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SAFETY AND EFFICACY OF INTRADERMAL INJECTION OF BOTULINUM TOXIN FOR THE TREATMENT OF OILY SKIN

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ABSTRACT

Objectives: To evaluate the safety and efficacy of intradermal injection of botulinum toxin for the treatment of oily skin and enlarged facial pores. **Methods:** Thirty-four patients with oily skin and enlarged facial pores were treated with intradermal injection of botulinum toxin type A on the face. Pore size was measured using a digital microscope. Patients were asked to assess their sebum production at baseline and post-treatment and to rate their satisfaction in terms of overall improvement of skin oiliness and pore size. **Results:** Treatment with intradermal botulinum toxin resulted in sebum production alteration. 14 subjects had moderate sebum production (41.2%) and 20 subjects had severe sebum production (58.8%) at baseline. After two weeks, most subjects had mild and very mild sebum production (39.4% and 21.2% respectively). No significant difference in pore size was noted between the first visit and follow-up visit using a digital microscope (0.33 cm ± 0.15) at baseline and after two weeks (0.31 cm ± 0.15) ($p < 0.05$, t-test). 16 patients reported they were satisfied (48.5%). No significant side effects were reported. **Conclusions:** Botulinum toxin reduced sebum production in oily skin. However, it had no significant effect on reducing pore size.

KEYWORDS: Botulinum toxin; oily skin; enlarged facial pores.

INTRODUCTION

Oily skin and facial pores are common complaints of patients presenting to dermatologic clinics. They represent a major cosmetic concern for women. Pore-minimizing treatments and lasers have different efficacy and longevity. Most of these treatments require daily or monthly application to see results. Sebum is secreted from sebaceous glands which are distributed variably within the skin. They are particularly well-developed in the face on the forehead, nose, and chin. The forehead region normally has higher sebum production than other regions because of a higher density of sebaceous follicles in the face (300–900/cm2).[1] Oil helps to lubricate the skin and has anti-inflammatory purposes.[2] However, excess sebum production results in seborrhea and other skin disorders like wide facial pores, acne vulgaris, and seborrheic dermatitis.[3] Facial pores are a visible topographic feature of skin surfaces and are generally the enlarged openings of pilosebaceous follicles.[4] The morphological subtypes of skin pores were classified into three different categories, using the Robo SkinAnalyzerCS50 (NIIC, Tokyo, Japan), as follows: "visible skin pores" (0.1–0.6 mm2), "enlarged skin pores" (0.3–0.6mm2), and "blackhead embedded skin pores".[5] Pathologic factors of facial pores include aging, sex, genetic predisposition, chronic ultraviolet exposure, seborrhea, decreased elasticity, and large hair follicles.[2,4-6] Thus, therapeutic modalities must be individualized according to the possible causes. The most effective medication to inhibit sebum production is isotretinoin (13-cis retinoic acid), the action of it includes suppression of sebaceous gland activity and normalization of the pattern of keratinization within the sebaceous gland follicle.[7] Also, hormonal therapies and spironolactone were used with varying outcomes.[8] Topically, retinoids and chemical peels have shown efficacy in treating oily skin and facial pores.[9] Lately, botulinum toxin has gained increasing popularity in treating oily skin and enlarged pores.[10] Many reports have demonstrated the effect of botulinum toxin on sebum production. Rose et al.[11] used the botulinum toxin to treat the forehead region of twenty-five patients with oily skin and found a significantly lower sebum production at 1 week 1, 2, and 3 months after injection ($p < .001$, t-test).

Li et al.[12] explained the effect of botulinum toxin on sebocytes by conducting in vitro studies that showed that cholinergic receptors are expressed in human sebocytes and that acetylcholine induces lipid synthesis in human sebocytes via the ERK pathway. Thus, sebum production could be inhibited by using botulinum toxin

which blocks the activity of acetylcholine at the motor unit.[12]

The purpose of this study was to evaluate the safety and efficacy of intradermal botulinum toxin for the treatment of oily skin and facial pores and study the durability of its effect to evaluate its cost-effectiveness compared to other available treatments.

MATERIALS AND METHODS

We conducted a prospective study, with the approval of our Hospital Ethical Research Committee (Tishreen University Hospital, Latakia, Syrian Arab Republic), thirty-four patients with oily skin and enlarged facial pores from the dermatology outpatient clinic were enrolled in the study. Inclusion criteria were age above 18. Exclusion criteria included treatment with isotretinoin within the previous 24 months, history of topical treatment affecting pore size, history of myasthenia gravis, pregnant or lactating, hypersensitivity to botulinum toxin or any of its components, immunocompromise, hepatitis, poor wound healing or keloid formation, history of filler or botulinum toxin injection within three months, history of steroids, antifungals and contraceptive. All subjects signed informed consent.

