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Dolna 17, Warsaw,
Poland 00-773
+48 226 0 227 03
editorial_office@rsglobal.pl

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UNVEILING THE EXPANDING CLINICAL HORIZONS OF BOTULINUM TOXIN ACROSS MEDICAL SPECIALITIES

Katarzyna Herjan *(Corresponding Author, Email: katarzyna_herjan@icloud.com)*
Center of Postgraduate Medical Education, Prof. W. Orłowski Memorial Hospital, 00-401 Warsaw, Poland
ORCID ID: 0009-0009-1439-3793

Piotr Armański
District Hospital in Sochaczew, 96-500 Sochaczew, Poland
ORCID ID: 0009-0003-4545-3740

Gabriela Łocik
Dr Anna Gostynska Wolski Hospital, Independent Public Health Care Institution, 01- 211 Warsaw, Poland
ORDIC ID: 0009-0000-8111-279X

Marta Bonarska
Student of Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
ORCID ID: 0009-0008-7201-2082

Joanna Wróbel
Department of Pediatric Surgery, Regional Hospital in Kielce, 25-736 Kielce, Poland
ORCID ID: 0000-0002-8996-6383

Katarzyna Kozon
Masovian Bródnowski Hospital, 03-242 Warsaw, Poland
ORCID ID: 0009-0009-6536-946X

ABSTRACT

Introduction: Originally identified for its potent neurotoxicity, botulinum toxin (BoNT) has been successfully repurposed into a highly versatile agent used across numerous medical specialities. Through targeted inhibition of acetylcholine release at neuromuscular synapses, BoNT induces localized, reversible muscle relaxation, effectively alleviating symptoms in a variety of neuromuscular and autonomic disorders.
Aim: This review aims to highlight the approved therapeutic uses of BoNT, its expanding applications, and the importance of proper technique and anatomical knowledge in maximizing efficacy and minimizing adverse events.
Materials and Methods: A comprehensive literature review was conducted to evaluate current therapeutic indications, mechanisms of action, safety profile, and emerging uses of BoNT.
Results: Approved therapeutic indications include dystonias, spasticity, chronic migraine, hyperhidrosis, bruxism, while growing evidence supports its emerging role in pain management, selected psychiatric disorders and certain cardiovascular conditions. In aesthetic medicine, BoNT remains primary non-surgical option for addressing dynamic facial lines and hyperfunctional musculature. The safty profile of BoNT remains favorable, however, the efficacy and safety of BoNT is strongly linked to appropriate dosing, product selection, formulation and precise injection technique, emphasizing the critical role of anatomical knowledge to maximize therapeutic benefit while minimizing adverse events.
Conclusion: Botulinum toxin has evolved from a potent neurotoxin to a valuable therapeutic agent across a broad range of medical disciplines. Its continued success depends on deep understanding of anatomy, product characteristics, and injection technique. Ongoing research into novel serotypes, delivery systems, and expanded indications will further solidify BoNT's role as a cornerstone in both therapeutic and aesthetic practice.

KEYWORDS

Botulinum Toxin, Acetylocholine Inhibition, Neuromuscular Blockade, Therapeutic Applications

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Introduction.

The history of botulinum toxin (BoNT) dates back to the first half of the 19th century. In 1817, a German physician, Justinus Kerner, described the symptoms of food poisoning caused by the consumption of spoiled meat, which he termed "sausage poisoning" (*Wurstvergiftung*). Suspecting that a toxin present in the meat was responsible for the symptoms, Kerner conducted numerous experiments to study the effects of this unknown substance on the human body, although he was never able to isolate it. It was not until 1897 that Belgian scientist Emile Pierre van Ermengem identified *Clostridium botulinum* bacteria as the source of the substance responsible for the foodborne illnesses that had occurred earlier that century. He named the substance botulinum toxin. The discovery of botulinum toxin sparked significant interest among scientists worldwide—initially due to its extreme toxicity and potential use as a biological weapon. The first therapeutic use of botulinum toxin was carried out in 1977 by American scientist Alan Scott, who used it to treat strabismus. Scott's research laid the groundwork for legal regulations allowing the therapeutic use of BoNT. The first botulinum toxin preparation approved for medical use was named Oculinum, and it received FDA approval on December 29, 1989, for the treatment of strabismus and blepharospasm in patients aged 12 and older. Since 1991, following the acquisition of the product by the pharmaceutical company Allergan, it has been marketed under the now widely recognized name Botox [1].

