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REVIEW ARTICLE

Botulinum toxin: a new ally in the fight against seborrheic dermatitis?

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ABSTRACT

The objective of this review was to provide information on the pathophysiology of seborrheic dermatitis (SD), the mechanism of action of botulinum toxin (BoNT), and the main findings regarding its benefits and limitations in the treatment of this condition. A literature review was conducted in the Scopus and Web of Science databases covering the period from 2019 to 2024, along with a bibliometric analysis of the related scientific output. A low level of scientific production was observed between 2019 and 2024, with an annual growth rate of 14.87%. Although the use of botulinum toxin type A (BoNT-A) has demonstrated benefits in the control of SD, several limitations regarding its applicability have been identified, including variations in skin type, genetic factors, and underlying health conditions. In addition, the limited number of specific studies on the subject, the methodological quality of available research, and the short duration of clinical trials may introduce bias and limit the assessment of long-term effects and risks associated with BoNT-A use. Current evidence suggests that BoNT represents a promising therapeutic option; however, a greater number of high-quality studies is required to confirm its efficacy and safety.

Toxina botulínica: ¿un nuevo aliado en la lucha contra la dermatitis seborreica?

Palabras clave:
toxinas botulínicas; dermatitis; fisiopatología; tratamiento farmacológico; terapéutica (fuente: DeCs-BIREME).

RESUMEN

El objetivo de la presente revisión fue proporcionar información sobre la fisiopatología de la dermatitis seborreica (DS), el mecanismo de acción de la toxina botulínica (BoNT) e información sobre los principales hallazgos relacionados con los beneficios y sus limitaciones de uso en el tratamiento de esta enfermedad. Se realizó una revisión bibliográfica en las bases de datos Scopus y Web of Science entre 2019 y 2024 y un análisis bibliométrico de la producción científica relacionada. Se observó una baja producción científica entre 2019 y 2024 con una tasa de crecimiento anual del 14,87 %. Si bien el uso de la toxina botulínica tipo A (BoNT-A) ha mostrado beneficios en el control de la DS, también existen algunas limitaciones sobre su aplicabilidad relacionadas con las diferencias en el tipo de piel, la genética y las condiciones de salud, además del sesgo en los análisis debido al limitado número de estudios específicos sobre el tema, la calidad de los estudios y la corta duración de los ensayos, lo cual limita la verificación de los efectos y riesgos a largo plazo del uso de BoNT-A. Los estudios muestran el uso de la BoNT como un tratamiento prometedor para enfermedades, sin embargo, se requiere realizar un mayor número de estudios de alta calidad para confirmar su eficacia y seguridad.

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INTRODUCTION

Seborrheic dermatitis (SD) is a chronic inflammatory disease characterized by immune dysregulation, inflammation, and impairment of the skin barrier [1]. These processes may be exacerbated by lipophilic metabolites produced by yeast of the genus *Malassezia*, a key component in the pathophysiology of the disease [2]. Its global prevalence is 4.38%, with a higher prevalence among adults (5.64%) than among children (3.70%) and newborns (0.23%) [3].

The clinical manifestations of SD differ clearly according to age group. In infants, it presents as yellowish, greasy patches with crusting ("cradle cap"), whereas in adolescents and adults symptoms include yellow, greasy scales over erythematous skin in seborrheic areas, such as the scalp, eyebrows, nasolabial folds, upper lip area, ears, retroauricular region, and upper chest, accompanied by skin inflammation and pruritus [2]. In adults, several environmental factors are likely to contribute to the development of SD, in addition to sebaceous gland activity and the influence of endocrine, neurogenic, and iatrogenic factors, as well as immunosuppression, which together appear to promote the proliferation of *Malassezia* spp. [4].

Several treatment options are available depending on the location and severity of the dermatitis; however, these treatments, ranging from shampoos to topical antifungal and anti-inflammatory agents such as corticosteroids, generally only reduce symptom severity or decrease the frequency of flare-ups [5]. Treatment modalities include keratolytic agents, topical corticosteroids, and antifungal therapies, as well as emerging approaches such as calcineurin inhibitors, metronidazole, and antimicrobial peptides, although some of these options remain controversial [6]. Topical shampoos, foams, and gels require frequent application, which may compromise hair moisture and integrity because of the presence of surfactants and high concentrations of alcohols [7].