Each 100-U vial of botulinum toxin A (Neuroxin) was diluted using 5 ml of bacteriostatic saline. The face was cleaned with saline serum. Anesthesia gel (prilocaine 2.5% and lidocaine 2.5%) was applied for 10 minutes under occlusion. The forehead, nose, and cheeks were injected intradermally with 20 U of botulinum toxin using a 30-G needle. The injection sites were 1 cm apart. The endpoint was the appearance of yellow papules. The injected sites were standardized for all the subjects. Patients were asked to keep their heads up for 4 hours, avoid exercise for 24 hours, and avoid the use of any products for oily skin like soaps or creams.

Subjects returned for follow-up visits 2 weeks 1,2, and 3 months after the initial visit. Digital photographs were taken of the treatment area at baseline and each follow-up visit using a mobile phone camera (iPhone15). Measurements of pore size were obtained using a digital microscope at baseline and each follow-up visit. In addition, self-reported evaluations of the oiliness of the patient's skin were collected (severe, moderate, mild, very mild, and dry skin).

At the end of the study, patients were asked to rate their satisfaction with the treatment regarding overall improvement in oily skin and facial pores (1=not satisfied at all,2=not satisfied, 3=somewhat satisfied,4=satisfied, 5=very satisfied). Patients were examined at follow-up to record any side effects like decreased muscle tone or paralysis in the treated area.

Sebum production was compared using the Wilcoxon test. Pore sizes were compared using the Student's T-test. Data were analyzed using the SPSS software. (version 12.0; SPSS Inc., Chicago, IL, USA). A P-value of <0.05 was considered statistically significant.

RESULTS

Thirty-four subjects were enrolled. Twenty-nine (85%) were females and five (15%) were males. Most subjects were below thirty years old (67.65%). Treatment with intradermal botulinum toxin resulted in sebum production alteration in the t-zone region according to patients' assessment at the follow-up visits. We asked patients at the first visit to assess the sebum production in their opinion (very mild, mild, moderate, severe). Fourteen subjects had moderate sebum production (41.2%) and twenty subjects had severe sebum production (58.8%). None of the subjects had mild or very mild sebum production, which is normal because having oily skin was an inclusion criterion in our study. After two weeks, only two patients had severe sebum production (6%), eleven had moderate sebum production (33.3%), and thirteen and seven subjects had mild and very mild sebum production (39.4% and 21.2% respectively) (Figure 1). One patient didn't come for a follow-up. The duration time of botulinum toxin effect was three months in twenty patients, two months in twelve patients, and four months in only one patient (Figure 2). The pore score showed no statistically significant difference between the first visit and follow-up visit using a dermoscopy (0.33 cm ± 0.15) and after two weeks (0.31 cm ± 0.15) ($p < 0.05$, t-test) (Figure 3).

Sixteen patients reported they were satisfied (48.5%) with the treatment, four patients were unsatisfied (12.1%) and thirteen patients were moderately satisfied (Figure 4). No subject reported sensitivity to the botulinum toxin. However, all subjects (100%) reported pain during injection. Ten subjects (29.4%) had erythema. One subject reported smile asymmetry caused by paralysis of the levator labii superioris.

DISCUSSION

Sebaceous glands produce sebum via holocrine secretion and have multiple biological functions, including hormonal and immune modulation. It also lubricates the skin, but it becomes bothersome when secreted in excess amounts (>1.5 mg/10 cm2 every 3 hours) and gives the skin a shiny and greasy appearance.[3,13] These glands are associated with hair follicles except for ectopic or free sebaceous glands of the vermilion lips, urogenital mucosa, and eyelids. Sebum consists of free fatty acids, wax and sterol esters, triglycerides, and squalene. A sebaceous follicle consists of four parts; the keratinized follicular infundibulum, the hair, the cauliflower-like convoluted sebaceous gland, and the sebaceous duct.[3] Several factors affect sebum production like sex, age, feeding, drugs (i.e. 13-cis retinoic acid and oral contraceptives), temperature, and stress.[2,3,14] The most effective treatment for oily skin is isotretinoin (13-cis-retinoic-acid) which is the strongest inhibitor of sebum

production, it inhibits sebaceous gland activity and modulates keratinization within sebaceous follicles. However, not everyone can tolerate the side effects of isotretinoin. Other treatments include hormonal therapies, such as combined oral contraceptives and spironolactone. Cyproterone acetate is a progestin that acts as an androgen receptor blocker and inhibits ovulation. Spironolactone is a potassium-sparing diuretic, taking 50-200 mg daily of spironolactone may decrease sebum production.[15] Using isotretinoin with other treatment options can significantly decrease facial pores' area and number via synergistic effects.[16]