Methodology

This narrative review is based solely on data obtained from publicly accessible sources. A comprehensive literature search was conducted in June 2025 using two major bibliographic databases: PubMed and Google Scholar. The search strategy included key terms such as "botulinum toxin", "BoNT", and "clinical application". Only articles published in English were included, and no limitations were applied regarding the year of publication. In addition, the reference lists of selected papers were manually reviewed to identify any further relevant studies.

Structure and types of botulinum toxin

Botulinum toxin is an exogenous neurotoxin produced by the anaerobic bacterium *Clostridium botulinum*, and less commonly by related species. It is composed of a light chain with a molecular weight of 50 kilodaltons (kDa) and a heavy chain of 100 kDa, linked by a disulfide bridge. In addition to these two chains, the botulinum toxin molecule is surrounded and stabilized by accessory proteins with a total molecular weight of approximately 750 kDa [2]. The heavy chain is responsible for binding to the receptor on the neuronal cell surface and for translocating the light chain, which—due to its enzymatic activity—enables the toxin to enter the interior of the neuron [3].

Seven types of botulinum toxin have been identified, labeled A through G. Within these types, 40 subtypes have been described, differing in the amino acid sequences of their protein chains. Botulinum toxins types A (BoNT/A), B (BoNT/B), E (BoNT/E), and F (BoNT/F) are associated with botulism in humans and animals. Type C (BoNT/C) and D (BoNT/D) cause symptoms only in animals. Type G (BoNT/G) has been isolated from soil, but no confirmed cases of botulism have been linked to it [2]. Currently, only two subtypes—BoNT/A1 and BoNT/B1—are used for therapeutic purposes [3].

Mechanism of action

Botulinum toxin acts at the neuromuscular junction, also known as the motor endplate. This is the site of synaptic contact between a muscle cell and the axon of a motor neuron. The neurotransmitter at this synapse is acetylcholine (ACh). In the axon terminal of the motor neuron, an action potential triggers the opening of voltage-gated calcium channels, leading to an influx of calcium ions (Ca^{2+}) into the neuron. This, in turn, causes the release of ACh-containing vesicles into the synaptic cleft. On the postsynaptic membrane, ACh

binds to ionotropic nicotinic receptors, causing ion channels to open and allowing sodium ions (Na^+) to enter the muscle cell. This influx results in depolarization of the muscle cell membrane.

Botulinum toxin blocks the release of ACh into the synaptic cleft by preventing vesicle fusion at the motor endplate, thereby inhibiting muscle contraction. Entry of BoNT into the neuron terminal is initiated by the binding of the heavy chain receptor domain to a neuronal surface receptor. Following this, additional surface receptors—synaptotagmin (Syt) and SV2 (synaptic vesicle glycoprotein 2)—mediate the internalization of the toxin, depending on the type and subtype of botulinum toxin. BoNT/A1 binds specifically to the SV2 receptor, while BoNT/B1 binds to the Syt receptor [2].

Once inside the neuron, the toxin is enclosed within vesicles derived from the neuronal membrane during internalization. The influx of hydrogen ions (H^+) into these vesicles causes a drop in pH, which activates proteins involved in transporting ACh into the vesicle. At this stage, the light chain of the toxin translocates across the vesicle membrane while remaining associated with the heavy chain. Enzymatic cleavage then separates and activates the light chain. The free, active light chain cleaves the SNARE protein complex—comprising VAMP (vesicle-associated membrane protein), SNAP-25 (synaptosomal-associated protein of 25 kDa), and syntaxin—which is essential for vesicle fusion with the presynaptic membrane and subsequent ACh release. (**Figure 1**)

The clinical effect of BoNT typically begins around 6.7 ± 5 days after injection and lasts for approximately 78.5 ± 28.4 days [4]. It is important to note that nerve terminals affected by botulinum toxin do not undergo degeneration, even though ACh release blockade is irreversible at the molecular level. Restoration of muscle contractile activity https://1drv.ms/w/c/2c84c575a0f7f606/EWkLe9Q9EPhJl_bXvZORqsQB4rI396NqcKbK9OeP9s-Ywwoccurs through the formation of new synaptic connections capable of releasing ACh, a process that takes approximately 2–3 months [5].

