



Using Mathematical Models within the Cosmetological Aid Organization in the Context of Botulinum Toxin Therapy of Upper Face Skin Age-Related Changes

Marina Aleksandrovna Pozdniakova, Olga Nikolaevna Krasilnikova*

Department of Preventive Medicine Privolzhsky Research Medical University» of the Ministry of Health of the Russian Federation.

*Corresponding Author: Olga Nikolaevna Krasilnikova

Abstract

Mathematical modeling is the language of modern science. This paper describes the application of the mathematical evaluation of the clinical efficiency of botulinum toxin therapy of age-related changes in the skin of the upper half of the face on the example of correcting the three zones of the patient. For this purpose, we used the scoring scale; schedules that help the doctor get new information about the effectiveness and quality of the procedure throughout the observation period, and master practical skills of quality examination. Such an approach in cosmetology will make it closer to evidence-based medicine, contributing to the objectification and systematization of the accumulated data.

Keywords: *Cosmetological care, Botulinum toxin therapy, Evaluation of the efficiency of injection correction of age-related facial skin changes, Quality of medical care, Integral quality factor.*

Introduction

Progress in the field of science and medicine has led to an increase in life expectancy and in interest in the quality of human life, an understanding of the basic mechanisms of aging and an increased interest in methods for correcting age-related manifestations. The so-called anti-age treatment regimens have become popular in many areas of medicine. Correction of endocrine and metabolic changes associated with natural aging processes is becoming one of the most relevant medical areas [1]. Thanks to these trends, botulinum “wonder toxin” became in the twenty-first century a widespread drug in the field of aesthetic and anti-aging medicine [2].

However, these are not the only areas of its application. Botulinum toxin (BT) has gained wide popularity in neurology, for the treatment of chronic migraines, myofascial pain [3-5], in urology - for the treatment of neurogenic bladder syndrome [6, 7], in ophthalmology -for the treatment of blepharospasm, neurotrophic keratopathy [8, 9], in neurosurgery - for a dysfunction of the facial nerve and the trigeminal nerve in neurinomas, meningiomas.

BT blocks the transmission of impulses from the nerve to the muscle, affecting the release process of the neurotransmitter acetylcholine from vesicles by the nerve ending [10]. Botulinum toxin injections have become the most common cosmetic procedure. According to the survey data of the American Society of Aesthetic Plastic Surgery (ASAPS) for 2016. Botulinum toxin injections rank first (over 4.5 million procedures) among all non-surgical interventions. The popularity of this method of wrinkle correction has increased 64.5 times since 1997 [11]. In 2002, the FDA approved the use of Botox (Botox Cosmetic) for cosmetic purposes - to eliminate facial wrinkles on the forehead and around the eyes [12].

After this official recognition, botulinum toxin injections, which have radically changed the approaches to the methods of rejuvenation [13], smoothing mimic wrinkles caused by excessive activity of the subcutaneous muscles, began to occupy a leading position among all cosmetic procedures in the world [1, 14, 15, 16].

The volume of injection cosmetology services in Russia in 2016 exceeded 104 billion rubles; more than 12 million procedures were carried out [17]. The volume of services of botulinum therapy in 2017 according to the Vademecum Analytical Center amounted to 19.5 billion rubles; the total consumption of botulinum toxins was 99.4 million units [18]. The result of the provision of these medical services is the improvement of the skin, facial rejuvenation, and hence an increase in self-esteem and quality of life [19, 22].

However, the practice not always shows a sufficient cosmetic effect. Repeated injections cause clinical resistance and loss of treatment effectiveness [23]. The time of onset and duration of response are key indicators of the effectiveness of botulinum therapy [24].

Studying and improving the evaluation of the effectiveness of the correction by both patients and the doctor, familiarizing the patient in order to increase his/her compliance and satisfaction with the results, contribute to further improvement of the quality of medical care, allow for self-control and self-education of the professional work of a cosmetologist.

Despite numerous developments in health care quality management, this issue remains relevant today. Objective: to develop and test a mathematical model for evaluating the clinical efficacy of botulinum therapy of age-related changes in the skin of the face for the standardization and objectification of the results of botulinum toxin injection therapy.

Material and Methods

We shall consider the results of zonal wrinkle correction, taking into account the mathematical model for calculating the integral quality factor (IQF) [25]. To form a mathematical model for assessing the quality of botulinum therapy for mimic age-related changes in the skin we followed the following stages.

