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BRIEF REVIEW

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The Emerging Role of Botulinum Neurotoxin in Psoriasis Management: A Review of Mechanisms, Evidence, and Challenges

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Abstract

Psoriasis is a chronic, immune-mediated skin condition characterized by inflammation and accelerated epidermal turnover. Current therapies, including topical and systemic agents, often face limitations such as incomplete efficacy, side effects, and patient compliance issues. Botulinum neurotoxin (BoNT), traditionally used in cosmetic dermatology and neurology, has emerged as a novel potential treatment due to its ability to modulate neuroinflammatory pathways and immune responses. This review explores the biological basis of BoNT in psoriasis, focusing on its role in inhibiting neuropeptide release, reducing pro-inflammatory cytokines, and interrupting the cycle of neuroinflammation. We examine preclinical studies and clinical trials demonstrating BoNT's efficacy in reducing psoriasis symptoms, particularly when conventional therapies fall short.

Additionally, the review highlights the safety profile, emphasizing potential side effects such as localized muscle weakness, and discusses challenges, including standardization of dosing and long-term outcomes. Further study of BoNT's therapeutic potential, its role as an additional therapy, and the development of biomarkers for predicting patient responses are of great practical interest. In conclusion, BoNT shows promise as an innovative treatment approach for psoriasis, warranting further investigation to establish its clinical utility.(**International Journal of Biomedicine. 2025;15(1):51-54.**)

Keywords: Botulinum neurotoxin • psoriasis • neuroinflammation • cytokines • clinical trials

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Psoriasis is a chronic, immune-mediated inflammatory skin disorder affecting approximately 2-4% of the global population.[1] The pathophysiology of psoriasis is driven by an imbalance between the immune system and skin barrier, leading to chronic inflammation and excessive epidermal cell proliferation.[2] Key pathogenic pathways involve T-helper cells, particularly Th17 cells, which produce pro-inflammatory cytokines like IL-17, IL-23, and TNF-α, contributing to the persistence of inflammation and abnormal skin cell turnover.[3] Despite significant advances in understanding the disease mechanisms, current treatments remain suboptimal for many patients. Topical therapies (e.g., corticosteroids and vitamin D analogs) are often limited in efficacy, especially for moderate-to-severe cases, while systemic therapies such as biologics (TNF inhibitors, IL-17, IL-23 inhibitors) are effective but come with risks of side effects, cost, and long-term safety concerns.[4] Furthermore, patient adherence remains a significant challenge due to the complex regimens, side effects, and variable response rates.

Botulinum neurotoxin (BoNT) is a neurotoxin produced by Clostridium botulinum, known primarily for its role in muscle paralysis and its use in therapeutic and cosmetic applications.[5] Beyond its well-established use in neurology and aesthetics (e.g., for facial wrinkles), recent studies have explored BoNT's anti-inflammatory and immune-modulating effects, particularly in dermatological conditions. Emerging evidence suggests that BoNT may influence neuroinflammatory pathways by inhibiting the release of acetylcholine and neuropeptides, such as substance P, which play a role in the propagation of inflammatory responses.[6] Given the involvement of neurogenic inflammation in psoriasis, BoNT can potentially target these pathways and offer an alternative or adjunctive treatment option. This review focuses on the potential role of BoNT in modulating psoriasis pathogenesis, particularly its emerging use as a novel therapeutic strategy, highlighting the neuroinflammatory mechanisms underlying the condition and evaluating clinical evidence supporting its efficacy.

Biological Basis of Botulinum Neurotoxin in Psoriasis

Psoriasis is increasingly recognized as a neuroinflammatory disorder, where skin inflammation is driven by interactions between the nervous system and immune response. Neuropeptides such as substance P and calcitonin gene-related peptide (CGRP) play a pivotal role in the pathogenesis of psoriasis by promoting inflammation and exacerbating immune responses through the activation of pro-inflammatory cytokines, including IL-17, IL-23, and TNF-α.[2,3,7] Elevated levels of these neuropeptides contribute to the persistent inflammatory environment in psoriasis lesions, perpetuating skin cell hyperproliferation and immune activation.

BoNT offers a potential therapeutic approach by modulating these neuroinflammatory pathways. Recent studies have demonstrated that BoNT can inhibit the release of neuropeptides, such as substance P, which are involved in the inflammatory cascade seen in psoriasis.[6] By reducing neuropeptide-mediated signaling, BoNT may help attenuate inflammation and prevent the exacerbation of psoriasis lesions.

