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## **Botulinum neurotoxin: Not only in Dermatology - Expanding Therapeutic Horizons Across Medical Specialties**

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## **Abstract**

**Background.** Botulinum neurotoxin (BTX) is commonly associated with cosmetic applications; however, its therapeutic relevance extends far beyond aesthetic medicine. Through inhibition of presynaptic acetylcholine release, BTX induces reversible chemodenervation and modulates sensory, autonomic, and inflammatory signaling, providing a biological basis for its wide range of clinical applications across multiple medical specialties.

**Aim.** The aim of this review was to summarize and critically appraise current evidence on established and emerging therapeutic applications of botulinum neurotoxin in dermatology, neurology, urology, gastroenterology, and selected novel indications.

**Material and methods.** A narrative review of the literature was conducted using recent clinical studies, systematic reviews, meta-analyses, and relevant experimental research focusing on the mechanisms of action, clinical efficacy, and safety of botulinum neurotoxin across different medical disciplines.

**Results.** Botulinum neurotoxin demonstrates well-established efficacy and an acceptable safety profile in dermatology, particularly in wound healing and hyperhidrosis, and in neurology, where it represents a cornerstone therapy for focal dystonias, spasticity, chronic migraine, and selected pain syndromes. In urology and gastroenterology, BTX provides effective, minimally invasive treatment options for refractory lower urinary tract dysfunctions and selected gastrointestinal and anorectal disorders. Emerging evidence further suggests potential roles for BTX in depression and immunomodulation.

**Conclusions.** Botulinum neurotoxin has evolved into a versatile therapeutic agent with broad clinical applicability across multiple medical specialties. While its established indications are supported by robust evidence, emerging applications highlight promising new therapeutic directions that warrant further high-quality clinical and translational research.

**Key words:** botulinum neurotoxin, botulinum toxin type A, neuromodulation, clinical applications, emerging indications

## **1. Introduction**

Botulinum neurotoxin (BTX) is commonly perceived either as a dangerous poison or as a cosmetic agent used to reduce facial wrinkles (1). However, its clinical utility extends far beyond aesthetic medicine, with established applications across numerous medical specialties. Historically, botulinum neurotoxin was primarily recognized as a highly potent and potentially lethal toxin, most notably associated with severe foodborne botulism (2). A major paradigm shift occurred when its ability to block neuromuscular transmission was identified, leading to the recognition of its therapeutic potential and subsequent development as a medical treatment for a wide range of neurological and non-neurological disorders (3). By inhibiting presynaptic acetylcholine release, botulinum neurotoxin induces reversible chemodenervation and modulates sensory, autonomic, and inflammatory signaling, providing a biological rationale for its expanding therapeutic applications (2). Importantly, growing high-quality evidence, including recent systematic reviews and meta-analyses, confirms that botulinum neurotoxin is both safe and effective across a broad range of non-neurological conditions, further supporting its expanding role beyond traditional indications (4).

## **2. Research materials and methods**

This narrative review was performed to summarize established and emerging therapeutic applications of botulinum neurotoxin across multiple medical specialties. A targeted literature search was performed using PubMed, Wiley Online Library, Springer Nature Link, Google Scholar, and ScienceDirect, focusing on clinical studies, systematic reviews, meta-analyses, and relevant experimental research. Search terms included combinations of “botulinum neurotoxin,” “botulinum toxin type A,” “BTX,” “BTX-A,” “dermatology,” “neurology,” “urology,” “gastroenterology,” “wound healing,” “hyperhidrosis,” “focal dystonia,” “spasticity,” “migraine,” “neuropathic pain,” “overactive bladder,” “urinary incontinence,” “interstitial cystitis,” “Hirschsprung’s disease,” “gastroparesis,” “chronic anal fissure,” “depression,” and “immunomodulation.” Preference was given to high-quality and recent publications (particularly from 2023–2025), while earlier landmark studies were included where necessary to provide mechanistic or historical context. Data were synthesized qualitatively and organized thematically according to the clinical domains and subtopics addressed in this review, without formal statistical analysis.

