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Review Article

Long-term botulinum therapy for overactive bladder: myths and reality

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The review article presents data on the efficacy and tolerability of intravesical injections of botulinum toxin in patients with overactive bladder. The pharmacological bases of the use of botulinum therapy in this category of patients are described in detail. Data on the history of the use of botulinum toxin for medical purposes are presented. Experience to date shows that intravesical botulinum toxin injections are highly effective and well tolerated in patients with refractory overactive bladder. Botulinum therapy is included in domestic and foreign clinical guidelines as a 3rd line treatment for idiopathic and neurogenic overactive bladder. Indications for its implementation are the inefficiency and/or poor tolerability of oral pharmacotherapy. It is noted that the only botulinum toxin recommended for use in clinical practice for the treatment of overactive bladder is onabotulinumtoxin A (Botox®). The results of clinical studies are presented, showing that the effectiveness and safety of botulinum therapy do not decrease over time.

Keywords: overactive bladder; detrusor overactivity; botulinum therapy; botulinum toxin; onabotulinumtoxin A; Botox®.

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Обзорная статья

Длительная ботулинотерапия гиперактивного мочевого пузыря: мифы и реальность

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В обзорной статье приведены данные об эффективности и переносимости внутрипузырных инъекций ботулинического токсина у пациентов с гиперактивным мочевым пузырем. Подробно описаны фармакологические основы применения ботулинотерапии у данной категории больных. Представлены данные об истории использования ботулинического токсина в медицинских целях. Накопленный на сегодняшний день опыт показывает, что внутрипузырные инъекции ботулинического токсина можно рассматривать как высокоэффективный и хорошо переносимый метод лечения пациентов с рефрактерным гиперактивным мочевым пузырем. Ботулинотерапия включена в отечественные и зарубежные клинические рекомендации в качестве 3-й линии лечения при идиопатическом и нейрогенном гиперактивном мочевом пузыре. Показанием к ее проведению становится неэффективность и/или неудовлетворительная переносимость пероральной фармакотерапии. Отмечено, что единственным ботулотоксином, рекомендованным к использованию в клинической практике для лечения пациентов с гиперактивным мочевым пузырем, является онаботулинумтоксин А (Ботокс®). Приведены результаты клинических исследований, показывающих, что эффективность и безопасность ботулинотерапии с течением времени не снижаются.

Ключевые слова: гиперактивный мочевой пузырь; гиперактивность детрузора; ботулинотерапия; ботулинический токсин; онаботулинумтоксин А; Ботокс®.

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ЭКО•ВЕКТОР

The term "overactive bladder (OAB)" refers to a symptom complex that includes an imperative urge to urinate, most often accompanied by its increase at daytime and night, with or without urge urinary incontinence in the absence of infectious, tumorous, and other obvious bladder lesions [1]. According to various estimates, the incidence of OAB is high and ranges from 15% to 25% among adults; therefore, it can be attributed to one of the most common urological disorders [2, 3]. According to epidemiological studies, at the age of up to 60 years, OAB is more often diagnosed in women, and after the age of 60 years, it is more often detected in men [2, 3]. Moreover, among representatives of both sexes, the prevalence of OAB is higher in older groups. OAB has two main forms: neurogenic and non-neurogenic (idiopathic). The former develops against neurological diseases (such as spinal injury, multilocular sclerosis, acute and chronic cerebrovascular accident, and Parkinson's disease). In turn, idiopathic OAB occurs in patients with intact neurological function and is most often caused by dysfunction of the detrusor and urothelium due to hormonal or metabolic disorders, infravesical obstruction, and other factors [4]. Bladder wall ischemia is also of great importance in the development of lower urinary tract dysfunctions, including OAB [5, 6].

The significance of OAB and associated urge urinary incontinence is determined not only by their high prevalence but also by a significant deterioration in the quality of life of patients. OAB symptoms affect almost all aspects of life, namely, professional, family, domestic, and sexual life, often causing serious social maladjustment of patients [7, 8]. The results of a study conducted at the Department of Urology, First Pavlov Saint Petersburg State Medical University, enabled us to reveal the relationship between the degree of deterioration in the quality of life of patients and the severity of clinical symptoms of OAB [9]. Serious emotional disorders and anxiety-depressive disorders are also often noted in patients with OAB. In addition, OAB contributes to the development of several severe complications that further worsen the quality of life. Thus, patients with OAB have a higher risk of falls leading to fractures, disability, and lower urinary tract infections, and urinary incontinence is often accompanied by skin irritation, followed by infection. In this regard, the quality of life should be assessed when examining patients with OAB, and its improvement is an important goal of therapeutic measures [8].

