контакти в стінці судин розширені, базальна мембрана пошкоджена, у просвіті гемокапілярів деформовані еритроцити, розміщені «монетним стовпчиком», часто прикріплюються до люменальної поверхні ендотеліоцитів. Стінка артерій та артеріол потовщена в зв'язку з набряком ендотеліоцитів та початковими ознаками склерозу. Через п'ять-шість тижнів наколосудинні набряки та крововиливи в паренхіму тимуса. Переважна більшість судин «порожні». Через один тиждень після відміни препарату зворотних змін не виявлено.

Ключові слова: налбуфін, щур, вена, артерія, гемокапіляр, ендотеліоцит, перицит.

Стаття надійшла 30.11.2017 р.

междуэндотелиальные контакты в стенке сосудов расширены, базальная мембрана повреждена, в просвете гемокапилляров деформированные эритроциты, размещенные «монетным столбиком», часто прикрепляются к люменальной поверхности эндотелиоцитов. Стенка артерий и артериол утолщена в связи с отеком эндотелиоцитов и начальными признаками склероза. Через пять-шесть недель околососудистые отеки и кровоизлияния в паренхиму тимуса. Подавляющее большинство сосудов «пустые». Через одну неделю после отмены препарата обратных изменений не обнаружено.

Ключевые слова: налбуфин, крыса, вена, артерия, гемокапилляр, эндотелиоцит, перицит.

Рецензент Єрошенко Г.А.

DOI 10.26724 / 2079-8334-2017-4-62-116-123
UDC 611.835+ 616.833-009+615.277

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CHANGES IN PERINEURIAL AND HEMATOENDONEURIAL BARRIERS OF THE SCIATIC NERVE IN PACLITAXEL-INDUCED PERIPHERAL NEUROPATHY

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The absence of a unified concept of paclitaxel-induced peripheral neuropathy morphogenesis determines the need for a detailed morphological study. This paper demonstrates ultramicroscopic changes in the structure of the perineurial and the hematoendoneurial barriers of the sciatic nerve in albino rats caused by paclitaxel. Chemotherapeutic agent was administered intraperitoneally at a dose of 2 mg/kg of body weight, each alternate day, 4 times. The experiment period was 120 days; during the experiment, samples were collected for morphometric study and electron microscopic study. In the experiment, there were determined changes in endoneurial blood flow manifested themselves as congestion, morphological signs of transendothelial transport abnormalities, dystrophic changes in endothelial cells of varying severity and stages, thickening and dissociation of the basement membrane. In the perineurium, the disorganization of fiber and cellular elements, deformation of the processes, hydropic dystrophy of perineurial cells and impaired permeability of the perineurium progressing within the first months of the experiment and gradually disappearing until the end of the experiment were observed.

Key words: Paclitaxel, perineurial barrier, hematoendoneurial barrier, peripheral neuropathy.

The article is a part SRW "Morpho-functional characteristic of lesions of the central and peripheral nervous systems, sensory organs caused by chemotherapeutic agents used for the treatment of oncological diseases, and the development of neuroprotective therapy" (state registration number 0117U000672).

Taxanes are a group of broad-spectrum chemotherapeutic agents which are highly effective [3, 9]; however, they have a negative impact on the peripheral nervous system [7, 14]. Paclitaxel (P) is one of the anti-neoplastic agents that affects the microtubules and prevents their depolarization resulting in abnormal intraneuronal transport. This is how most researchers explain peripheral neurotoxicity of P [6, 11]. It is a dose-dependent effect which manifests itself in most oncological patients treated with P as numbness, burning pain, paresthesia mainly in "gloves and socks" areas, joint and muscle pain, disordered motor function [8, 14]. Despite numerous studies, there are currently no effective neuroprotective schemes being able to significantly affect the clinical course of P-induced neuropathy. It is due to lack of knowledge of the pathomorphogenetic mechanisms of peripheral neuropathy which occur under the influence of the preparation. The overwhelming majority of research is limited to the study of qualitative and quantitative aspects of the damage to conducting component of the peripheral nerves since they are considered as the main ones in the development of P-induced peripheral neuropathy (PIPN) [4, 5]. Some authors indicated the possible role of the disorganization of connective tissue elements and the microcirculation system in the pathogenesis of PIPN; however, these issues were rarely considered in the context of the pathomorphogenesis in general [12]. Changes in nerve fibers of the sciatic nerve (SN) described in our previous studies, were accompanied by endoneurial edema of different severity degrees [1]. Therefore, particular attention has been paid to the study of the effect of P on the endoneurial capillaries as well as the perineurium of the SN under the influence of P.

