METHODS OF NEUROMODULATION IN THE TREATMENT OF SPASTIC SYNDROME AND THEIR ROLE IN COMPLEX REHABILITATION OF PATIENTS AFTER SPINE AND SPINAL CORD INJURIES

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Objective. To present an algorithm for consistent application of neuromodulation techniques to improve the effectiveness of spastic syndrome relief and to specify its role in the rehabilitation of patients after spine and spinal cord injuries.
Material and Methods. The study included 105 patients with increased muscle tone after spinal cord injury. To relieve muscle spasticity, a staged therapy was performed including electrical stimulation of the spinal cord, simultaneous epidural drug therapy with electrical stimulation, and local hypothermia of the spinal cord.
Results. Positive results were obtained after each stage of neuromodulation therapy. They became a basis for the development of an algorithm of surgical treatment of patients with excessive muscle spasticity.
Conclusion. The proposed algorithm for consistent application of neuromodulation techniques in patients with spastic syndrome after spinal cord injuries allowed significant reducing the degree of spasticity and creating conditions for further rehabilitation in 88.6 % of cases.
Key Words: spinal cord injury, spastic syndrome, treatment, neuromodulation.

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Spine and spinal cord injuries are among the most common and severe injuries of the central nervous system. Spine and spinal cord injuries annually occur in ~8,000 people, 70–80 % of them become disabled (group I or II disability status). In 65–78 % of these patients, traumatic spinal cord disease is complicated by the development of spastic syndrome [3]. In 80 % of cases, the injured patients are relatively young working-age people. The required relief of the spastic syndrome and motor function restoration present an extremely challenging task [8].

Conservative procedures, including a broad range of drugs, physiotherapeutic and other reflexology treatment methods do not provide the long-term and reliable positive outcome in most cases [2]. Since conservative therapy was not successful, open and percutaneous destructive surgeries for various structures of the central and peripheral nervous system were performed until recently; the positive outcome was achieved in 60–80 % of cases. However, a high rate of relapse and aggravation of the spinal cord function was also observed, which worsens the quality of life of these patients [1, 7]. Local hypothermia of the spinal cord, a minimally invasive method complying with the principles of functional neurosurgery, is an alternative to destructive interventions to a certain extent [9].

Today, the neurosurgeons' toolbox for treating spastic syndromes includes the novel technologies (electrical stimulation of the spinal cord, intrathecal administration of opiates and baclofen), which are widely used abroad and make it possible to sufficiently effectively control the increased muscle tone. However, the use of these techniques in the chronic variant often results in a number of annoying complications (such as suppuration, termination of stimulation or drug feeding, pseudomeningocele formation, or granulomas in the inner catheter tip, etc.) that require replacing the stimulating system, the catheter, and the implanted pump or total refusal of this type of therapy [4].

An analysis of the literature has demonstrated that each of the existing methods for treating spastic syndromes provides a certain positive outcome, which varies for the aforementioned procedures and requires further comprehensive investigation. In addition, their role

in the rehabilitation system for this category of patients is still to be specified.

The objective of this study is to present an algorithm for consistent application of neuromodulation techniques to improve the effectiveness of spastic syndrome relief and to specify its role in the rehabilitation of patients after spine and spinal cord injuries.

Material and Methods

A total of 105 patients with severe and persistent muscle spasticity caused by complicated spine injury were examined and treated. The male-to-female ratio was 80 (71.6 %) to 25 (23.9 %). Most patients (>80 %) were young. All of them had earlier undergone urgent surgery aimed at elimination of compression of the spinal cord and its vascular structures by reconstructing the deformed spinal canal and reliably stabilizing the injured spinal segment using various constructs (cervical plate systems and cages, transpedicular and ventral devices, as well as prosthetic vertebral bodies). One hundred and five patients were admitted to the neurosurgical department of the Saratov Research Institute of Traumatology and Orthopedics after the ineffective conservative procedures for treating the spastic syndrome: 70 (66.6 %) – one year or more after the injury and 35 (33.4 %) patients, 3–11 months after the injury.