Despite the availability of multiple treatments, therapeutic response is often incomplete and recurrences are frequent, prompting the search for innovative options. In this context, botulinum toxin (BoNT), a potent neurotoxin produced by the bacterium *Clostridium botulinum*, has shown benefits in several dermatologic conditions, including hyperseborrhea and SD, by reducing sebum production through inhibition of the neural signals that regulate it [8,9]. Previous studies have shown that BoNT injections can reduce sebum production and pore size by up to 80%, while also improving skin texture, with no significant adverse effects reported [10,11]. Despite its increasing use in dermatology, the available findings remain inconclusive. Therefore, this review analyzed the potential applications of BoNT in the management of SD based on published evidence.

METHODS

A literature review was conducted on the pathophysiology of SD, the mechanism of action of BoNT, and its use in the treatment of this condition.

In addition, a bibliometric analysis was performed using the Scopus and Web of Science databases to assess the current state of research on the use of BoNT in the treatment of SD.

The search strategy used the following terms and Boolean combinations: "seborrheic dermatitis" AND "botulinum toxin"; "seborrheic dermatitis" AND "botulinum toxin type A" AND "treatment"; "BoNT-A" AND "sebaceous glands" AND "dermatology"; "botulinum toxin" AND "sebum" AND "facial skin disorders"; and "botulinum toxin" AND "seborrhea". Scientific articles, systematic reviews, and clinical studies published in English, Spanish, or Portuguese between 2019 and 2024 and available as free full text were included. Articles without access to the full text and those that did not specifically address the use of BoNT for the treatment of SD were excluded. The search yielded 11 articles related to the topic (Figure 1).

For the quantitative and visual analysis, the bibliometrix R package, together with Biblioshiny, was used to export and organize data from Scopus.

RESULTS

Overall, a low level of scientific production on the use of BoNT for the treatment of SD was observed between 2019 and 2024. The years with the highest number of publications were 2021 and 2023, with three articles published in each year, followed by 2024 with two articles, representing an annual growth rate of 14.87% (Figure 2). Regarding the most relevant journals publishing on this topic, two main sources were identified: *Journal of Cosmetic Dermatology* and

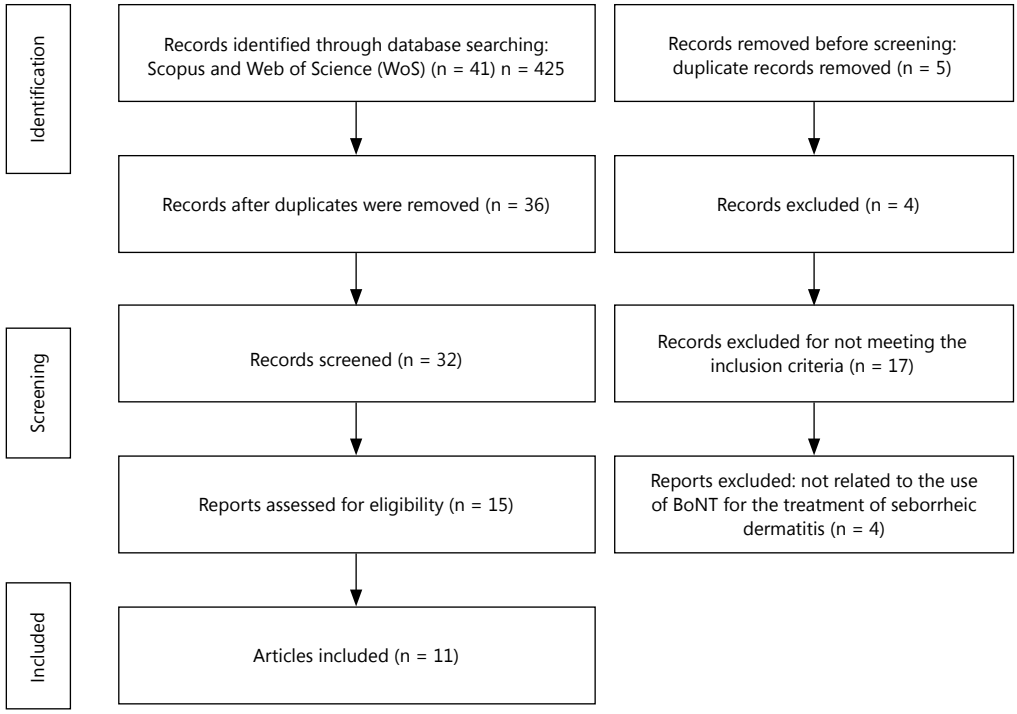


Figure 1. PRISMA-style flow diagram

Journal of Drugs in Dermatology, with 4 and 2 articles, respectively (Figure 3).

