Intradermal Botulinum Toxin A Injection for Scalp Sebum Secretion Regulation: A Multicenter, Randomized, Double-Blinded, Placebo-Controlled, Prospective Study in Chinese Subjects

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Abstract

Background: Although botulinum toxin type A (BTX-A) injection has been proved to reduce topical sebum secretion, the impact of intradermal BTX-A injection on scalp sebum production has never been reported.

Objectives: The purpose of this study was to investigate the efficacy and safety of intradermal BTX-A treatment vs intradermal normal saline (NS) injection for scalp sebum secretion regulation.

Methods: This multicenter, randomized, double-blinded, prospective study recruited patients complaining of oily scalp and/or hair. The patients were randomly allocated to receive either 1 session of intradermal BTX-A or NS injection. The baseline and posttreatment scalp sebum secretion at 24, 48, 72, and 96 hours postshampooing was measured with a Sebumeter SM815 (Cutometer Dual MPA 580, Courage & Khazaka, Cologne, Germany) at 1, 3, 4, and 6 months after treatment. The patients' comments, satisfaction, and adverse events were evaluated and compared.

Results: In total, 25 patients in the BTX-A group and 24 patients in the NS group completed the follow-up. For the treated region, compared with NS, intradermal BTX-A treatment (50-65 U) significantly reduced scalp sebum secretion at 24, 48, and 72 hours postshampooing at the 1- and 3-month follow-up visits ($P < 0.05$). No significant difference between the 2 groups was observed at 4 and 6 months after the treatment. The patients' satisfaction ratings were significantly higher for the BTX-A treatment ($P = 0.000$). No serious adverse events occurred.

Conclusions: Compared with NS, 1 session of intradermal BTX-A injection (50-65 U) effectively and safely reduced scalp sebum secretion and greasiness perception in the treated region at 24 and 48 hours postshampooing for 3 months.

Level of Evidence: 4

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Botulinum toxin type A (BTX-A) has been utilized for more than 2 decades for various neurologic conditions and aesthetic treatments. Recently, insights into the effect of BTX-A on sebum production have been published. Intramuscular BTX-A treatment for forehead rhytides exhibited significant sebum alteration at the injection site, with a sebum gradient surrounding the injection point. Sebum production recovered to normal levels at the 16-week follow-up.[1] Studies have suggested that intradermal BTX-A injection may represent a promising new treatment for oily skin and other related dermatologic problems, including enlarged pores, acne, and seborrheic dermatitis.[2] Greasy scalp and hair, like oily facial skin, have a negative influence on personal image and social activities.

Shah et al described intradermal injection of onabotulinumtoxin type A to the T-zone for the treatment of oily skin and enlarged facial pores. In their retrospective study, 17 of 20 patients reported improvement in oiliness at 1 month after only 1 treatment.[3] Rose et al treated patients with oily skin in the forehead region with intradermal injections of botulinum toxin. Significantly lower sebum production was noticed at 1 week and 1, 2, and 3 months after injection. Ninety-one percent of patients reported that they were satisfied with intradermal botulinum toxin as a treatment for oily skin. Subjective differences in pore size could also be seen photographically, and were associated with the activity of the arrector pili muscle and the activation of local muscarinic receptors in the pilosebaceous unit by acetylcholine.[4] Similarly, intradermal microdroplet injection of diluted BTX-A has been proved to decrease sweat and sebaceous gland activity, improve skin texture and sheen, and improve facial skin laxity and facial pores.[5,6]

Several studies on BTX-A treatment for androgenic alopecia (AGA) have demonstrated alteration of scalp sebum secretion. Zhang et al reported treating AGA by intramuscularly injecting 50 U BTX-A into the muscles surrounding the scalp, including the frontalis, temporalis, periauricular, and occipitalis muscles, in equally divided doses at a minimum of 30 injection sites. They reported that 19 out of 25 patients showed a significant decrease in grease secretion at 3 months and the grease content was close to the healthy level. After 6 months of treatment, grease secretion gradually restored to the baseline state.[7] Zhou et al treated AGA patients by injecting 100 U BTX-A intramuscularly at 30 sites located in the frontal muscle, temporal muscle, periauricular muscle, and occipital muscle. The patients received BTX-A treatment every 3 months for a total of 4 times. After treatment, 16 out of 30 patients reported they exhibited moderate and marked improvement in fewer symptoms of scalp oil secretion, pruritus, and dandruff.[8] The studies above classified a reduction in sebum production as an additional benefit of BTX-A treatment for AGA.

The impact of intradermal BTX-A injection on scalp sebum production has not previously been reported. In the current study, we aimed to investigate the efficacy and safety of intradermal BTX-A treatment for scalp sebum secretion regulation postshampooing, in comparison with intradermal normal saline (NS) injection.