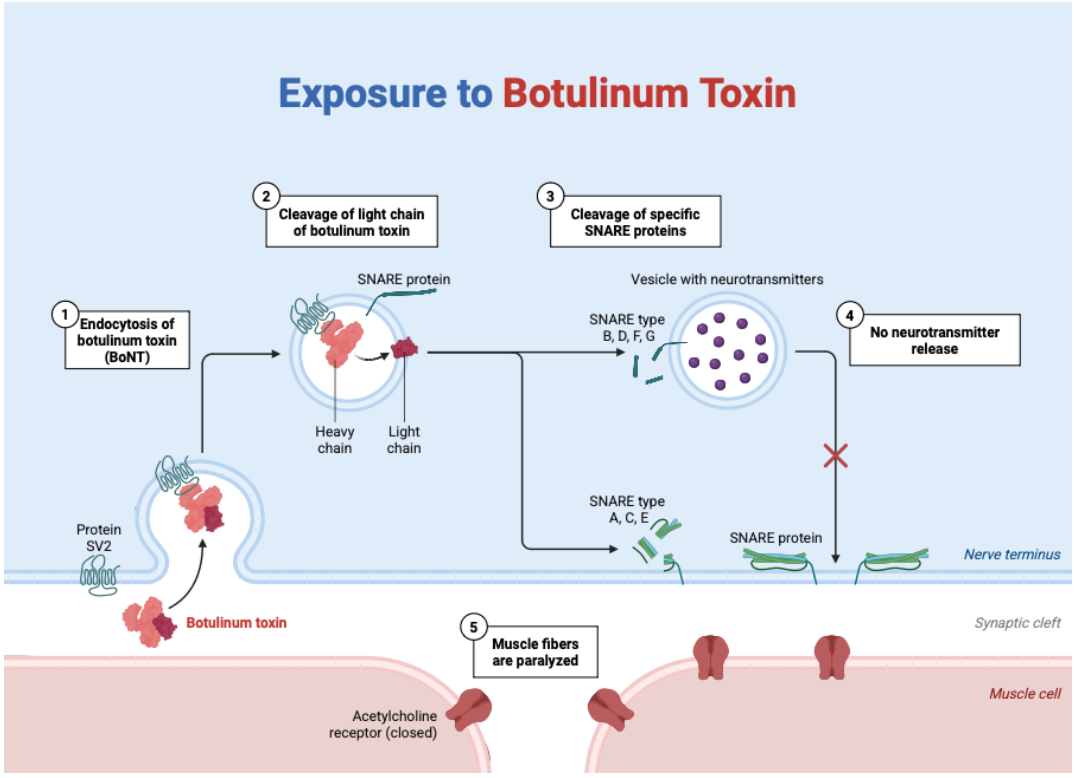

Fig. 1. *Mechanism of action of botulinum toxin.*
Source: The figure was created using BioRender.com

Immunogenicity of botulinum toxin

BoNT is an immunogenic compound. The proteins it contains act as antigens and can trigger an immune response leading to the production of both neutralizing and non-neutralizing antibodies. From a clinical perspective, neutralizing antibodies are particularly important, as they bind to the heavy chain of BoNT and inhibit its therapeutic effect. Risk factors for the development of neutralizing antibodies include repeated

administration of BoNT within one month of the initial injection, the use of more than 200 units in a single treatment, and frequent injections. To prevent the formation of neutralizing antibodies, BoNT should be administered at the lowest effective dose, repeat injections should be avoided within one month of the initial procedure, and a minimum interval of three months should be maintained between treatments [6]. This is especially important for patients undergoing long-term therapy.