Research purpose was to determine the patterns of structural and functional rearrangement of the components of the hematoendoneurial and the perineurial barriers of the SN in dynamics of experimental PIPN.

Materials and methods. Experiment was conducted on the random bred albino rats, weighing 150-200 g, that were divided into 3 groups. 35 animals of the 1st experimental group were administered

chemotherapeutic agent Paclitaxel (Actavis, Romania) at the dose of 2 mg/kg of body weight, intraperitoneally, previously dissolved in isotonic NaCl solution, on every alternative day to reach the total dose of 8 mg / kg as recommended by S. Polomano et al. [2]. 15 Rats of the 2nd group were injected isotonic NaCl solution in the equivalent volume (0.2 ml) intraperitoneallyfor control. The 3rd group of 10 intact animals was made to establish the performance standards. Tissue sampling for microscopic study was performed on the 1st, 7th, 15th, 27th, 60th, 90th and 120th days after the last Paclitaxel injection. The research objects were SN. Transverse sections of the SN, 1 micron thick, made of material blocks and intended for electron microscope examination, were stained with toluidine blue. Semithin and ultrathin sections were made on ultramicrotome UMTP- 2M. Ultrathin sections stained preliminarily with uranyl acetate and lead citrate were examined with an electron microscope PEM-125K. Morphometric study was performed using image analyzer, which consists of microscope LYUMAM 8-P with photometric nozzle MFN-10-1. For measuring metric characteristics, software UTHSCSA Image Tool® for Windows® (version 2.00) was used online. There were measured such morphometric parameters: cross-sectional area of the endoneurial capillaries, lumen and wall area of the endoneurial capillaries. To calculate statistical analysis of measurement results, there were used spreadsheets Microsoft Excel 2000, StatPlus program and Statistica 6.0 for Windows. Due to the fact that the distribution of metric characteristics in variation rows was different from normal (Kolmogorov-Smirnov/Lilliforca, Shapiro-Wilkie, Fisher d'Ahostino criteria), reliability of performance differences between the groups was assessed using the nonparametric Mann-Whitney test.

Results and its discussion. In dynamics of PIPN development, the morphometric analysis of the endoneurial capillaries showed that on the 1st day after the last administration of chemotherapeutic agent, the mean surface area of the capillary profile on semi-thin sections increased significantly as compared to controls (Table 1). On the 7th day, the cross-sectional area of the capillaries in the endoneurium of the SN increased dramatically exceeding the indicators of control animals by 1.8 times being significantly different from the indicators obtained in the previous observation period. The mean vessel lumen area increased and there were no significant changes in wall thickness as compared to the previous observation period. On the 15th day of the experiment, the mean value of the cross-sectional area of the capillaries decreased to (140.27±6.62) μm^2 that was accompanied by the appearance of large numbers of vessels with sharply thickened endothelial lining and narrowed lumen. The mean value of the lumen area was close to controls constituting (41.37±3.35) μm^2. At the same time, the profile area of the capillary wall increased progressively to (98.90±4.18) μm^2 exceeding that in the control group by 1.9 times. On the 27th day of the experiment, the increase in the number of congested capillaries with sharply dilated lumen and thickened wall was typical. The mean value of the cross-sectional area of the capillary profile reached maximum values being (178.73±9.84) μm^2. The lumen of most capillaries was dilated; its mean value increased by 1.9 times as compared to the previous observation period. The mean values of the profile area of the capillary wall did not differ significantly from those obtained during the previous observation period.