METHODS

Patients

From October 2020 to November 2021, this multicenter, randomized, double-blinded, prospective study recruited Chinese patients (Fitzpatrick skin types II-IV) aged 25 to 45 years who complained of oily scalp and/or hair. The baseline calvarium scalp sebum levels of the patients, according to the measurement at 24 hours postshampooing, exceeded 100 μg/cm^2. The exclusion criteria included the presence of scalp infection or skin abnormality, seborrheic dermatitis, AGA, trichotillomania, scarring alopecia, and alopecia areata. Patients with symptoms or history of autoimmune disease, neuromuscular disease, cancer, bleeding tendency, coagulation disorder, diabetes, hypertension, hepatitis, immunocompromise, severe systemic disease, and hypersensitivity to botulinum toxin or any of its components were excluded. Patients who were prone to scarring, were pregnant or lactating, or had received laser, chemical peeling, soft tissue filling, mesotherapy, BTX-A injection, or other surgeries on the head within 3 months of screening were excluded. Patients who had had their hair permed and/or dyed within 1 month of screening were also excluded. The exclusion criteria also included history of systemic corticosteroids, antifungals, isotretinoin, or oral contraceptive use in the last 3 months. Patients who had used topical corticosteroids or antifungal shampoos or solutions within the past 4 weeks were excluded as well.

The study was approved by the Sichuan Shesays Aesthetic Plastic Surgery Hospital Institutional Ethical Committee (No. 2020-07-02) and was conducted in compliance with the 1975 Declaration of Helsinki. All patients provided written informed consent prior to enrollment.

Treatment

The patients were randomly allocated to either the intradermal BTX-A injection group or the NS injection group. The randomization was achieved by means of a random number table.[9–11] Briefly, a number was selected randomly in the random number table, and the following 49 numbers were then selected sequentially. Each selected number represented 1 enrolled patient. A patient was randomly allocated to the BTX-A treatment if the number was odd, or to the NS treatment if the number was even. Both the patients and the physicians were blinded to treatment.

BTX-A Treatment

A 100-U vial of onabotulinum toxin type A (Hengli, Lanzhou Institute of Biology, Lanzhou, China; Botox, Allergan,

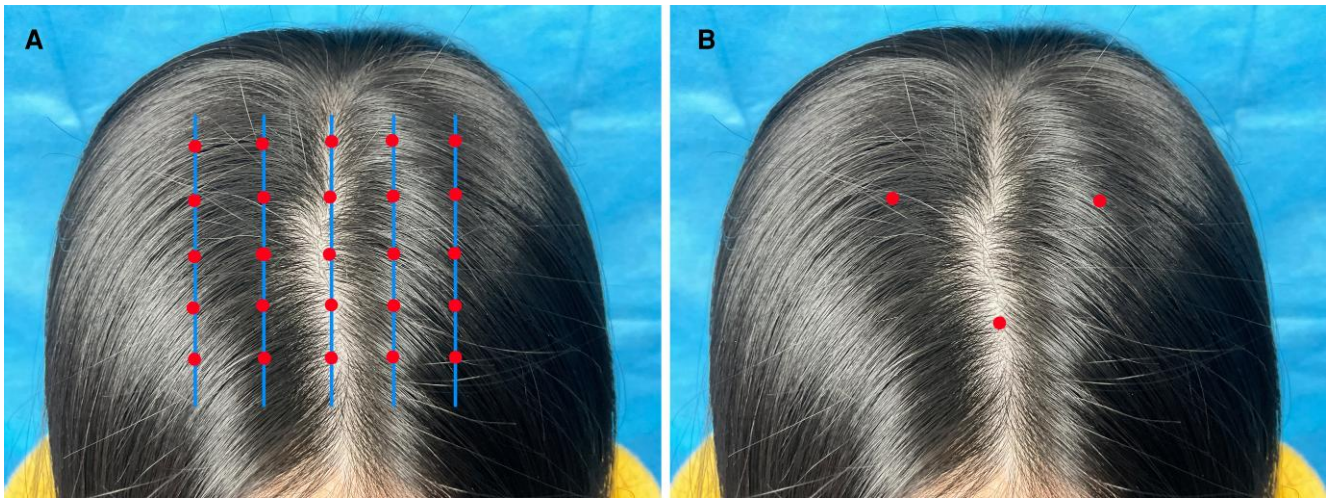

Figure 1. (A) The injection sites, marked with red dots, and (B) scalp sebum measurement sites within the treated region, marked with red dots, shown on a 28-year-old female patient.