All patients underwent comprehensive clinical neurological, electrophysiological, and radiological examination on admission. The motor and sensory disturbance was assessed using the ASIA/IMSOP impairment scale that is subdivided into 5 grades: grade A – no motor or sensory function of the spinal cord is preserved; B – sensory but no motor function is preserved in the sacral segments; C – motor function in the extremities is preserved, but muscles have a muscle grade less than 3; D – partial disturbance (the key muscles have a muscle grade 3 or greater); E – motor and sensory function are normal. However, the increased muscle tone makes it impossible to clearly classify the severity of traumatic injury to the spinal cord; hence, grades A and B, C and D were combined into two groups: group 1 – AB and group 2 – CD.

Group 1 included 58 (55.2 %) patients diagnosed with spastic tetra- and paraplegia; group 2, 47 (44.8 %) patients with clinical signs of spastic tetra- and paraparesis. The intensity of muscle hypertonia was measured according to the modified Ashworth scale (grades 0–5) before and after treatment [11].

All the patients underwent conventional spine radiography; 35 patients, CT examination in order to assess the condition of the spine segment operated on and the reliability of its stabilization. MRI was performed in 66 cases to study the severity and the pattern of structural damage in the spinal cord at the injury level.

Electrophysiological examination was carried out in all 105 patients using a Keypoint elecromyograph (Denmark – USA) before and during pulsed electric field and pharmaceutical neuromodulation, as well as after the treatment course. The latent period, H-reflex and M-response amplitude and the H/M ratio were examined.

In order to compare the electroneuromyography (ENMG) data recorded in patients with spinal cord injury complicated by the spastic syndrome, we examined 10 healthy volunteers (5 male and 5 female individuals) aged 25–45 years. The resulting parameters of the electrophysiological examination were assumed to be the conditional normal parameters.

One hundred and five patients with increased muscle spasticity were treated consistently: at stage I they underwent electrical stimulation of the spinal cord (ESSC); at stage II, 46 patients in whom ESSC proved ineffective received epidural drug therapy (EDT) combined with ESSC; at stage III – 25 patients in whom EDT proved ineffective received local hypothermia of the spinal cord (LHSP).

ESSC was performed by placing electrodes into the epidural space of the spinal cord; the electrodes were arranged above the posterior columns 1–2 vertebrae above and below the lumbar enlargement segments. Parameters of pulsed electric field stimulation were selected individually; pulse frequency was 100–150 Hz; pulse width varied from 0.2 to 0.5 ms; the amplitude and voltage, from 8 to 10 V. The patients underwent 30–40 min long stimulation sessions using the Medtronic equipment (USA) for 3–4 weeks.

A catheter was additionally inserted at the T12–L1 level, between the electrodes, in order to simultaneously perform EDT combined with ESSC. A drug cocktail consisting of 2.0 ml of 0.01 % clonidine, 2.0 ml of 1 % morphine hydrochloride and 20.0 ml of normal saline was infused continuously using the standard VEDA-3 dosing devices (Russia) or WalkMed portable devices (USA) at an infusion rate varying from 0.1 to 0.5 ml/h during 10–12 days, in combination with ESSC (the ESSC scheme remained unchanged).

LHSC was performed using the infusion/perfusion technique in the operating room under general anesthesia using relaxants and artificial ventilation. In the perfusion method, a lumbar puncture between the L3 and L4 vertebrae is performed using a special needle; after removing 60–80 ml of cerebrospinal fluid, the normal saline cooled to +18–22 °C was slowly (10 ml/min) insufflated and, if there were no cardiovascular system complications, another 40–60 ml of the solution was insufflated at +2–0 °C. During the perfusion procedure, needles were additionally inserted into the subarachnoid space 2–3 positions above the initial level. The patients were perfused with 1500–2000 ml of normal saline cooled to –2–0 °C through the lower needle during 60–120 min.