The current Russian and international clinical guidelines distinguish three lines of treatment for patients with OAB [10–12]. Lines 1 and 2 include conservative non-drug and drug therapy. Line 1 includes behavioral therapy (restriction of fluid intake and diuretic products and bladder training), pelvic muscle exercises, and physiotherapy. Line 2 of treatment for OAB includes oral pharmacotherapy, which is recommended to be started simultaneously with line 1. For drug treatment, different pharmacological groups are used, with the main ones being M-cholinoblockers and β3-adrenoceptor agonists [13–16]. Numerous studies have shown the efficiency of pharmacotherapy in the treatment of OA; however, drug therapy is unsuccessful in several patients (10%–20% according to various estimates) [17]. In these cases, OAB is designated as refractory (resistant). The causes of refractoriness to standard pharmacotherapy of OAB are not fully understood. It may be due to predominance in these patients of mechanisms, other than cholinergic, of increased sensitivity and contractile activity of the bladder, particularly purinergic mechanisms [18]. An equally significant problem in the prescription of pharmacotherapy is the tolerability of treatment, which is not always satisfactory. Anticholinergic drugs can have severe side effects (such as dry mouth, constipation, nausea, and visual impairment) [19] and increased risk of dementia [20]. The intake of β3-adrenoceptor agonists is often accompanied by intense headaches, gastrointestinal symptoms, and significant increase in blood pressure [21].

Intravesical injections of botulinum toxin in the treatment of patients with OAB

The ineffectiveness or unsatisfactory tolerance of non-drug and oral pharmacotherapy becomes an indication for the transition to line 3 of OAB treatment, namely, intravesical injections of botulinum toxin (botulinum therapy).

Botulinum toxin (botulotoxin) is a protein-based neurotoxin produced by the anaerobic Gram-positive bacteria *Clostridium botulinum*. The botulinum toxin is a unique compound, being one of the most complex proteins in nature, and has exceptional biological activity. Thus, 1 ng (10^{-9} g) of this substance can already cause specific effects. For example, all botulinum toxins used in its pure form worldwide for 1 year for medical and cosmetic purposes could fit a tablespoon [22]. It is hardly an exaggeration to state also that botulinum toxin is the most bioactive of all currently known substances of natural and synthetic origins.

Botulinum toxin has been studied for 200 years. In 1822, the German physician and naturalist Justinus Kerner for the first time described the clinical signs of poisoning with canned foods, proposed using the term botulism to refer to this condition, and suggested its connection with some unknown toxin. In 1897, the Belgian bacteriologist Émile van Ermengem first described *C. botulinum*. In 1928, botulinum toxin was isolated, and in 1949, its ability to block acetylcholine release from nerve endings and thereby disrupt neuromuscular transmission was discovered [22]. Over the past 50 years,

important discoveries have been made in the field of molecular biology of botulinum toxin. It consists of heavy (100 kDa) and light (50 kDa) strands linked by a disulfide bridge. The heavy chain has both a binding domain and a translocation domain. In the late 1990s, the crystal structure of botulinum toxin was determined, and cell receptors for it were identified.

To date, seven serotypes of botulinum toxin have been identified, designated by Latin letters from A to G. All botulinum toxin serotypes are metalloproteinases with a common ability to disrupt neuromuscular function through chemodenervation. For medical purposes, botulinum toxin type A (BT-A) is most often used, which is widely applied in clinical practice [23]. BT-A was first approved as a drug by the United States Food and Drug Administration (FDA) in 1989 for the treatment blepharospasm and strabismus. In Russia, BT-A was registered in 1994 for the treatment of the above ophthalmic diseases, hemifacial spasm, and cervical dystonia. Later, the indications for BT-A were expanded, and at present, it is used for the treatment of various diseases in neurology, orthopedics, gynecology, cosmetology, urology, and other fields. The clinical effects of BT-A use (muscle relaxation, decreased sensitivity, and decreased secretion of glands in the injection zone) appear already within 2–5 days and persist for several months.

According to their chemical structure and biological activity, BT-A is divided into three types, namely, onabotulinumtoxin A, abobotulinumtoxin A, and incobotulinumtoxin A. The most famous and studied of them is onabotulinumtoxin A, which is widely known under the brand name Botox®. Since only onabotulinumtoxin A (Botox®) is registered as a drug for the treatment of urological diseases, hereinafter, we imply exactly this subtype of botulinum toxin as BT-A.