The most highly cited articles were mainly reviews and studies on the use of BoNT for the control of SD. The article entitled "Efficacy and possible mechanisms of botulinum toxin treatment of oily skin," published in *Journal of Cosmetic Dermatology* by Shuo et al. [12], has received 45 citations. This was followed by the article entitled "The efficacy of intradermal injections of botulinum toxin in the management of enlarged facial pores and seborrhea: a split face-controlled study," published by Sayed et al. [13] in *Journal of Dermatological Treatment*, which has received 22 citations. Finally, the review article "Botulinum neurotoxin type A in the treatment of facial seborrhea

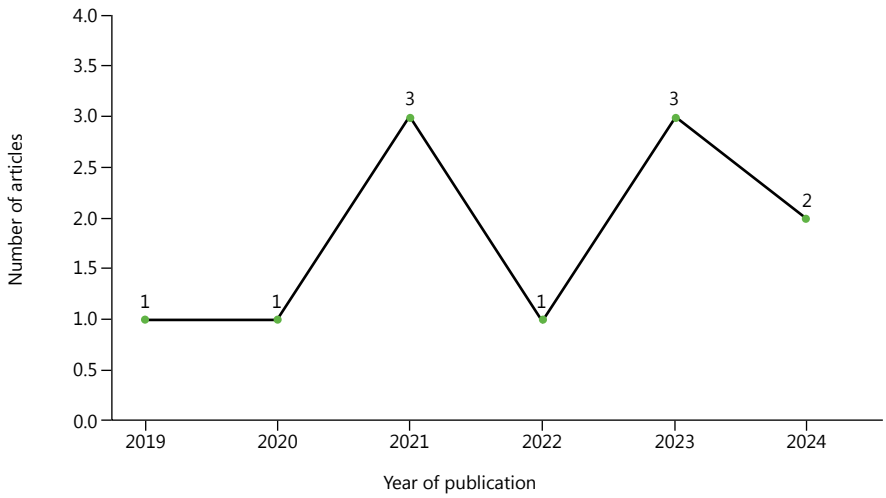


Figure 2. Annual scientific production related to the use of botulinum toxin for the management of seborrheic dermatitis.

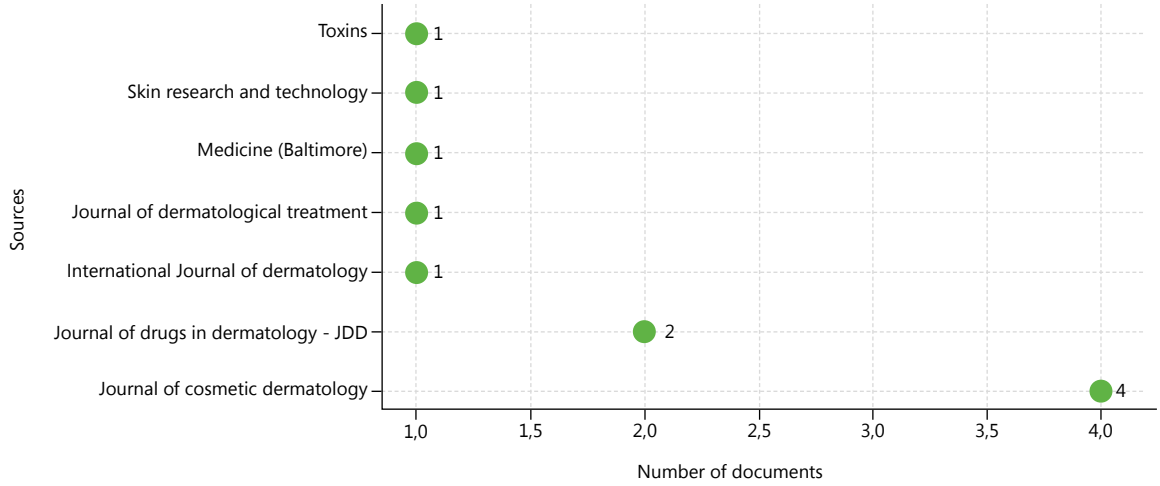


Figure 3. Leading journals publishing on topics related to the use of botulinum toxin for the management of seborrheic dermatitis.

and acne: Evidence and a proposed mechanism," by Rho et al. [14], published in *Toxins*, has received 19 citations since publication.