Table 1

Morphometric parameters of the endoneurial capillaries of the SN in rats with PIPN (M±m, n=20)

		Cross-sectional area of the endoneurial capillary (μm^2)	Lumen area of the endoneurial capillary (μm^2)	Wall area of the endoneurial capillary (μm^2)
1-st day	Experiment	131,65±5,03*	46,93±3,67	84,72±4,25*
	Control	93,71±6,84	41,29±5,07	52,42±3,29
7-th day	Experiment	169,24±7,83*•	89,71±6,25*•	79,53±3,48*
	Control	92,46±5,27	43,16±4,89	49,30±2,84
15-th day	Experiment	140,27±6,62*•	41,37±3,35•	98,90±4,18*•
	Control	96,13±6,69	43,79±4,73	52,34±3,06
27-th day	Experiment	178,73±9,84*•	79,84±6,13*•	98,89±5,11*
	Control	94,17±5,31	42,06±3,52	52,11±4,31
60-th Day	Experiment	172,11±10,29*	65,26±6,93*	106,85±8,04*
	Control	93,61±7,02	42,85±4,70	50,76±3,82
90-th day	Experiment	119,64±7,83*•	63,81±4,17*	55,83±2,96•
	Control	95,88±6,27	44,01±5,39	51,87±4,62
120-th day	Experiment	90,16±5,29•	37,36±2,49•	52,80±5,21
	Control	94,81±4,62	43,57±3,99	51,24±2,85

The difference is significant (p <0,05): * - compared to control; • - compared to the previous experiment term.

On the 60th day after the last administration of P, metric indicators of the cross-sectional area of the capillaries in the endoneurium, their lumen area and the profile area of their wall did not differ significantly from those obtained during the previous observation period; however, they dramatically exceeded the control

values. On the 90th day, there was a tendency for decrease in the studied parameters. The mean value of the cross-sectional area of the capillary profile in the endoneurium decreased significantly as compared to the previous observation period; however, it exceeded that in the control group. The lumen area of the capillaries did not differ significantly being higher than that in the control group. The mean value of the section area of the wall decreased dramatically; its value was normalized and did not differ significantly from controls. Until the end of the experiment (the 120th day), the mean values of all the studied parameters of the endoneurial capillaries decreased and did not differ from the controls.

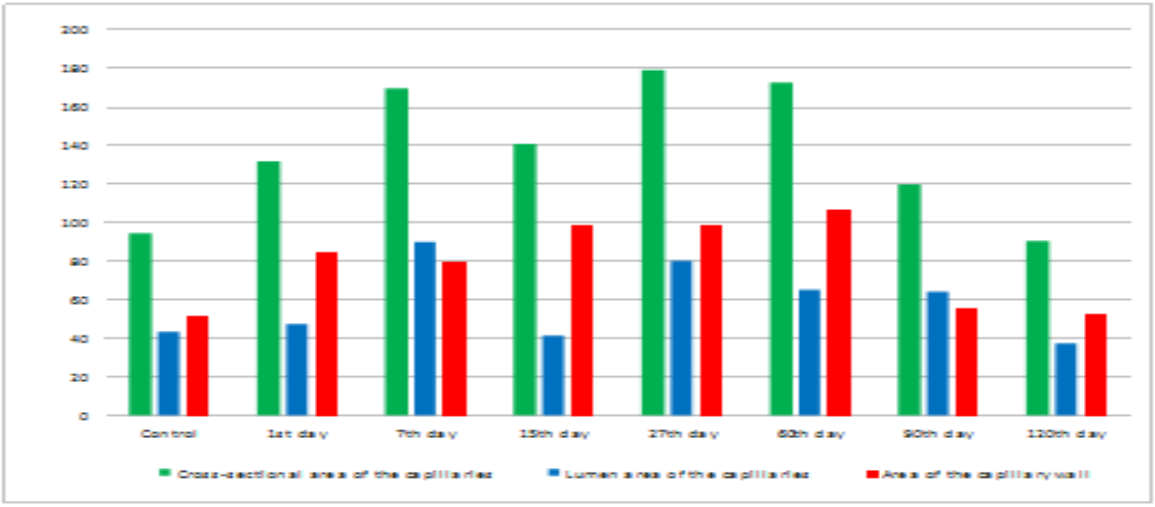

Fig. 1. Changes in morphometric parameters of the endoneurial capillaries of the SN in rats with PIPN.