Westport, Ireland) was diluted with 2.5 mL NS to prepare a 4-U/0.1-mL solution. A central hair parting was made with a cotton tipped applicator, using the nose as an anatomic landmark. The first injection line was then determined as the central hair parting line, and another 2 lines were allocated on both sides of this central one with each line 2 cm apart. Five injection sites were allocated for each line, giving 25 sites in total for the treatment. The first injection site was 1 to 1.5 cm posterior to the hairline, followed by the other 4 injection sites with each site approximately 2 cm apart (Figure 1A). The patient was placed in the horizontal position, and the scalp was cleansed 3 times with povidone-iodine solution 5% and an alcohol swab. After the hair was separated and fixed with hair clips, injections were performed intradermally with a 34G needle (Kangcheng, Changcheng Medical Devices Ltd., Yangzhou, China) with the bevel up. For each site, 2 to 3 U BTX-A was delivered, and the total dosage was 50 to 65 U. It was not possible to guarantee delivery of an identical toxin dose to each point; the dose may vary slightly within the intended range: it could be 2 U, 3 U, or a value between 2 and 3 U (for instance, 2.5, 2.6, or 2.8 U). The minimal dosage of 50 U and the maximal dosage of 65 U were determined based upon literature review and the physicians' experience, given this was an explorative study and the dosage tended to be conservative. Gauze was then pressed on the injection sites with moderate pressure for 10 seconds to prevent hemorrhage (Video 1).

NS Treatment

The injection sites and methods were the same as for the BTX-A group. For each site, 0.05 to 0.075 mL NS was injected intradermally, and the total volume was 1.25 to 1.875 mL. Patients in both groups were instructed to avoid shampooing or applying haircare products for 24 hours.

Follow-up and Evaluation

Follow-up

Standardized digital photographs of the scalp and hair in the treated region were taken at baseline and at 1, 3, 4, and 6 months after the treatment. Touch-ups were not allowed during the follow-up. The patients were instructed to keep their hairstyle and haircare routine, including shampooing frequency (3-4 times per week), consistent and to avoid perming and/or dyeing the hair during the follow-up. Haircare products described as "deep cleans," "clarifying," "antidandruff," or "for oily hair" were prohibited. In addition, the patients were asked not to use haircare products containing salicylic acid, tea tree oil, ketoconazole, piroctone olamine, or 1% zinc pyrithione. The patients were not allowed to receive any topical or systemic antiseborrhea management during the follow-up.

Scalp Sebum Measurement

The baseline and posttreatment scalp sebum secretion at 24, 48, 72, and 96 hours postshampooing was measured with a Sebumeter SM815 (Cutometer Dual MPA 580, Courage & Khazaka, Cologne, Germany).[12–15] Prior to the measurements, the patients were instructed to acclimate for 20 minutes to the environment with controlled temperature (20-22°C) and relative humidity (45%-55%). The sebum levels were measured between 10:00 and 11:00 am to avoid diurnal variation.[16] All procedures were performed by the same assessor. For each patient, 5 sites on the scalp were selected for the sebum secretion measurement. Three sites were within the treated region, located on the 3 vertexes of an equilateral triangle with an approximate side length of 6.5 to 7.5 cm (Figure 1B). The other 2 sites were outside of the treated region and located on the lateral scalp 3.5 to 4.5 cm superior to the auricles of both sides.

Video 1. Watch now at http://academic.oup.com/asj/article-lookup/doi/10.1093/asj/sjac236

The hair was parted and fixed with hair clips before the measurement. A fresh tape section was applied to calibrate the Sebumeter SM815 to 0 before each measurement. Under a constant pressure of 10 N, sebum was taken from the sites on a plastic strip for 30 seconds. The average values of the first 3 sites and the other 2 sites were regarded as the sebum secretion for the treated and the untreated region, respectively.

Patient-Evaluated Outcomes

Patients' satisfaction with the treatment outcomes was evaluated on a 7-point scale questionnaire (−3, very dissatisfied; −2, dissatisfied; −1, slightly dissatisfied; 0, neutral; 1, slightly satisfied; 2, satisfied; 3, very satisfied) on the final follow-up visit. In addition, the patients were allowed to state any comments and/or concerns they might have during the study. Patients were also given the opportunity to report any possible adverse events (AEs) that occurred during the study.

Complications/AEs

Immediately after the treatment, the patients indicated their degree of pain on a visual analog scale (VAS) from 0 (no pain at all) to 10 (unbearable pain). Complications and AEs were recorded throughout the study.

Statistical Analysis

All quantitative data were expressed as mean [standard deviation]. All categoric data were presented as frequencies or percentages. Analysis was conducted with SPSS 23 (SPSS, Inc., Chicago, IL). An independent *t*-test or analysis of variance was used to compare continuous variables. A chi-square test or Fisher's exact test was used to compare the ratios. A value of $P < 0.05$ was considered statistically significant.

Table 1. Patients' Baseline Demographics

Characteristics	BTX-A treatment group (n = 25)	NS treatment group (n = 24)	*P* value
Gender, n (%)			
Female	24 (96)	24 (100)	1.000
Male	1 (4)	—	—
Age (years)	35.2 [3.6]	34.9 [3.5]	0.752
Fitzpatrick skin phototype, n (%)			
III	16 (64)	13 (56)	—
IV	9 (36)	11 (44)	—
Baseline scalp sebum (μg/cm^2), 24 hours postshampooing			
Treated region	144.8 ± 12.9	139.2 ± 14.8	0.167
Untreated region	84.0 ± 11	81.7 ± 5.9	0.38

Values are n (%) or mean [standard deviation]. BTX-A, botulinum toxin type A; NS, normal saline.