Of the total documents identified, six corresponded to clinical studies or research articles (Table 1), and five to review articles (Table 2).

Table 1. Clinical studies related to the use of botulinum toxin for the management of seborrheic dermatitis

Title	Authors/ Year	Journal	Study type	Method	Results
Evaluation of the effect of botulinum toxin injection in aggravating or improving seborrheic dermatitis symptoms: A prospective, single-arm clinical trial	Bazargan et al. (2023) [40]	*Skin Research and Technology*	Prospective clinical study	Injection of 150 units of BoNT in 20 patients with SD and facial wrinkles	No significant improvement in SD symptoms was observed after 1 month of follow-up ($p > 0.05$)
Microbotox injection versus its topical application following microneedling in the treatment of wide facial pores: A split face comparative study	Salem et al. (2023) [41]	*Journal of Cosmetic Dermatology*	Split-face study	Intradermal microbotox injection on one side of the face and topical application followed by microneedling on the other side	Significant improvement in pore and sebum scores on both sides, with better results on the side treated with intradermal injection. Higher satisfaction was reported with injection ($p < 0.001$)
Botulinum Toxin in the Oily Skin: Advantage of a Multi-Needle Device for a Controlled Release	Guarino et al. (2023) [43]	*Journal of Drugs in Dermatology*	Clinical study	Subdermal injection of onabotulinumtoxinA in 10 patients, evaluated at 15 days, 1 month, and 3 months	Significant improvement in skin quality, with reductions in sebum production and enlarged pores; the procedure was virtually painless and no serious adverse effects were reported
Microneedle delivery of botulinum toxin type A combined with hyaluronic acid for the synergetic management of multiple sternal keloids with oily skin: A retrospective clinical investigation	Zhang et al. (2022) [42]	*Journal of Cosmetic Dermatology*	Retrospective study	Combination of BoNT-A and hyaluronic acid administered by microneedling in 58 patients with keloids	Reduced sebum production and improved skin barrier function. No keloid recurrence was observed in the intervention group, with greater patient satisfaction ($p < 0.001$)
The effectiveness of botulinum toxin type A (BTX-A) in the treatment of facial skin oily seborrhea, enlarged pores, and symptom complex of post-acne.	Shirshakova et al. (2021) [10]	*International Journal of Dermatology*	Clinical study	Intradermal injection of 0.125–0.250 units of BoNT-A in 12 patients	Increased skin hydration (4%), decreased porosity (7%), and significant improvement in pores and pigmentation (10%) at 15 days
The efficacy of intradermal injections of botulinum toxin in the management of enlarged facial pores and seborrhea: a split face-controlled study	Sayed et al. (2021) [13]	Journal of Dermatological Treatment	Split-face clinical study	Intradermal injection of 100 units of botulinum toxin on one side of the face and saline on the other	Significant improvement in pore size and sebum production on the BoNT-A-treated side ($p < 0.001$). Persistent improvement was also observed at 4 months on the treated side

Table 2. Review articles related to the use of botulinum toxin for the management of seborrheic dermatitis

Title	Results
Dermatologic Procedures for the Treatment of Seborrheic Dermatitis [44]	A PubMed search was conducted on various dermatologic procedures related to SD in human patients. Most of the treatments evaluated showed significant efficacy in small cohorts with high patient satisfaction; however, the role of BoNT in SD is still being explored, as the available evidence does not support its use.
The role of botulinum neurotoxin BoNT-A in the management of oily skin and acne vulgaris: A comprehensive review [34]	This review provides promising perspectives on the use of BoNT-A for sebum regulation and reduction of inflammation and pore size, based on relevant studies and clinical trials in which significant reductions in sebum production and pore size were demonstrated after BoNT-A treatment, together with greater patient satisfaction.
Botulinum neurotoxin type a in the treatment of facial seborrhea and acne: Evidence and a proposed mechanism [14]	In clinical practice, BoNT-A is used to reduce facial skin oiliness. According to the authors, evidence suggests that acetylcholine (ACh) plays specific roles in sebum production, supporting its potential use to reduce sebum secretion by interfering with cholinergic transmission between sebaceous glands and autonomic nerve endings. Botulinum neurotoxins may also inhibit several pathogenic components involved in acne development, suggesting that they may represent a safe and effective treatment for acne and other skin disorders associated with sebaceous gland hyperactivity.
Oily sensitive skin: A review of management options [45]	A literature search was conducted using PubMed, considering publications related to the Baumann skin type indicator and oily sensitive skin. Oily sensitive skin is a combination of oily and sensitive skin that causes considerable discomfort and is often resistant to treatment. Sebaceous dysfunction and hypersensitivity may play key roles in the development of sensitive skin. Considering the pathogenesis of oily sensitive skin, treatment should target both seborrhea and hypersensitivity.
Efficacy and possible mechanisms of botulinum toxin treatment of oily skin [12]	A retrospective review of published data was performed. Most studies suggest that intradermal BoNT-A injection decreases sebum production and pore size, possibly through blockade of cholinergic signaling and neuromodulatory effects. This treatment achieved high patient satisfaction, with no significant adverse effects reported.

