Novel approaches to the treatment of cervical dystonia. The concept of dual navigation control

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Cervical dystonia (CD) is the most common type of focal dystonia (up to 50% of all dystonia cases). Botulinum neurotoxin (BoNT) injections is the treatment choice for CD. However, the effectiveness and tolerability of botulinum therapy in CD depends on the correct choice of target muscles and the accuracy of the BoNT injection. The publication presents literature data and our own clinical experience regarding the use of navigation in BoNT injections in CD.
According to the majority of authors, the use of navigation equipment, such as ultrasound (US) and electromyography (EMG), definitely increases the effectiveness of CD treatment and reduces the likelihood of adverse events. For the first time, an algorithm for the diagnosis and treatment of CD is proposed, based on the use of the method of «double- (EMG and US) guided navigation», a variant for determining the comparative activity of muscles by the intensity of the EMG signal and the design of an individual «passport» of the CD. The possibilities of analyzing the US of muscles, drawing up an accurate treatment regimen, targeted administration of BoNT, and using a non-injectable EMG electrode are shown. We present 4 clinical cases demonstrating the advantages of the double- (EMG+US) guided navigation method over the EMG-guided navigation for injection.
The proposed algorithm for the diagnosis and treatment of CD makes it possible to increase the effectiveness of treatment, optimize the costs of BoNT and diagnostic equipment (injection EMG needle).

Keywords: *cervical dystonia; botulinum neurotoxin; ultrasound; electromyography; guided navigation for injection; dystonic activity assessment.*
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Cervical dystonia (CD) is the most common form of dystonic hyperkinesis with an incidence of up to 20 cases per 100 thousand people. As a rule, the debut of CD occurs at the age of 35–43 years, the diagnosis of CD is obvious. Nevertheless, in 50% of patients, the diagnosis of «dystonia» is established only after a year, and in 24% – after 5 years from the onset of the first manifestations of the disease [1, 2].

According to the existing recommendations for CD treatment, injections of botulinum neurotoxin (BoNT) belong to the first-line therapy with proven efficacy and safety [3, 4]. About a half of patients return to work after BoNT treatment, 56% are absolutely satisfied, 25% are satisfied, and 20% are not satisfied with the results of treatment [5]. The reasons for dissatisfaction include insufficient or short-term effect of injections. Thus, in 45% of cases, it is not possible to achieve complete relief of the symptoms of CD, which is primarily due to the complexity of the diagnostic analysis of the existing muscle pattern of CD and the peculiarities of the use of BoNT drugs [5–7].

The work of Gerhard Reichel et al. [8], devoted to the verification of CD patterns, made it possible to differentiate any possible trajectory of movement of the neck and head (Fig. 1), identifying the muscles responsible for the formation of each posture. In total, 10 main forms of pathological head and neck positions have been identified, plus, additionally, shoulder and scapula lift. The combination of these patterns can give up to 730 individual forms of CD, each determined by the pathological activity of various muscles and their numerous combinations [7]. Obviously, trying to focus only on the appearance of the patient and choosing from a formalized list of muscles responsible for a specific muscle pattern, especially in difficult cases, minimizes the effectiveness of treatment.

Thus, the usefulness of determining the dystonic muscles and the accuracy of injection into them are of paramount importance for improving the effectiveness of CD treatment.

Needle insertion in accordance with anatomical landmarks has traditionally been the most commonly used method of BoNT injections [9, 10]. This method consists of palpation of muscles, detection of increased tone or contraction in them, determination of possible muscles involved in the phenomenology of the dystonic posture [11]. Some anatomical landmarks are also taken into account to determine the target muscles. This method requires deep knowledge of the anatomy of the neck, moreover, physical characteristics of each patient add to the possibility of errors, so the accuracy and side effects depend significantly on the specialist's experience. The only advantage of this method is saving time during the procedure.

Studies with the use of needle electromyography (EMG) during the examination of patients with CD have shown that clinical examination alone is not sufficient to determine which muscles contribute to the dystonic movement [12]. Without the use of EMG, specialists in motor disorders correctly identified only 59% of active muscles. The choice of wrong muscles and inaccuracy of injections explain why some patients have a suboptimal effect and develop undesirable phenomena [12, 13].

