Mielniczek Katarzyna. Botulinum toxin in the treatment of neuralgia and neuropathic pain. Journal of Education, Health and Sport. 2021;11(9):310-314. eISSN 2391-8306. DOI http://dx.doi.org/10.12775/JEHS.2021.11.09.038
https://apcz.umk.pl/JEHS/article/view/JEHS.2021.11.09.038
https://zenodo.org/record/5515785

The journal has had 5 points in Ministry of Science and Higher Education parametric evaluation. § 8. 2) and § 12. 1. 2) 22.02.2019.

The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 05.09.2021. Revised: 18.09.2021. Accepted: 18.09.2021.

Botulinum toxin in the treatment of neuralgia and neuropathic pain

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Abstract

Introduction: Botulinum toxin is one of the most powerful neurotoxins currently known, with high affinity to the cholinergic synapse, which sufficiently inhibits the release of acetylcholine. Its use has proved to be effective in the treatment of many diseases of the musculoskeletal system. Although most of the therapeutic effects of botulinum toxin are due to the temporary relaxation of skeletal muscles (caused by inhibition of acetylcholine release), research is ongoing into its effects on the nervous system.

Purpose of the work: The aim of the study is to analyze the effectiveness of botulinum toxin in the treatment of neuralgia and neuropathic pain.

Method: The relevant samples were accessed by means of an electronic search in the PubMed database. The analysis used reviews and meta-analyzes posted on the platform over the last 10 years.

Conclusions: Botulinum toxin has great potential in the treatment of pain. It is multitasking due to its favorable safety profile and long-lasting relief from a single injection compared to other pain medications. The side effects caused by it were assessed to be mild to moderate and

included a local skin reaction (swelling), injection site pain, muscle weakness, flu symptoms, nausea and vomiting.

Key words: botulinum toxin; neuropathic pain; pain treatment; neuralgia; BoNT / A

Introduction:

Botulinum toxins (BTX) are protein neurotoxins (exotoxins) produced by Clostridium botulinum (gram (+) anaerobic bacteria) as well as by a few other members of the genus Clostridium. Botulism is caused by flaccid paralysis following the inhibition of neurotransmitter release from peripheral cholinergic nerve endings of the skeletal and autonomic nervous systems. [1]The paralysis begins in the eye muscles, continues to spread to the facial muscles, eventually reaches the respiratory muscles, and can cause respiratory failure.

There are several types of this toxin, marked with successive letters of the alphabet from A to H. The most important for human health are types: A, B and E, and in veterinary medicine C and D. Type H is the most poisonous. These serotypes share similar molecular weights and common subunit structures, but differ in reaction mechanisms, duration of action, and side effects.

On average, the toxin has a molecular weight of 150 kDa, it consists of an inactive single-chain polypeptide that forms a 3-domain structure. It is composed of two polypeptide chains: light, with a molecular weight of approx. 50 kDa, and heavy, with a molecular weight of approx. 100 kDa, connected by a disulfide bridge. The light chain is a zinc-dependent

[1] Park J, Chung ME. Botulinum Toxin for Central Neuropathic Pain. Toxins (Basel). 2018 Jun 1; 10 (6): 224. doi: 10.3390 / toxins10060224. PMID: 29857568; PMCID: PMC6024683.

protease that is an active toxin and cleaves the soluble receptor complex. The heavy chain (100 kDa) consists of the N-terminal translocation domain and the C-terminal receptor binding domain and acts in neuron-specific binding [1].