In cases where anti-BoNT/A antibodies are present, treatment with BoNT/B may be effective, although the therapeutic effect is often not long-lasting. It is important to note that primary non-response to BoNT—defined as less than a 25% improvement despite increasing doses or after 2–3 treatment sessions—may be due to low individual sensitivity to the toxin, incorrect diagnosis and patient qualification, insufficient dosing, or improper intramuscular injection technique [6]. In the case of secondary treatment failure—understood as the loss of efficacy despite previous therapeutic response—possible causes include disease progression (requiring higher doses to achieve effect) or the development of neutralizing antibodies against BoNT.

Application of botulinum toxin in medicine.

Botulinum toxin (BoNT) is primarily known for its use in aesthetic medicine procedures. However, it is important to emphasize that due to its unique mechanism of action—blocking the release of acetylcholine at neuromuscular synapses—it also demonstrates high efficacy in the treatment of neuromuscular disorders. Interest in its therapeutic potential is also growing in the context of chronic conditions such as migraine, dystonia, hyperhidrosis, and chronic pain syndromes. The versatility of BoNT makes it a valuable tool in modern medical practice. (**Table 1**)

Table.1. Most important uses of botulinum toxin.

Application	Main therapeutic effect
Strabismus	Selective weakening of the overactive extraocular muscle, which allows for the restoration of the correct position of the eyeball
Focal and segmental dystonias	Reduction of involuntary muscle contractions
Spasticity	Reduction of excessive muscle tension, improvement of range of movement
Migraine	Reduction of the number and severity of migraine episodes
Overactive bladder	Reduction of the frequency of micturition, episodes of sudden urge to urinate and urinary incontinence
Chronic pain (e.g. neuropathic pain)	Relief of chronic pain
Bruxism	Reduction of pain, reduction of maximum bite force, improvement of chewing function
Hyperhidrosis	Reduction of sweat secretion
Aesthetic medicine	Smoothing of facial wrinkles, improvement and rejuvenation of appearance, correction of asymmetry

Ophthalmology

Botulinum toxin plays an important role in ophthalmology, which is the first area of its clinical application. Initially used in the treatment of strabismus, it enables selective weakening of the overactive extraocular muscle, which allows for the restoration of the correct position of the eyeball, without the need for surgical intervention. [7] BoNT is also used in the treatment of nystagmus, i.e. involuntary, uncontrolled eye movements. [8] Another important indication for its use is blepharospasm, which belongs to focal dystonias, consisting of involuntary, often bilateral, contraction of the orbicularis oculi muscle, leading to uncontrolled eyelid closure. [7] Botulinum toxin injections into the orbicularis oculi muscle effectively alleviate symptoms and improve the quality of life. Botulinum toxin has also been used in Bogorad's syndrome, also known as "crocodile tears syndrome", which involves excessive tear secretion following taste stimulation. The cause of the syndrome is post-traumatic or idiopathic facial nerve paralysis. BoNT administration to the lacrimal gland reduces the amount of tear secretion, improves visual acuity and quality of life.[9] In lagophthalmos and non-healing corneal ulcers, the seemingly undesirable effects of botulinum toxin, consisting of drooping eyelids, are used as an alternative to surgical intervention. [10] BoNT can also be used as a bridging therapy, aimed at minimizing symptoms and reducing the risk of complications. Botulinum toxin is used for this purpose in the

treatment of entropion. Pathological inward turning of the eyelid is associated with great discomfort and carries the risk of corneal damage due to continuous irritation of its surface by the eyelashes. Botulinum toxin reduces symptoms and the risk of complications, making it a good alternative in cases of contraindications to surgery or long waiting times for surgical intervention. [7,11]

Neurology

Botulinum toxin, through the selective inhibition of acetylcholine (ACh) release at the neuromuscular junction, blocks neuromuscular transmission, allowing for a reduction in excessive muscle activity. These properties have made botulinum toxin (BoNT) a valuable tool in neurology.