The peculiarity of using EMG as a diagnostic and navigation method in the treatment of CD is that the needle is inserted into the projections of the muscles selected during the preliminary examination to the depth at which an audible signal indicating the dystonic activity of the muscle will be received. This approach does not allow to target complexly oriented or thin muscles, such as, for example, *m. obliquus capitis inferior* and *m. longissimus cervicis*. Even when injecting into the projection of large muscles with registered dystonic activity, the specialist does not know for sure which muscle has been reached, and although this allows for a sufficient therapeutic effect, it does not give confidence in the accuracy of verification of the injected muscle. EMG helps detect hyper-reactivity of a muscle when it hits it, but it does not allow to accurately target and reach a specific muscle and cannot help avoid traumatization of anatomical structures of the neck, such as blood vessels (vertebral artery, carotid artery or jugular veins), the cervical plexus, vagus nerve or spinal nerve roots. This is another important limitation of EMG as a navigation tool for BoNT injections [14, 15]. In the future, with subsequent injections, a specialist may be mistaken in assessing the role of muscles previously selected on the basis of EMG activity in the formation of a particular CD phenotype, and thus provoke the emergence of more complex, combined patterns.

The exclusive use of EMG control has another very serious drawback P excessive trust in the signal and acting only in accordance with the signal. Thus, the work of a doctor forfeits one of its most important aspects P a conscious clinical search and pursuit of diagnostic excellence. In this case, the clinical analysis of patterns, their dynamics and individuality are practically not taken into account. In addition, the use of EMG significantly increases the cost of botulinum therapy, which is associated with the cost of electromyographic injection needles.

Thus, even if it is possible to perform EMG, there is a number of serious drawbacks: high cost, insufficient quality of diagnosis and the risk of injury to the vessels and nerves of the neck.

The lack of technical capabilities for many years fixed this diagnostic algorithm, and despite the known shortcomings, EMG was the best method that could be used in the treatment of CD. Recently, there has been a rapid development of methods of visual navigation control of injections (ultrasound and computed tomography). They make it possible to visualize muscles that were previously identified clinically and phenomenologically associated with abnormal postures [8, 16–21], but even now no proposals have been formulated to improve the technology of diagnosis and treatment of CD.

The ultrasound navigation method has already taken its strong positions in botulinum therapy of spasticity, displacing EMG control [22]. The main advantage of ultrasound navigation over EMG is the possibility to make an accurate injection into the selected muscle and control the real distribution of BoNT in it.

There are indirect ultrasound signs that allow to identify dystonic muscles: registration of its contraction at the time of ultrasound examination or bilateral comparison of the muscles of the same name, which allows to reveal the asymmetry of their ultrasound picture – hypertrophy or hyperechogenicity of one of them [22]. Muscle hypertrophy indicates the most hyperactive muscles involved in abnormal posture or movement. The conclusion about dystonic activity is made after comparing the thickness of this muscle with the contralateral one of the same name. An increase in the intensity of the echo signal in the dystonic muscle is a change caused by the development of intramuscular fibrosis or a decrease in the amount of intercellular fluid as a result of a prolonged muscle spasm [22–25].

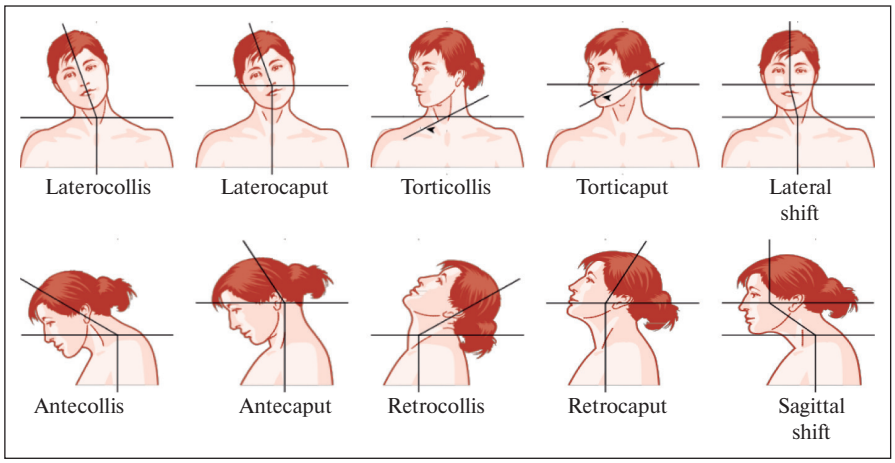

Fig. 1. *Clinical forms of cervical dystonia [8]*

Table 1. *An example of dystonic pattern «passport» in CD*

Pattern	Muscles	Ultasound		EMG-activity
		hypertrophy	hyper-echogenicity	
Torticollis	SCM SC	+ +		++ +++
Torticaput	OCI			+++
Scapula lifting	LS	+	+	+

Note. SCM – *m. sternocleidomastoideus*; SC – *m. splenius capitis*; OCI – *m. obliquus capitis inferior*; LS – *m. levator scapulae*.