The first report on the successful use of BT-A in urology dates back to 1988 when Dykstra et al. [24] used botulinum toxin to treat 11 patients with detrusor-sphincter dyssynergia and a history of a spinal injury. BT-A was injected directly into the external urethral sphincter percutaneously and through the ureteroscope. At the control examination, electromyographic signs of sphincter denervation, decrease in intraurethral pressure, and decrease in the volume of residual urine were noted. In 2000, the results of the first use of BT-A for the treatment of bladder diseases were published [25]. We monitored 31 patients with neurogenic detrusor hyperactivity, refractory to anticholinergic therapy. All patients under cystoscopic control underwent intravesical injections of BT-A at a dose of 200–300 units (10 units at 20–30 points). The authors registered high clinical efficacy (cessation of urinary incontinence and increase in maximum bladder capacity) and good tolerability of treatment. Subsequently, multicenter clinical studies have confirmed the high clinical efficacy of botulinum therapy in the treatment of patients with OAB [26–28]. Clinical improvement was noted within a few days after injections, reaching a maximum after 1.5–2 weeks and lasting for 6–9 months on average [29]. The results were used as the basis for the approval of botulinum therapy as a treatment for neurogenic (FDA, 2011) and idiopathic (FDA, 2013) OAB. The high clinical efficacy of BT-A in the treatment of patients with OAB is due to the pharmacological characteristics of the drug, which can inhibit the release of neurotransmitters in both efferent and afferent nerve synapses [30]. The dual motor and sensory mechanism of action of BT-A contributes to a decrease in both contractile activity and a sensitivity of the bladder wall [31].

Currently, intravesical BT-A injections are included in Russian and international clinical recommendations as the third line of treatment for neurogenic and idiopathic OAB and are used in cases of ineffectiveness or poor tolerability of pharmacotherapy [10–12]. In Russia, botulinum therapy is also successfully used to treat patients with OAB in many medical institutions [32–34]. Moreover, studies are conducted on the possibility of using BT-A in other bladder diseases [35]. Despite more than a decade of experience in the successful use of BT-A in the treatment of patients with OAB, the approval of this treatment method by regulatory authorities and inclusion in clinical guidelines, as well as its distribution in Russia, is still not extensive enough. The reasons for this can be objective and subjective. The former include: the lack of specialists with the skills to perform intravesical injections of BT-A and organizational issues of botulinum therapy (purchase of special needles for injections and the drug itself, provision of conditions for its storage, etc.), and the interdisciplinary nature of the problem of treating OAB, which often requires interaction of urologists, neurologists, and gynecologists. The main subjective reason is the lack of awareness of practicing urologists about this treatment method; therefore, their ideas about the efficiency and safety of botulinum therapy are often far from the truth. Based on our experience with the use of botulinum toxin therapy in urology, communicating both with healthcare professionals and directly with patients, we have identified the main misconceptions that reduce the propagation of this treatment technique. What are the main myths of botulinum therapy? We attributed the following to them. With chronic botulinum therapy, its efficiency decreases over time; after botulinum therapy, a return to oral pharmacotherapy is not possible. Performing many intravesical injections of BT-A increases the risk of bladder sclerosis, and intravesical botulinum therapy is always accompanied by urinary tract infection and urinary retention. The results of studies conducted in recent years, demonstrating the state of the art in reality, are presented below.

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Does the efficiency of long-term botulinum therapy of OAB decrease over time?

No, it does not decrease. This is evidenced by the results of many studies, the largest of which is a multicenter randomized controlled trial [36]. This study involved 829 patients with refractory idiopathic OAB, who received BT-A injections at a dose of 100 IU on demand, that is, the patients themselves chose the time when; in their opinion, it was necessary to administer the drug. The mean follow-up time was 3.4 years, and the mean interval between injections was 7.6 months. Moreover, not only was there no reduction in the intervals between injections, but vice versa, this period increased with subsequent injections. Similar results were obtained in another large study of the efficiency of long-term botulinum therapy in patients with neurogenic detrusor hyperactivity [37]. The final analysis included 227 patients with a follow-up period of 4 years. The overall average duration of the BT-A effect over this period reached 9 months, and in 26% of the patients, it exceeded 12 months. Thus, in patients with neurogenic detrusor hyperactivity, who have been treated with botulinum toxin therapy for 4 years, with each subsequent injection, there is a progressive improvement in symptoms without worsening the treatment tolerance. The results of clinical studies were used as the basis for the inclusion in the clinical guidelines of indications that there is no decrease in the efficiency of botulinum therapy in patients with OAB and repeated injections of BT-A [11].

