

PODRAZA, Anna, SACHER, Karolina, MACIASZEK, Oliwia, TUREMKA, Mariola and CHMIEL, Marianna. Botulinum Toxin: An Innovative Approach to Treating Acne and Acne Scars: A systematic review. Journal of Education, Health and Sport. 2025;79:57875. eISSN 2391-8306.

<https://doi.org/10.12775/JEHS.2025.79.57875>

<https://apcz.umk.pl/JEHS/article/view/57875>

The journal has had 40 points in Minister of Science and Higher Education of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences).

Punkty Ministerialne 40 punktów. Załącznik do komunikatu Ministra Nauki i Szkolnictwa Wyższego z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu). © The Authors 2025;

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

Received: 16.01.2025. Revised: 02.03.2025. Accepted: 02.03.2025. Published: 06.03.2025.

Botulinum Toxin: An Innovative Approach to Treating Acne and Acne Scars – A systematic review

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Abstract

Introduction and Objective: Acne is one of the most common dermatological diseases. It mainly affects young people, but is more and more common in older people. There are reports on the effectiveness of treatment with botulinum toxin in acne vulgaris, acne rosacea and in the treatment of acne scars. The article takes into account research examining the effect of BTX as a method of treating acne. The results indicate that the use of BTX therapy as the method of treating acne may be effective. However, further research on its use in this therapy is necessary.

Methods: The article is a review on the effect of botulinum toxin on acne vulgaris, rosacea and on the treatment of scars. works from 1999-2024 were used to create the article. On their basis, conclusions were drawn.

Results: The results obtained based on the research review indicate a great potential for the use of botulinum toxin in the treatment of acne and acne scars. However, more research is needed

on a larger population of patients to clearly assess the effectiveness of botulinum toxin therapy and adjust the appropriate doses of the preparation.

Key words : Botulinum Toxin, Acne vulgaris, Hidradenitis suppurativa, Rosacea, Acne scars management

Introduction:

Acne vulgaris is one of the most common dermatological diseases that usually affects the young population, but in recent years the percentage of adults struggling with the disease has been increasing. Acne vulgaris is manifested by the appearance of blackheads, pimples, inflammation on the skin, often with purulent pus. Among the main factors mentioned are, among others, the influence of excessive sebaceous gland activity, which is related to hormonal disorders, especially excess production of androgens, which affect increased sebum production, and disorders in the process of keratinization of the sebaceous glands' exit ducts. Another factor confirmed to influence the onset of acne vulgaris is the proliferation of *Propionibacterium acnes* bacteria inside blackheads. Other factors influencing the occurrence of acne vulgaris are genetic factors, immunological disorders, excessive reactivity of hair follicles, psychological, physical and even iatrogenic factors. There are indications that BTX has a positive effect on reducing acne lesions and scars caused by acne.

Acne rosacea is a chronic skin condition that manifests itself by the appearance of erythema and telangiectasias, especially in the central part of the face and tissue hypertrophy, mainly in the nose. It occurs in people mainly between the ages of 30 and 50. The causes of rosacea are not fully understood. They include: abnormalities in the functioning of the immune system, genetic factors, ultraviolet radiation, microorganisms such as *Desmodex folliculorum* and *Helicobacter pylori* as well as the hyper-reactivity of blood vessels.. There are indications that botulinum toxin may be a good treatment for rosacea.

Acne inversa is, like other types of acne, a chronic inflammatory skin disease. It is characterized by the formation of painful nodules, usually located in areas where the skin rubs against itself. The resulting nodules may rupture and then heal with the formation of scars. It can happen that

the inflammatory nodules create a fistula and surgical intervention and antibiotic administration will be necessary. The disease usually affects people around the age of 40, and is influenced by a couple of factors, which we can include obesity, female gender, genetic conditions, mechanical irritation of the skin and most patients with acne inversa are smokers. There are reports of an effective treatment for Hidradenitis suppurativa using botulinum toxin.