RESULTS

Baseline Demographics

In total, 50 Chinese patients (49 female and 1 male), aged 26 to 43 years (mean, 35.1 [3.5] years), were enrolled in the study. The follow-up time ranged from 6 to 7.5 months (mean, 6.4 [0.4] months). Forty-nine patients completed all follow-up visits; 1 patient in the NS treatment group dropped out due to insufficient efficacy. The mean age of the BTX-A treatment group was 35.2 [3.6] years (range, 27-43 years). The mean age of the NS treatment group was 34.9 [3.5] years (range, 26-42 years). The patients' baseline characteristics are listed in Table 1.

Clinical Outcomes

Scalp Sebum Production

For the treated region, compared with NS, intradermal BTX-A treatment significantly reduced the scalp sebum secretion at 24, 48, and 72 hours postshampooing at the 1- and 3-month follow-up ($P < 0.05$). The sebum secretion was lower at 96 hours postshampooing for the BTX-A group although this was not statistically significant. No significant difference between the 2 groups was noticed at the 4- and 6-month follow-up.

For the untreated region, according to the Sebumeter measurements, the scalp sebum was higher for the BTX-A treatment group at 96 and 72 hours

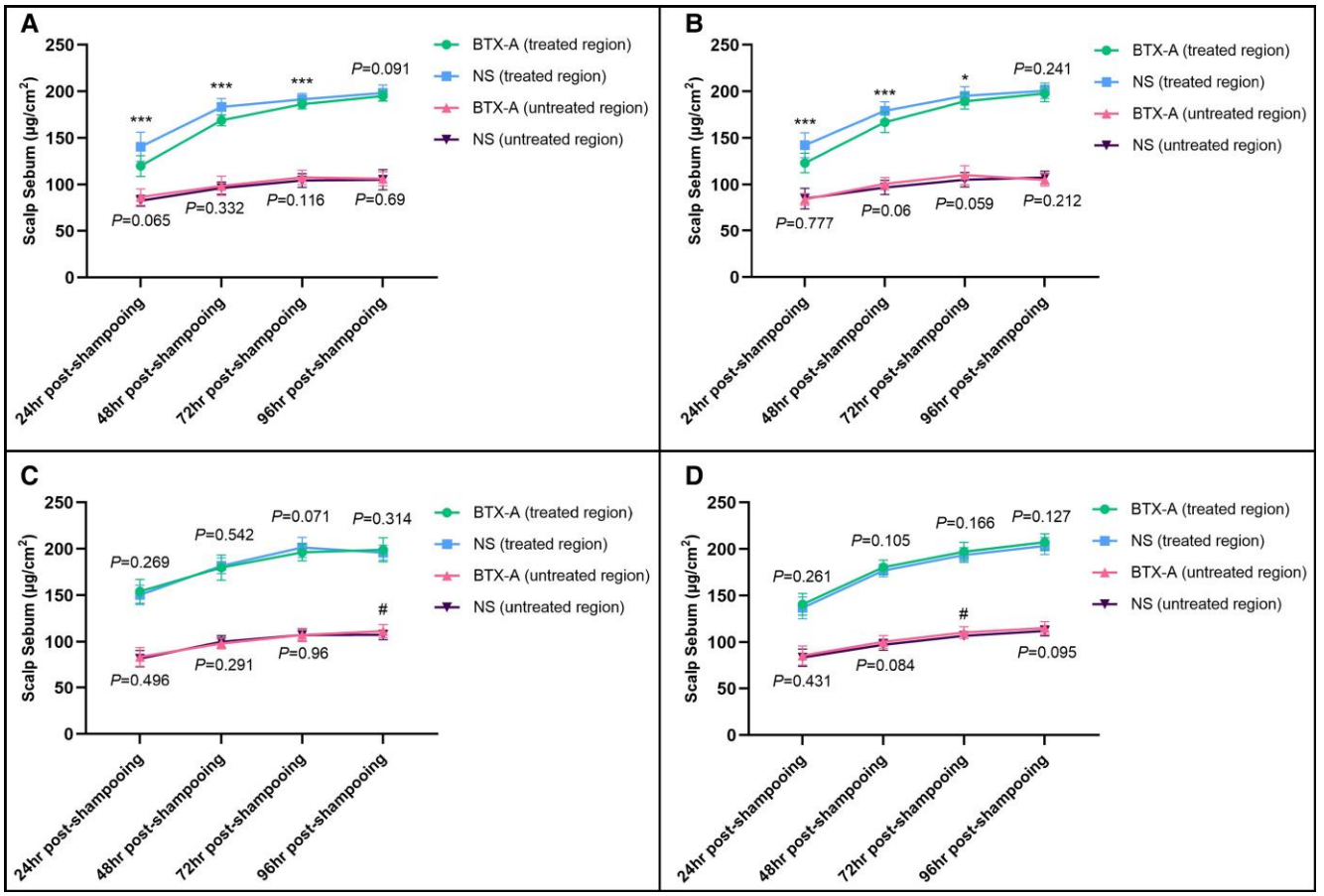

Figure 2. Scalp sebum secretion at 24, 48, 72, and 96 hours postshampooing at (A) 1-month follow-up, (B) 3-month follow-up, (C) 4-month follow-up, and (D) 6-month follow-up. BTX-A vs NS, treated region: $^{*}P < 0.05$; $^{***}P < 0.001$. BTX-A vs NS, untreated region: $^{\#}P < 0.05$. BTX-A, botulinum toxin type A; NS, normal saline.

postshampooing at the 4- and 6-month follow-up ($P < 0.05$), respectively. No significant difference between the 2 groups was noticed on the other follow-up visits. Additionally, the sebum production of the untreated region was significantly lower than that of the treated region at the 4 postshampooing time points at all follow-up visits (Figures 2-4).