The morphometric analysis of the endoneurial capillaries indicated that, their cross-sectional area increased within the first week – the section area of their wall increased on the 1st day, while their lumen size increased on the 7th day. On the 15th day, the lumen area of the capillaries slightly decreased; however, the wall remained thickened. On the 27th day, the vessel lumen area increased; we tend to regard it as a compensatory reaction aimed at increasing the level of metabolic supply to the nerve trunk. Since the 90th day, a gradual restoration of metric parameters of the endoneurial capillaries was observed; on the 120th day, they were close to controls (Fig. 1).

Electron microscopic study of endoneurial microcirculation in the SN on the 1st day after the last administration of P revealed luminal narrowing of the endoneurial capillaries as well as rather polymorphic changes. In some of them, a few digitiform protrusions were formed by the luminal plasmalemma of endothelial cells. In the perinuclear space, the dilated cisternal lumen of the rough endoplasmic reticulum was found. The mitochondria with partially destroyed cristae were of normal size. The micropinocytotic vesicles were evenly distributed throughout the cytoplasm. The nuclei of endothelial cells were oval in shape or somewhat flattened with evenly distributed euchromatin. The structure of endothelial tight junctions was preserved; contiguous membranes were separated in certain areas. The basement membrane was thickened; its dissociation was seen in some areas. The vacuolar transformation of the endoplasmic reticulum cisternae and swollen mitochondria with partially destroyed cristae were found in the cytoplasm of pericytes. Perivascular edema of endoneurial connective tissue was observed.

More pronounced changes manifested themselves as the swollen cytoplasm of endothelial cells were detected in many capillaries (Fig.2). The mitochondria were deformed; most mitochondria were found with destroyed cristae, while focal dissolution of the outer membrane was seen in certain ones only. The dictyosomes of the Golgi apparatus were somewhat enlarged. In the cytoplasm, there were moderate amounts of the micropinocytotic vesicles, most of which were found beneath the luminal plasmalemma. The latter formed a few digitiform protrusions into the vessel lumen. The nuclei were frequently deformed; their heterochromatization with predominantly peripheral euchromatin condensation was seen. The swelling of the nucleoplasm was often observed. The swelling, thickening and dissociation of the basement membrane were frequently detected. In the cytoplasm of pericytes, hydropic dystrophy, nuclear deformation, dissociation and swelling of the basement membrane were observed. At the same time, the integrity of endothelial tight junctions was preserved.

On the 7th day of the experiment, the signs of an increased mobility of the luminal plasmalemma of endothelial cells were found. In endothelial cells, numerous cytoplasmic protrusions were observed; microclasmatosis was often seen. In the subplasmalemmal spaces, vacuoles were frequently visualized. In certain areas, the luminal plasmalemma was indistinct. In the cytoplasm of the peripheral zones of

endothelial cells, there were many micropinocytotic vesicles which sometimes merged to form small vacuoles or multivesicular bodies forming transendothelial chains. The cisternae of the endoplasmic reticulum were somewhat dilated. Mitochondrial disruption consisted in mild swelling, deformation, partial or total dissolution of their cristae as well as the enlightenment or the increase in electron density of the mitochondrial matrix. Numerous free ribosomes and polyribosomes were observed in the cytoplasm of most endothelial cells. Large numbers of the micropinocytotic vesicles were localized directly beneath the abluminal plasmalemma or attached to its inner surface. The zones of endothelial tight junctions were somewhat indistinct; however, their opening was not observed. The abluminal plasmalemma formed single superficial invaginations; its contours were frequently indistinct. The basement membrane was thickened with the foci of the dissolution and homogenization.

Severe hydropic dystrophy, in some cases ballooning degeneration involving endothelial cells was seen in many capillaries mainly with the dilated lumen. The appearance of "light" and "dark" endothelial cells differing in the nature of morphological changes was worth noting. The first type of cells was characterized by total swelling of the cytoplasm and reduced number of organelles that formed mainly focal aggregates. There were polymorphic mitochondria with destroyed cristae; sometimes, focal dissolution of the outer membrane was found. Some mitochondria underwent vacuolar transformation. The micropinocytotic vesicles were not numerous. The luminal plasmalemma was usually smooth. The cisternae of the endoplasmic reticulum as well as the dictyosomes of the Golgi apparatus being few in number were enlarged. The contours of cytoskeletal elements were not seen clearly; there was a sharp reduction in the number of free ribosomes and polyribosomes, while in certain areas, they were absent. In "dark" endothelial cells, the luminal plasmalemma had a wavy contour being often indistinct. The cytoplasm contained large numbers of microfilaments, ribosomes, micropinocytotic vesicles. The contours of the abluminal plasmalemma were indistinct, especially in the areas of pericyte-endothelial cell contacts. The basement membrane was sharply expanded; it often contained the fragments of endothelial cell cytoplasm surrounded by the membrane. Vacuolar transformation of organelles and cytoplasmic swelling were found in pericytes. At the same time, the structure of endothelial tight junctions was not significantly disrupted.