Collection of Material

The collection of material begins from the initial correction with BTA and lasts for 6 months. We assume several visits of the patient for the purpose of control: 14 days, 1 month, 3 months, and 6 months after the correction (if there is no need for the next botulinum therapy procedure earlier).

Material collection includes information on the wrinkles depth of the corrected facial areas (the assessment is carried out at each visit), the dose of the drug administered at the first visit and at the second visit again after 14 days, if there is a need for an additional correction, introduction scheme (number of rows, number of points), etc.

Material Processing and Optimal Scheduling

Statistical processing of the collected material, the choice of the optimal variant of the injection correction of a specific facial area, which will ensure minimum depth of wrinkles during the observation period. For both static and dynamic wrinkles, the corresponding diagrams can be constructed. Let's call them *optimal diagrams*. Now choose a diagram containing the best indicators throughout the observation period and use it as a reference for further assessments using different doses and drug administration regimen.

Analysis

Statistical analysis of the quality of the botulinum therapy procedure is carried out by processing and comparing all indicators of injection correction in real clinical cases with selected optimal values of these indicators. The lack of standards of medical care in the "Cosmetology" profile makes it difficult to control the results and quality. Botulinum therapy ICF can be determined by a simplified calculation formula taking into account only real and reference indicators throughout a certain period of observation.

Analysis Algorithm

We find R_i - the relative value of deviations of real indices of botulinum therapy from optimal (reference):

$$R_i = (A_i - K_i) / A_i$$

Where $i=1, N$, N - is the number of temporary cases of observation after the correction (in our case, the patient re-visits in 14 days (visit No.2), after 1 month (visit No.3), 3 months (visit No.4) and 6 months (visit No.5)). Therefore, in the above situation, the number of cases of observation (N) will be equal to 4);

K_i - the indicator of assessment of the correction quality of a real case at the i -th time point (measured from 1 to 5);

A_i - the indicator of assessment of the correction quality of the optimal (reference) case at the i -th time point (the reference quality indicator will always be equal to 5). If $R_i = 0$ (or <0 ?), we consider the result of the correction as achieved (this indicator will be equal to 0 when $K_i = A_i$).

We propose to calculate the value of ICF - the integral quality factor of botulinum toxin therapy during a certain period of observation, as follows:

$$BCF = (1 - \frac{\sum R_i}{N}) \times 100\%$$

Results

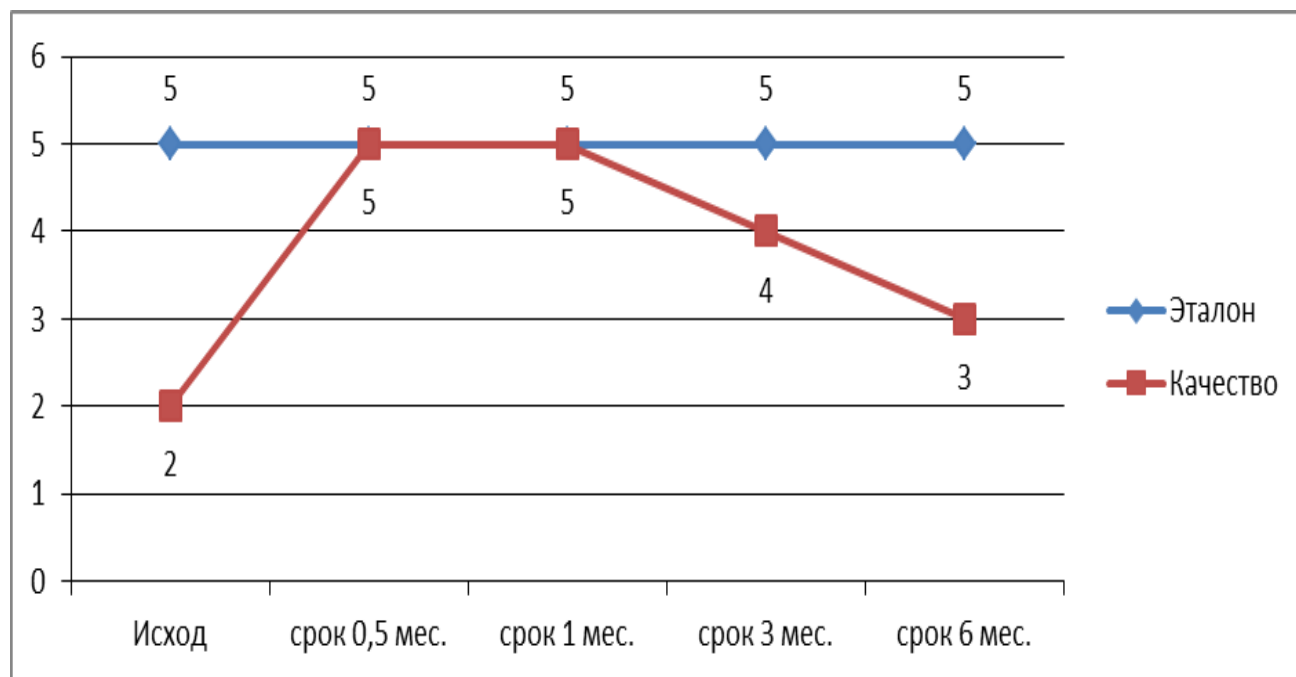
As an example, we present the following clinical observation, taking into account the mathematical model for calculating ICF, the visual diagram.