The Effect of Botulinum Toxin on Different Types of Acne

1. Hidradenitis suppurativa

The study by Li in. a double-blind placebo-controlled study involved 20 healthy volunteers who were divided into groups with oily and dry skin. OnabotulinumtoxinA (MEDITOXIN) (2 U/cm²) was injected intradermally into one half of the face. Saline was used in the placebo. [1][4]

In the study by Shirshakov et al. 12 patients with acne vulgaris took part. 0.25 U/cm² of BTX-A of unspecified brand was injected intradermally. [2][4]. In contrast, a retrospective review by Shar AR. examined 20 consecutive patients with excessive sebum production who were injected once intradermally with onabotulinumtoxinA of unknown donor. All patients were requested to rate their satisfaction with the treatment. [4][7]

In the study by Calvisi et al. 40 women and 10 men participated. The first group consisted of 35 people and were those with mild to moderate acne, while the remaining 15 people struggling with erythematous-teleangiectasic rosacea made up the second group. The treatment included Onabotulinum A (Microbotox) in specific dilutions. Photographs were taken of the patients before treatment and after 4 weeks. Patients were also asked to rate aesthetics according to the sGAIS scale. [8]

Botulinum toxin solution was prepared using a vial containing 50 units of Botox (UB) Onabotulinum A toxin (Vistabex; Allergan Spa, Via Salvatore Quasimodo, 134-138, 00144 Rome) with 0.75 ml of saline and 0.5 ml of lidocaine (0.5%) without epinephrine for dilution, to a total volume of 1.25 ml. From this solution, 0.5 ml (20 UB) was taken and 0.5 ml of saline or lidocaine (0.5%) without epinephrine was added to make 1 cm³ for facial injection. Droplets of 0.2UB were injected in a regular grid with 1cm² spacing. [5]

Intramuscular injections of onabotulinumtoxinA were used to treat Hidradenitis suppurativa (HS). The two-year study included 13 patients. Intramuscular injections of 0.05ml of onabotulinumtoxinA diluted in 7 ml of saline per 100 units were administered. Multiple injections into the affected area of the cheek averaged 8 to 12 units. [6]

Hidradenitis suppurativa (HS) is a chronic inflammatory skin condition characterized by painful lesions, abscesses, and sinus tracts, which can significantly impact quality of life. [9] Traditional treatments are often not fully effective, leading to the need of exploration of alternative therapies. One of recently suggested is use of botulinum toxin (BTX). Evidence from case reports and small studies suggests that botulinum toxin, can reduce pain, shrink abscesses, and promote healing in draining sinuses associated with severe HS.

A systematic review of seven studies involving 31 patients found that 96.8% experienced either clinical improvement or enhanced quality of life after BTX treatment [9]. The Grimstad et al. randomized, placebo-controlled trial demonstrated that HS patients treated with BTX-B had significant improvements in the Dermatology Life Quality Index (DLQI), with scores decreasing from a median of 17 at baseline to 8 after 3 months. In contrast, the placebo group where the reduction was smaller - from 13.5 to 11 ($p < 0.05$) [9,10]. The Grimstad study also reported a substantial decrease in the total lesion count, with median lesions in the BTX-B group dropping from 9 to 4 at 3 months ($p < 0.01$). Pain scores, measured on the Visual Analogue Scale (VAS), decreased from a baseline median of 8 to 3.5, while the placebo group experienced no significant change.[9] Other studies also showed reductions in pain and discomfort, with notable improvements in nodules and abscess, especially for patients receiving multiple BTX treatments [9][10][11][12].

The benefits of BTX in HS treatment may be partly attributed to its anhidrotic effects, as hyperhidrosis often coexists with HS and promotes flare-ups by creating a moist environment conducive to bacterial growth. BTX effectively reduced sweating in affected areas, potentially disrupting the local microbiota and reducing inflammation. Additionally, BTX may have an anti-inflammatory effect by blocking acetylcholine release, which could help reduce neurogenic inflammation associated with HS. This dual mechanism—addressing both hyperhidrosis and inflammation—suggests that BTX may be particularly effective for HS patients with hyperhidrosis as a comorbidity.[9,10,11]

Botox was well-tolerated among HS patients, with no significant adverse effects reported in the reviewed studies. This favorable safety profile supports BTX as a viable option for HS patients who do not respond well to conventional therapies [9,10,11].

Botulinum toxin, shows significant potential as an adjunctive therapy for Hidradenitis Suppurativa, particularly for patients who do not respond to conventional treatments. Across reviewed studies, most patients reported considerable clinical and quality-of-life improvements. The dual mechanism of action—reducing sweat-induced bacterial growth and potentially

lowering inflammation—makes BTX a particularly valuable option for HS patients with hyperhidrosis as a comorbidity.