On the15th day of the experiment, the deformation of endothelial cells and their nuclei were found in the capillaries of the endoneurium. The luminal plasmalemma formed numerous digitiform and sail-like protrusions; microclasmatosis was observed. In the cytoplasm of endothelial cells, there were numerous mitochondria with disrupted structure of the inner membrane, destroyed cristae and enlightened matrix. There were observed large numbers of vacuoles. The nuclei were characterized by uneven distribution of chromatin with small condensation foci and enlightened areas localized mainly in the central region of the nucleoplasm. In the zones of endothelial tight junctions, contiguous membranes of endothelial cells were separated; however, the full disclosure was not observed. The cytoplasm of pericytes was enlightened containing numerous micropinocytotic vesicles most of which were attached to the plasma membrane along the outer cell contour. The basement membrane was found to be thickened, locally dissolved and dissociated. In some areas of the endoneurium of the SN, the capillaries with pronounced swelling of endothelial cell hyaloplasm were seen. These cells were characterized by the reduction in the number of free ribosomes and polyribosomes, the disorganization and rarefaction of microtubules and neurofilaments, dilation, in some cases vacuolar transformation of the endoplasmic reticulum cisternae. At the same time, the micropinocytotic vesicles - both free and those attached to the plasmalemma were numerous. The nuclei of endothelial cells underwent some deformation; euchromatin was evenly distributed throughout the nucleoplasm. The perinuclear space was slightly expanded in some areas; the foci of the nuclear membrane dissociation were found. Particular attention should be paid to a high activity of the transendothelial transport in the areas of pericyte-endothelial cell contacts. Changes in pericytes generally correlated with the nature of morphological changes in endothelial cells. Their cytoplasm was found to be enlightened; there were seen slightly deformed mitochondria with partially destroyed cristae, focal damage to the outer and inner membranes, reduced number of ribosomes and polyribosomes, rarefaction of cytoskeletal elements. The structure of the basement membrane was preserved.

On the 27th day, ultramicroscopic changes in endothelial cells of the endoneurial capillaries manifested themselves as the reduction in both the number of the luminal plasmalemma protrusions and damage to mitochondria. There was observed no dilation of the endoplasmic reticulum cisternae as well as the Golgi apparatus dictyosomes. A rapid vesicle formation was detected; the areas of the thickened luminal plasmalemma as well as its disrupted structure were preserved. The basement membrane was thickened; in some areas, it appeared as a homogeneous structure. In pericytes, there were observed

moderate disruptions of mitochondrial ultrastructure, large numbers of the micropinocytotic vesicles, as well as the areas of plasmalemma homogenization.

On the 60th day, in the endoneurium of the SN, most capillaries were congested; their lumen was found to be dilated. The depletion of the nucleated capillary zones was seen. The luminal plasmalemma was smooth; in some areas, it was somewhat indistinct. The number of the micropinocytotic vesicles reduced as compared to the previous observation period. The cytoplasm of endothelial cells contained normal organelles; there were found several mitochondria with partially destroyed cristae. The nuclei were elongated with evenly distributed euchromatin in the nucleoplasm. The contours defining the nuclear membrane were well-defined along the entire perimeter. The structure of endothelial tight junctions was preserved. The separation and thickening of the basement membrane were seen in certain areas only. The mitochondria with destroyed cristae and enlightened matrix were found in the peripheral zones of pericyte cytoplasm.

Moderate swelling of the cytoplasm and significantly disrupted ultrastructure of cytoplasmic organelles were seen in endothelial cells of the endoneurial capillaries significantly more rarely as compared to the previous observation period (Fig.3).