The reasons for the increase in the efficiency of botulinum therapy during its long-term use are associated with a change in the expression of receptors in the bladder wall under the influence of BT-A [38].

Is it possible for patients with refractory OAB to return to effective oral pharmacotherapy after botulinum toxin therapy?

Yes, it is possible. Intravesical injections of BT-A should not be a reason to withhold subsequent oral anticholinergic therapy in patients with refractory OAB. This is evidenced by the results of a uniquely designed study by Elbaset et al. [39], who investigated the efficacy and safety of M-cholinoblockers in patients with refractory OAB after the end of botulinum therapy. They monitored 100 patients with idiopathic OAB refractory to anticholinergic therapy, who underwent intravesical injections of BT-A at a dose of 100 IU. After the termination of the effect of the botulinum therapy, the patients were distributed into two groups. In the main group, the M-cholinoblocker solifenacin was prescribed at a dose of 10 mg per day for 12 weeks, whereas the control group received a placebo at the same period. The study results demonstrated that the main group, who received anticholinergic therapy, had a significant decrease in the severity of OAB symptoms and an increase in the quality of life compared with the baseline and the group that received placebo. Clinical improvement was accompanied by improvement in urodynamic parameters. Thus, the main group showed a decrease in the frequency and amplitude of involuntary detrusor contractions and an increase in the maximum cystometric capacity ($p < 0.0001$, $p = 0.03$, and $p = 0.007$, respectively, compared with the index before treatment). The results enabled the authors to conclude that the re-administration of anticholinergic therapy to patients with refractory idiopathic OAB is justified and that it is an effective treatment option after the termination of the effect of botulinum therapy.

How can the effect of M-cholinoblockers be explained in patients with refractory OAB after intravesical botulinum therapy? Most experts tend to believe that a possible mechanism is an increase in the expression of muscarinic receptors under the influence of BT-A. Therefore, according to one of the hypotheses, cholinergic resistance develops with a decrease in the expression of muscarinic receptors and, conversely, an increase in the expression of other receptors, mainly purinergic ones, which provide the motor and sensory activities of the bladder [18]. In this regard, Datta et al. [38] proved an increase in the density and activity of muscarinic receptors in the urothelium and suburothelium after intravesical injections of BT-A and a simultaneous decrease in the expression of suburothelial purinergic and vanilloid receptors. Moreover, to date, all aspects of the effect of BT-A on the sensitization of muscarinic receptors in the bladder wall are still unknown.

Thus, botulinum therapy in patients with OAB not only does not limit the possibility of subsequent use of anticholinergic drugs but also, apparently, contributes to an increase in susceptibility to M-cholinoblockers in patients with refractory OAB. In addition, very few studies have focused on the simultaneous or sequential administration of anticholinergic drugs and intravesical botulinum therapy. In this regard, the synergistic or additive action of M-cholinoblockers and BT-A in refractory OAB appears to be a very promising subject of scientific research.

Can intravesical injections of BT-A increase the risk of bladder wall sclerosis?

No, the risk of bladder sclerosis does not increase after BT-A injections. This is evidenced by the results of numerous morphological studies of the bladder wall before and after this procedure, including repeated injections [40–42]. Multiple injections of BT-A into the bladder wall do not cause inflammatory, dysplastic, and sclerotic changes in the urothelium and suburothelium [43] and do

not affect the morphological state of the detrusor, as no changes in the structure of smooth muscle cells, width of intercellular spaces, and type of intercellular junctions were noted [44].

Moreover, BT-A injections have opposite effects and reduce the risk of bladder wall fibrosis. Compérat et al. [40] revealed that patients with neurogenic OAB after BT-A injections had less pronounced sclerotic changes in the bladder wall than untreated patients. Pascali et al. [42] examined 46 biopsy specimens of the bladder wall from 40 pediatric patients with neurogenic detrusor overactivity aged 2–18 years and noted less signs of fibrosis after multiple intravesical injections of BT-A.

