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ABSTRACT

At the same time, the issues of assessing the severity of spinal cord injury are a serious problem in forensic practice, affecting not only the medical field, but also the legal field and social aspects. The aim of this review was to objectively evaluate the currently available methods for investigating functional, biological, and molecular markers of nerve tissue damage in spinal cord and spinal cord injuries of various genesis. The article highlights the diagnostic and prognostic value of neurophysiological methods, in particular electroneuromyography and neurospecific proteins of which glial fibrillary acidic protein and neurospecific enolase are the most informative and specific according to a number of experts. Formation of immediate and long-term prognostic criteria for spinal cord injury is a challenging task, and their determination will not only allow a more accurate assessment of the severity of patients with spinal cord injury, but also predict the further course and possibilities of recovery of spinal cord function activity, both in the early and in the distant posttraumatic period.

Key words: vertebral column injury, spinal cord injury, diagnostic significance, prognostic significance, electroneuromyography, glial fibrillary acidic protein, neurospecific enolase, posttraumatic period.

INTRODUCTION

The problem of injuries associated with injuries of the spine and spinal cord has not lost its relevance in recent decades. This phenomenon is determined by the development of industry, high-rise construction, steady motorization, military conflicts and other reasons. The high degree of disability in this category of patients is a major medical and social problem. According to the World Health Organization (WHO), up to 2 million people die from injuries every year. At the same time, in the structure of indicators, the trauma of the spine and spinal cord in the volume of all injuries of the musculoskeletal system (MSA) ranges from 8% to 20-26.2%. Also, according to the WHO, annually in the world up to half a million people suffer from spinal cord injuries, among which a significant proportion are young people (20-35 years old). Spinal cord injury is a serious health problem, often leading to lifelong disability for patients.

It is necessary to emphasize the high social significance of this type of injury, since the loss of ability to work, a high percentage of disability and social maladjustment, and, consequently, the financial damage with injuries of the spine and spinal cord is much higher than with other types of injuries. The need for lifelong care and rehabilitation for patients with spinal cord injury generally places a heavy burden on patients, their families and communities. Another negative aspect is that the category of persons most susceptible to traumatic injuries of the spine and spinal cord includes persons of young and working age. Spinal fractures are characterized by severe complications, the development of traumatic illness, persistent shifts in the internal organs, in particular, loss of functions of the pelvic organs, disorders of the endocrine system, an extremely high level of social and psychological maladjustment of patients, limited opportunities for independent movement and self-care.

The share of uncomplicated spinal injury is 50-54% of cases, in which men predominate - 58.2% -65.5% of cases and women are less susceptible, among whom this pathology is detected in 34.5-41.8% of cases, and in general the ratio of men and women is 1.8 / 1. Spinal injuries more often occur in men aged 20 to 50, and in women the greatest number of spinal fractures is observed in the age of 60-80, while the average age of patients with this type of injury is about 45 years old.

In clinical practice, the main research methods for trauma of the spine and spinal cord are instrumental and X-ray research methods: a combination of computed X-ray tomography (CT) and magnetic resonance imaging (MRI), lumbar puncture, including liquorodynamic tests, and vertebral angiography ... In general, these instrumental research methods require expensive specialized equipment, highly qualified specialists and, at the same time, cannot always allow objectively

and fully assess the degree of involvement of the spinal cord in the pathological process.

The problem of diagnosing spinal injuries, especially in combination with intracavitary bleeding, in the presence of concomitant or severe traumatic brain injury, unfortunately, is not always recognized in a timely manner, which ultimately leads to an incorrect assessment of the patient's objective condition, and as a result, the provision of inadequate medical care.

The need for affordable methods that do not require expensive high-precision equipment and highly qualified narrow specialists-radiologists or radiologists necessitates further study of various aspects of the etiopathogenesis of spinal injury in order to search for new criteria for early diagnosis, objective expert assessment and development of modern prediction algorithms. At the same time, the issues of assessing the severity of spinal cord injury are a serious problem in forensic practice, affecting not only the field of medicine, but also the legal field and social aspects. An objective assessment of the victim's condition, the prospects for restoring the functional usefulness of the damaged areas largely determine the fate of a particular person. That is why it is extremely important for forensic doctors to give a scientifically based objective assessment of the nature and possible consequences of injury.

The purpose of this review was an objective assessment of the currently existing research methods for functional, biological, and molecular markers of nerve tissue damage in spinal and spinal cord injuries of various origins.