Botulinum toxin is a leading therapeutic option in the treatment of focal and segmental dystonias, such as cervical dystonia, blepharospasm, writer's cramp, Meige's syndrome, and spasmodic dysphonia [12,15]. Dystonias are a diverse group of disorders characterized by involuntary muscle contractions that lead to abnormal postures, twisting movements, and sometimes tremors in various parts of the body. Precise injections of botulinum toxin allow for weakening of pathologically overactive muscles, restoring more physiological movement and body alignment.

BoNT has also found application in the treatment of spasticity, which involves increased, involuntary muscle tone resulting from upper motor neuron damage. The most common causes of spasticity in adults include traumatic brain injury, stroke, and multiple sclerosis, while in children it is most often caused by cerebral palsy. The main goals of therapy are to increase the range of motion, reduce pain, facilitate daily functioning, and decrease the risk of joint contractures [13,15].

Another indication for botulinum toxin is chronic migraine, defined as headache occurring on at least 15 days per month, with at least 8 of those days meeting criteria for migraine, persisting for at least 3 consecutive months. Injection of BoNT into the frontal, temporal, occipital muscles, and trapezius muscles presents a promising alternative for patients who are intolerant of or unresponsive to oral pain medications [14,15,16].

Botulinum toxin has also significantly improved the quality of life for patients with overactive bladder. BoNT injections help reduce urinary frequency, urgency episodes, and incontinence. Standardized questionnaires indicate a notable improvement in health-related quality of life, better sleep, and fewer limitations in social activity. Furthermore, the use of botulinum toxin allows for a reduction in anticholinergic drug dosages, leading to fewer side effects and greater overall satisfaction with therapy [17,18].

Chronic pain management

Pain is a subjective, unpleasant sensory and emotional experience associated with actual or potential tissue damage. Pain, especially chronic pain—defined as lasting more than three months—has a significant impact on patients' quality of life. It can lead to mood disturbances, reduced physical functioning, sleep disorders, depression, and ultimately decreased occupational and social activity.

As we know, BoNT inhibits the release of acetylcholine from presynaptic nerve endings, resulting in muscle relaxation. This mechanism can be utilized in pain syndromes with a spastic component. Reduction in muscle tone decreases pressure on neural structures, reduces local swelling within the fascia and interfascial spaces, and enhances blood flow and lymphatic drainage. These effects help remove inflammatory mediators, improve tissue metabolism, and accelerate microenvironment regeneration.

It is also worth noting that in the context of pain management, BoNT's ability to inhibit the release of neurotransmitters involved in pain transmission—such as substance P, glutamate, and calcitonin gene-related peptide (CGRP)—is equally important. By blocking the release of these pain-related neurotransmitters, botulinum toxin reduces the transmission of pain signals to the dorsal horns of the spinal cord, thereby lowering pain intensity [19,20].

Another beneficial effect of BoNT in pain relief is the reduction of pro-inflammatory cytokines (IL-1β, IL-6, TNF-α) and prostaglandins (PGE2) in tissues where the injections are administered. This leads to a decrease in inflammation at the injection site and results in downregulation of pain receptors such as TRPV1 (Transient Receptor Potential Vanilloid 1) and TRPA1 (Transient Receptor Potential Ankyrin 1) in nociceptors. As a consequence, these receptors become less sensitive to stimuli, leading to a reduction in peripheral hyperalgesia [19,20,21].

Although the direct effect of botulinum toxin on the central nervous system remains unclear, it is hypothesized that by reducing the influx of pain signals to the dorsal horns of the spinal cord, BoNT may attenuate central sensitization processes, which clinically translates to a decrease in the extent of allodynia. By reducing chronic pain intensity, BoNT enables a decrease in analgesic doses, which in turn lowers the risk of

side effects and dependency. These mechanisms of action make botulinum toxin a valuable tool in the treatment of patients with myofascial pain syndrome, chronic migraine, and neuropathic pain. In patients with neuropathic pain, BoNT has been used effectively for conditions such as trigeminal neuralgia, postherpetic neuralgia, postoperative neuralgia, spinal cord injury-related neuralgia, and diabetic neuropathy [20,22].