Female patient, 34 years old, correction of forehead wrinkles, total dose of Dysport - 16U, injections in 2 rows, 6 points. Assessment of the severity of dynamic wrinkles is 2 points (deep wrinkles). The observation period is 6 months (Table 1; Fig. 1).

Table 1: Dynamic forehead wrinkles in terms of quality and time of observation

Parameter	Time (months)				
	Ref.	0.5	1	3	6
Reference A_i	5	5	5	5	5
Actual K_i	2	5	5	4	3
Relative R_i	-	0	0	0.2	0.4

ICF=85%



Эталон	Reference
Качество	Quality
Исход	Baseline
Срок 0,5 мес.	0.5 month
Срок 1 мес.	1 month
Срок 3 мес.	3 months
Срок 6 мес.	5 months

Fig. 1: The correction quality of dynamic forehead wrinkles subject to the observation period

Female patient, 34 years old, correction of crow's feet wrinkles, total dose of Dysport - 40U, injections on both sides, 6 points.

Assessment of the severity of dynamic wrinkles is 1 point (very deep wrinkles). The observation period is 6 months (Table 2; Fig. 2).

Table 2: Dynamic periorbital wrinkles in terms of quality and time of observation

Parameter	Time (months)				
	Ref.	0.5	1	3	6
Reference A_i	5	5	5	5	5
Actual K_i	1	5	5	4	2
Relative R_i	-	0	0	0.2	0.6