State of knowledge :

Botulinum toxin has found its use in the treatment of pain. [2] According to research, BTX can inhibit the release of acetylcholine from the neuromuscular junction, causing the muscles to relax. In addition, experimental studies have shown that BTX-A affects the presynaptic vesicles of neurons by inhibiting the release of certain neurotransmitters such as acetylcholine and nociceptive neuropeptides, substance P, calcitonin gene related peptide and glutamate. It has also been shown to inhibit the expression of the vanilloid TRPV1 receptor on the surface of peripheral nociceptors responsible for inflammatory hyperalgesia. [2] And most importantly, the analgesic effect of BTX-A is independent of muscle relaxation. [34]

The International Association for the Study of Pain (IASP) defines neuropathic pain as pain caused by damage or disease to the somatosensory nervous system. Neuropathic pain is a clinical description that requires a demonstrable damage or disease that meets established neurological diagnostic criteria. It has two common symptoms: allodynia and hyperalgesia. In the treatment of neuropathic pain, it causes a reduction in muscle spasms. The hypothesis is that BTX inhibits the secretion of neuropeptides, thereby reducing peripheral inflammation and thereby suppressing inflammation and pain.[3] Moreover, it has been shown that BTX preferentially attenuates the slow phase of KCl-induced glutamate release, which may be related to the mobilization of synaptic vesicles. According to studies, BTX may also inhibit the secretion of substance P and significantly reduce TRPV1 expression. Subcutaneous administration of BTX-A significantly and bilaterally reduces mechanical allodynia and inhibits P2X3 overexpression

Trigeminal neuralgia (TN) is one of the most painful conditions that presents with recurrent unilateral short but severe electric shock-like pain with rapid onset and short duration (up to 2 minutes) in the distribution of the trigeminal nerve. TN is etiologically classified as idiopathic (without a reliable organic substrate), classical (due to the neurovascular conflict between the

[2] Kumar R. Therapeutic use of botulinum toxin in pain treatment. Neuronal Signal. 2018 Aug 31; 2 (3): NS20180058. doi: 10.1042 / NS20180058. PMID: 32714587; PMCID: PMC7373233.
[3] Sandrini G, De Icco R, Tassorelli C, Smania N, Tamburin S. Botulinum neurotoxin type A for the treatment of pain: not just in migraine and trigeminal neuralgia. J Headache Pain. 2017 Dec; 18 (1): 38. doi: 10.1186 / s10194-017-0744-z. Epub 2017 Mar 21. PMID: 28324318; PMCID: PMC5360746.
[4] Egeo G, Fofi L, Barbanti P. Botulinum Neurotoxin for the Treatment of Neuropathic Pain. Front Neurol. 2020 Aug 11; 11: 716. doi: 10.3389 / fneur.2020.00716. PMID: 32849195; PMCID: PMC7431775.

abnormal vessel and the trigeminal root near the entrance to the pons), and secondary (due to serious neurological diseases such as multiple sclerosis or angular tumors) in the cerebellum-sternum).[3] TN is twice as common in women and usually in the elderly (over 50). It can also manifest itself as constant pain between attacks in the affected area of moderate intensity.

Patients with classical TN were studied and randomized to multiple intradermal and / or submucosal injections of BoNT / A. It significantly reduced pain intensity at week 2 and pain attack frequency at week 1 compared to placebo (68.2 vs 15.0%; p <0.01), demonstrating sustained efficacy and good tolerability. The effectiveness was also shown in the case of difficult-to-treat cases of the disease. Significantly reduced the intensity of pain and the acute intake of pain medications. Most importantly, its effectiveness is dose independent. [45] Already at low doses, patients report significant improvement. It is also successful in TN caused by microvascular decompression surgery. [67]

Conclusions:

Botulinum toxin may be a promising therapeutic tool for pain due to its proven efficacy and tolerance in a wide range of neuropathic diseases. Its analgesic effect is mediated by neurons and glial cells, especially microglia. Injection with botulinum toxin type A is a safe and effective method of treating trigeminal neuralgia. No differences were found between the doses of botulinum toxin type A in the treatment of neuralgia. Its effect appears after 4-8 weeks [after 1 week in TN] and lasts up to 6 months after treatment. However, for neuropathic pain, the effectiveness depends on the dose of the toxin, injection site, number and depth of injections. The overall tolerability of BoNT / A under various clinical settings was good and the adverse events were usually transient and mild. Side effects were assessed as mild to moderate and included local skin reaction (swelling), injection site pain, muscle weakness, flu symptoms, nausea and vomiting. The use of botulinum toxin should be carefully considered in patients with NP who do not meet current standards of care and to avoid undesirable side effects.

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