### **3. Results**

#### **3.1. Dermatology**

##### **Wound healing**

Botulinum neurotoxin has been increasingly used to promote wound healing without tension by temporarily limiting excessive muscular activity that contributes to tension across developing scar tissue. Recent studies indicate that BTX can improve the management of scars, enhancing overall clinical effectiveness. (5) Research by Kasyan et al. further supports these observations by demonstrating that BTX alleviates tension, decreases collagen synthesis and inhibits fibroblast proliferation that can prevent and treat scarring (6). Moreover a recent meta-analysis also reported that botulinum neurotoxin improves cosmetic outcomes and decreased the incidence of hypertrophic scar development after facial surgery. (7)

##### **Hyperhidrosis**

Hyperhidrosis still remains a common problem among patients. It is associated with decreased life quality and it can lead to social embarrassment, anxiety and depression (8). BTX acts by inhibiting acetylcholine release at cholinergic sympathetic nerve terminals that innervate sweat glands, leading to a reversible reduction in sweat production. (9) Multiple clinical studies have confirmed the efficacy of BTX in the management of axillary, palmar, plantar and frontal hyperhidrosis. The limitations of this method include a relatively short duration of effectiveness and discomfort related to intradermal injections. Nevertheless, studies consistently demonstrate that patients are highly willing to continue BTX therapy, valuing the significant reduction in sweating and the associated improvements in social functioning, confidence, and overall life quality. (9-11)

These represent only two of the many dermatologic indications for botulinum neurotoxin. Beyond wound healing and hyperhidrosis, BTX has been effectively used in the management of rosacea-related erythema and flushing, various forms of pruritus and neuropathic itch, excessive sebum production, and certain inflammatory dermatoses (12,13). Emerging evidence also supports its application in conditions such as hidradenitis suppurativa, keloid modulation, and even disorders of the scalp, including alopecia-associated scalp tension (13,14). This broadening spectrum of dermatologic uses highlights BTX as a versatile neuromodulator with expanding relevance in both aesthetic and therapeutic dermatology.

To date, BTX has therefore become an established and widely accepted therapeutic option in dermatology—both for functional and aesthetic indications. Given its well-documented neuromodulatory properties, its applications extend far beyond the skin. This expanding

therapeutic profile has particularly reshaped the field of neurology, where botulinum neurotoxin plays a central role in the management of numerous neuromuscular and pain-related disorders.

### **3.2. Neurology**

Neurology remains the medical speciality in which botulinum neurotoxin has achieved the most extensive validation and the strongest clinical evidence. Owing to its ability to produce reversible chemodenervation by inhibiting acetylcholine release at the neuromuscular junction, BTX has become a cornerstone therapy in several neuromuscular disorders. Over the past decades, its indications have expanded from focal dystonias to spasticity, chronic migraine, neuropathic pain syndromes, and other movement-related conditions (14). The following subsections summarize the major neurological applications supported by the current literature.

#### **Focal dystonias**

Focal dystonias represent one of the neurological conditions in which botulinum neurotoxin demonstrates the most consistent therapeutic benefit. Clinical evidence from both early and contemporary studies suggests that targeted injection into overactive muscles leads to measurable reductions in abnormal postures, muscle spasms, and pain, making it the preferred symptomatic treatment across cervical, cranial, and limb dystonias (14,15). Treatment outcomes are typically robust and reproducible, with improvements maintained over successive injection cycles (14). Recent analyses also indicate that the therapeutic value of botulinum neurotoxin extends to less typical dystonic patterns. A review of axial extensor dystonia reports clinically meaningful benefit in the majority of treated patients, highlighting the adaptability of this approach even in complex or atypical presentations (16). Although individual muscle patterns differ among dystonia subtypes, the injection strategy is consistently based on precise identification of involved muscles and tailored dosing, contributing to optimized clinical results (14). Overall, focal dystonias remain one of the clearest examples of the targeted, phenotype-specific application of botulinum neurotoxin, with an evidence base that continues to expand through both clinical experience and systematic evaluations (14-16).

#### **Spasticity**

Spasticity is a common consequence of upper motor neuron lesions and contributes to muscle overactivity, functional limitations, and reduced quality of life (17). Botulinum neurotoxin is well established as an effective focal treatment, with clinical studies demonstrating reductions in muscle tone and improved passive function following targeted injection into spastic muscles (17). Benefits are maintained across repeated treatment cycles, and BTX can facilitate rehabilitation by improving limb positioning and enabling more efficient therapeutic interventions. Recent bibliometric analysis indicates a growing global interest in BTX for

spasticity, documenting nearly 1500 publications and showing sustained expansion of research activity in neurology and rehabilitation fields (18). Together, these findings confirm the central role of BTX in contemporary spasticity management and its broad clinical relevance across diverse neurological populations.