However, indirect signs cannot be a sufficient criterion for choosing a target muscle in CD, since we also need to know the functional activity of the muscle. This can be provided by EMG which has undoubted advantages over ultrasound diagnostics, because it allows to determine dystonic activity in the area of needle insertion, while having an undoubted disadvantage: it does not allow to make sure that the needle is located in the active muscle.

Another advantage of ultrasound over EMG is the minimization of side effects, since ultrasound allows to visualize nerves and vessels in real time, which provides a chance to avoid injuries to anatomical structures such as the cervical plexus, jugular veins, carotid or vertebral arteries, etc. [22, 26, 27].

It is obvious that each of the methods has its advantages and disadvantages, which significantly limit the improvement of the quality of diagnosis and treatment.

The solution of the problem lies in the simultaneous use of these two navigation methods: EMG and ultrasound. Such a «double control» option allows to use ultrasound navigation to verify any muscle and target it with an EMG needle, thereby checking the activity of the muscle. These methods, complementing each other, create a full-fledged diagnostic picture of the CD pattern. A sequential check of all the muscles capable of providing this pathological movement or posture gives a unique opportunity to create an individual «passport» of CD with the identification of specific dystonic muscles, which allows to choose an individual treatment regimen for the patient.

One of successful recent methodological findings is the gradation of sound of dystonic muscle activity in percent or using «crosses» to mark the intensity of the EMG signal. Despite the fact that assessment in each study is made subjectively, depending on the extremes of different signal intensity from minimum to maximum, the specialist has an opportunity to distribute the muscles according to the degree of their participation in the formation of a dystonic pattern (Table 1).

Creating an individual «passport» of CD during the initial examination allows to minimize the time of subsequent injection sessions, avoid using EMG during these sessions, and use only ultrasound navigation, or use EMG only in the case of a change in the dystonic pattern. This significantly reduces the cost of BoNT procedure, except for the cost of an injectable EMG needle.

Thanks to ultrasound navigation, it is possible to completely eliminate the cost of an injectable EMG needle. To do this, it is enough to use a conventional EMG electrode for detection of dystonic muscles and inject BoNT under ultrasound control. Creating a list of active muscles will allow to perform subsequent injections guided only by ultrasound navigation if the CD phenotype remains unchanged. If the pattern changes, the methodology can be modified, as in the initial selection of a treatment regimen.

The creation of a CD passport increases the time spent on the initial diagnosis, but a significant improvement in the quality of treatment, decreased time spent on subsequent injection sessions, and a reduction in the cost of treatment compensate for this disadvantage.

Another advantage of ultrasound picture and EMG activity is the possibility of tracking the dynamics of muscle condition during the treatment and creating a full-fledged registry of patients with a high-quality observation history.

Here are some clinical observations.

***Patient T.**, 21 years old. BoNT treatment was started 5 months after the first symptoms appeared. A combination of patterns was as follows: right-sided latero- and torticollis, lifting of the shoulder blade and shoulder on the right. The CD score on the*

Table 2. *A dystonic pattern «passport» of a 21-year-old male patient T. with CD*

Pattern	Muscles	EMG-activity	Dysport, U
Torticollis on the right	SCM sin., SC dex.	++ ++	150 200
Laterocollis on the right	Long. cerv. dex.	+++	150
Scapula lifting on the right	LS dex.	+	200

Note. SCM sin. – *m. sternocleidomastoideus sinister*; SC dex. – *m. splenius capitis dexter*; Long. cerv. dex. – *m. longissimus cervicis dexter*; LS dex. – *m. levator scapulae dexter*.