Researchers continue to search for new objective methods for assessing the neurophysiological state of patients with spinal trauma. One of the diagnostic methods of considerable interest to researchers is electroneurophysiological methods and, in particular, or its modern version, electroneuromyography, which is an objective electrophysiological method for assessing the functional activity of skeletal muscles and individual muscle elements (myocytes, motor units) as components of the musculoskeletal system. ENMG is a hardware-instrumental method for studying the degree of conduction of nerve endings and electrical activity of muscles and diagnostics of the peripheral nervous system. The two main options for ENMG are: the use of cutaneous electrodes attached over the muscle, or needle electrodes inserted into the muscle tissue. The potential fluctuations captured in this case are recorded depending on the type of storage medium. ENMG is considered a painless and harmless method, and therefore, it is actively used to determine the bioelectric activity of ODA. ENMG is used to determine the electrical potentials in the muscle in the states of rest, tonic tension and voluntary

contraction, thus providing. a complete picture of the diagnostic picture of the state of the nervous system and muscles innervated by it.

The main stages of ENMG when used to assess the severity and depth of damage to spinal functions in spinal cord injury:

• registration of the potential of spinal motoneurons;

• assessment of the occurrence and conduction of excitation in the muscle;

• comparative analysis of ENMG data from patients with spinal cord injury with reference electroneuromyographic criteria;

• diagnosis of spinal cord injuries based on the above data.

ENMG can be successfully used to verify the functionality of spinal motoneurons in spinal cord injury and in the post-traumatic recovery period. ENMG takes a leading place in obtaining an objective assessment of the state of the neuromuscular apparatus, the severity of CNS damage in spinal cord injuries and the results of ongoing rehabilitation measures, on the basis of which an early and long-term prognosis of recovery can be built.

Based on the foregoing, neurophysiological monitoring and, in particular, electromyography in complicated and uncomplicated spinal trauma can serve as a method for assessing the severity of damage to the conductive function and predicting the dynamics and completeness of its recovery in the post-traumatic period.

Electroneurophysiological methods make it possible to clarify the diagnosis and assess the degree and severity of conduction and segmental disorders in spinal cord injury, and also allow assessing the body's capabilities in terms of restoring impaired sensory and motor neuronal functions in the long term. For example, a new method of transcranial magnetic stimulation, which is proposed to be used along with the "classical" ENMG, has significant potential. According to researchers, in the recovery period of uncomplicated spinal cord injury, as a rule, positive dynamics of electroneuromyography and transcranial magnetic stimulation indices is revealed, which was manifested by a tendency to increase the amplitudes of motor responses of the small and tibial nerves.

The development of medical science requires the development and creation of new publicly available modern methods for assessing the severity and predicting long-term outcomes of spinal cord injury, which could be performed by standard methods of clinical and laboratory diagnostics.

Recently, the importance of so-called neurospecific proteins in damage to nerve tissue has attracted more and more attention of researchers. Their potential in assessing the severity of spinal cord injury, as well as in the recovery period after injuries and injuries has not been fully explored. The use of biochemical markers

of damage to nerve tissue, in particular, neurospecific proteins of blood plasma, taking into account the sufficient clinical availability, the possibility of minimally invasive diagnosis and assessment of the prognosis of damage to nerve tissue are extremely relevant for many related branches of medicine, in particular for forensic medicine. diagnostics with the determination of neurospecific proteins in blood or cerebrospinal fluid (CSF) as potential biomarkers can be considered an urgent trend in the study of spinal cord injury.

The gradual death of neurons and microglia cells during traumatic injury to the spinal cord leads to the release of neuron-specific enzymes and their isoenzymes into the extracellular environment, which makes it possible to assess the depth and severity of its damage.

As you know, as a result of damage to the central nervous system, a certain part of nerve cells die, as a result of which protein substances are formed and released, which are involved in the regulation of the vital activity of glial and nerve cells (neurons) and the so-called neurotrophic factors (NTF) or neurospecific proteins. Among the most well-known of these proteins are neurotrophins, which include: neurotrophins: NT-3, NT-4/5, NT-6, brain neurotrophic factor (BDNF), nerve growth factor (NGF), neuroglial protein S- 100 and myelin basic protein (MBP).