Patients' Satisfaction Ratings and Comments

The patients' mean satisfaction ratings were 2 [0.5] and 0.6 [0.8] for the BTX-A treatment and NS treatment, respectively ($P = 0.000$) (Figure 5A). Notably, according to the patients' comments, 14 (56%) patients reported "treatment postponed postshampooing regreasing for 1-2 days" in the BTX-A treatment group, compared with 2 (8.3%) patients in the NS treatment group ($P = 0.000$). Eleven (44%) patients mentioned "scalp itchiness alleviated" in the BTX-A treatment group, compared with 2 (8.3%) patients in NS treatment group ($P = 0.005$). In addition, 7 (28%) patients reported "less hair loss", and 13 (52%) patients mentioned "efficacy did not last long enough" for the BTX-A treatment (Table 2).

Complications/AEs

The mean pain visual analog score for the BTX-A treatment and the NS treatment was 4.3 [0.7] and 4 [0.8], respectively ($P = 0.2$) (Figure 5B). The treatment-associated complications or AEs in both groups are listed in Table 3. Seven (28%) patients experienced dizziness in the BTX-A treatment group, compared with 2 (8.3%) in the NS treatment group ($P = 0.138$). Six (24%) patients experienced insomnia in the BTX-A treatment group, compared with 3 (12.5%) in the NS treatment group ($P = 0.463$). Five (20%) patients reported itchiness in the BTX-A treatment group, compared with 7 (29.2%) in the NS treatment group ($P = 0.456$). Four (16%) patients reported folliculitis in the BTX-A treatment group, compared with 6 (25%) in the NS treatment group ($P = 0.496$). Topical scalp tightness (n = 10, 40%) and tinnitus (n = 1, 4%) presented only in the BTX-A treatment group. Generally, the AEs were mild/moderate and