The study results were analyzed using the Statistica 10.0 for Windows (StatSoft Inc.) statistical software; the parametric method involving determining the arithmetic mean and the error of mean ($M \pm m$) were used along with the normal distribution of the sample using the Shapiro – Wilk test. Intergroup comparison was carried out using Student's t-test. The results were considered statistically significant at $p \leq 0.05$.

Results

The effectiveness of the neuromodulation methods was assessed according to the level of muscle tone, the ratio between the H/M amplitudes on electroneuromyograms, and the neurological status before and after treatment; allowance was made for the positive and unsatisfactory outcomes. In order to reduce subjectivity in interpreting the intensity of muscle spasticity, we suggested employing a coefficient (K) calculated using the formula:

$$K = N1/N2,$$

where N1 and N2 is the score before and after treatment, respectively.

At $K \geq 2$, the therapeutic effect was considered positive, at $K < 2$ it was unsatisfactory.

In 58 group 1 patients, the average degree of increased muscle tone was 4.50 ± 0.06 points; in 47 group 2 patients, 3.80 ± 0.07 points (or 90.0 ± 1.2 % and 76.0 ± 1.4 %, respectively).

The condition of the neural apparatus of the lumbar region of the spinal cord before treatment according to the electroneuromyography data is shown in Table 1.

In 58 patients with spastic tetra- and paraplegia, the electroneuromyograms show a statistically significant ($p < 0.05$) increase in H-reflex amplitude and a decrease in muscle response, which increased the H/M ratio (%) compared to the control group (the norm).

In 47 group 2 patients, the H-reflex and M-response values turned out to be lower than the normal values; the percentage values of H/M amplitudes were statistically significant ($p < 0.05$) compared to those in the control group. Comparison of the ENMG parameters in group 1 and 2 patients demonstrated that in patients with partial damage to the spinal cord, the decrease in H-reflex amplitude and the ratio between the H-reflex and the M-response (%) is statistically significant ($p_1 < 0.05$) compared to those in patients with severe damage to the spinal cord.

ESSC. The results of assessing the effectiveness of ESSC according to the intensity of the spastic syndrome and the indicators of the H/M amplitude ratio (%) are shown on the histogram in Fig. 1.

In 23 (39.7 %) patients with severe neurological deficit (group 1), the positive treatment outcome involved the statistically significant reduction of muscle tone from 90.0 to 42.0 % and the average H/M ratio, from 81.3 to 49.5 %, which is indicative of significant decrease in hyperreactivity of the neural apparatus in the lumbar spinal cord. The positive outcome was achieved in 36 (76.6 %) patients with partial traumatic injury to the spinal cord structures (group 2) and was accompanied by reduction of the degree of muscle spasticity from 76.0 to 30.0 % and the H/M amplitude ratio, from 56.3 to 40.5 %, which demonstrates that the reflex function of the spinal cord was normalized. Thirty-five (60.3%) group 1 patients and 11 (23.4 %) group 2 patients showed an unsatisfactory outcome. The muscle spasticity indicators and the H/M amplitude ratio (%) did not differ statistically significantly from the initial data before treatment.

The generally positive outcomes after the ESSC course were recorded in 59 (56.2 %) patients; unsatisfactory outcomes, in 46 (43.8 %) patients.

EDT and ESSC. ESSC as the only procedure proved ineffective in 46 (43.8 %) patients; these patients simultaneously underwent EDT and ESSC. Interestingly, 35 (33.3 %) patients were group 1 patients, while 11 (10.5 %), group 2 patients. The results of this type of neuromodulation are shown on the histogram in Fig. 2.