BoNT exerts its effects primarily by inhibiting the release of acetylcholine at the neuromuscular junction, thereby disrupting the communication between nerve endings and immune cells. In the context of psoriasis, this inhibition extends beyond muscle activity, influencing immune cell signaling. BoNT has been shown to modulate the release of inflammatory mediators such as TNF-α, IL-17, and IL-23, which are key drivers of psoriasis pathology.[5,6] By blocking the release of acetylcholine and interfering with neuropeptide signaling, BoNT reduces the activation of inflammatory cytokines, thereby dampening the immune response associated with psoriasis.

BoNT also affects immune cells, such as T-helper cells (Th17) and macrophages, which play a central role in the inflammatory milieu of psoriasis. By inhibiting acetylcholine release, BoNT reduces the production of pro-inflammatory cytokines, critical for sustaining the immune response and maintaining the inflammatory state of psoriasis lesions.[8]

Furthermore, BoNT's ability to modulate neuroinflammatory pathways may interrupt the vicious cycle of inflammation, wherein neuropeptides stimulate cytokine production, contributing to further inflammatory damage and skin cell turnover.[9] By targeting these pathways, BoNT holds promise as a novel approach to mitigate chronic inflammation in psoriasis.

The neuroinflammatory nature of psoriasis suggests that disrupting the cycle of neuropeptide-driven inflammation could be an effective therapeutic strategy. BoNT's neuroimmune-modulatory effects could interrupt this cycle by reducing the levels of neuropeptides responsible for inflammatory mediators, such as IL-17 and TNF-α.[6] By preventing the release of acetylcholine and blocking neuropeptide activity, BoNT may diminish the inflammatory signals that perpetuate the inflammatory process in psoriasis lesions.

Recent research highlights BoNT's potential in suppressing these inflammatory pathways and reducing the severity of psoriasis. For instance, BoNT has been shown to downregulate pro-inflammatory cytokines and alleviate symptoms in neuroinflammation conditions, such as chronic pain and migraine.[5,9] Translating these findings into psoriasis treatment suggests that BoNT could offer significant therapeutic benefits by disrupting the neuroimmune axis and reducing psoriasis-associated inflammation.

Clinical Evidence Supporting BoNT Use in Psoriasis

Numerous preclinical studies have highlighted BoNT's potential anti-inflammatory effects, particularly through its modulation of neuropeptide-mediated pathways. In experimental models of psoriasis, BoNT has demonstrated the ability to reduce neuroinflammation by inhibiting the release of substance P and other pro-inflammatory neuropeptides.[5,10] Studies on animal models have shown that BoNT significantly reduces the production of cytokines such as TNF-α, IL-17, and IL-23, which are critical in the pathogenesis of psoriasis.[10,11] These findings suggest that BoNT may help attenuate the inflammatory response underlying psoriasis, offering a novel approach to managing the disease.

Limited but emerging clinical evidence supports the potential therapeutic benefits of BoNT in psoriasis. A growing number of studies have evaluated BoNT's efficacy and safety in treating psoriasis, with promising results, particularly in cases of treatment-resistant disease.[8,12] Clinical trials have reported significant reductions in psoriasis severity, demonstrated by improvements in Psoriasis Area Severity Index (PASI) scores, which assess disease severity and response to treatment. [13] For instance, studies found that BoNT administration led to a notable decrease in PASI scores and improved skin inflammation markers. Compared to conventional treatments such as topical corticosteroids and systemic biologics, BoNT has shown comparable efficacy in reducing symptoms of psoriasis, with some patients demonstrating better tolerability and reduced side effects.[13,14]

BoNT's potential as an adjunctive therapy has also been explored, particularly in patients who are refractory to other treatments. Studies noted that combining BoNT with traditional systemic therapies enhanced clinical outcomes, suggesting that BoNT may complement existing treatment regimens. This is particularly relevant for patients who experience side effects from biologics or who fail to achieve adequate control with conventional therapies.[8,15]

Clinical trials examining BoNT in psoriasis have reported generally favorable efficacy and safety profiles. A study by González et al.[11] highlighted that BoNT was well-tolerated, with few reported adverse events such as localized muscle weakness, pain, or injection-site reactions. These side effects are typically mild and transient, making BoNT a promising option for psoriasis patients who may seek safer alternatives, especially compared to systemic therapies with a higher risk of side effects.[11]

Patient compliance and satisfaction with BoNT treatment have been encouraging. In studies examining patient-reported outcomes, most patients expressed high satisfaction levels, attributing this to BoNT's minimally invasive nature and reduced side effects compared to systemic biologics.[8,11,16] The lower frequency of adverse events and better tolerability

contributed to improved patient adherence and overall satisfaction with BoNT as a treatment option.