ICF=80%

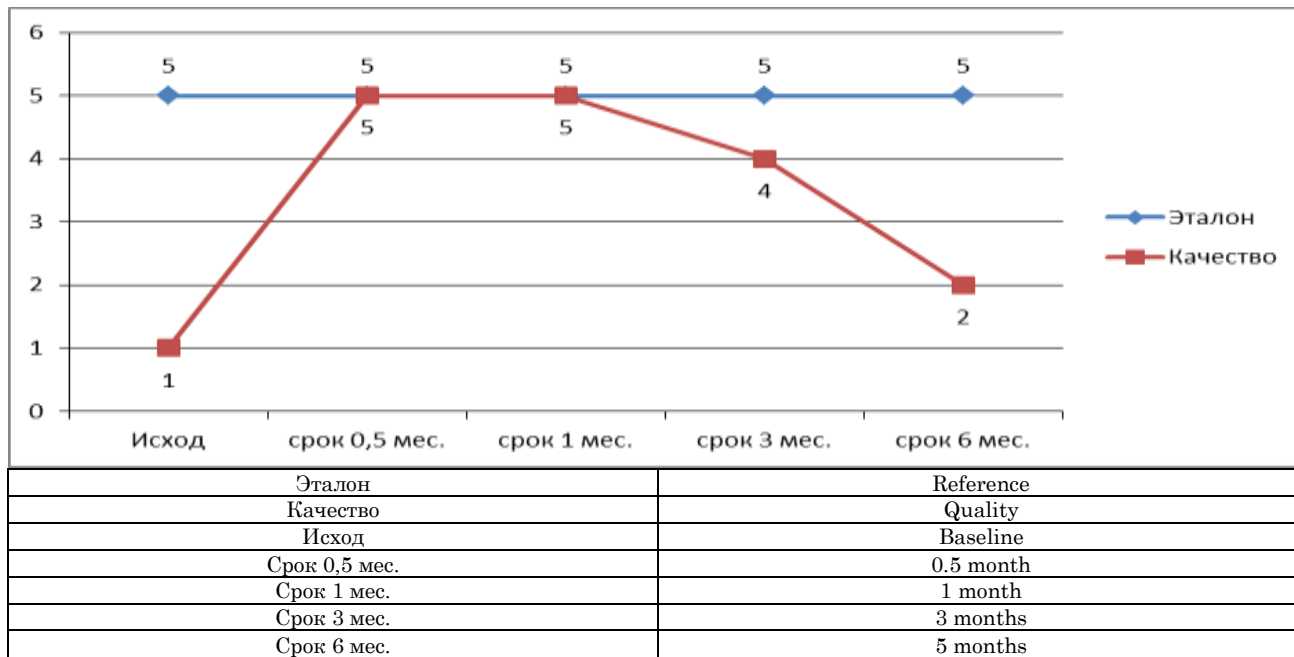


Fig. 2: The correction quality of dynamic periorbital wrinkles subject to the observation period

Female patient, 34 years old, correction of glabellar lines, total dose of Dysport - 44U, injections in 3 points. Assessment of the

severity of dynamic wrinkles is 2 points (deep wrinkles). The observation period is 6 months (Table 3; Fig. 3).

Table 3: Dynamic glabellar lines in terms of quality and time of observation

Parameter	Time (months)				
	Ref.	0.5	1	3	6
Reference A_i	5	5	5	5	5
Actual K_i	2	5	5	4	3
Relative R_i	-	0	0	0.2	0.4

ICF=85%



Fig. 3: The correction quality of dynamic glabellar lines subject to the observation period

Discussion

The aesthetic procedures evaluation scales is a necessary tool not only for the medical specialist and the administration, but also a way to systematize the accumulated experience, predict and develop new methods and techniques. However, it is not always possible to create a tool for assessing the quality of medical care due to subjectivity. Based on the analysis of the compiled questions and answers, the satisfaction questionnaire may not always be the optimal form for studying the result for the patient and the doctor [21].

The ideal rating scale should be simple, convenient, objective, and have a mathematical and graphical application [25]. The proposed scale is based on the existing GAIS, Merz Aesthetics scales. The Merz Aesthetics scale allows you to evaluate evolutionary changes in various zones (face,

neck, hands), including mimic wrinkles in statics and dynamics on a five-point system (from 0 to 4, where 0 is the absence of wrinkles or folds, and 4 is the most prominent feature: deep wrinkles at rest, turning into deep folds when changing the facial expression).

For example, "horizontal frontal wrinkles at rest scale": 0 - no wrinkles, 1 - no wrinkles at rest, fine wrinkles when changing facial expressions, 2 - thin wrinkles at rest, aggravating when changing facial expressions, 3 - thin wrinkles at rest, deep wrinkles when changing facial expressions, and 4 - deep wrinkles at rest, turning into deep folds when changing facial expressions. The GAIS (Global Aesthetic Improvement Scale) is used to assess the clinical efficacy of treatment. According to this scale, the result of the procedure is estimated by points from -1 to 3 by the doctor and patient (Table 4) [26].

Table 4: Global Aesthetic Improvement Scale (GAIS)

Score	Doctor's assessment	Patient's assessment
3	Optimal cosmetic result for this patient	Completely satisfied with the result
2	Significant improvement, but incomplete correction	Satisfied with the result, but would like to slightly improve
1	Improvement, but needs additional correction	Minor improvement, additional correction is desirable
0	No change, the state is the same as before the procedure	No change
-1	Worse compared with the initial state	The condition is worse than before the procedure

To describe the severity of wrinkles, we propose to apply the following characteristics using a 5-point system, where 5 points would mean no wrinkles; 4 - subtle wrinkles; 3 - fine wrinkles; 2 - moderate, deep wrinkles; and 1 - very deep wrinkles. The proposed scale has descriptive and graphic parts. The descriptive part of the scale is created by combining clinical, evaluative indicators and modification of the scoring [27] (Table 5), the graphic part is attached with a "Harmonious Face" photo, compiled using a computer program. We use photos BEFORE and AFTER the procedure, additionally creating the "Harmonious Face" photo, taking the

image BEFORE as a basis. We remove in the image the signs of aging of the treated skin areas of the upper half of the face and compare it further with the image AFTER the procedure (we do not correct the existing face asymmetry, if any, for example, asymmetry of eyebrow position in statics or dynamics, due to the complexity of execution and in order to save the doctor and patient time). Initially, we used only photos with wrinkles in dynamics, later, especially with combination correction; we began to compare photos of static and dynamic wrinkles BEFORE correction and the "Harmonious Face" photo.