The results indicate that the positive outcome was confirmed by the statistically significant ($p < 0.05$) reduction of muscle tone from 64.0 to 30.0 % and the H/M amplitude ratio from 68.3 to 40.1 % in 13 (12.4 %) patients, which allows one to assess the actual decrease in hyperreactivity of motor neurons at the level of the lumbar spinal cord. The statistically significant reduction of the increased muscle tone from 62.0 to 28.0 % and the H/M amplitude ratio, from 56.3 to 40.5 % in 8 (7.6 %) group 2 patients demonstrate that the positive outcome was achieved. The ENMG data showed neither statistically significant positive dynamics of muscle tone nor the corresponding indicators in 25 group 1 and 2 patients in whom treatment proved ineffective.

LHSC was performed in 25 patients after the aforedescribed neuromodulation procedures proved ineffective: 22 (88.0 %) of these patients with paraplegia were group 1 patients and only 3 (12.0 %) patients with spastic tetraparesis were group 2 patients. The data on effectiveness of LHSC are summarized in Table 2.

The positive outcome was achieved in 52 % of patients. It was confirmed by the statistically significant ($p < 0.05$) reduction of the average indicators of muscle spasticity and the H/M amplitude ratio compared to the initial data; a clear

Table 1

Electromyography parameters of patients with the spastic syndrome before the treatment was started (M ± m)

Groups	H-reflex amplitude, mV	M-response amplitude, mV	H/M ratio, %
Control (n = 10)	1,09 ± 0,10	2,55 ± 0,20	42,80 ± 2,10
Group 1 (n = 58)	1,48 ± 0,10	1,55 ± 0,13	81,30 ± 2,50
	p < 0,05	p < 0,05	p < 0,05
Group 2 (n = 47)	0,62 ± 0,17	1,12 ± 0,14	56,30 ± 5,30
	p < 0,05	p < 0,05	p < 0,05
		p^1 < 0,05	p^1 < 0,05

p – statistical significance compared to the parameters in the control group;
p^1 – statistical significance compared to the parameters in group 1.

decrease in involuntary muscle spasms in the extremities was observed. LHSC showed no effect in 48% of patients. However, this value will be only 11.4 % if compared to the total number of patients (n = 105), while the outcome of neuromodulation therapy was positive in 88.6 % of patients.

The results of this study lay the basis for elaborating the algorithm for surgical treatment of spastic syndromes in clinical practice (Fig. 3).

According to the proposed algorithm, the neuromodulation therapy was started with ESSC (stage I). If the therapeutic effect was positive, patients were offered a system for chronic electrical stimulation of the spinal cord to be implanted. If the patents refused, they were discharged and provided recommendations for rehabilitation treatment. If no satisfactory outcome was achieved, stage II (EDT combined with ESSC) was started. If the positive outcome was achieved, the patients were discharged to receive rehabilitation measures. If the outcome was unsatisfactory, these patients underwent LHSC (stage III), the final stage of functional neuromodulation therapy. The achieved positive outcome allowed one to proceed to the scheme of rehabilitation therapy to restore the lost functions.

Discussion

Most clinicians assess spasticity according to the generally used Ashworth scale, which is a subjective method, since the reliability of measurements fully depends on physician's experience and expertise. In order to unify the assessment of treatment outcomes, we proposed the procedure for calculating its effectiveness coefficient by comparing the score or percentage before and after a therapy course, which allows one to interpret the outcomes of treating pain and/or spastic syndrome [6]. Some authors suggest using electroneuromyography to make assessment more objective as they believe that this method enables refining the Ashworth scale data [5]. However, the points of view in the available literature are exactly converse [12].