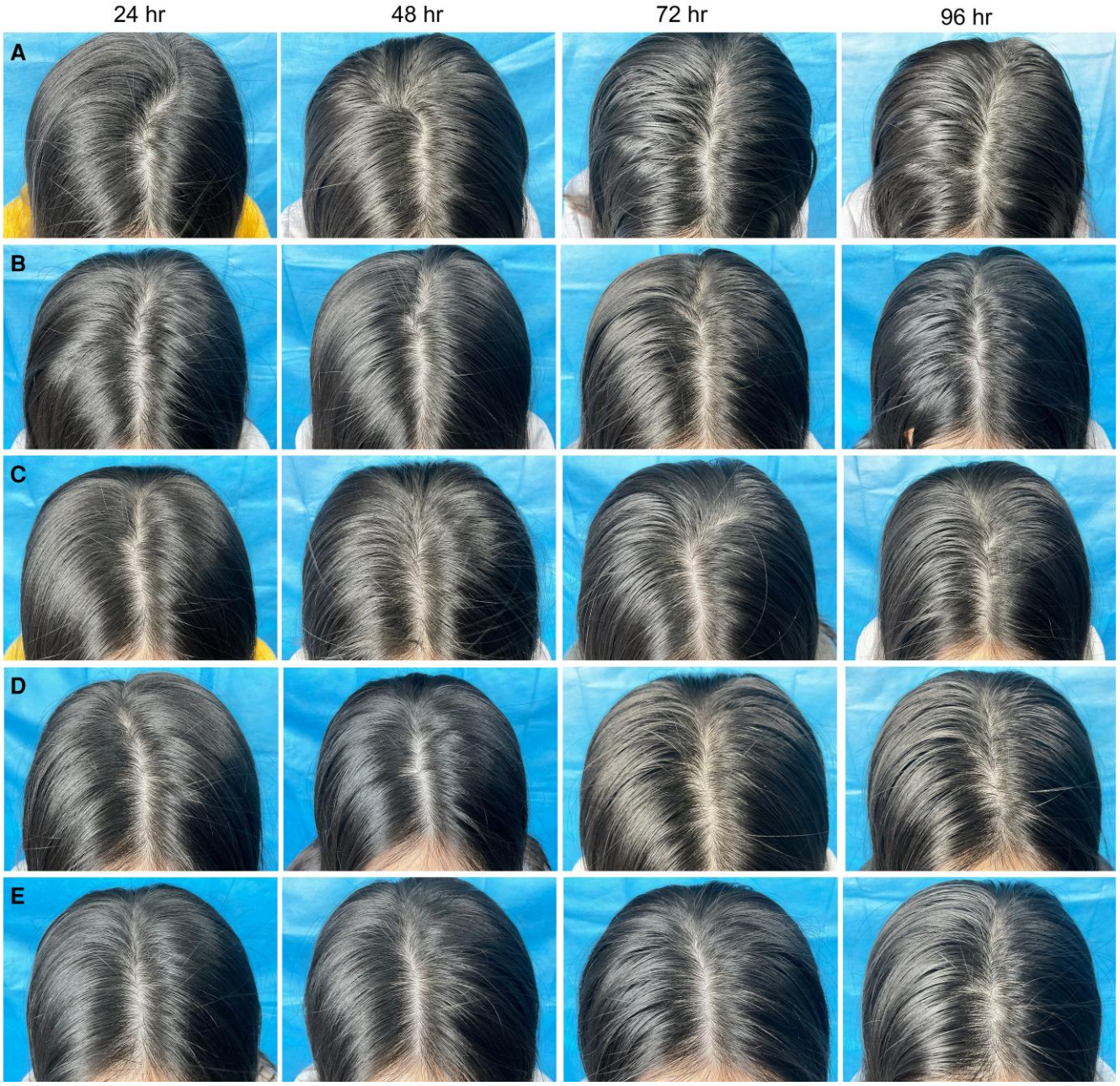

Figure 3. A 28-year-old female patient who received 1 session of 60 U intradermal BTX-A treatment shown at (A) baseline, (B) 1-month follow-up, (C) 3-month follow-up, (D) 4-month follow-up, and (E) 6-month follow-up. From left to right: 24, 48, 72, and 96 hours postshampooing. BTX-A, botulinum toxin type A.

managed conservatively. Postinflammatory hyperpigmentation, infection, and scarring were not observed during the study.

DISCUSSION

Previous studies revealed that the scalp regreasing process postshampooing followed a hyperbolic-like kinetics over days, and the highest amount of sebum was found at 2 to 3 days postshampooing. Lower amounts of sebum presented in the older age class in all ethnicities, as compared to the younger one, and male subjects were found to be higher sebum producers than women, irrespective of ethnicity. Diet, occupation, smoking, climate, ultraviolet radiation, pollutants, personal hygiene, and circadian rhythms have been identified as contributing factors to this process. Excessive scalp sebum secretion facilitates the regreasing process

Figure 4. A 26-year-old female patient who received 1 session of 1.6 mL intradermal NS treatment shown at (A) baseline, (B) 1-month follow-up, (C) 3-month follow-up, (D) 4-month follow-up, and (E) 6-month follow-up. From left to right: 24, 48, 72, and 96 hours postshampooing. NS, normal saline.

and leads to greasy scalp and hair. Coated with sebum, greasy hair progressively sticks together, trapping external dirt and particles. Undesirable sebum blocks the pores, and fuels bacteria and yeasts, resulting in itchiness, dandruff, folliculitis, and acne in susceptible individuals.[13]

Clear scalp and volumized hair help create a young, decent, and healthy image. Unlike facial oiliness, which can be modified with cosmetics, greasy scalp and hair are difficult to conceal. Frequent washing may help to alleviate scalp and hair oiliness, but also may lead to sensitive or irritable skin. Compared with oily facial skin, few therapeutic options for greasy scalp and hair are available. The efficacy of energy devices to treat scalp sebum excretion remains controversial, and the usage of lasers on hairy scalps appears difficult and restricted.[17,18] Although systemic treatments such as antifungals, isotretinoin, spironolactone, herbal medicines, and oral contraceptives have been proven to reduce sebum production with varying degrees of

Table 2. Patients' Comments

Patients' comments	BTX-A treatment group (n = 25), n (%)	NS treatment group (n = 24), n (%)	*P* value
Treatment postponed postshampooing regreasing for 1-2 days	14 (56)	2 (8.3)	0.000
Efficacy did not last long enough	13 (52)	—	—
Scalp itchiness alleviated	11 (44)	2 (8.3)	0.005
Less hair loss	7 (28)	—	—
Less dandruff	6 (24)	1 (4.2)	0.098