### Migraine

Chronic migraine represents a highly disabling neurological disorder characterized by persistent headache burden and central sensitization phenomena. Botulinum neurotoxin has emerged as a validated preventive intervention, particularly for individuals exhibiting refractoriness to standard oral treatment. Experimental and clinical evidence indicates that BTX modulates trigeminovascular neurobiology by attenuating the release of CGRP, substance P, and glutamate, thereby reducing both peripheral and central nociceptive transmission (19). A Cochrane systematic review reported clinically meaningful reductions in migraine frequency among patients with chronic migraine receiving BTX relative to placebo (20). Observational studies further demonstrate that BTX maintains effectiveness across repeated treatment cycles and provides clinical benefit even in more complex patient groups, including those with medication-overuse headache or multiple prior preventive treatment failures (19). Collectively, current evidence reinforces the role of BTX as an essential component of preventive therapy in chronic migraine.

### Neuropathic Pain

Emerging data indicate that botulinum neurotoxin exerts clinically meaningful analgesic effects in selected neuropathic and myofascial pain syndromes. Experimental models consistently results in reductions in mechanical hypersensitivity and allodynia following peripheral BTX administration, mediated by inhibition of key neurotransmitters such as CGRP, glutamate, and substance P, as well as modulation of TRPV1- and TRPA1-dependent nociceptive signalling (21). Additional studies demonstrate that BTX attenuates neuroinflammatory pathways by suppressing cytokines including IL-1 $\beta$  and TNF- $\alpha$  and by reducing microglial activation, thereby limiting central sensitization processes relevant to chronic pain (22). Clinical observations in neurological practice further indicate that BTX may provide symptom relief in conditions such as trigeminal neuralgia, post-herpetic neuralgia, and myofascial pain, particularly in patients unresponsive to conventional therapies (15). Taken together, these findings support a growing role for BTX as a targeted adjunctive option in refractory neuropathic and myofascial pain disorders.

Overall, the neurological indications of botulinum neurotoxin represent the most evidence-rich and clinically impactful domain of its therapeutic use. The growing literature base underscores

its versatility across movement disorders, spasticity, migraine, and neuropathic pain. Beyond neurology, however, BTX continues to expand into other medical specialties, including urology, gastroenterology, ophthalmology, and otolaryngology (2,14,15).

### **3.3. Urology**

Botulinum toxin type A has become an established therapeutic option in functional urology, particularly in the management of lower urinary tract dysfunctions that are refractory to conventional pharmacological treatment. Its ability to modulate detrusor and sphincter activity through inhibition of acetylcholine release provides a strong mechanistic rationale for its use in a range of urological disorders (4,23,24).

#### **Overactive bladder (OAB)**

Botulinum neurotoxin type represents an established option for patients with refractory overactive bladder, offering meaningful short-term improvement in urgency, frequency and incontinence when conventional therapy fails. However, long-term data demonstrates that many patients discontinue treatment over time, most often due to tolerability issues such as need for clean intermittent self-catheterisation or urinary tract infections rather than lack of efficacy (23). Evidence from paediatric populations similarly indicates that BTX can be effective in selected cases of therapy-resistant OAB, providing symptomatic improvement with acceptable safety, although the need for repeated injections remains a limiting factor (25). BTX represents a valuable adjunct in OAB management, though long-term continuation depends heavily on patient tolerance and treatment-related challenges.

#### **Urinary incontinence**

Urinary incontinence is a frequently reported patient-related problem. It commonly occurs in patient with central nervous system disorders such as stroke, Parkinson's disease, multiple sclerosis, dementia and intracranial lesions. Oral pharmacotherapy may provide limited symptom control and may induce unacceptable adverse effects. Intravesical BTX injection offers an effective approach to improve urinary incontinence, while targeted urethral sphincter injection can enhance voiding dynamics (26). Although it might be associated with adverse events such as hematuria, urinary tract infections and epididymitis, usually they are mild and manageable (26). Overall BTX provides meaningful symptom improvement and represents a valuable therapeutic option for patients with urinary incontinence (26,27).

