Botulinum Toxin A in the Management of Acne Vulgaris: Evidence and Recommendations

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Botulinum toxin type A (BTX-A) is widely used in aesthetic practice for its primary role in local muscle paralysis. There is also a growing body of evidence supporting the use of BTX-A in the treatment of acne vulgaris. The pathophysiology of acne vulgaris is multifactorial, with major contributors being increased sebum production, colonization of follicles with *Propionibacterium acnes*, and excessive keratin deposition.[1]

BTX-A has been shown to reduce the production of sebum in sebaceous glands,[2-7] with proposed mechanisms involving blocking acetylcholine release in sebocytes[2] and inducing flaccid paralysis in the arrector pili smooth muscle of follicular units.[8] Because arrector pili contraction is needed for sebum secretion,[9] its paralysis results in reduced sebum on the skin surface. There is no evidence to suggest an antibacterial role of BTX-A,[10] making it likely that this reduction in sebum is the primary mechanism behind BTX-A's ability to reduce acne vulgaris. Table 1 summarizes the literature supporting this BTX-A effect.

Current treatment for acne vulgaris includes topical treatment with retinoids, antibiotic creams, and azelaic acid, and systemic treatment with oral antibiotics, combined oral contraceptive pills in women, and oral isotretinoin in severe disease.[11] All of these treatments come with their own side-effect profile, in particular isotretinoin with its propensity to derange liver function and cause teratogenicity.[12] Nonpharmacological therapies such as laser treatments are in use and can be efficacious, although their effects are often short lived and require regular follow-up treatments.[11]

Li et al's placebo-controlled, double-blinded study found a statistically significant reduction in sebum produced in patients with oily skin when treated with BTX-A.[2] The effects were most evident 4 weeks posttreatment. Kesty and Goldberg's study, which was also placebo-controlled and double-blinded, found the same statistically significant reduction in sebum production ($P < 0.05$).[5] Rose and Goldberg's study lacked blinding and a control group, but they also found a statistically significant ($P < 0.001$) reduction in sebum production with BTX-A (an 80% reduction from baseline sebum measurements at 1 month, comparable to isotretinoin,[13] $P < 0.01$).[4] BTX-A treatment was also found to significantly reduce sebum production compared with pretreatment sebum measurements in studies by Shirshakova et al[6] ($P \leq 0.01$) and Min et al.[7]

The studies used either onabotulinumtoxinA (Botox; Allergan, Inc., Irvine, CA) or abobotulinumtoxinA (Dysport; Ipsen Ltd, Slough, UK). It is estimated that the dose conversion ratio of Botox to Dysport is between 1:2 and 1:4,[14] and given this wide range, the precise doses used in different studies are not exactly comparable. Due to varying study design regarding the pattern of injection of the BTX-A, the dose administered per cm^2 was difficult to elucidate; Li et al[2] used 2 U/cm^2 of Botox and Shirshakova et al[6] used

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Table 1. Literature Review of BTX-A in the Reduction of Sebum Production