BTX-A, botulinum toxin type A; NS, normal saline

Table 3. Treatment-Associated AEs and Incidence

Treatment-associated AEs	BTX-A treatment group (n = 25), n (%)	NS treatment group (n = 24), n (%)	*P* value
Topical scalp tightness	10 (40)	—	—
Dizziness	7 (28)	2 (8.3)	0.138
Insomnia	6 (24)	3 (12.5)	0.463
Itchiness	5 (20)	7 (29.2)	0.456
Folliculitis	4 (16)	6 (25)	0.496
Pain	3 (12)	4 (16.7)	0.702
Hematoma	1 (4)	1 (4.2)	1.000
Tinnitus	1 (4)	—	—

AE, adverse event; BTX-A, botulinum toxin type A; NS, normal saline.

efficacy, the potential adverse effects, especially with long-term use, cannot be ignored.[12,19,20]

Basic research has confirmed that human skin sebaceous glands in vivo and sebocytes in vitro express nicotinic acetylcholine receptor α7, and that acetylcholine increases lipid synthesis in a dose-dependent manner. A marked decrease in sebum production on the intradermal botulinum toxin–treated side has been found in healthy volunteers with oily skin.[16] Intradermal botulinum toxin appears to be a viable option for patients with oily scalp.

To our knowledge, this is the first study that explored the impact of intradermal BTX-A treatment on the scalp sebum secretion and postshampooing regreasing process. Self-perceptions of the scalp and hair greasiness are highly subjective and vary largely. The sebum measurement reference value for "oily scalp" remains undetermined, even though several studies have been completed.[12–15,21,22]

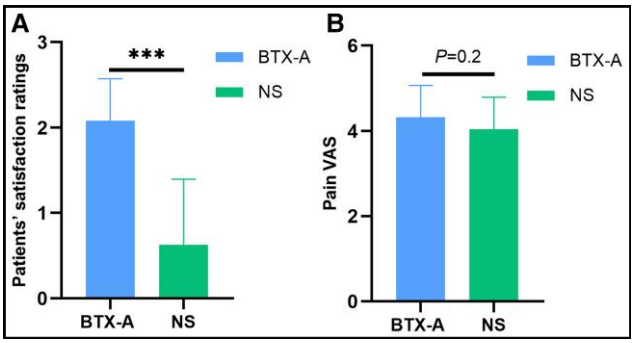

Figure 5. Bar graphs depicting (A) patients' satisfaction ratings for the treatment outcomes and (B) pain visual analog scale. ***$P < 0.001$.

The previous study suggested that botulinum toxin effectively reduced sebum production and pore size in the oily skin group, but had no effect in the dry-to-normal skin group.[16] We excluded subjects aged over 45 and with baseline scalp sebum 24 hours postshampooing of <100 μg/cm^2. Considering it was an investigative therapy, we selected the vertex scalp as the treatment region, rather than the whole scalp. Another consideration was that the greasiness of the vertex scalp and hair was most noticeable, and hence most influential on personal image. A relatively conservative toxin dosage (50-65 U) was selected for safety reasons.

Min et al reported that sebum production on the forehead had a positive correlation with the distance from the BTX-A injection point. Intramuscular injection of BTX-A significantly reduced sebum production at the injection site but increased the sebum production of the surrounding skin at a radius of 2.5 cm. They presumed that the sebum gradient surrounding the injection point was due to a compensatory mechanism for human skin sebum control.[1] Nevertheless, the scalp sebum measurement cannot be as accurate as that of the hairless skin. In addition, regular hair combing may lead to the redistribution of scalp sebum. In the current study, we measured the sites both within and outside of the treated region to comprehensively assess the scalp sebum production. Additionally, unlike that previous study which measured sebum production at only 1 post-shampooing time point,[12] we tracked and assessed a series of time points, which allowed us to evaluate the impact of BTX-A on the entire regreasing process.

In agreement with previous findings, the postshampooing regreasing process presented a hyperbolic-like slope.[13] Based upon our observation, at the 1- and 3-month follow-ups, intradermal BTX-A injection significantly impacted the overall kinetics of the regreasing process by reducing the sebum secretion at 24, 48, and 72 hours postshampooing. This finding agrees with patients' comments that the BTX-A treatment "postponed the regreasing process

postshampooing for 1-2 days." We believe the outcomes are clinically relevant, given most people, especially individuals with seborrheic scalp, tend to wash their hair much more frequently than every 72 or 96 hours.

According to the sebum measurements of the untreated region, the scalp sebum was higher in the BTX-A treatment group at 96 and 72 hours postshampooing at the 4- and 6-month follow-up, respectively. However, whether this was due to the BTX-A treatment or to a compensatory mechanism for sebum secretion needs further investigation. In addition, the sebum production threshold for "perceptible greasiness" remains to be determined, given neither the investigators nor the patients observed or reported any difference in the untreated regions between the 2 groups. It is noteworthy that, for both groups, the sebum production of the untreated region (lateral scalp) was considerably lower than that of the treated region (vertex scalp) during the follow-up. The regional sebum secretion variation verified that only the vertex scalp, rather than the whole scalp, required toxin intervention.