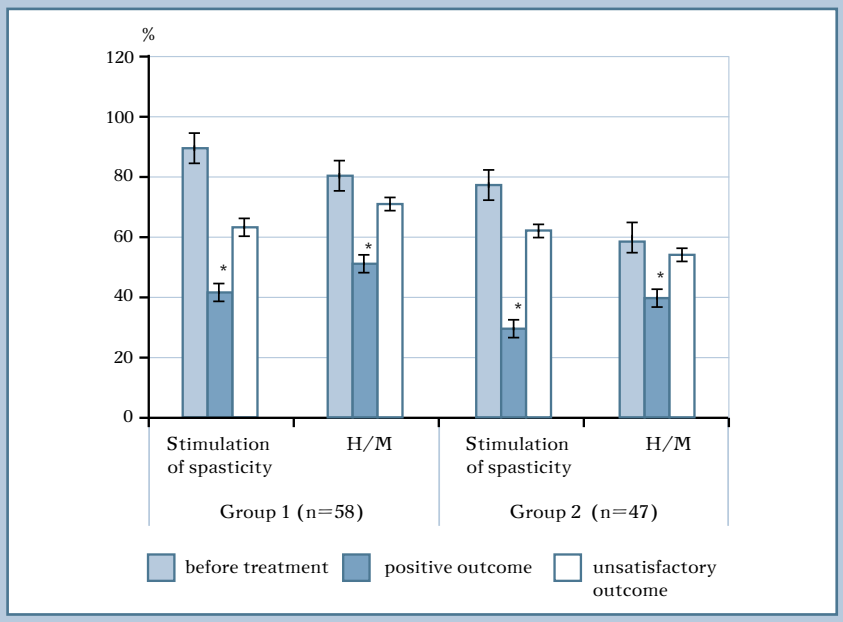

Fig. 1
Outcomes of electrical stimulation of the spinal cord: * – the indicators are statistically significant ($p < 0.05$) in groups 1 and 2 for the positive outcome compared to the initial data before treatment; H/M is the ratio between the H-reflex and the M-response

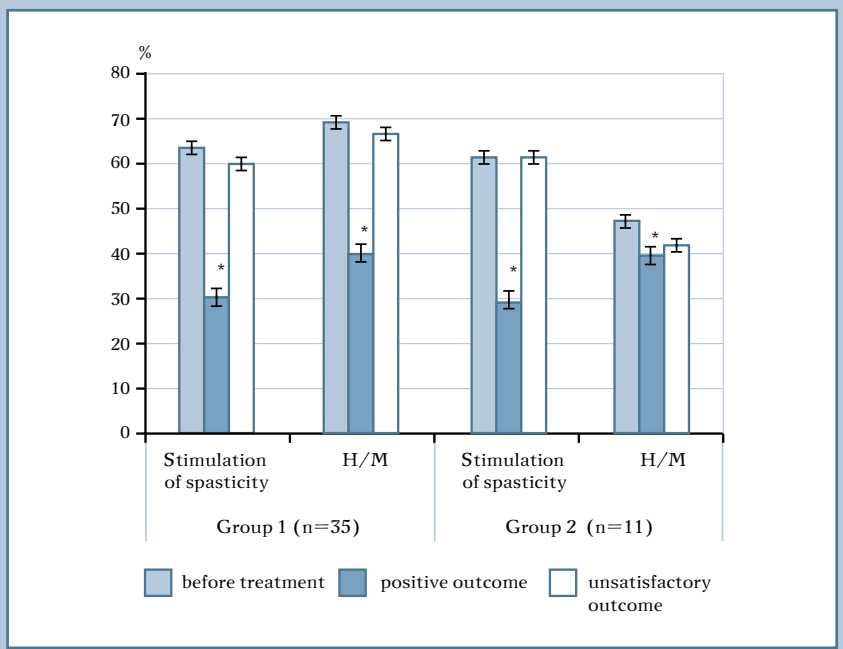

Fig. 2
Outcomes of epidural drug therapy and electrical stimulation of the spinal cord: * – the indicators are statistically significant ($p < 0.05$) in groups 1 and 2 for the positive outcome compared to the data obtained after the ineffective electrical stimulation; H/M is the ratio between the H-reflex and the M-response

In this connection, the potential of electroneuromyography needs to be further studied and refined. Our investigations demonstrated that the positive treatment outcome is almost always accompanied by a decrease in the degree of muscle spasticity, which was associated with a decrease in the ratio between the maximum amplitudes of the H-reflex and the M-response. These results agreed with the data reported by the foreign authors [13].