### Painful urological syndromes

According to current guidelines, botulinum neurotoxin may be considered in selected groups of patients with chronic pelvic syndrome (CPPS) and interstitial cystitis/bladder pain syndrome (IC/BPS). This approach is especially beneficial in patients who still remain symptomatic, despite pharmacological therapies or other medical interventions (24). BTX reduces pelvic floor muscle hyperactivity and spasm in CPPS, contributing to alleviation of pain and overall symptom severity. In IC/BPS intravesical BTX acts on sensory and inflammatory pathways, resulting in decreased bladder pain, urgency, and frequency (4,24). Nevertheless, current studies emphasise careful patient selection and underline the need of repeated treatments and unpredictable duration of therapeutic benefit (24).

Botulinum neurotoxin has become an established therapeutic tool in functional urology. The treatment outcomes are satisfactory for patients and are associated with a low rate of adverse effects, most of which are being acceptable and manageable. Emerging evidence supports the expanding role of BTX in urology, with potential applications in benign prostatic hyperplasia and dysfunctional voiding (23,24,28)

### **3.4. Gastroenterology**

Botulinum neurotoxin has found increasing application in gastroenterology, primarily as a minimally invasive therapeutic option for selected functional and obstructive gastrointestinal disorders (29,30). Its ability to induce reversible smooth muscle relaxation and modulate enteric neurotransmission provides a mechanistic basis for its use in both pediatric and adult populations (29-31).

#### Hirschsprung's Disease (HD)

In Hirschsprung's disease, botulinum neurotoxin is mainly used in children who require further medical interventions after surgical treatment. Intrasphincteric injections of BTX results in a temporary blockade of presynaptic acetylcholine release, resulting in lower resting internal anal sphincter pressure, reduced obstructive symptoms and events, and fewer number of hospitalizations (29-31). In the study by Han-Geurts et al., short-term improvement is observed in approximately 76% of patients, primarily related to a reduction in hospitalizations for enterocolitis. However, it should be noted that the prevalence of enterocolitis decreased with age, therefore these findings should be carefully interpreted (31). Similar findings were also

confirmed by Patel et al., demonstrating that BTX injections in children with Hirschsprung's disease are associated with clinical improvement and lower number of hospitalizations (29).

#### Gastroparesis (GP)

Intragastric botulinum neurotoxin injections have found applications in gastroparesis. It is associated with clinical efficacy in reducing gastroparesis symptoms such as nausea, vomiting, early satiety and postprandial fullness. The study highlights that pyloric BTX may provide symptomatic relief in selected patients, but its overall benefit appears less pronounced and potentially less durable than achieved with gastric peroral endoscopic myotomy. (Gastric peroral endoscopic myotomy versus botulinum toxin injection for the treatment of refractory gastroparesis: results of a double-blind randomized controlled study). Similar findings were observed in other studies, suggesting that BTX has a limited duration of action and need for repeated procedures under anesthesia. Also cost-effectiveness remains an important consideration given the likelihood of repeated treatments. Although the treatment is generally well tolerated with minimal adverse effects, the potential for pyloric scarring may pose limitations or increase the complexity of subsequent surgical interventions (29).

#### Chronic anal fissure

Botulinum neurotoxin has emerged as a minimally invasive therapeutic option for chronic anal fissure, aiming to reduce internal sphincter hypertonia while preserving sphincter integrity and continence (29,32,33). BTX injections is an effective non-surgical treatment for this condition, achieving fissure healing in approximately 73% of patients after the first injection (33). The therapeutic effect of BTX is mediated through temporary chemical sphincterotomy, resulting from inhibition of acetylcholine release and subsequent relaxation of the internal anal sphincter (29,32,33). Compared with lateral internal sphincterotomy, BTX treatment is associated with more favourable safety profile, particularly with respect to continence preservation, although recurrence of symptoms may occur (32,33). Consequently, recent reviews support BTX as a reversible and well-tolerated first-line or bridging therapy in selected patients (29).

Botulinum neurotoxin has an established role in the management of selected gastrointestinal and anorectal disorders in both children and adults as a minimally invasive and reversible therapeutic option. In Hirschsprung's disease and chronic anal fissure, BTX reduces internal anal sphincter hypertonia, leading to clinical improvement and fewer hospitalizations while preserving continence, although the effect is often transient and may require repeat treatment (29-33). In gastroparesis, intrapyloric BTX can provide short-term symptomatic relief in selected patients, but its benefit appears to be less durable than definitive endoscopic or surgical

interventions (29). Overall, BTX is best positioned as a safe, well-tolerated first-line or bridging therapy in carefully selected patients (29,32,33).