However, further research is essential to solidify the therapeutic role of BTX in HS. High-quality trials are needed to establish optimal dosing regimens, evaluate long-term safety, and explore the efficacy of BTX across different disease severities. Additionally, focused studies on the mechanisms by which BTX provides relief in HS may clarify its utility and help refine its application. The promising early results suggest that botulinum toxin could become an important treatment option for underserved HS populations, and larger studies could strengthen its therapeutic recommendations[9,10,11,12,13].

2. Acne Vulgaris

Acne vulgaris is a common disorder of sebaceous gland function, affecting up to 80–85% of adolescents and young adults [14,15]. Its impact goes beyond skin changes, imposing a significant psychological burden comparable to that of systemic disorders [15,16], affecting both men and women [14].

The pathogenesis of acne vulgaris is multifactorial. Key contributing factors include excessive sebum production by sebaceous glands, follicular colonization by *Cutibacterium acnes*, and impaired keratinization, which together promote the development of inflammatory lesions [25,16]. Given the significant cosmetic and psychological impact of acne, it is crucial to develop effective treatments that minimize systemic effects while enabling patients to enjoy healthy, clear skin. One promising method is the intradermal application of botulinum toxin type A (BTX-A).

In cosmetic and aesthetic medicine, BTX-A is best known for its ability to paralyze facial muscles, thereby preventing wrinkle formation [18]. This effect is achieved by blocking the release of acetylcholine (ACh) at the neuromuscular junction, causing temporary muscle denervation [19]. However, ACh also influences keratinocyte proliferation, sebum production, and inflammation, all of which contribute to acne development [20]. Research suggests that these mechanisms make BTX-A a viable option for treating acne vulgaris⁴ by inhibiting these acne-promoting processes.

Intradermal injections of botulinum toxin have been shown to reduce sebum production and pore size, likely due to BTX-A's anti-inflammatory and muscle-relaxing properties [18,19]. The contraction of the arrector pili muscle is necessary for sebum secretion; its paralysis inhibits this process [18].

In 2001, a technique for administering microdoses of BTX-A was developed. This method, known as Microbotox, improves facial skin quality, reduces excessive sebum production, minimizes pore size, and smooths fine wrinkles while preserving the function of the frontalis muscle [20]. It was determined that effective doses for reducing sebum production are lower than those used in standard aesthetic procedures, with doses as low as 10–20 U (Dysport) proving effective [21,22]. Optimal results are typically observed between the first and fourth week post-injection [18].

In 2021, Kesty and Goldberg conducted a study to assess the safety and efficacy of BTX-A injections for treating oily skin on the forehead. They found that administering 30–45 U (Dysport) significantly reduced skin oiliness, with effects lasting approximately six months and no significant adverse effects reported [18].

Thus, minimally invasive therapy with botulinum toxin may be an effective treatment option for acne vulgaris. The broad impact of BTX-A on skin health, including its well-known anti-wrinkle effects and the ability to reduce pore size, combined with its ability to limit sebum production, may result in comprehensive skin improvement and high patient satisfaction. However, as with most therapeutic approaches, the use of BTX-A in acne treatment has its limitations. These include its temporary effects and the need for repeat injections, which may be uncomfortable for some patients. Additionally, not all cases of acne vulgaris are driven by excessive sebum production; in such cases, treatment with botulinum toxin may prove ineffective.

3. Acne scars management

Integrating botulinum toxin A (BTX-A) in acne scar treatment, particularly using techniques like microtoxin therapy, has shown considerable promise. Studies suggest that microtoxin injections reduce sebum production, refine skin texture, and promote collagen remodeling, leading to smoother and more uniform skin [23,26].

A randomized split-face study showed that BTX-A delivered via microneedling significantly improved acne scars compared to a saline control. Over 70% of patients experienced substantial improvements in scar appearance, with enhanced patient satisfaction and minimal side effects [23]. Similarly, microtoxin injections were noted to improve pore size, fine lines, and skin elasticity, with noticeable benefits in younger patients and those with oily skin [26].

The mechanisms include modulating fibroblast activity, stimulating vascular endothelial growth factor, and reducing skin tension around scars. These factors collectively enhance collagen synthesis and reorganization, reducing scar depth and improving texture [24,25].

Using botulinum toxin A in acne scar management, particularly through intradermal microinjections and microneedling, offers a minimally invasive, safe, and effective treatment option. This approach not only refines skin appearance but also reduces the psychological impact of scarring. Further studies to standardize treatment protocols and long-term evaluations are warranted to optimize its clinical applications [25,26].

