endings [50–52].

Previous studies of PIPN have examined various doses, regimens and combinations of paclitaxel with other, often neurotoxic, chemotherapeutic agents. In addition, a modified, reduced and clinical version of the TNS was used in most studies. Thus, the relevance of these scientific papers to our study is difficult to assess.

Prevention and treatment of peripheral neuropathy caused by many commonly used chemotherapeutic agents, such as taxanes and platinum drugs, continues to be an important issue for both clinicians and cancer patients. CIPN can cause significant neuropathic pain and even lead to disability of patients, causing significant loss of functional abilities and reduced quality of life [53]. The current standard of prevention of peripheral neuropathy is the reduction of drug doses or refusal to use taxanes, which certainly affects the treatment potential [54].

Our study showed that the use of ALA in combination with an acetylcholinesterase inhibitor — ipidacrine hydrochloride, significantly reduces the symptoms and severity of PIPN. Patients in the control group suffered from significantly more severe degrees of PIPN, compared with the group in which the study drugs were used. Therefore, it may be concluded that the combination proposed by us (ALA and ipidacrine hydrochloride) in patients of study group II led to a statistically significant reduction in the severity of PIPN, and thus to improvement of the functional capacity and quality of life of patients. The combination of ALA and acetylcholinesterase inhibitor (ipidacrine hydrochloride) could be recommended for prophylaxis of PIPN.

REFERENCES


ОЦІНКА ЕФЕКТИВНОСТІ ЗАСТОСУВАННЯ АЛЬФА-ЛІПОЄВОЇ КИСЛОТИ ТА ІПІДАКРИНУ ГІДРОХЛОРИДУ ДЛЯ ПРОФІЛАКТИКИ ПАКЛІТАКСЕЛ-ІНДУКОВАНОЇ ПЕРИФЕРИЧНОЇ НЕЙРОПАТІЇ ЗА ДАНИМИ ОЦІНОЧНОЇ ШКАЛИ TOTAL NEUROPATHY SCORE

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Мета: Оцінити ефективність призначення комбінації альфа-ліпоєвої кислоти та інгібітора ацетилхолінестерази — іпідакрину гідрохлориду для запобігання розвитку та по- кращення перебігу паклітаксел-індукованої периферичної нейропатії у пацієнтів з раком грудної залози за даними оціночної шкали Total Neuropathy Score.

Матеріали та методи: 32 хворих на рак грудної залози T1–4N0–3M0–1, яким була показана поліхіміотерапія за схемою АТ (паклітаксел, доксорубіцин) або ЕТ (паклітаксел, епірубіцин), рандомізовано у дві групи. Хворі першої групи (n = 16) не отримували додатково препаратів для профілактики нейропатії. Хворі другої групи (n = 16) з метою профілактики нейропатії призначали альфа-ліпоєву кислоту та іпідакрину гідрохлорид. Проведено комплексне неврологічне обстеження пацієнтів за всіма десятьма параметрами оціночної шкали Total Neuropathy Score до початку хіміотерапії й після 3-го та 6-го циклів хіміотерапії. Кожен параметр оцінювали від 0 (відсутність дефіциту) до 4 (відсутність функції/найважчий дефіцит). Отримані за результатами обстеження бали підсумовували, щоб отримати загальний бал від 0 до 40.

Результати: Застосування альфа-ліпоєвої кислоти в поєднанні з інгібітором ацетилхолінестерази — іпідакрину гідрохлоридом достовірно зменшує вираженість симптомів та тяжкість паклітаксел-індукованої периферичної нейропатії. Прояви паклітаксел-індукованої периферичної нейропатії у хворих контрольної групи були достовірно важчими порівняно з групою, в якій застосовували досліджувані препарати. Середня ступінь важкості нейропатії після 3 та 6 циклів становила 1,75 та 2,62 у I групі та 1,12 та 1,62 у II групі відповідно (покращення на 15,75% (р < 0,05) та 25,00% (р < 0,001) після 3 та 6 циклів відповідно).

Ключові слова: паклітаксел, хіміотерапія, нейропатія, Total Neuropathy Score, альфа-ліпоєва кислота, інгібітори ацетилхолінестерази.

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