### **3.5. Emerging Indications**

Beyond its established clinical indications, increasing experimental and clinical evidence suggests that botulinum neurotoxin may exert broader neuromodulatory and immunological effects, opening new therapeutic perspectives (34-36).

#### **Depression**

Botulinum neurotoxin (BTX) has emerged as a novel therapeutic approach for depression, based on the facial feedback hypothesis, which posits that facial muscle activity can modulate emotional experience. Glabellar BTX injections reduce the activity of corrugator and procerus muscles associated with negative emotions, thereby interrupting maladaptive emotional feedback loops and alleviating depressive symptoms (34,37). Randomized controlled trials and meta-analyses have demonstrated significant reductions in depressive symptom severity following BTX treatment, including in patients with treatment-resistant depression (34,35,37). Reported response and remission rates are comparable to those achieved with standard antidepressant therapies, with some studies suggesting a faster onset of clinical improvement (35). Neurobiological studies indicate that the antidepressant effects of BTX extend beyond peripheral muscle paralysis and involve central mechanisms, including modulation of amygdala activity and limbic circuits (34,35). Additional proposed mechanisms include increased BDNF expression and enhanced monoaminergic transmission, supporting a broader neuromodulatory role of BTX in mood regulation (35). BTX treatment is generally well tolerated, with a favourable safety profile and long-lasting effects, often requiring only a limited number of injections per year (35,37). Taken together, contemporary reviews conclude that BTX represents a promising adjunctive or alternative therapy for depression, although larger, well-designed phase III trials are still needed before its routine adoption in psychiatric practice (35,37).

#### **Immunomodulation**

Botulinum neurotoxin has been increasingly recognized as a modulator of inflammatory and neuroimmune pathways, extending its effects beyond neuromuscular blockade. Clinical and experimental data indicate that BTX inhibits neurogenic inflammation by blocking SNAP-25-mediated release of pro-inflammatory neuropeptides, particularly calcitonin gene-related peptide (CGRP) and substance P. At the molecular level, BTX has also been shown to modulate

immune signaling at the molecular level by downregulating gene sets involved in cytokine signaling, lymphocyte activation, and innate immune responses (36). Experimental studies further demonstrate that BTX suppresses cytokine-driven inflammatory cascades by inhibiting intracellular signaling pathways such as Smad2/3 and ERK1/2, resulting in reduced expression of key pro-inflammatory cytokines. In addition, BTX reduces the expression of neuroimmune mediators involved in chronic inflammation and pruritus, including IL-31, IL-33, CGRP, and substance P, highlighting its role in neuroimmune cross-talk (38). Although accumulating evidence suggests that botulinum neurotoxin exerts immunomodulatory effects through cytokine and neuroimmune pathways, current data remain limited, and further mechanistic and clinical studies are required to fully elucidate its role (36,38).

#### **4. Conclusions**

Botulinum neurotoxin has evolved from a potent biological toxin and cosmetic agent into a versatile therapeutic tool with well-established applications across multiple medical specialties (1-3). Robust clinical evidence supports its central role in dermatology, neurology, urology, and gastroenterology, where BTX provides effective, minimally invasive, and generally well-tolerated treatment options for a wide range of functional, neuromuscular, and pain-related disorders (5-7,14-20,23).

Beyond its traditional indications, accumulating experimental and clinical data highlight emerging roles for botulinum neurotoxin in psychiatry and immunomodulation, suggesting broader neuromodulatory and neuroimmune effects that extend beyond peripheral chemodenervation (34-38). Although findings in these areas are promising, they remain supported primarily by early clinical trials, systematic reviews, and experimental studies, underscoring the need for further large-scale, well-designed investigations (32,35-38).

Overall, the expanding therapeutic profile of botulinum neurotoxin reflects its unique mechanism of action and favourable safety characteristics across diverse patient populations (2-4,27). Continued interdisciplinary research will be essential to better define optimal indications, long-term outcomes, and patient selection, thereby facilitating the responsible integration of BTX into both established and emerging areas of clinical practice (28,36,38).

#### **Disclosure:**

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### **Conflict Of Interest**

The author declare no conflict of interest.

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