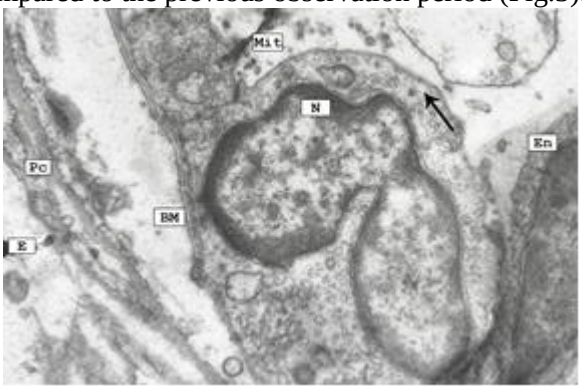

Fig. 2. Deformation of the nucleus, swelling of the mitochondria, edema of the endothelial cytoplasm (↑), dissociation of the basement membrane of the endoneurial capillary in SN on the 1st day of the experiment. Electron micrograph. Magnification: x8000. Designation: En - endothelial cell, N – nucleus of the endothelial cell, Pc - pericyte, BM - basement membrane, E - endoneurium, Mit - mitochondria.

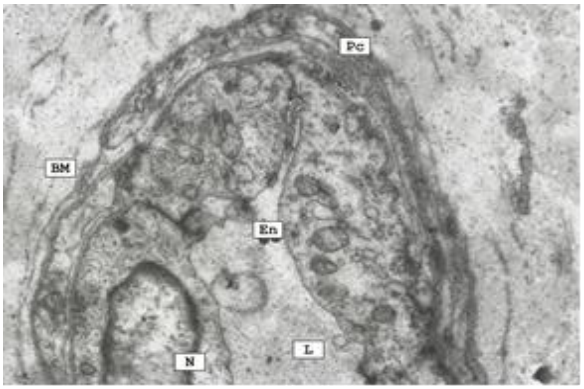

Fig. 3. Edema of cytoplasm of the endothelial cells and pericytes in the capillary of endothelium in SN on the 60th day of the PIPN. Electron micrograph. Magnification: x12000. Designation: En - endothelial cell, L - lumen of the capillary, BM - basement membrane, N – nucleus of endothelial cell, Pc - pericyte.

The peripheral zones of individual endothelial cells were thickened; the enlightenment of their hyaloplasm was seen. The number of ribosomes reduced; membranous organelles formed aggregates. The mitochondria were polymorphic in size and shape; predominantly shortened and dissolved cristae were observed. Single profiles of the endoplasmic reticulum were deformed and dilated. The micropinocytotic vesicles were found in depleted areas of endothelial cells with less pronounced cytoplasmic swelling. The contours of the luminal plasmalemma were smooth; there were only single cytoplasmic protrusions into the capillary lumen most of which were seen close to endothelial tight junctions. Their structure was preserved. The nuclei of endothelial cells were characterized by mild edema and unevenly distributed euchromatin. The basement membrane was thickened; the dissolution foci were detected. Pericyte processes were swollen and thickened.

On the 90th day of the experiment, in the capillaries, moderate deformation and luminal dilation were seen. In the cytoplasm of most endothelial cells, the number of free ribosomes and polyribosomes increased; the number of the micropinocytotic vesicles reduced; the mitochondrial structure was restored. The structure of the endoplasmic reticulum and the Golgi apparatus was normalized. The contours of cytoskeletal elements were clearly identified. The contours of the luminal and abluminal plasmalemma were predominantly clear. The structure of pericyte-endothelial cell contacts became normal. There were no signs of pathological changes in the basement membrane.

On the 120th day of the experiment, the ultrastructure of endoneurial capillaries was normalized. The lumen dilation was preserved; there was a mild focal swelling of the basement membrane.

Electron microscopic study of the perineurial structures in PIPN revealed that severe destructive changes were seen on the 1st day of the experiment already. There was a disruption of the orderly arranged bundles of collagen fibers as well as the deformation of perineurial cells and uneven swelling. The processes of perineurial cells were deformed. The destruction of organelles was observed on the background of severe hydropic dystrophy. The basement membrane was of uneven electron density; in some areas, it was thickened, dissociated. Severe subperineurial edema was found. In the next stages of

the experiment, within the first month after the last administration of P, the similarity of changes in the perineurial membrane was noted.