The antifibrotic effect of intravesical injections of BT-A is most probably associated with blood flow improvement in the bladder wall. Possible mechanisms of this effect are an increase under the influence of BT-A in the expression of vascular endothelial growth factor and membrane adhesin protein platelet/endothelial cell adhesion molecule one and inhibition of sympathetic nerve endings [45]. In addition, with detrusor hyperactivity, due to an increase in intravesical pressure, the bladder wall perfusion decreases [46]; therefore, a decrease in the detrusor contractile activity also improves blood flow. A direct antifibrotic effect of BT-A in the bladder cannot be ruled out. This is evidenced by the results of Jia et al. [47], who experimentally revealed the suppression of the expression of transforming growth factor β1 (TGF-β1), a key cytokine that promotes fibrosis, under the influence of intravesical injections of botulinum toxin.

Thus, botulinum therapy not only does induce fibrosis of the bladder wall but has an anti-sclerotic effect.

Will intravesical injections of BT-A cause cystitis?

The administration of BT-A into the bladder wall does increase the probability of cystitis, however not significantly, and the risk of a bladder infection is almost completely eliminated by the prophylactic administration of antibacterial drugs. In 2020, the results of a meta-analysis of 19 randomized controlled trials of the efficacy and safety of BT-A use in OAB were published, which enrolled a total of 3499 patients with idiopathic and 2097 patients with neurogenic disease [28]. The risk of urinary tract infections after intravesical injections of BT-A was slightly greater than that after placebo. Thus, when BT-A was administered at a dose of 100 IU to patients with idiopathic OAB, the relative risk of cystitis was 2.55 times higher, and with the administration of 200 IU, it was 2.68 times higher than placebo. A similar tendency was also noted for neurogenic detrusor hyperactivity, where urinary tract infections were recorded 1.44 times more often with the administration of 200 units of BT-A than with the diagnostic control. Female sex and initial residual urine volume of >100 mL were indicated as risk factors for cystitis after BT-A injections [48]. Moreover, the prescription of antibacterial drugs significantly reduces the risk of a urinary tract infection after intravesical injections of BT-A. Thus, in the large prospective observational study GRACE, conducted in four European countries, all patients received antibiotic prophylaxis of cystitis before intravesical injections of BT-A, and a clinically significant urinary tract infection was registered only in 0.4% of the patients [49]. According to Bickhaus et al. [50], the best results are achieved when antibiotic prophylaxis was started 1 day before botulinum toxin injection and continued for 4 days after the procedure.

An important practical issue is the timing of botulinum therapy after an earlier urinary tract infection. The retrospective study by Bickhaus et al. [51] demonstrated that the initial injection of BT-A in women with refractory OAB within 30 days after an episode of cystitis does not increase the probability of relapse after the procedure. The authors recommend not postponing botulinum therapy due to a previous urinary tract infection.

Several publications indicate a significantly higher incidence of urinary tract infection after botulinum therapy, namely, 24.1%–35% [26, 27, 52–54]. However, when analyzing the results of these studies, the criterion for diagnosing a urinary tract infection was a positive urine culture (bacteriuria $>10^5$ CFU/mL) or leukocyturia (>5 leukocytes per field of view), regardless of the presence of clinical symptoms of cystitis, and antibiotic prophylaxis was not a prerequisite for BT-A injections.

Thus, the prophylactic administration of antibacterial drugs minimizes the risk of urinary tract infections after intravesical injections of BT-A.

Intravesical botulinum therapy is accompanied by urinary retention, requiring intermittent catheterization

The mechanism of the pharmacological effect of BT-A in patients with OAB is based on a disorder of neuromuscular transmission, resulting in a decrease in the contractile activity of the detrusor. In patients with detrusor hyperactivity, this contributes to the elimination of involuntary detrusor contractions and is clinically manifested by a decrease in the severity of OAB symptoms. Moreover, a decrease in the force of detrusor contraction can result in impaired bladder emptying. In this regard, in the clinical guidelines for OAB treatment in the section on botulinum therapy, there is an indication of the risk of developing urinary retention and the need to teach the patient to perform intermittent self-catheterization. In many cases, the fear of not being able to urinate independently keeps patients from choosing this treatment method. However, how high is this risk of developing

urinary retention? In the previously mentioned meta-analysis by Gong et al. [28], the risk of worsening urinary outflow in patients with neurogenic OAB when using BT-A at a dose of 200 IU was 5.85 times higher than the placebo and 13.99 times higher than idiopathic OAB when using 100 IU of BT-A. In addition, the need for catheterization due to an increase in the residual urine volume or urinary retention was only 1.53 times greater in patients with neurogenic OAB with the administration of 200 IU of BT-A and 2.31 times greater in case of idiopathic OAB with the administration of 100 IU of BT-A. A. However, if it is referred to absolute values based on the results of clinical studies, the risk of urinary retention is low. In a multicenter randomized controlled trial of men and women with refractory OAB, only 4% of the patients required intermittent catheterization after the initial intravesical injection of BT-A at a dose of 100 IU [36]. In patients who did not require self-catheterization after the initial injection of BT-A, the risk of urinary retention and the need for catheterization in subsequent injections were even lower, namely, <2%. In other clinical studies, the incidence of urinary retention after intravesical injections of BT-A requiring intermittent catheterization was similar, namely, 5.4% [27] and 6.9% [26].