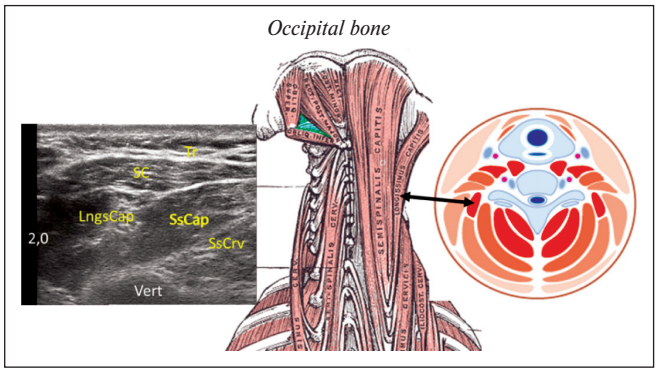

Fig. 2. *The location of m. longissimus capitis et cervicis on the screen of the US-scanner, in the anatomical atlas and on the diagram of the neck section at the C_{VI} level*

Table 3. *A dystonic pattern «passport» of a 43-year-old male patient P. with CD*

Pattern	Muscles on both sides	EMG-activity	Dysport, on both sides in each muscle, U
Retrocollis	SCM SC S/s cap. et cerv.	+ +++ ++	50 300 100
Shoulders and scapulae lift	LS Tr	+ +++	50 100

Примечание: SCM – *m. sternocleidomastoideus*; SC – *m. splenius capitis*; S/s cap. et cerv. – *mm. semispinalis capitis et cervicis*; LS – *m. levator scapulae*; Tr – *m. trapezius*.

Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) was 30 points. The choice of target muscles was carried out according to the form of movement and under EMG control. During 2 years of observation, the clinical picture changed dynamically, the effect was insufficient and unstable, and there was a tendency toward the pattern change. The effectiveness of different injection sessions varied, which led to a constant change of drug doses and the list of target muscles. The drug Dysport was used. The doses reached 1000–1200 units. TWSTRS score was 24 points. The patientXs and familyXs satisfaction with the treatment was low. At the 6th injection session, after 2 years of treatment, ultrasound navigation was introduced. The compilation of an individual «passport» of the patient revealed an increase in hyper-echogenicity of m. longissimus cervicis on the right. The targeted insertion of an EMG needle into the muscle showed «+++» activity.

Changing the method of introduction enabled us to achieve the best effect. TWSTRS score reached 3 points. The total dose of Dysport was decreased to 700 units. The use of this scheme for a year led to a stable remission lasting for 3 years. TWSTRS score became 0 points, accompanied by absolute satisfaction with the treatment.

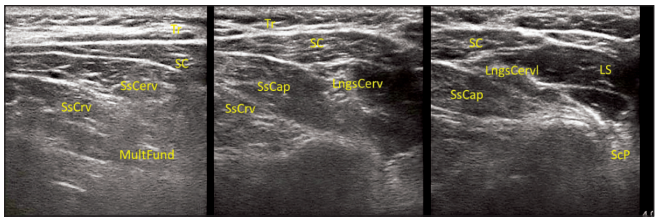

Рис. 3. *Расположение мышц задней поверхности шеи на экране УЗ-сканера*

Table 4. *A dystonic pattern «passport» of a 40-year-old female patient V. with CD*

Pattern	Muscles	EMG-activity	Dysport, U
Torticollis to the left	SCM dex. SC sin.	++ +++	150 300
Torticaput to the left	OCI sin.	+++	120

Note. SCM dex. – *m. sternocleidomastoideus dexter*; SC sin. – *m. splenius capitis sinister*; OCI sin. – *m. obliquus capitis inferior sinister.*

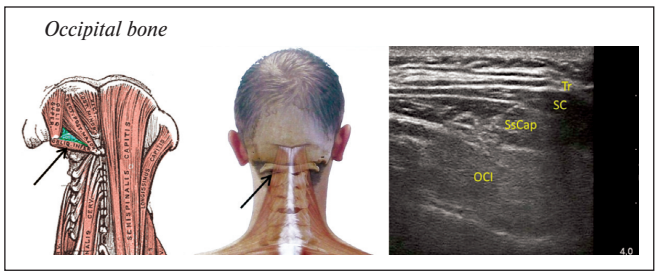

Fig. 4. *The location of m. obliquus capitis inferior in the anatomical atlas and on the screen of the US-scanner (C_{II} level)*

Table 5. *A dystonic pattern «passport» of a 37-year-old female patient V. with CD*

Pattern	Muscles	EMG-activity	Dysport, U
Torticollis to the right	SCM sin. SC dex. S/s cerv. et multifidii sin.	++ ++ +++ +++	150 200 200 100
Scapula lifting on the right	LS dex.	++	150

Note. SCM sin. – *m. sternocleidomastoideus sinister*; SC dex. – *m. splenius capitis dexter*; S/s cerv. et multifidii sin. – *m. semispinalis cervicis et multifidii sinistri*; LS dex. – *m. levator scapulae dexter.*