DISCUSSION

Pathophysiology of seborrheic dermatitis

a) Role of the sebaceous glands and excessive sebum production

Sebaceous glands are exocrine structures that develop alongside hair follicles in the mid-dermis and empty into the follicular canal. They are most densely distributed on the scalp, face, upper chest, and back [15,16]. These glands are composed mainly of sebocytes; their size and activity progressively increase with age, reaching a peak during adrenarche and puberty under the influence of sex hormones [17].

Nevertheless, it remains unclear whether changes in sebaceous gland density or activity influence the pathophysiology of SD or other dermatologic diseases such as rosacea, atopic dermatitis, psoriasis, or hidradenitis suppurativa. Likewise, the effectiveness of sebum-modifying therapies in inflammatory skin diseases remains an underexplored area of research [16].

b) Relationship between *Malassezia* spp. and seborrheic dermatitis

Multiple factors are associated with the development of SD; however, the disease appears to be related to the interaction among skin surface lipids, individual susceptibility, and the cutaneous microflora, particularly yeasts of the genus *Malassezia* [2,18].

Malassezia is a genus of commensal basidiomycetous fungi of the skin that, under certain conditions, may trigger inflammatory reactions [19,20]. The genus comprises 18 species and numerous strains that form part of the skin microbiome, where they contribute to skin homeostasis and function. However, some species may cause diseases such as SD, psoriasis, and Crohn's disease, among others, demonstrating their potential pathogenic role [21,22]. Of the 18 known species, seven have been associated with SD: *M. globosa, M. restricta, M. sympodialis, M. furfur, M. slooffiae, M. arunalokei*, and *M. yamatoensis*.

c) Predisposing factors for seborrheic dermatitis: genetic, hormonal, immunological, and environmental factors

Host-related factors such as genetic variation, environmental conditions, lifestyle, hygiene, and immune status may induce changes in skin microbial communities associated with SD [23]. In addition to sebaceous activity and *Malassezia* colonization, other factors may also contribute to individual susceptibility to the pathogenesis of SD, including epidermal barrier integrity, the host immune response, neurogenic factors, emotional stress, and nutritional habits [24].

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According to Jackson [25], the role of genetics in SD has been investigated in only a limited number of studies, in which 11 genetic mutations or protein deficiencies were identified as causes of the disease, with the affected genes predominantly involved in epidermal differentiation or immune function. These studies identified dominant and recessive hereditary forms of inherited seborrheic dermatitis (ISD) in autosomal recessive mice, characterized by enlarged sebaceous glands, hyperkeratosis, parakeratosis, acanthosis, and inflammatory infiltrates in the epidermis and dermis [24].

Although genetic predisposition has not been clearly established, recent studies have reported genetic mutations in certain human leukocyte antigen (HLA) subtypes that appear to impair the immune system's ability to restrict *Malassezia* growth, thereby increasing the risk of developing the disease [26].

Furthermore, alterations in the skin microbiota, particularly abnormal immune responses to *Malassezia* and *Demodex* species; the effects of certain medications, including dopamine antagonists, immunosuppressants, psoralen plus ultraviolet A, and lithium; hormonal factors; and increased levels of inflammatory cytokines, including interleukin (IL)-1α, IL-1β, IL-2, IL-4, IL-6, IL-8, IL-10, IL-12, IL-17, and tumor necrosis factor (TNF)-α, have been associated with SD [27].