The release of myelin basic protein (MBP) into the cerebrospinal fluid occurs when nerve tissue of various etiologies is damaged. An increase in its concentration was noted in traumas of the central nervous system, tumor lesions of the central nervous system, neurodegenerative diseases, in particular in multiple sclerosis, inflammatory processes of the central nervous system - in subacute sclerosing panencephalitis and viral encephalitis and other diseases and pathological processes associated with damage to the nervous tissue.

The expression of another neumarker, a neurotrophic factor of the brain, occurs on neurons, astrocytes, in the area of damage on Schwann cells, fibroblasts, megakaryocytes / platelets, and, according to researchers, on smooth muscle cells. Functionally, BDNF is responsible for the formation of synapses, participation in the processes of differentiation, maturation and survival of neurons during the development of the organism, and in the adult state, its main function is to protect neurons. There is information about the participation of BDNF in the neuroprotection of motoneurons during axon removal.

Another neuromarker of interest to researchers is the calcium-binding neuroglial protein S-100, which originates from astrocytic glia, which forms a branched network. S-100, is able to remain dissolved in a saturated solution of ammonium sulfate. Structurally, S-100 consists of 17 tissue-specific monomers,

including monomers “a” and “b”, which form homo- and heterodimers, which are found in high concentrations in cells of the nervous system: homodimer S-100 (bb) - in glial and Schwann cells, S-100 (aa) in liver, kidney, and striated muscle cells, and S-100 (ab) heterodimer in glial cells. An increase in the concentration of S-100 (ab) and S-100 (bb) can serve not only as a qualitative, but also as a quantitative marker of CNS damage, reflecting the degree of damage.

However, the most informative and specific, according to some experts, are glial fibrillar acidic protein and neurospecific enolase.

NSE is a specific enzyme found in the cells of the nervous system of neuroectodermal origin, i.e. neurons and neuroendocrine cells of both the central nervous system and the peripheral nervous system. NSE is currently the only known common marker of all differentiated neurons. To date, data have been accumulated concerning the possibility of using NSE as a marker for assessing CNS damage. Measurement of the NSE level according to researchers is able to signal the violation of the integrity and permeability of the blood-brain barrier (BBB) and the severity of neuronal damage, and NSE can serve as a marker of acute spinal cord injury.

In a study conducted by Chabok S.Y. et al. (2012) studied the relationship between clinical outcomes in patients with diffuse axonal injury and serum NSE levels during the first 3 days of the post-traumatic period. The regularities of changes in the NSE concentration in the post-traumatic period after CNS injury, studied by other researchers, revealed significant differences in its levels in patients with axonal injuries caused by focal cerebral contusions and in patients with cerebral edema without local changes. The highest NSE levels were observed during the first day of the post-traumatic period, gradually decreasing during the 4-day period after CNS damage. A correlation was established between the concentration of NSE in the blood serum of patients on the one hand and the volume of the contusion lesion focus and the severity of CNS damage on the other hand. All this prompted the researchers to the following conclusions: the quantitative determination of NSE in diseases with direct involvement of the central nervous system has diagnostic value.

Similar changes were obtained in the studies of Du W. et al (2018), in which it was found that serum NSE levels were significantly increased in patients in the acute phase of spinal cord injury and gradually decreased in the post-traumatic period. The moderately recovered group had an increased NSE level, while the fully recovered group had significantly lower levels. According to Du W. et al (2018), the sensitivity of the NSE study as an evaluative marker of functional neurological recovery was characterized by a sensitivity of 74.4% and a specificity

of 71.4%. In this case, the threshold values of the NSE content in the blood serum were 29,1 мg/L. Serum NSE concentrations exceeding threshold values in patients were highly likely to indicate a poor prognosis for recovery of neurological functions.

However, despite the data presented, the effectiveness of the NSE study for assessing the severity and prognosis of spinal cord injury, its isolated assessment does not allow its use as a highly specific criterion for CNS damage. It is also known that an increase in NSE can be detected in conditions not directly related to damage to the central nervous system, and therefore changes in the level of this protein cannot be considered a sufficient criterion for damage to the nervous tissue. Thus, the level of NSE can increase not only with traumatic damage to the central nervous system, but also with other diseases accompanied by damage to the central nervous system of various etiologies: hemorrhagic and ischemic strokes, with schizophrenia, hepatic encephalopathy, bacterial and purulent meningitis, epilepsy, neurodegenerative processes (parkinsonism, Alzheimer's disease) perinatal-hypoxic damage to the central nervous system, neuritis. According to these authors, NSE activity increases more significantly when the pathological process spreads to the cerebral membranes, in contrast to cases when only the brain parenchyma is damaged.