Test ESSC was the first modulation procedure used by most Russian and foreign clinicians; it was the key criterion for selecting patients to perform other types of therapy [10]. However, it proved effective only in half of the patients with post-injury spastic syndrome, while in the remaining patients, the increased muscle tone was eliminated by simultaneously using EDT, ESSC, and LHSC. It should be emphasized once again that among the total number of patients (n = 105), consistent application of the functional methods did not result in therapeutic effect in 11.4 % of patients. Hence, destructive surgeries (selective rhizotomy, coagulation of the posterior root entry zones, myelotomy, etc.) are indicated for these patients if intrathecal administration of baclofen or opiates using implanted pumps is impossible.

Conclusions

The proposed algorithm for consistent application of the methods for neuromodulation in patients with spastic syndrome after spinal cord injury made it possible to significantly reduce the severity of muscle spasticity in 88.6 % and laid the basis for further rehabilitation procedure, which justifies its use in clinical practice.

Table 2
Outcomes of local hypothermia of the spinal cord according to the Ashworth scale and the electroneuromyography data (M ± m)

Outcome	Muscle spasticity, score	Muscle spasticity, %	The H/M amplitude ratio, %
Initial data	2,90 ± 0,10	58,00 ± 2,00	59,80 ± 2,00
Positive outcome (n = 13)	1,40 ± 0,05*	28,00 ± 1,00*	40,80 ± 1,20*
Unsatisfactory outcome (n = 12)	2,50 ± 0,10	50,00 ± 2,00	52,40 ± 1,50

*the result statistically significantly (p < 0.05) differs from the initial data.

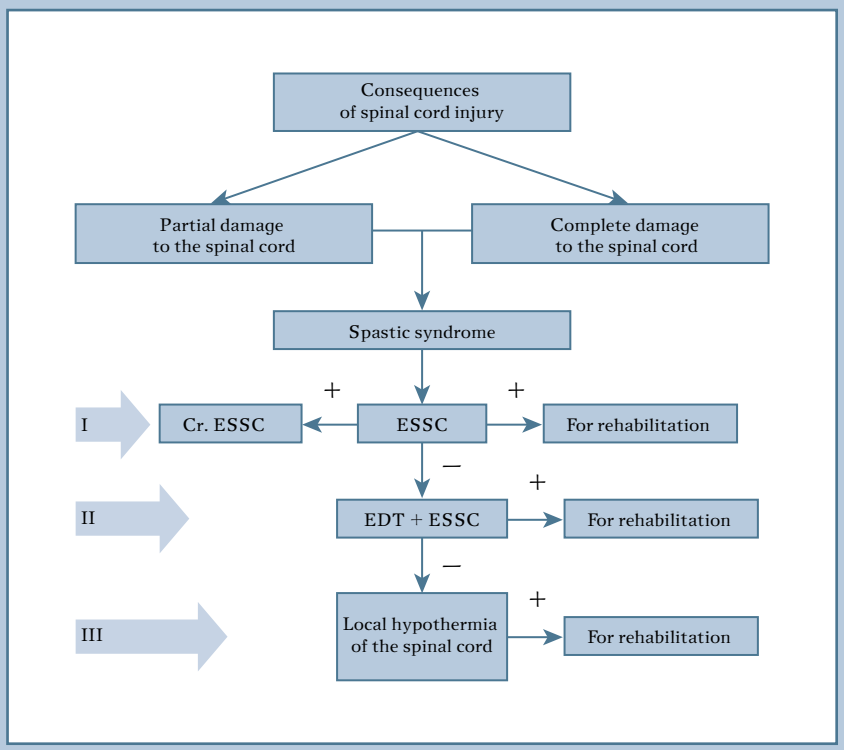

Fig. 3
Algorithm for surgical treatment of spastic syndromes: ESSC – electrical stimulation of the spinal cord; Cr. ESSC – chronic stimulation of the spinal cord; EDT – epidural drug therapy

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