In addition, this disease may be exacerbated by psychological stress and is commonly observed in individuals with psychotic disorders. It may also be associated with chronic diseases such as HIV infection and Parkinson's disease. In the latter, the occurrence of SD may possibly be related to increased sebum production and impaired immune responses to *Malassezia* spp.; however, there are no conclusive data regarding its etiology [27,28].

d) Botulinum toxin: definition, mechanism of action, and uses

Botulinum toxin (BoNT) is a neurotoxin produced by the bacterium *Clostridium botulinum*, which produces eight antigenically distinguishable exotoxins (A, B, C1, C2, D, E, F, and G). All of them interfere with neuronal transmission by blocking the release of acetylcholine (ACh), the main neurotransmitter at the neuromuscular junction [29].

Each BoNT serotype consists of a light chain with metalloprotease activity (50 kDa) and a heavy chain (100 kDa), linked by a disulfide bond. These are organized into three functional domains: the "binding" domain, in which the C-terminal end of the heavy chain binds to the receptor site; the "translocation" domain, located centrally, which facilitates toxin passage into the neuronal cytoplasm and contributes to protection of the active site; and the "catalytic" domain, represented by the light chain, which acts as a zinc-dependent endopeptidase that inhibits neurotransmitter release [30].

Neurotransmitter inhibition by botulinum neurotoxins begins with BoNT binding to specific receptors on motor neurons, followed by internalization through endocytosis and a conformational change. Subsequently, the toxin light chain is translocated into the neuronal cytosol, where it cleaves proteins involved in ACh release, preventing fusion of synaptic vesicles with the presynaptic membrane and thereby inhibiting ACh release and producing muscle paralysis [31].

Traditionally, botulinum toxin type A (BoNT-A) has been used to treat hyperactive muscle disorders and chronic pain [32]. Studies have shown that BoNT-A may undergo retrograde axonal transport to the central nervous system and to the axonal compartment of peripherally injected regions, leading to SNAP-25 cleavage with an antinociceptive effect, as well as transport toward the dorsal root ganglion, where it reduces the expression of IL-1β and TNF-α, two key cytokines in the inflammatory response, thereby producing anti-inflammatory effects [33]. However, these anti-inflammatory effects have not been clearly established.

This mechanism underlies the therapeutic effects of BoNT in conditions characterized by excessive muscle contraction, as well as its cosmetic applications for reducing wrinkles through paralysis of facial muscles.

e) Effects on sebaceous glands: inhibition of sebum secretion

Inhibition of ACh release into the synaptic cleft by BoNT-A, thereby preventing its binding to postsynaptic cholinergic receptors, produces decreased muscle tone at neuromuscular junctions and interferes with cholinergic sympathetic nervous system function in specific glandular tissues [34]. The ability of BoNT-A to disrupt cholinergic transmission has generated interest in investigating its potential clinical applications in autonomic disorders characterized by excessive glandular secretion, including hyperhidrosis and sialorrhea [12,14].

Clinical evidence suggests that the nervous system plays a fundamental role in regulating sebaceous gland activity, as findings obtained with BoNT-A for the treatment of excessive sebum production point to possible modulation of the neuroendocrine mechanisms that regulate sebaceous secretion [12].

f) Adverse effects of botulinum toxin, prevention, and management

BoNT has high specificity for neuronal cells; however, several factors may contribute to the occurrence of adverse effects, including product quality, characteristics of the diluent, insufficient professional expertise in terms of knowledge and technical skill, and variability in facial anatomy [35,36]. In addition, adverse reactions may be associated with each patient's immune response and may manifest through different clinical presentations, including edema, nodules, or indurated plaques, and different histopathological patterns, such as granulomatous reaction, sarcoidal granuloma, foreign-body granuloma, and eosinophilic panniculitis [37].

According to Di et al. [37], the most common adverse effects include hematomas and ecchymoses, headache and ophthalmologic disturbances, hypotonia and compensatory hypertonia of antagonist muscles, blepharoptosis and ectropion, urticaria, anaphylaxis, dyspnea, and soft-tissue edema, among others. Most of these reactions are mild, transient, reversible, and nonspecific and are related to the procedure and the short-term inflammatory response [38].

Other more severe effects include filler-induced skin necrosis resulting from inadvertent intravascular injection and the occurrence of bacterial, viral, or fungal infections [39].