Despite the fact that the swelling of collagen layers was preserved (Fig.5), the fibers in some areas were disorderly arranged; cytoplasmic swelling and damaged organelles were found in the processes of individual perineurial cells only. The number of vesicles reduced. The nuclei contained predominantly euchromatin; the nuclear membrane was smooth. The basement membranes were preserved. Their thickening and dissociation alongside with impaired adhesion to the plasmalemma by perineurial cells were detected in several areas only. On the 60th day of the experiment, collagen fibers were thinner and mild swelling was detected in several perineurial cells. The number of the micropinocytotic vesicles reduced significantly. Cytoplasmic swelling was observed in the perinuclear space of several cells only. The contours of the basement membranes were clearly discernible. There were no perineurial cell separations from the plasmalemma. On the 120th day of the experiment, mild edema of collagen fibers and the processes of perineurial cells as well as moderate swelling of the endoplasmic reticulum in the perinuclear spaces was preserved.

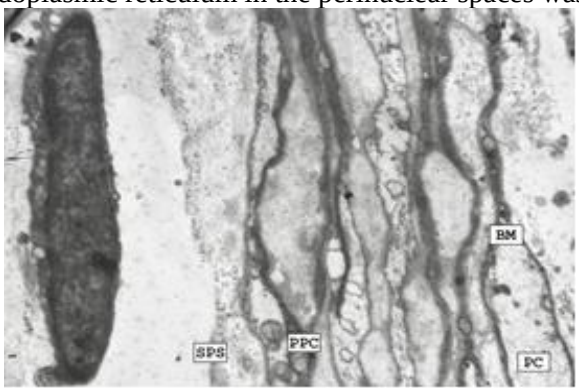

Fig 4. Violations of the perineurium in SN on the 1st day of the PIPN. Electron micrograph. Magnification: x8000. Designation: PC - perineurial cell, PPC - processus of perineurial cell, BM - basement membrane, SPS - subperineral space.

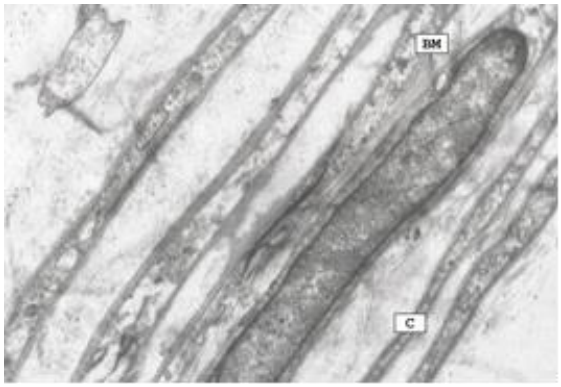

Fig. 5. Edema of the collagen layer (C), focal dissociation of the basement membrane (BM) in the perineurium of the SN on the 27th day of the experiment. Electron micrograph. Magnification: x8000.

Thus, using the morphometric methods and electron microscopic study, we have revealed morphological signs of transendothelial transport abnormalities and capillary recalibration in endoneurial microcirculation. Our data are consistent with Kirchmair R et al., who indicated the possible role of the disorganization of connective tissue elements and the microcirculation system in the pathogenesis of PIPN. Also we support the findings made by the Lim T.K.Y. et al., that showed that peripheral nerve injury causes alteration in endoneurial vessels structures, endoneurial fibrosis and hypoxia. We have demonstrated the role of the disrupted structure of the perineurial barrier and suggested its significant role in the development of endoneurial swelling for the first time ever. Some authors, for example Horner S. A et al, in their work devoted to the study of the pathomorphogenesis of peripheral neuropathies, have proven the possibility of increasing the permeability of perineurial structures to proteins that easily extend beyond epineurial vessels resulting in endoneurial swelling [13]. These phenomena require further study using tracer techniques; however, they can be considered as the trigger mechanism playing an important role in the pathomorphogenesis of PIPN.