In several other studies, the frequency of intermittent catheterization was significantly lower. In a study by Patel et al. [55], 187 intravesical injections of BT-A at a dose of 100 IU were performed in 99 women with idiopathic OAB. Intermittent catheterization was required after only three injections (1.6%), where acute urinary retention developed in two cases, and in two cases, the residual urine volume increased to 350 mL. In all patients, the recovery of urination occurred no later than 8 weeks after injection. Hamid et al. [49] analyzed the results of the GRACE multicenter study on the use of botulinum therapy in the real clinical practice in 505 patients with OAB and indicated the need for intermittent catheterization in only 5 (1%) of them.

The difference in the frequency of the need for intermittent catheterization in some studies is associated with different indications for its initiation. Thus, in the studies of Nitti et al. [27], Chapple et al. [26], and Nitti et al. [36], intermittent catheterization was performed when the residual urine volume increased to ≥200 mL, even if spontaneous urination persisted. In addition, Patel et al. [55] and Hamid et al. [49] recommended intermittent catheterization only in cases of impossibility of spontaneous urination or a significant increase in the residual urine volume of more than 350–400 ml.

Currently, there is no consensus on the amount of residual urine at which intermittent catheterization should be started in a patient with natural urination. A residual urine volume of >400 ml has an adverse effect on the upper urinary tract; therefore, urine should not exceed this value in the bladder. Nitti et al. [27], Chapple [26], and Nitti et al. [36] accepted ≥200 ml of residual urine as an indication for the start of intermittent catheterization, and Marcelissen et al. [56] indicated even 150 ml. Other researchers have used significantly less stringent criteria for initiating intermittent catheterization [49, 55].

The medical community is more unanimous in assessing the risk factors for urinary retention after botulinum therapy. The main factor is recognized as a disorder of the urine outflow from the bladder with an increase in residual urine volume before the procedure, which is often noted in men with benign prostatic hyperplasia, women with pelvic organ prolapse, and older patients [57, 58]. There is also complete agreement that the risk of urinary retention associated with the administration of BT-A disappears completely 2 weeks after the procedure [58].

Thus, the experience accumulated to date demonstrates that intravesical BT-A injections are a highly effective and well-tolerated method of treating patients with refractory OAB. Botulinum therapy is included in the Russian and international clinical guidelines as the third line of treatment for idiopathic and neurogenic OAB. The indication for its use is the ineffectiveness and/or poor tolerability of oral pharmacotherapy.

Currently, the only botulinum toxin listed in the clinical guidelines is onabotulinumtoxin A, known by the trade name Botox®. This drug is the world's first registered botulinum toxin for medicinal use (1989). For the treatment of patients with idiopathic OAB, a dose of Botox® of 100 IU is recommended, whereas for patients with neurogenic OAB, 200 IU is recommended. Other doses of onabotulinumtoxin A and other BT-A preparations (abobotulinumtoxin A and incobotulinumtoxin A) are not recommended for use in urology, and dosages of onabotulinumtoxin A (Botox®) should not be extrapolated to other brands of botulinum toxin [11]. The clinical effect of BT-A is dose-dependent and lasts for several months, after which repeated injections of the drug are required. Moreover, they are recommended to be performed no earlier than 3 months after the previous injection [10]. When prescribing botulinum therapy to patients with OAB, side effects must be considered, the most common of which are urinary tract infections and worsening of urine outflow from the bladder. Although the risk of their development is relatively low, antibacterial prophylaxis of infectious complications and teaching patients to perform self-catheterization are recommended.

Thus, botulinum toxin therapy is an effective, minimally invasive, and well-tolerated treatment for patients with refractory OAB. When performing intravesical injections of BT-A for a long time, their efficiency does not decrease, and tolerability does not worsen. It seems expedient to use this method of treatment more extensively in practical medicine.

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ADDITIONAL INFORMATION

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