Dentistry

In recent years, botulinum toxin has found wide application in dentistry. A smile is one of the most complex facial expressions, involving the coordinated action of numerous facial muscles. It serves as a positive, universal signal that enhances social interactions [23,24]. One common variation is the gummy smile, characterized by excessive gingival display during smiling. This condition is particularly prevalent in women and occurs in approximately 10.5% to 29% of the population [23]. The cause of a gummy smile can stem from dysfunctions in the lips, teeth, or skeletal structure. Treatment depends on the underlying etiology. The most common cause is hyperactivity of the upper lip elevator muscles, and in such cases, treatment with botulinum toxin has proven effective. BoNT relaxes the overactive muscles, particularly the levator labii superioris alaeque nasi, thereby reducing excessive gingival exposure and restoring a more natural smile [24]. Another key dental application of BoNT is in the treatment of bruxism—a repetitive activity involving the masseter muscles, leading to involuntary clenching and grinding of the teeth during the day or night. This muscle overactivity results in dental wear, enamel erosion, cavities, pain in the masseter and temporal muscles, temporomandibular joint (TMJ) dysfunction, sleep disturbances, and significantly reduced quality of life [25]. Standard treatment protocols involve bilateral, selective BoNT injections into the masseter muscle, which block acetylcholine release, weakening the muscle contractions and reducing tension [26]. Randomized trials have demonstrated that BoNT decreases the frequency of bruxism, reduces pain intensity, lowers bite force, and improves chewing function [27,28]. Thanks to its ability to reduce muscle tension and pain—via effects on neurotransmitters and inflammatory mediators—botulinum toxin is also used in the treatment of temporomandibular disorders (TMDs). TMDs typically present with pain, limited joint mobility, and a sensation of joint surfaces rubbing against each other, sometimes accompanied by distinctive joint noises. BoNT offers a valuable therapeutic option for patients with myogenic forms of TMD, with injections shown to reduce pain intensity and improve chewing function [29]. However, meta-analyses suggest that these benefits may not always surpass those of conventional therapies, such as occlusal splints or physiotherapy [30]. Evidence for intra-articular (joint-related) forms of TMD is more limited. Most studies show no significant advantage over placebo in reducing joint friction or increasing the maximum mouth opening range [30].

Treatment of Hyperhidrosis

Sweating is a natural physiological mechanism responsible for thermoregulation. However, when it occurs excessively and uncontrollably—as in the case of hyperhidrosis—it can significantly impact quality of life. Individuals affected by this condition often face difficulties in both professional and social settings. Despite its prevalence, hyperhidrosis is still frequently underestimated, both by patients and their surroundings. Only about 51% of people suffering from hyperhidrosis seek medical help for their symptoms [32].

Hyperhidrosis is classified into primary hyperhidrosis, which accounts for approximately 90% of cases, and secondary hyperhidrosis. The causes of primary hyperhidrosis are not fully understood, but it is believed to result from abnormal functioning of the autonomic nervous system, leading to excessive stimulation of cholinergically innervated sweat glands. Primary hyperhidrosis is strongly associated with stress-related mechanisms. Although the exact etiology remains unclear, overactivity of the sympathetic nervous system is thought to play a central role. In individuals with primary hyperhidrosis, psychological tension, stress, anxiety, or uncomfortable social situations can trigger excessive sweating, especially in specific areas such as the palms, underarms, soles, or face [33,34]. Secondary hyperhidrosis may result from neurological disorders, endocrine diseases, infections, malignancies, or adverse effects of medications [35]. The use of botulinum toxin, which blocks the release of acetylcholine from nerve endings and thereby inhibits stimulation of sweat glands, presents a logical and effective therapeutic approach to hyperhidrosis. Clinical studies confirm that BoNT injections into affected areas effectively reduce sweat gland activity, lower sweat production, and significantly improve patients' quality of life [36]. This treatment is characterized by high efficacy, long-lasting effects, and a relatively low incidence of side effects, making it one of the most commonly recommended therapies for managing hyperhidrosis [32].