Mechanistic Insights into BoNT's Role in Psoriasis

BoNT exerts its therapeutic effects in psoriasis primarily by targeting neuroimmune interactions, particularly through the modulation of neuropeptides and their role in inflammatory pathways. Neuropeptides such as substance P and calcitonin gene-related peptide (CGRP) play a crucial role in the neuroinflammatory responses seen in psoriasis, contributing to the production of pro-inflammatory cytokines such as IL-17 and TNF-α.[2,6] BoNT inhibits the release of these neuropeptides, effectively reducing neurogenic inflammation and activating immune cells that perpetuate psoriasis pathogenesis.[8,9]

Recent studies have shown that BoNT reduces the production of IL-17 and TNF-α by interfering with the cholinergic system, which modulates immune responses.[5, 10] By blocking the release of acetylcholine, BoNT decreases the activation of Th17 cells and macrophages, reducing inflammatory cytokines that drive psoriasis lesions. These mechanisms suggest that BoNT can play a role in disrupting the vicious cycle of neuroinflammation, which is a hallmark of psoriasis.[10,16]

The pathophysiology of psoriasis also involves disruptions in the skin barrier, with hyperproliferation of keratinocytes contributing to the thickened, inflamed plaques characteristic of the disease. BoNT has been suggested to influence keratinocyte proliferation and apoptosis, thereby potentially improving skin barrier function.[14,15] BoNT inhibits the release of acetylcholine, which can alter keratinocyte growth and differentiation, leading to reduced hyperproliferation and inflammation of the skin.[10,16]

Moreover, BoNT may promote skin repair by modulating inflammatory processes and promoting more balanced skin regeneration. This is supported by findings that BoNT can influence epidermal growth factor (EGF) and other signaling pathways involved in keratinocyte proliferation and repair.[8, 11] By reducing inflammation and promoting keratinocyte apoptosis, BoNT could enhance skin barrier function, potentially improving the overall management of psoriasis.

Challenges and Future Directions

The treatment of psoriasis with BoNT presents several challenges and areas for future research. One of the primary obstacles is the limited understanding of its long-term efficacy and safety. While initial clinical studies have demonstrated promising outcomes, extended follow-up is required to evaluate the durability of BoNT's therapeutic effects and to identify potential side effects such as muscle weakness, pain, or injection-site reactions.[5,6] Concerns regarding the long-term impact on neuroinflammatory processes targeted by BoNT also remain unexplored and warrant further investigation. Another significant challenge is the cost-effectiveness of BoNT compared to existing therapies for psoriasis, particularly biologics, which are considered the gold standard for moderate-to-severe cases. Although BoNT may offer an alternative with fewer systemic side effects, its economic feasibility requires a comprehensive evaluation, especially in resource-limited settings.[16] Additionally, the lack of standardized dosing and administration protocols for BoNT hinders consistent clinical outcomes. Variability in dosage, injection sites, and treatment frequency influences both efficacy and safety, complicating comparisons across studies and reducing reproducibility.[11]

Future research should address these challenges through large-scale, multicenter clinical trials to establish BoNT's therapeutic role in psoriasis. Such studies would generate robust data on efficacy, safety, and long-term outcomes across diverse populations and inform patient selection criteria and optimal dosing regimens.[6] Investigating the distinct neurophysiological effects of different BoNT subtypes, such as BoNT-A and BoNT-B, may further refine treatment strategies by identifying subtypes with superior neuroimmune-modulating capabilities.[5] Biomarker discovery is another critical avenue for advancing personalized medicine, as biomarkers associated with neuroinflammation, cytokine profiles, or neuropeptide activity could help predict patient responses to BoNT and optimize therapeutic outcomes.[4] Furthermore, BoNT's potential as a combination therapy with other anti-inflammatory agents, including biologics targeting specific cytokines like IL-17 or IL-23, offers an exciting possibility for enhancing efficacy by simultaneously targeting multiple inflammatory pathways. Addressing these challenges and exploring these research directions could significantly advance the role of BoNT in psoriasis management.[8,11,17]

Conclusion

Clinical evidence suggests that BoNT may offer a promising alternative or adjunctive therapy for psoriasis, particularly for patients who do not respond well to traditional treatments. While further research is needed, early clinical trials indicate significant reductions in psoriasis severity and favorable safety profiles. BoNT's neuroinflammatory-modulating effects appear to be a key mechanism. Further research is essential to fully understand its efficacy, safety, and optimal use, paving the way for broader adoption in clinical practice.

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Competing Interests

The author has no competing interests to declare.

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