For an objective assessment of the patient's condition after spinal cord injury and the compilation of an objective and reliable prognostic picture of the restoration of the functional activity of the central nervous system, it is necessary to study at least two neuromarkers. Only this approach can make it possible to more accurately assess the patient's condition and predict possible outcomes with a greater degree of confidence.

Another neurospecific protein that is also being investigated for the possibility of its use as a biomarker, in our opinion, may be gliofibrillar acidic protein (GFAP), discovered by researchers led by L.F. Eng in 1969 This protein is a structural component of astrocytic glia and, accordingly, is responsible for its main functions: providing an energy substrate for astrocytes and their differentiation and, accordingly, determines the formation and functioning of the cytoskeleton of the central nervous system formed by astrocytic glia, in particular in the growth of astrocytic processes and establishing contacts of the latter with oligoendrocytes, myelin sheaths, synapses. In this regard, it can be argued that GFAP is directly involved in the formation of the blood-brain barrier (BBB).

GFAP is mediated, through the inductive effect of astrocytes on the vascular endothelium, is a stimulator of vascularization of the white matter of the brain. The absence of GFAP leads to disruption of normal myelin synthesis. GFAP is

involved in astrocyte mitosis and is of exceptional importance for CNS injuries and spinal injuries in particular. Thus, an increase in GFAP in the blood indicates the destruction of astrocytes and, accordingly, the blood-brain barrier (BBB) and may serve as a predictor of neurocyte death. GFAP consists of structural units - monomeric molecules with a molecular weight of 40-53 kDa, sizes from 8 to 12 nm and consisting of a "head" containing the amino acid arginine with an aromatic residue and a "tail" that form a complex structure. Each of these molecules (N and C-terminals) form a dimer, twist together around the longitudinal axis. At the center of such a dimer, there is a basic rod structure, which is called a supercoiled polypeptide L-helix. In turn, the dimers form tetramers that form protofilaments. Aggregation of tetramers occurs on a head-to-head basis. Polymerization of intermediate GFAP fibers, each of which is formed by eight protofilaments, leads to the formation of stable non-polar polymer molecules of this neuroprotein. The C-terminal of the GFAP molecule contains a significant amount of aspartic and glutamic acids, leucine, glycine and alanine, and the N-terminal residue is alanine or blocked methionine. Three forms of GFAP are known - α, β and γ, with γ prevailing in the central nervous system, and α in the peripheral nervous system. GFAP expression is associated with the activation of astrocytic glia by cytokines or hormones. In mature CNS cells, GFAP is concentrated primarily in glial filaments within gray matter protoplasmic astrocytes and white matter fibrous astrocytes. A significant amount of GFAP is concentrated in astrocytes located at the surface of the brain on the outer membrane, as well as paraventricularly in subependymal astrocytes.

Research by Fraser D.D. et al. (2011), the level of GFAP in the cerebrospinal fluid after CNS injury reached its maximum values on the first day. At the same time, during this period, the level of GFAP in the cerebrospinal fluid was significantly - more than 25 times higher than its same value in the blood serum: 15.5 ± 6.1 ng / ml versus 0.6 ± 0.2 ng / ml, respectively. Over time, the concentration of GFAP in the cerebrospinal fluid decreased, normalizing by the 7th day of the post-traumatic period and reaching the reference values by the 10th day. Moreover, according to Fraser D.D. (2011) the level of GFAP in blood serum on the 1st day did not correlate with the assessment of trauma at admission, indices of CNS injury obtained during magnetic resonance imaging (MRI) and physiological parameters immediately after trauma, but did correlate with assessments of pediatric brain functions determined six months after the injury. Thus, the data obtained by the researchers indicate the presence of the predictive value of this biomarker in CNS injury.

The combination of measuring the level of neurospecific proteins and studying the correlations between changes in their level and electroneuromyography indicators can reveal and develop new criteria and an algorithm for an objective and accessible assessment of the severity of predicting the severity of cerebrospinal injury in the early and late periods of recovery.

Conclusion. Thus, the formation of criteria for the short-term and long-term prognosis in spinal cord injury is a difficult task and the subject of further in-depth research. The definition of such criteria will undoubtedly enrich forensic medicine with new objective research criteria, which will allow not only to more accurately assess the severity of the condition of patients with spinal cord injury, but also to predict the further course and the possibility of restoring the activity of spinal functions, both in the early and in the long-term post-traumatic period.

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