4. Rosacea

Rosacea is a chronic, inflammatory skin disease that is characterized by clinical symptoms such as erythema, telangiectasia, flushing episodes, papules, pustules, plaques and phymatous changes. It can also affect eyes. A characteristic feature is the presence of persistent erythema in the central part of the face, which worsens under the influence of aggravating factors [26,27]. There are four subtypes of rosacea: erythematotelangiectatic (ERT), papulopustular, phymatous, and ocular rosacea. Rosacea can occur at any age, but it most commonly appears between 30 and 50 years old. [28] The pathogenesis is complex. It can be triggered by: genetic factors, exposure to UV radiation, microbiological factors (Demodex), immune system dysfunction, and epidermal barrier dysfunction [4]. Vasodilation may result from the overproduction of VEGF and neuromediators involved in neurogenic inflammation. Many treatment options for rosacea have been proposed so far, but none are fully effective or free from side effects. Managing rosacea still remains a challenge, mainly in refractory/ recalcitrant cases [30]. Evidence from case reports and clinical trials shows that botulinum toxin type A may be an alternative method of treating rosacea. The mechanism of action of botulinum toxin involves inhibiting the release of acetylcholine into the synaptic cleft. It also modulates the secretion of other neuropeptides, such as substance P and VIP (vasoactive intestinal peptide), which are responsible for vasodilation and the appearance of erythema. Inhibiting these neuropeptides is important in the treatment of rosacea. Recent studies show that botulinum toxin also inhibits mast cell degranulation, thereby reducing the inflammatory component of rosacea [31].

In a clinical study conducted by Kim et al., the effectiveness and safety of botulinum toxin (BTX) were evaluated using the split-face method. BTX was injected on one side of the face, while saline was applied on the other side. On the side where BTX was administered, a significant reduction in CEA (Clinical Erythema Assessment) was observed, along with an increase in GAIS (Global Aesthetic Improvement Scale). Scientists also observed the improvement in skin elasticity and hydration after 4 weeks from BTX injection. What is more,

the intensity of erythema decreased. No significant differences were observed in transepidermal water loss or sebum secretion. The study demonstrated that transdermal BTX injections effectively and safely reduce erythema and rejuvenate the appearance of the skin in patients with rosacea [32].

In the similar study conducted by Bloom the scientists observed that after administering toxin(15-45U) to the nasal tip, nasal bridge and nasal alae, the facial erythema decreased from 1.80(+/- 0,56) to 1.00(+/-0,38) three months after treatment.

Rosacea and its symptoms can also strongly influence patients mental health. It is proved in the study by Eshghi et al. focused on assessing the quality of life of patients with rosacea who were treated with BTX. The participants completed the DLQI (Dermatology Life Quality Index) questionnaire. In all 24 female patients, the DLQI score improved, and after two months of observation, the average DLQI score improved from 8.08 +/- 1.17 to 4.5 +/- 1.21 [34].

There are some studies with a description of clinical cases. For example Silve et al. evaluated the impact of BTX on improving erythema and redness in 6 patients with erythematotelangiectatic rosacea. BTX was administered intradermally (0.2-0.5 U) at the affected areas. The study showed improvement in erythema and facial redness for 3 consecutive months, after which the symptoms worsened [35].

Similarly, in 2022 Yang et al. observed that the positive effects last for the first 3 months after injection, followed by a deterioration in results. The study concluded that botulinum toxin type A alleviates persistent erythema and redness in patients with the erythematotelangiectatic form of rosacea, but there is a need for repeating the injection[36].

Several studies have also shown the effectiveness of combining BTX with other treatment methods. In a clinical study conducted by Tong et al. in 2022, the effectiveness and safety of botulinum toxin combined with broadband light (BBL) were assessed. The study involved 20 patients, and the patient's face was randomly divided into two groups: an experimental group that received botulinum toxin and BBL, and a control group that received saline and BBL. The results showed that the experimental group, compared to the control group, experienced increased hydration, reduced redness, a lower erythema index, decreased transepidermal water loss, and less sebum secretion. After 6 months of observation, an increase in sebum secretion was noted, which correlated with the duration of botulinum toxin's effect. The study demonstrated that intradermal injection of botulinum toxin, combined with BBL, has a significant therapeutic effect in improving erythema and redness associated with rosacea, which is more effective than BBL alone and is highly safe. [37]

Al-Niimi et al. observed that combining pulsed-dye laser (PDL) with subsequent intradermal botulinum toxin injections reduced erythema, telangiectasia, and flushing more effectively than PDL alone. Patients reported high satisfaction with the treatment and minimal side effects. The study noted synergistic effects of both methods [38].