Conclusions

1. Using the morphometric methods and electron microscopic study during the experiment, we have revealed morphological signs of transendothelial transport abnormalities and capillary recalibration in endoneurium resulting in endoneurial swelling of the SN persisting for 27 days after the last administration of P.
2. The obtained results concerning the submicroscopic structure of the perineurium have demonstrated that within the first months after the last administration of P, changes indicating the disorganization of fiber and cellular elements of the perineurial barrier as well as possible impairment of its permeability were observed. Since the 27th day, the signs of damage gradually disappeared until the end of the experiment that correlated with the severity degree of endoneurial connective tissue swelling.
3. Taking into account the obtained data, endoneurial swelling which is caused by both impaired permeability of the hematoendoneurial barrier and the disorganization of the perineurial one can be considered to play a significant role in the pathomorphogenesis of PIPN.

Prospects for further research. *Revealed changes in neuro-vescular-desmal component of the SN caused by P complete the concept of PIPN pathomorphogenesis that can be used in future experiments as well as in clinic to develop effective neuroprotective schemes for the prevention and treatment of toxic peripheral neuropathies.*

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Реферати

ЗМІНИ ПЕРИНЕВРАЛЬНОГО ТА ГЕМАТО-ЕНДОНЕВРАЛЬНОГО БАР'ЄРІВ СІДНИЧОГО НЕРВА ПРИ ПАКЛІТАКСЕЛ-ІНДУКОВАНІЙ ПЕРИФЕРІЙНІЙ НЕЙРОПАТІЇ

Гевка О. І.

Відсутність єдиної концепції морфогенезу паклітаксел-індукованої периферійної нейропатії визначає необхідність проведення детальних морфологічних досліджень. Дана експериментальна робота демонструє ультрамікроскопічні зміни в будові гемато-ендоневрального та периневрального бар'єрів сідничих нервів білих щурів під впливом Паклітакселу. Хіміопрерарат вводили тваринам через день 4 рази внутрішньоочеревинно в дозі 2 мг/кг маси тіла, забір матеріалу для морфометричного та електронномікроскопічного дослідження проводили протягом 120 діб. У динаміці експерименту визначалися зміни гемомікроциркуляторного русла ендоневрію, які проявлялися повнокров'ям, морфологічними ознаками порушень процесів трансендотеліального транспорту, дистрофічними змінами ендотеліоцитів різного ступеня вираженості, потовщенням та дисоціацією базальної мембрани. У периневрії спостерігалася дезорганізація волоконних та клітинних елементів, деформація відростків гідропічна дистрофія периневральних клітин та порушення проникності периневрію, що прогресували протягом першого місяця досліду та поступово зникали до завершення терміну експерименту.

Ключові слова: паклітаксел, периневральний бар’єр, гематоендоневральний бар’єр, периферійна нейропатія.

Стаття надійшла 1.10.2017 р.

ИЗМЕНЕНИЯ ПЕРИНЕВРАЛЬНЫХ И ГЕМАТО-ЭНДОНЕВРАЛЬНЫХ БАРЬЕРОВ СЕДАЛИЩНОГО НЕРВА ПРИ ПАКЛИТАКСЕЛ-ИНДУЦИРОВАННОЙ ПЕРИФЕРИЧЕСКОЙ НЕЙРОПАТИИ

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Отсутствие единой концепции морфогенеза паклитаксел-индуцированной периферической нейропатии определяет необходимость проведения детальных морфологических исследований. Данная экспериментальная работа демонстрирует ультрамикроскопические изменения в строении гемато-эндоневрального и периневрального барьеров седалищных нервов белых крыс под влиянием Паклитаксела. Химиопрерарат вводили животным через день, 4 раза, внутр.-брюшинно в дозе 2 мг / кг массы тела, забор материала для морфометрического и электронномикроскопического исследования проводили в течение 120 суток. В динамике эксперимента определялись изменения гемомикроциркуляторного русла эндоневрия, которые проявлялись полнокровием, морфологическим признакам нарушений процессов трансэндотелиальных транспорта, дистрофическими изменениями эндотелиоцитов различной степени выраженности, утолщением и диссоциацией базальной мембраны. В периневрие наблюдалась дезорганизация волоконных и клеточных элементов, деформация отростков гидропическая дистрофия периневральных клеток и нарушение проницаемости периневрием, что прогрессировали в течение первого месяца опыта и постепенно исчезали до завершения срока эксперимента.

Ключевые слова: паклитаксел, периневральный барьер, гемато-эндоневральный барьер, периферическая нейропатия.

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