Gynecology

Botulinum toxin is also finding increasing application in gynecology, particularly in the treatment of conditions associated with excessive muscle tension and chronic pelvic pain. BoNT has been used in cases of dyspareunia, vaginismus, vulvodynia, and chronic pelvic pain syndromes, especially when other therapeutic methods prove ineffective [37]. In vaginismus, the administration of botulinum toxin reduces involuntary vaginal muscle spasms, facilitating penetration and reducing pain during intercourse. In vulvodynia and chronic pelvic pain, BoNT injections exhibit analgesic effects by modulating the release of neurotransmitters involved in pain signal transmission [37,38]. Botulinum toxin presents a promising therapeutic option in gynecology. However, due to inconsistent research findings, there is a clear need for further well-designed clinical trials to determine optimal dosing, injection sites, long-term efficacy, and the safety profile of BoNT in gynecological use [37].

Aesthetic Medicine

Botulinum toxin is one of the most commonly used tools in aesthetic medicine. Thanks to its unique properties allowing for the precise inhibition of neuromuscular transmission by blocking acetylcholine release at neuromuscular junctions, BoNT enables controlled selective weakening of the overactive facial muscles responsible for the formation of expression lines. This results in a smoother more youthful and radiant facial appearance. Botulinum toxin injections are most frequently used in the upper third of the face to reduce the appearance of dynamic wrinkles that form as a result of repeated muscle activity. These include horizontal forehead lines, which develop due to the excessive activity of the frontalis muscle; glabellar lines, also known as frown lines, which are formed by the combined action of the corrugator supercilii and procerus muscles; and crow's feet, the fine lines that appear at the outer corners of the eyes, resulting from overactivity of the orbicularis oculi muscle [39,40]. BoNT is also used to elevate the eyebrows creating a more open-eye appearance and a brighter more refreshed facial expression [40]. In the lower third of the face BoNT is used to treat vertical lines around the mouth commonly referred to as "smoker's lines" caused by the orbicularis oris muscle. Caution is essential in this area as starting with minimal doses is recommended since improper injection may affect important muscle functions potentially impairing speech eating or drinking. Another aesthetic concern where BoNT can be applied is the "cobblestone" or "pebbled" chin resulting from overactivity of the mentalis muscle and volume loss in subcutaneous tissues. BoNT injections combined with dermal fillers can help smooth the surface and significantly improve the skin's appearance [40,41]. BoNT is also used to elevate downturned mouth corners which can give the face a sad or tired look. This is achieved by weakening the depressor anguli oris muscle using targeted BoNT injections. [41] Botulinum toxin can also improve the appearance of the neck which is just as important for a youthful look as the face. In the neck area BoNT injections are used to reduce the visibility of horizontal wrinkles and vertical bands (commonly referred to as "turkey neck") caused by overactivity of the platysma muscle and loss of skin elasticity with aging. By relaxing these muscles and smoothing the skin BoNT offers a noticeable aesthetic improvement in the neck region [42].

Safety Profile

Despite being one of the most potent known neurotoxins, botulinum toxin demonstrates a relatively favorable safety profile. Although its laboratory toxicity is high (the lethal dose LD50 for humans is approximately 1 ng/kg of body weight when administered intravenously), the therapeutic doses used in clinical practice are significantly lower and thus considered safe [43,44]. Adverse effects associated with botulinum toxin largely depend on the total dose administered, the site and depth of the injection, and the experience of the practitioner performing the procedure. The most frequently reported complications are local in nature and stem directly from the toxin's mechanism of action. Common local side effects include pain at the injection site, erythema, bruising, swelling, paresthesia, temporary muscle weakness in the treated area, eyelid ptosis (particularly after injections in the forehead and glabellar region), and facial asymmetry [45,46]. When higher doses are used—mainly in the treatment of neurological conditions such as dystonia and spasticity—systemic symptoms may occur due to toxin diffusion beyond the injection site. These can include dysphagia, dysarthria, dysphonia, limb muscle weakness, and even respiratory muscle weakness [45]. An important safety consideration is the previously mentioned risk of immunogenicity, which may lead to the formation of neutralizing antibodies and reduced clinical efficacy of the treatment. Despite these potential adverse effects, clinical studies and long-term observations confirm that, with proper patient selection and adherence to correct injection protocols, botulinum toxin has a very favorable safety profile, demonstrating high therapeutic efficacy with a relatively low risk of complications [44,45,46].