Table 5: The "Harmonious Face" scale for evaluating the efficiency of injection correction of some wrinkles of the upper half of the face with botulinum toxin type A (descriptive part)

Localization of wrinkles	Scale	Clinical, subjective assessment and scoring of the effectiveness				
		5 Excellent	4 Good	3 Improvement, partial correction	2 No change	1 Deterioration, complications
Static glabellar lines (frown wrinkles)	A	No wrinkles	Subtle wrinkles	Thin but noticeable wrinkles	Moderate wrinkles	Deep wrinkles/complications
Dynamic glabellar lines (frown)	B	No wrinkles	Thin wrinkles	Moderate wrinkles	Deep wrinkles	Very deep wrinkles/complications

wrinkles)						
Static forehead wrinkles	C	No wrinkles	Subtle wrinkles	Thin but noticeable wrinkles	Moderate wrinkles	Deep wrinkles/complications
Dynamic forehead wrinkles	D	No wrinkles	Thin wrinkles	Moderate, superficial wrinkles	Deep wrinkles	Very deep wrinkles/complications
Static periorbital wrinkles (crow's feet)	E	No wrinkles	Subtle wrinkles	Thin but noticeable wrinkles	Moderate wrinkles	Deep wrinkles/complications
Dynamic periorbital wrinkles (crow's feet)	F	No wrinkles	Thin wrinkles	Moderate, superficial wrinkles	Deep wrinkles	Very deep wrinkles/complications

The developed scale has turned out to be attractive for assessing the effectiveness, but requiring computed correction of the photo, additional equipment and additional time for analysis. We have been able to improve the methodology for assessing effectiveness through the development and implementation of a mathematical model for evaluating the effectiveness of botulin toxin therapy.

Conclusion

The mathematical model, as the language of modern medical science, allows assessing the quality of the medical botulin toxin therapy of age-related changes of the facial skin, reflecting it visually, mathematically and graphically at all stages of observation, and developing and adjusting the clinical way of managing the patient from the first session to the final result - reducing the number and severity of wrinkles. The introduction of an assessment of the quality of wrinkles

correction of the upper third of the facial skin with the help of ICF allows us to bring medical interventions in cosmetology closer to the principles of evidence-based medicine. Mathematical analysis of the scoring of wrinkles and qualitative assessment of the correction procedure considering the dose of the drug used makes it possible to trace the changes in the effectiveness of the drug.

ICF allows evaluating the quality of the procedure of injection correction of a specific zone during dynamic observation, and determining the time for the re-correction at the stage of control examination. The use of ICF during staged observation makes it possible to assess the correctness of the applied dosages of the drug, taking into account the depth of wrinkles, the number of points of injection, to revise the accepted provisions of certain doses of botulin toxin therapy in the applied correction areas.

References

1. Ko AC, Korn BS, Kikkawa DO (2017) The aging face. *Surv. Ophthalmol.*, 32(2): 190-202.
2. França K, Kumar A, Fioranelli M, Lotti T, Tirant M, Rocchia MG (2017) The history of Botulinum toxin: from poison to beauty. *Wien Med. Wochenschr.*, 167 (1): 46-48.
3. Natoli JL, Manack A, Dean B et al (2010) Global prevalence of chronic migraine: a systematic review. *Cephalalgia*, 30, 599.
4. National Institute for Health and Clinical Excellence (2016) Botulinum Toxin Type A for the Prevention of Headaches in Adults with Chronic Migraine.
5. Khalil M, Zafar HW, Quarshie V et al (2014) Prospective analysis of the use of OnabotulinumtoxinA (BOTOX) in the treatment of chronic migraine; real-life data in 254 patients from Hull. U.K. *J. Headache Pain*, 15: 54.
6. Jhang JF, Kuo HC (2016) Botulinum toxin and lower urinary tract dysfunction: pathophysiology and mechanisms of action. *Toxins (Basel)*, 8: 120.
7. Kuo HC (2007) Comparison of effectiveness of detrusor, suburothelial and bladder base injections of botulinum toxin a for idiopathic detrusor over activity. *J. Urol.*, 178, 1359-1363.