Patient P.*, 43 years old. The patient was observed by various specialists for 6 years, received BoNT treatment without proper effect. During the examination, retrocollis was diagnosed. TWSTRS score was 34 points. The drug Dysport was administered under EMG control with a pronounced effect, but it was not possible to achieve a complete correction of the position of the head and neck. Doses reached 1000–1200 units. TWSTRS was 18 points. The complex use of ultrasound and EMG allowed to verify target muscles for injections and correct the formulation, as well as to clarify the activity in mm. trapezius and levator scapulae, m. sternocleidomastoideus. The total dose remained at the level of 1000–1200 units. TWSTRS score decreased to 3 points, with absolute satisfaction with the treatment.*

Patient V.*, a 40-year-old woman, complained of a forced tilt of the head and neck to the left; the symptoms appeared about a year ago. During the examination, torticollis was diagnosed. TWSTRS was 39 points, the angle of rotation of the head was 60-70°. Dysport injection was performed into m. sternocleidomastoideus sinister and m. splenius capitis dexter – 150 and 300 units, respectively, without instrumental control. At the control examination after 21 days, an improvement was diagnosed, but it was not possible to achieve the middle position of the head; the angle of rotation of the head was about 30°. Analysis showed the middle position of the neck. It was concluded that there was an additional pattern in the form of a torticaput. An EMG needle was inserted under ultrasound control into m. obliquus capitis inferior sinister, and dystonic activity «+++» was obtained. The dose of 120 units of Dysport was introduced. At the control examination after 21 days, the middle position of the head and neck was recorded. The total dose of Dysport was 570 units. TWSTRS decreased to 5 points, the patient was satisfied with the treatment.*

Patient D.*, a 37-year-old woman, complained of a forced tilt of the head and neck to the right and backwards. On examination, a right-sided torticollis with retrocollis elements and a right shoulder blade lift was diagnosed. TWSTRS was 36 points. Dysport injections were performed into mm. sternocleidomastoideus sin., splenius capitis dex. et levator scapulae dex. (200, 300 and 200 units, respec-*

tively) under EMG control. At a follow-up examination after 21 days, a slight improvement was observed. Laterocollis was preserved to a large extent. TWSTRS was 26 points. Diagnostic search using double control revealed dystonic activity «+++» in mm. semispinalis cervicis et multifidi sin. At the next visit (after 12 weeks), the treatment regimen was adjusted. The total dose of Dysport was 800 units. At the control examination after 21 days, the middle position of the head and neck was recorded. TWSTRS decreased to 5 points, together with absolute satisfaction with treatment.

Discussion

Even 5–6 years ago, no one expressed an idea about the possibility of using ultrasound systematically for navigation in the treatment of CD. In the clinical guidelines for the diagnosis and treatment of dystonia published in Russia in 2014, only 12 muscles involved in CD patterns were mentioned, and EMG was the only method for navigating BoNT injections [28]. In 2016, we began to use ultrasound more and more actively to verify muscles, and identified up to 18 neck muscles. At the same time, the idea of using «dual (EMG and ultrasound) control» of injections began to take shape [11, 21, 22, 29].

There is no doubt that the transition to a new level of diagnosis and treatment of CD is a timely and reasonable process associated with the awareness of the need for a combination of ultrasound and EMG control methods. This is confirmed by accumulating experience of specialists from different countries and the appearance of the first independent publications [11, 17, 21, 22, 29–31], which mention the use of both ultrasound and EMG control in the treatment of CD.