Skin pores are enlarged openings of the pilosebaceous follicles on the skin that can be affected by several factors including age, gender, exposure to UV light, ethnicity, and sebum secretion. With increased age, facial pores expand on the nose and cheeks especially the medial aspect.[2,4,13,14,17] Using the Robo Skin Analyzer CS50, facial pores are divided into three categories: "visible skin pores" (0.1–0.6 mm2), "enlarged skin pores" (0.3–0.6mm2), and "blackhead embedded skin pores".[5] Many treatments modalities have been suggested to treat oily skin and facial pores, including oral and topical medication (isotretinoin, contraceptive pills, spironolactone, and chemical peeling) as well as different wavelengths of lasers.[4] The sebaceous gland is not innervated by the parasympathetic nervous system. However, it was recently proved to prominently express distinct nAchR subunits, including nAchRα7, and release Ach by autocrine mechanisms. The regulated expression of AchR in sebaceous glands advocates a role for Ach in sebum production and as a promoter of sebocyte differentiation, thus offering an explanation for the decrease of the activity of sebaceous gland after intradermal injections of botulinum toxin type A (BTX-A)[12] To investigate the role of cholinergic signaling in the human sebaceous glands, primary sebocytes were treated with Ach (Acetylcholine). When sebocytes were treated with 10 nM Ach, an increase in lipid accumulation in the cytoplasm was detected by microscopy after Oil Red O staining. Then these cells were treated with A-bungarotoxin which is an Ach receptor antagonist, it suppressed Ach-induced lipid synthesis in sebocytes. Also, botulinum toxin had neuromodulator effects on the arrector pili muscles.[12] Anecdotal reports of patients noting tighter, smoother skin after botulinum toxin in addition to these observations of oily skin and enlarged facial pores, have promoted speculation that botulinum toxin may be an effective and safe treatment for oily skin and enlarged pores.

Our results suggest that intradermal injection of botulinum toxin reduces sebum production in patients with oily skin, with a high degree of patient satisfaction. However, it had no significant effect on large facial pores. Even though, previous studies had shown a significant effect on pore size. Thus, botulinum toxin represents a solution for oily skin but not for facial pores.

Ahmad el Attar et al.[18] study showed that a single session of microbotox improved pore size by 3.7 (0-4 scale). The average patient satisfaction after the end of therapy was 4.7 (1-5 scale). Dermoscopic evaluation confirmed the reduction in the size and number of pores. There were no serious or long-term side effects. In our study, no reduction in pore size was detected using dermoscopy after a single session of microbotox.

Kesty et al.[19] study showed that receiving either 30 or 45 units of neurotoxin showed a significant reduction in oily skin. This effect was present for 6 months. A high level of satisfaction was reported with no side effects. This is similar to our study. Both studies showed a reduction in oily skin with a high satisfaction rate in improving the oiliness of skin and no side effects were reported.

Sapra et al.[20] study showed no significant effect of botulinum toxin type A on pore size which is similar to our study. However, it also showed no effect on sebum production in contrary to our study which showed a decrease in sebum production.

Salem et al.[21] study compared the efficacy and longevity of intradermal mesobotox injection versus its topical application with microneedling for the treatment of wide facial pores and seborrhea. It showed more satisfaction when injected intradermally compared to topical application with microneedling. Both methods were safe.

Parvar et al. study recommended long-term topical therapy that includes AHA chemical peeling followed by systemic treatments in younger patients and mesobotox which can be used in all face areas. For older age groups they recommended a combination of rejuvenation and reduction of facial pores' size therapies such as lasers, particularly the ablative ones, ultrasonography, and radiofrequency in 3–5 sessions with 2–4 weeks intervals.[16]

CONCLUSION

The current study concluded that intradermal injection of botulinum toxin led to improvement of oily skin but had no effect on pore size. More studies on the effect of botulinum toxin in the treatment of oily skin and pore size are required with a larger sample size and objective methods of measuring skin oiliness like sebumeter. The limitation of our study is the lack of objective tools to assess the oiliness of skin like a sebumeter. We recommend mesobotox for young and elderly patients who complain of greasy skin and shiness. However, we recommended adding it to other pore-minimizing treatments like lasers and oral medicine to reduce pore size.

Sebum Production	At Baseline	Percentage	Post-Treatment	Percentage	P-Value
Very mild	0	0%	7	21.2%	0.00
Mild	0	0%	13	39.4%	
Moderate	14	41.2%	11	33.3%	
Severe	20	58.8%	2	6%	

Figure 1: Sebum Production According to Patients' Assessment at Baseline and Post-Treatment. (Wilcoxon-Test).

Durability of effect (months)	Subjects number	Percentage	p-value
2	12	36.4%	0.00
3	20	60.6%	
4	1	3%	

Figure 2: durability of botulinum toxin effect on sebum production.

	Mean	N	Std. Deviation	Std. Error Mean
Maximum pore size at baseline	.3339	33	.14760	.02569
Maximum pore size at follow-up	.3176	33	.15334	.02669

Figure 3: maximum pore size at baseline and follow-up. (Student T-test).

Satisfactory scale	Subjects number	Percentage
Not satisfied	4	12%
Moderately satisfied	13	39.4%
Satisfied	8	24.2%
Very satisfied	8	24.2%

Figure 4: Patient satisfaction post-treatment (Friedman-test).

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