The clinical studies reviewed showed divergent findings regarding the efficacy of BoNT injections for the treatment of SD. According to Bazargan et al. [40], BoNT-A is not recommended as a therapy for controlling SD symptoms because, although intramuscular injection produced a slight reduction, this improvement was not statistically significant. The authors suggested repeating the study with modifications to post-treatment follow-up intervals, standardization of the injection technique and toxin type, and a more detailed analysis of disease symptoms and their relationship with other conditions. In contrast, the remaining published studies reported positive effects of BoNT-A [10,13,41–43].

According to Guarino et al. [43], one of the recommended treatments for oily skin involves subdermal injection of onabotulinumtoxinA, a pharmaceutical formulation of BoNT-A, which requires numerous microinjections into the subdermis. This procedure is generally poorly tolerated by patients and may occasionally cause bruising. In their study, the authors proposed the use of a disposable device for BoNT injection at a depth of 1.5 mm, confirming its advantages because it allows homogeneous drug distribution at the appropriate tissue plane, without pain, while reducing the risk of common complications.

Additionally, Zhang et al. [42] demonstrated that microneedle delivery of BoNT-A/HA, a combination of BoNT-A and hyaluronic acid, reduced sebum production and improved skin barrier function. In contrast, Salem et al. [41] reported that microneedle application of microbotox requires several sessions and a greater amount of toxin to achieve the desired effects, thereby requiring more time and greater expense, whereas administration of microbotox through multiple intradermal injections can effectively and safely reduce enlarged pore size without requiring recovery time, thus increasing patient satisfaction because of its efficacy and duration after a single session. These findings are consistent with those of Sayed et al. [13], who concluded that intradermal BoNT injection is an effective and safe procedure for the management of excessive sebum production and enlarged facial pores, with acceptable results lasting an average of 4 months.

Similarly, review articles have not provided conclusive findings regarding the potential benefits of BoNT for controlling SD. Jaalouk et al. [44] stated that the role of BoNT in SD is still under investigation because the available evidence does not currently support its use; therefore, further research is required, particularly studies focusing on protocol standardization and comprehensive assessment of long-term outcomes.

Although the review by Dayel et al. [34] highlights the advantages of BoNT-A for the management of oily skin and acne, it also emphasizes several limitations affecting its applicability. These include individual differences in skin type, genetics, and health status, as well as limited population diversity, which together may restrict generalizability across different demographic groups. The authors also identified other factors that may limit the depth of analysis and

consequently introduce bias, including the limited number of studies specifically addressing the topic, possible publication bias favoring positive findings, variability in study quality, and the short duration of clinical trials, which limits the assessment of long-term effects and risks associated with prolonged BoNT-A use.

According to recent studies, intradermal BoNT injection has been proposed as a new strategy for treating excessive sebum production and enlarged pores, as some studies have shown that it may reduce sebum production by up to 80% after 1 month. Nevertheless, a sound understanding of the underlying pathogenesis is necessary for effective treatment; therefore, further research is required to reach consensus regarding the underlying pathophysiology and optimal treatment guidelines for oily sensitive skin [12,45].

g) Clinical perspectives on the use of botulinum toxin

BoNT has traditionally been used to reduce facial wrinkles, but more recently it has shown potential for the management of certain conditions in clinical dermatology, such as SD, because of its ability to modulate sebaceous gland activity and reduce neurogenic inflammation [46,47].

In severe SD, the action of BoNT on sebaceous glands could represent an alternative adjunct to conventional treatment, providing a potential option for patients in whom topical applications or oral or injectable medications have failed to produce significant improvement [14]. Nevertheless, further studies are required to evaluate and promote the development of personalized treatment strategies in which doses and injection sites are adapted to maximize efficacy and minimize adverse effects, particularly in conditions in which clinical characteristics vary considerably among patients.

In this context, BoNT represents a promising therapy that requires additional controlled studies to validate its efficacy and safety in patients [34].

Conclusions

Recent studies suggest that BoNT is a promising therapeutic option for certain dermatologic conditions, including SD, because of its ability to modulate sebaceous gland activity, reduce neurogenic inflammation, and alter neurotransmitter release. This opens a range of therapeutic possibilities for dermatologic conditions such as SD and may improve patients' quality of life, particularly among those in whom other therapeutic approaches have not produced satisfactory results. However, several factors limit its implementation, highlighting the need for high-quality clinical studies to confirm its efficacy and safety.

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