The maintenance time of the toxin efficacy seems to be associated with the injection technique. Jun et al compared intradermal and intramuscular injection of BTX-A for forehead wrinkles in a double-blinded, split-face, pilot study, and observed that the intramuscular injection side showed a slightly longer duration of effect.[23] Wanitphakdeedecha et al documented that the facelifting effect of abobotulinumtoxinA intradermal injection sustained for up to 3 months after treatment.[24] Min et al reported that the alteration in sebum production following intramuscular BTX-A treatment for forehead rhytides recovered to normal levels at the 16-week follow-up.[1] Our study, in accordance with these previous findings, implied the sebum returned to baseline levels at the 4-month follow-up.

Multiple mechanisms are likely involved in scalp sebum regulation by BTX-A. The primary mechanism would be toxin interfering with cholinergic transmission between autonomic nerve terminals and sebaceous glands. The oily skin may be more susceptible to cholinergic regulation than normal skin due to the greater abundance of sebocytes with more cholinergic receptors.[16] Second, intradermal botulinum toxin may reduce sebum production through its neuromodulatory effects on the arrector pili muscles, the contraction of which are required for sebum excretion.[4] Third, toxin may have influenced the topical hormonal equilibrium. Androgens are the major influence controlling sebaceous gland development and sebum production. A few studies documented that BTX-A injection at the muscles surrounding the scalp produced a marked decrease in scalp oil secretion. Toxin relaxed the muscles, reduced pressure on the perforating vasculature, and increased blood flow and oxygen concentration. More testosterone was converted into estradiol with a high concentration of oxygen, leading to a decline in grease secretion and consequently hair loss.[7,8] Fourth, the patients' perceptions of less greasiness may partially be due to the inhibition of sweat gland activities by BTX-A.[25,26] Finally, the patients' perceptions of "less itchy" and "less dandruff" may be associated with alteration of the scalp microbiome. The clinical outcomes indicated that scalp sebum secretion was likely regulated by complicated interactions between multiple factors. More studies are needed to clarify these mechanisms.

Previous studies demonstrated that sebum excretion was subject to a variety of influential factors, including ethnicity, genetics, gender, age, climatic variation, and pregnancy.[2,13,27] Pouradier et al found quantitative differences between different ethnic groups, resulting from different sebaceous production levels and scalp hygiene routines. The scalp regreasing process followed a hyperbolic-like kinetics over days. The amounts of collected sebum highly varied with ethnicity. The highest amount of sebum 2 to 3 days postshampooing was found in African Americans, followed in descending order by Caucasian American, Japanese, Chinese, Thai, Caucasian European, and Indian subjects.[13] The Chinese population's scalp sebum level ranked in the middle of the ethnicities. The botulinum toxin dosage range used in our study has been determined after reviewing previous studies, including Pouradier et al's. We assume the positive effects of toxin on scalp sebum secretion in the current study may not be simply generalized to the other scenarios, given it was relatively conservative and generated moderate scalp sebum secretion regulation.

Because there was only 1 male subject enrolled in the study, we did not perform a gender variability analysis. One major reason why male subjects were less willing to participate in the study, we speculate, was that hair-washing may be easier and less time consuming for them. Male subjects, especially ones with oily scalps, may alleviate scalp greasiness through frequent hair-washing. Men were found to be higher sebum producers than women, irrespective of ethnicity.[13] A further study with a larger study group and more male subjects is warranted.

In generally, intradermal BTX-A treatment on the scalp was well-tolerated. We noticed that topical scalp tightness and dizziness were the 2 most frequent complications for the BTX-A treatment group, which were assumed to be associated with the toxin effect. Based upon the efficacy and safety profiles, a higher toxin dosage could be utilized. How to maintain a balance between toxin dosage, clinical efficacy, and risks of complications deserves further investigation. Topical anesthesia was not applied in our study because most patients rated the pain associated with intradermal toxin injection to the scalp as moderate and tolerable. For pain-sensitive individuals, we would recommend ice bags or vibration anesthesia.[28]

There are several limitations to the present study worthy of further exploration. With only 1 toxin dosage, 1 treatment

session, and a restricted scalp region being explored, the efficacy and safety of higher-dosage, repetitive treatments, and treatment of extended regions, need further study. Given the limited sample size of predominantly female patients, a larger study group with more male subjects would be highly desirable. In addition, the age in the current research was relatively young, and toxin application for more age groups would also be worth investigating.

CONCLUSIONS

This randomized, double-blinded, placebo-controlled, and prospective study has demonstrated that compared with NS, 1 session of intradermal BTX-A injection (50-65 U) effectively and safely reduced scalp sebum secretion and greasiness perception in the treated region at 24 and 48 hours postshampooing for 3 months.

Supplemental Material

This article contains supplemental material located online at www.aestheticsurgeryjournal.com.

Disclosures

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

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