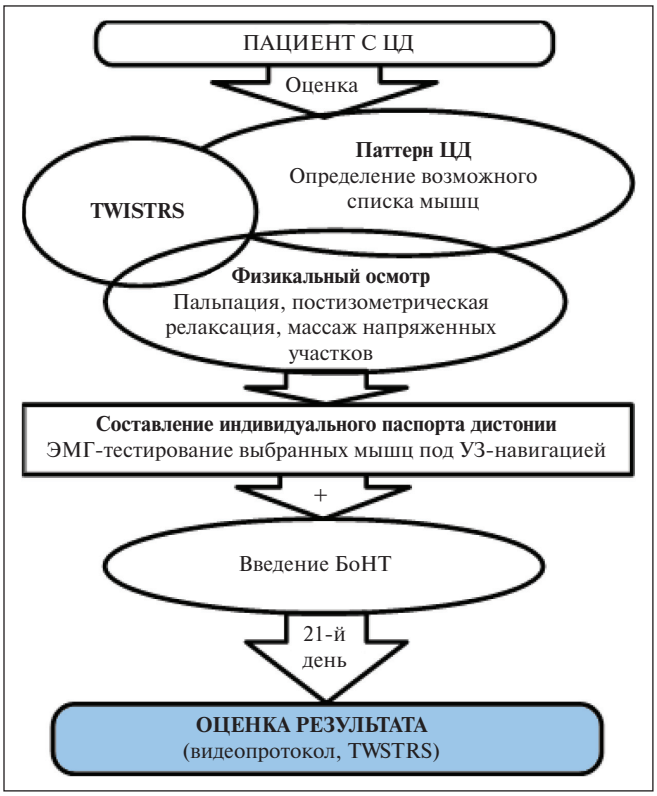

Fig. 5. *CD diagnostic algorithm*

One of the first such publications is a work by S.K. Allison and I.R. Odderson (2016) [29], which describes an approach to the treatment of antecollis, and a review work by A. Castagna and A. Albanese published in 2019 [11]. In the next 2 years, two more works were published: in 2020, a work of M. Farrell et al. [30], also devoted to the treatment of antecollis, and in 2021 - a review publication by G. Salazar et al. [31], in which the possibilities of EMG and ultrasonic navigation are analyzed in sufficient detail from a practical point of view. It should be noted that the algorithm of CD diagnostics proposed in our work, the option of determining the comparative activity of muscles by the intensity of the EMG signal and the design of an individual «CD passport» have not yet been found in the literature (Fig. 5).

Although CD is often a therapeutic problem due to the difficulty of determining the muscles involved in the abnormal posture, and there are reports of side effects and ineffectiveness of BoNT injections, instrumental injection is not always used for such patients, and manual needle insertion is often preferred, despite the evidence of better results obtained with instrumental methods, such as EMG and ultrasound, and especially their combination [9, 11, 13–17, 22]. The accuracy of BoNT injections and, accordingly, effectiveness of the therapy are clearly reduced when instrumental navigation is not used, and side effects are obviously amplified, which is reflected in most publications [9, 11, 13–17, 22, 25–31]. While ultrasound devices are being technically improved every year, and are becoming more and more accessible, the degree of use of ultrasound navigation in clinical practice of botulinum therapy of CD is still insufficient. Increasing the availability and simplification of technical devices (EMG and ultrasound devices) should also facilitate instructing doctors how to use them, and improve effectiveness and tolerability of BoNT therapy in patients with CD. Studies dedicated to proving the benefits of navigation control, especially when using «dual (EMG and ultrasound) control», are still needed and can help to implement these techniques more actively.

Currently, several botulinum toxin type A drugs have been registered on the territory of the Russian Federation for the treatment of CD. The most commonly used drugs are abobotulotoxin A (Dysport), onabotulotoxin A (Botox) and incobotulotoxin A (Xeomin). The choice of the drug Dysport in all presented clinical cases was associated with a broad evidence base (meta-analysis of observational studies; n=920) in the field of CD treatment; In particular, there was a persistent statistically significant decrease in TWISTRS scores: -12.9 (95% CI -13.9 -11.8) at the 4th week of the injection cycle and -3.2 (95% CI -3.8-2.7) at the end of the cycle. At the same time, the average time before repeated treatment was 14 weeks [32].

The use of the «double control» allowing examination and checking the activity of each muscle, for the first time clearly shows conditional character of CD patterns. The analysis of the presented clinical cases demonstrates that certain muscles are active in different patterns, and some patterns occur when the action of several muscles atypical for this clinical picture is combined. Obviously, with the increasing use of this diagnostic algorithm, the significance of correlating an individual form of CD with a specific pattern will decrease.

Conclusion

The complex use of ultrasound and EMG navigation (double control) in CD allows: to perform a preliminary analysis of the ultrasound picture of the muscles; to verify with the help of EMG the degree of dystonic activity of the muscles; to choose an accurate treatment regimen; to perform targeted needle insertion into a particular muscle; to monitor and analyze muscle changes during BoNT therapy and dynamic observation; to use a non-injection EMG needle.

The proposed algorithm for the diagnosis and treatment of CD, which includes the method of «double (EMG and ultrasound) navigation control» with determining comparative muscle activity by the intensity of the EMG signal and creating an individual «passport» of CD, allows to increase the effectiveness of treatment, optimize the costs of BoNT drugs and the diagnostic equipment (injection EMG needle).

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