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The application of botulinum toxin in the treatment of overactive bladder

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Abstract

Introduction:

Urinary incontinence is an involuntary, decision-dependent urination that leads to partial or complete emptying of the bladder. The causes include overactive bladder syndrome, which is diagnosed on the basis of clinical symptoms, such as urgency to urinate, increased frequency of voiding, nocturia caused by increased reactivity of the detrusor muscle. Treatment of this condition includes, but is not limited to, pharmacotherapy, behavioral therapy, and pelvic floor exercises. It is also possible to use an innovative method of local injection of botulinum toxin into the bladder. It inhibits the release of acetylcholine, which results in the inhibition of the contractile activity of the detrusor muscle.

The aim of the study:

The purpose of the systemic review was to collect and analyze material of application of botulinum toxin in the treatment of urinary incontinence caused by overactive bladder.

Material and methods:

The work is a review of the literature on the use of botulinum toxin in the treatment of overactive bladder, published in 2002-2020.

Description of the state of knowledge:

The use of the described method gives long-lasting results compared to pharmacotherapy. In addition, it eliminates the side effects caused by drugs because the administration of drugs is reduced or discontinued. The use of botulinum toxin has many more benefits than simply improving the lives of people affected by urinary incontinence. When selecting the therapy, one should also pay attention to possible side effects resulting from the use of the described drug.

Summary:

Intravesical administration by means of botulinum toxin cystoscopy is a modern, safe, effective and minimally invasive method of treating urinary incontinence, possible on an outpatient basis, allowing to improve the urodynamic parameters. Side effects are very rare. The botulinum toxin serotype A used in this method is the most studied serotype used for therapeutic purposes. The conducted research shows that over 90% of women reported a clinically significant improvement in sexual function after using the method.

Key words: urinary incontinence, botulinum toxin, overactive bladder

Introduction:

Incontinence, or involuntary urination, is caused by a variety of factors and can result in a wide range of urinary symptoms that can affect a woman's physical, mental and social

well-being and can sometimes place significant restrictions on lifestyle. There are three main types of urinary incontinence in women: stress incontinence, urge incontinence and mixed urinary incontinence. Most women cope better with the symptoms of stress urinary incontinence and report a poorer quality of life due to urination urgency, which is often symptoms of an overactive bladder (OAB) [1]. Overactive bladder syndrome is disorder that includes urgency to urinate, usually accompanied by frequent urination and nocturia, with or without the presence of urgency incontinence. OAB cannot be explained by other pathological factors, such as diabetes, infection, calculi, cancer of the urinary tract epithelium. OAB is generally responsible for 11–19% of the total incidence of urinary incontinence worldwide. This disease also affects many other aspects of the patient's life, by significantly reducing productivity at work, lower sexual satisfaction, higher percentage of depressive symptoms and poorer quality of sleep caused by nocturia.

There are many risk factors associated with OAB such as obesity, history of pelvic organ prolapse, old age, and menopause [2]. It has also been reported that women born vaginally show a stronger association with OAB, which is consistent with many other studies conducted elsewhere [3]. Multiple vaginal deliveries are believed to damage the integrity of the supporting structures of the pelvic organ, weakening their tensile strength, which is significantly related to OAB. The presence of comorbidities such as hypertension and diabetes has also been shown to influence the prevalence of OAB. Although the risk ratio varies, this means that diabetes has a greater impact on the condition than with hypertension. [4]

Initial treatment should be based on clinical signs and the results of basic diagnosis. OAB treatment options include lifestyle modifications, behavioral therapy, pharmacotherapy, neuromodulation, botulinum toxin therapy and surgical interventions. The choice of the therapeutic route should take into account the patient's preferences [5].

The aim of the study:

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Discussion:

Botulinum toxin A is the only botulinum toxin currently approved for the treatment of urinary incontinence in OAB [6]. Botulinum neurotoxin A is derived from the gram-negative anaerobic bacterium *Clostridium botulinum* [7]. The end organ effect of botulinum toxin is mediated by the parasympathetic presynaptic nerve end. Efferent fibers significantly affect the clinical efficacy of botulinum toxin by direct inhibition of acetylcholine and adenosine-5-triphosphate, which causes reversible chemodenervation and relaxation of muscle paralysis [8]. It usually takes 48-72 hours to the onset of action and may last from 6 to 9 months. From about the seventh day after the injection of botulinum toxin, the process of muscle

reinnervation begins. It consists of restoring innervation by budding nerve fibers. As a result, axon branches without myelin sheaths are produced. Some of the mentioned endings end "blind". The effect of the reinnervation process is a change in the innervation of muscle fibers. As a consequence of these changes, a single neuron innervates many muscle fibers with the help of axonal projections. However, after some time axons regenerate, which ultimately weakens the therapeutic effect and the procedure needs to be repeated. Studies have shown that administration of higher doses and shortening the intervals between individual injections of botulinum toxin A contribute to the development of resistance [9]. Therefore, it is currently recommended to maintain 3 month intervals between consecutive doses of neurotoxin and to use the lowest dose of the drug that will allow to achieve the desired clinical effect [10]. It was found that after repeated administration of botulin, blocking antibodies may be produced, and the conducted studies indicate that keeping the 3 month intervals between injections will allow for an almost complete elimination of the immunization development risk [11].

Further diagnostics should be performed prior to injection of botulinum toxin to determine the possible causes of prior therapy failure. Urethrocystoscopy should be performed to exclude a bladder tumor. The absolute contraindications for the use of botulinum toxin include: acute UTI, lack of willingness or ability to ISK, use of botulinum toxin in the last 3 months due to the development of resistance and possible cumulative effect, hypersensitivity to botulinum toxin or components of the solution for injection, pregnancy and breastfeeding; the relative contraindications are: coagulation disorders, oral anticoagulants administration and neuromuscular diseases such as myasthenia gravis [14].

The benefits of using botulinum toxin include not only an improvement in urinary incontinence. It has also been found that botulinum toxin A enables patients to reduce the dose or even dechallenge anticholinergic drugs. This effect was found to be permanent [15]. It has also been reported that botulinum toxin A injections helped to reduce the number of UTIs, especially pyelonephritis, orchitis and prostatitis [16].

Summary:

Urinary incontinence is a common problem that is often rarely reported due to its embarrassing nature and associated social stigma. It can have a significant impact on reducing an individual's quality of life, however it can be significantly improved with proper assessment, treatment and management. OAB is a chronic and complex disease that is often difficult to treat. A holistic approach that takes into account the physiological and anatomical changes is likely to improve treatment outcomes. First-line treatment options like lifestyle modification, behavioral therapy and pharmacotherapy combined together can significantly improve outcomes. Botulinum therapy is believed to produce spectacular results in patients with OAB that is difficult to treat, but is limited due to its side effects and the need for a repeated therapy.

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