Future Perspectives

The future development of botulinum toxin (BoNT) applications appears highly promising, encompassing both an expansion of therapeutic indications and improvements to the toxin formulations themselves. Ongoing research is focused on molecular modifications of BoNT aimed at extending its duration of action, enhancing its specificity for targeted receptors, and reducing its immunogenicity. Significant advancements are also being made in imaging techniques, particularly ultrasonography, which allow for more precise localization of anatomical structures and help minimize adverse effects. Increasing attention is being given to the potential use of botulinum toxin in previously unexplored medical fields, including psychiatry (for treatment-resistant depression and anxiety disorders), cardiology (for arrhythmias and arterial hypertension), and in the management of inflammatory and autoimmune diseases. Moreover, the development of nanotechnology and targeted drug delivery systems may, in the future, enable even more selective and safer BoNT-based therapies for well-defined cell populations. [47,48,49]

Discussion

Botulinum toxin (BoNT) has evolved from a specialized treatment for select neuromuscular disorders to a widely used therapeutic agent across a broad spectrum of medical fields. Its unique ability to induce temporary chemodenervation through inhibition of acetylcholine release has made it a cornerstone therapy in conditions characterized by muscular hyperactivity and autonomic dysfunction. The early clinical successes in ophthalmology and neurology laid the foundation for its expansion into other specialties, where its localized action, favorable safety profile, and reversible effects offer considerable advantages over systemic pharmacological treatments.

The clinical applications of BoNT now extend into dermatology for hyperhidrosis, pain medicine for chronic pain and migraine, dentystry for bruxism and gummy smile , and aesthetic medicine for dynamic wrinkles. More recently, there has been growing interest in exploring its use in psychiatry—such as in the treatment of depression and anxiety disorders—and cardiovascular medicine, particularly for conditions involving abnormal autonomic tone. These emerging indications are supported by earl clinical trials and mechanistic studies, though larger randomized controlled studies are needed to validate efficacy and safety in these domains.

Furthermore, advances in molecular engineering of BoNT, development of novel serotypes, and improvements in delivery techniques (e.g., ultrasound-guided injections) are opening new avenues for treatment optimization. However, challenges remain, including the potential for immunogenicity, variable duration of effect among patients, and the need for repeat administration, which may limit patient compliance and long-term effectiveness.

Despite these limitations, the versatility of botulinum toxin is unmatched among current therapeutic agents, and its evolving role in clinical medicine reflects ongoing innovation and discovery.

Conclusions

Botulinum toxin represents one of the most dynamic and versatile therapeutic agents in modern medicine. Its established efficacy in neuromuscular and autonomic disorders, combined with expanding applications in diverse medical fields, underscores its clinical value. Continued research into novel indications, refined dosing strategies, and advanced formulation technologies holds promise for further broadening its therapeutic potential. As our understanding of its mechanisms and clinical impact deepens, botulinum toxin is likely to remain an essential component of both established and emerging treatment protocols in the years to come.

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Author's contributions:
Conceptualization: Katarzyna Herjan, Piotr Armański.
Methodology: Gabriela Łocik, Piotr Amrański.
Software: Marta Bonarska, Joanna Wróbel, Katarzyna Kozon.
Check: Katarzyna Herjan, Piotr Armański, Joanna Wróbel.
Formal analysis: Gabriela Łocik, Marta Bonarska, Katarzyna Kozon.
Investigation: Katarzyna Herjan, Katarzyna Kozon.
Data curation: Joanna Wróbel, Gabriela Łocik, Marta Bonarska.
Writing – rough preparation: Katarzyna Herjan, Piotr Armański, Joanna Wróbel.
Writing – review and editing: Gabriela Łocik, Marta Bonarska, Katarzyna Kozon.
Visualization: Katarzyna Herjan, Piotr Armański.
Supervision: Gabriela Łocik, Marta Bonarska, Katarzyna Kozon.
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