Research also suggests that botulinum toxin may be effective for patients who are resistant to previously applied treatment. In a pilot study conducted by Park et al., patients with treatment-resistant and persistent erythema (symptoms lasting for at least 3 months despite prior use of at least two standard therapeutic options) participated. Each patient received intradermal BTX injections on both cheeks at a total dose of 20 U. The erythema index decreased from the second week, with the greatest improvement observed at 4 weeks after BTX injection. A statistically significant reduction in telangiectasia was also noted [39].

In a study by Calvisi et al., the effect of BTX on the course of both acne vulgaris and rosacea was evaluated. They used microbotox (multiple tiny blebs of BTX injections). In the rosacea group, 15 patients with erythematotelangiectatic rosacea who had previously been treated with various methods without success were included. Patients received two microinjections of BTX two weeks apart. Two weeks after the last dose, a reduction in erythema and flushing was observed, along with improved patient satisfaction measured by DLQI (average increase in quality of life by >47.73). The results remained stable for 4 months after the procedure [40].

Numerous studies focus on case reports highlighting the benefits of using botulinum toxin in patients with recurrent erythema who are resistant to conventional treatments [16,17,18]. In their study, Luque et al. focus on the cases of three patients who, despite previous treatment with standard methods, did not achieve clinical improvement. In all cases, the administration of botulinum toxin (BTX) led to significant improvement. Patient 1 showed a 75% improvement in flushing and a 65% improvement in erythema, Patient 2 had a 70% improvement in both flushing and erythema, and Patient 3 experienced a 60% reduction in erythema [41].

In 2021 in the study by Vasconcellos et al., a review of a series of 10 rosacea patients was conducted, evaluating the impact of BTX on reducing persistent erythema and facial flushing. Patients received 10-15 U per hemisphere. A reduction in the intensity of erythema and redness was observed in 75% of patients [43].

There are discrepancies in the doses of botulinum toxin used across studies. In the study by Dayna et al., 8-12U was administered to each cheek, which led to clinical improvement in

rosacea. In the study by Eshghi, 15 U was injected into each cheek, and in Park's study, 10 U was injected into each cheek, both resulting in clinical improvement.

There are also studies evaluating the effectiveness of different methods of administering BTX. In Gaon's study, the aim was to evaluate which method of administering botulinum toxin is more effective and safer for Patients with rosacea. Subjects received 5U of Botulinum toxin through intradermal injection on the right side of the face and the same amount was administered by electroporation technique on the left side of the face. Both techniques turned to be safe and effective in reducing the erythema. Researchers have highlighted the potential use of electroporation as a method for administering botulinum toxin (BTX), because this is just as effective as intradermal injection but less traumatic for patients [44].

The studies conducted so far show the effectiveness of using botulinum toxin as an alternative treatment for patients with rosacea. However, it is important to note that the studies mentioned in the article involved small sample sizes. Further research on a larger group of patients is necessary to evaluate the effectiveness, safety, long-term use, and cost-effectiveness of BTX treatment. Additionally, such studies will help establish the optimal dosage and method of administering BTX, as well as the time interval at which the dose should be repeated.

Conclusion:

Based on the articles presented above, we can draw conclusions about the likely positive effects of botulinum toxin in the treatment of rosacea, acne vulgaris, acne scars and Hidradenitis suppurativa. Due to studies on small groups of subjects, these conclusions are not entirely reliable, but they are a rationale for claiming that therapy with BTX can be an effective method of combating acne and scars, and an alternative to classical treatment. However, there is a need to develop specific guidelines for the use of this therapy and to conduct new studies, especially randomized trials on a larger population of people struggling with these problems.

Disclosure:

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Receiving funding: Not applicable.

All authors have read and agreed with the published version of the manuscript.

Declaration of the use of generative AI and AI-assisted technologies in improving the language and readability. In preparing this work, the authors used <https://chatgpt.com> for the purpose of improving the language and readability in English language. After using this tool/service, the

authors have reviewed and edited the content as needed and accept full responsibility for the substantive content of the publication.

Funding Statement: No funding received.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Acknowledgments: Not applicable.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Conflicts of Interest: The author declares no conflict of interest.

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