8. Dutton JJ, Fowler AM (2007) Botulinum toxin in ophthalmology. *Surv. Ophthalmol.*, 52: 13-31.
9. Bentivoglio AR, Fasano A, Ialongo T, Soleti F, Lo Fermo S, Albanese A (2009) Fifteen-year experience in treating blepharospasm with Botox or Dysport: same toxin, two drugs. *Neurotox Res.*, 15, 224-231.
10. Brennan A, Hickey M (2019) Botulinum toxin in women's health: An update. *Maturitas*, 119, 21-24. DOI: 10.1016/j.maturitas.2018.10.005.
11. ASAPS (2016) Please credit the American Society for Aesthetic Plastic Surgery when citing statistical data. Retrieved from <https://www.surgery.org/sites/default/files/ASAPS-Stats2016-page7.pdf> (Accessed on April 5, 2018).
12. US Food and Drug Administration (USFDA) (2013) Drug Safety Labeling. Botox (onabotulinumtoxinA) FDA.
13. Rohrich RJ, Janis JE, Fagien S, Stuzin JM (2003) The cosmetic use of botulinum toxin. *Plast Reconstr Surg.*, 112: 177-188.
14. Ashera B, Landau, M. (Eds.). (2016) Injection methods in cosmetology. 2nd ed. Moscow: MEDpress-inform.
15. Goldberg DJ (Eds.). (2011) Facial rejuvenation. Modern non-surgical methods. Moscow: Practical medicine.
16. Dorizas A, Krueger N, Sadick NS (2014) Aesthetic uses of the botulinum toxin. *Dermatol. Clin.*, 32(1), 23-36.
17. Goncharova OO (2017) Key trends in the market of injection cosmetology in Russia in 2016. *Injection methods in cosmetology*, 2: 4-9.
18. Goncharova OO (2018) Key trends in the market of injection cosmetology in Russia in 2017. *Cosmetics and medicine*, 2: 26-30.
19. Gubanova EI (2015) Cosmetology today: development guidelines and major trends. *Kosmetik international*, 2: 16-25.
20. Obagi ZE (2016) Art of skin revitalization: restoration and rejuvenation. Scientific basis of clinical practice. Moscow: Practical medicine.
21. Scharschmidt D, Mirastschijski U, Preiss S, Brähler E, Fischer T, Borkenhagen A (2018) Body image, personality traits, and quality of life in Botulinum Toxin A and dermal filler patients. *Aesthetic Plast. Surg.*, 42(4), 1119-1125.
22. Ruiz-Rodriguez R, Martin-Gorgojo A (2015) Diez errores a evitar en la inyección de toxina botulínica. *Actas Dermo-Sifiliográficas*, 106(6): 458-464.
23. Stephan F, Habre M, Tomb R (2014) Clinical resistance to three types of Botulinum toxin type A in aesthetic medicine. *J. Cosmet. Dermatol.*, 13(4): 346-348.
24. Nestor M, Ablon G, Pickett A (2017) Key parameters for the use of abobotulinumtoxinA in aesthetics: onset and duration. *Aesthet. Surg. J.*, 37 (1): 20-31.
25. Gubanova EI, Krasilnikova ON, Pozdniakova MA (2018) Botulinum toxic therapy: a mathematical model for evaluating clinical efficacy in the correction of mimic wrinkles. *Metamorphoses*, 24: 82-87.
26. Talarico S, Hassun KM, Monteiro EO, Parada MOB, Buratini LB, Arruda L, Bagatin E (2010) Safety and efficacy evaluation of a new hyaluronic acid based filler in the treatment of nasolabial folds and lips outline. *Surg. Cosmet. Dermatol.*, 2(2): 83-86.
27. Gubanova EI, Pozdniakova MA, Gladko VV, Krasilnikova ON (2018) Standardization of the procedure for the correction of age-related changes in the skin of the upper half of the face with a botulinum toxin type A drug (the "novice cosmetologist" technique): a study guide. Nizhny Novgorod: Publishing House of Volga Research Medical University.