Study	Journal	Author	Year	Methodology	Results
Regulation of lipid production by acetylcholine signalling in human sebaceous glands[2]	*J Dermatol Sci*	Li et al	2013	20 healthy volunteers, placebo-controlled, double-blinded study. Volunteers classified into oily skin and dry skin groups. One side of face injected intradermally with onabotulinumtoxinA (MEDITOXIN) (2 U/cm^2), other side placebo (normal saline). Facial sebum secretion measured with sebumeter	Statistically significant reduction in sebum secretion in oily skin group. No change in dry skin group. Effect most prevalent 4 weeks posttreatment. No significant side effects
Use of intradermal botulinum toxin to reduce sebum production and facial pore size[3]	*J Drugs Dermatol*	Shah	2008	Retrospective chart review of 20 patients who received onabotulinumtoxinA (Botox) (dose not stated) for excessive sebum production or large pores. Subjective opinion on patients measured at 1-month follow-up.	17/20 patients noted reduction of sebum production and 17/20 patients noted reduction in pore size. No significant side effects
Safety and efficacy of intradermal injection of botulinum toxin for the treatment of oily skin[4]	*Dermatol Surg*	Rose and Goldberg	2013	25 patients with oily skin injected with abobotulinumtoxinA (Dysport) (3-5 U per point, 10 points total, horizontally across forehead) intradermally. Measurements taken at follow-up with sebumeter and subjective patient opinion also recorded	Statistically significant reduction in sebum at follow-up. Effect greatest at 1 week but still statistically significant reduction at 3 months. No significant side effects
A randomized, double-blinded study evaluating the safety and efficacy of abobotulinumtoxinA injections for oily skin of the forehead: a dose-response analysis[5]	*Dermatol Surg*	Kesty and Goldberg	2021	50 healthy volunteers, double-blind, randomized control trial. Various doses (0, 15, 30, or 45 U) of abobotulinumtoxinA (Dysport) injected into forehead. Sebumeter and subjective patient and investigator scores used	Patients given 30 or 45 U reported significant reduction in oily skin. The effect was present for 6 months. No significant side effects
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[6]	*Int J Dermatol*	Shirshakova et al	2021	12 patients with acne. Injected intradermally across face with 6-8 U BTX-A (brand unspecified) per injection area (0.25 U/cm^2). Sebum secretion measured with sebumeter	Statistically significant reduction in skin oiliness. Greatest effects seen 2 weeks posttreatment. No significant side effects
Sebum production alteration after botulinum toxin type A injections for the treatment of forehead rhytides: a prospective randomized double-blind dose-comparative clinical investigation[7]	*Aesthet Surg J*	Min et al	2015	42 female volunteers with facial rhytides. Double-blind, randomized control trial. 2 or 4 U of onabotulinumtoxinA (Botox) per site (5 sites total, horizontally across forehead), injected intramuscularly. Control group injected with saline Sebum secretion measured with sebumeter. Followed-up at 2, 4, 8, and 16 weeks	Statistically significant reduction in amount of sebum secreted. Efficacy not improved at higher dose (no statistically significant difference between 2- and 4-U regimes). Sebum production reduction greatest around 2-4 weeks after treatment, levels returned to normal at 16 weeks Reduction in sebum greater in <40-year-old subgroup. One adverse event (relapse of photosensitive dermatitis) but not related to treatment

BTX-A, botulinum toxin type A.

0.25 U/cm^2 of an unspecified BTX-A product, with the remaining studies not detailing the dose in their methods.

The aesthetic starting doses for treatment of glabellar lines is 20 units of Botox or 50 units of Dysport.[15] Li et al[2] used 8 units of MEDITOXIN (Medytox, Seoul, South Korea), a Botox biosimilar, and Min et al[7] used 10 to 20 units of Botox. Rose and Goldberg[4] used 30 to 50 units of Dysport, and Kesty and Goldberg[5] used 30 to 45 units of Dysport. All of these doses were effective in reducing sebum secretion. From this we can infer that a slightly lower dose may be used in the treatment of acne than would be normal practice for aesthetic treatments. Moreover, both intradermal and intramuscular routes were used in the studies; Min et al suggested that the intradermal route may be more effective.[7]

The greatest effect of the treatment appears to be between 1 and 4 weeks postinjection. The length of the effects varied in the studies; Min et al[7] (10-20 units of Botox) found that levels of sebum production returned to normal after 16 weeks, whereas Kesty and Goldberg[5] (30-45 units of Dysport) found that the effects were still present at 6-month follow-up: the duration of these effects, therefore, may be dependent on dose and brand. Participants in the studies reported minimal side effects (2 reports of

frontalis muscle reduced tone at 2-month follow-up, and 1 relapse of photosensitive dermatitis that was unrelated to the treatment)—consistent with BTX-A's high safety profile when taken at therapeutic doses.[16]

The limitations of administering BTX-A to treat acne vulgaris include its temporary nature and need for repeat treatments, and although minimally invasive, injections can be painful, and the use of needles may be unacceptable to some patients. Furthermore, although increased sebum production is implicated in the pathophysiology of acne vulgaris, not all cases are caused primarily by this, and therefore treatment with BTX-A may be ineffective in these patients.

There is sufficient evidence to indicate the need for further studies evaluating the effects of BTX-A on patients with acne vulgaris. These studies should be double-blinded randomized control trials, and use several doses of BTX-A, in order to elucidate therapeutic benefit, minimal viable dosing, and dose-response relations. If the treatment is found to be efficacious, it would be a safe and local management option to consider, particularly in those hoping to avoid treatment with the high-side-effect alternatives that currently form the foundation of acne management.

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