Original Article

Comparison of the effect of intra-dermal injection of botulinum toxin and normal saline in the treatment of facial skin pores

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Abstract

Background and Purpose: Skin pores (SPs) are normal and benign skin structures that are mostly located on the face (nose, cheeks, etc.) that cause many aesthetic concerns or complaints. One known effective treatment is botulinum toxin A (BTXA), which is also approved for the treatment of strabismus, blepharospasm, muscle spasm, cervical dystonia, glabella wrinkles, and primary axillary hyperhidrosis. Therefore, the aim of this study was to compare the effect of intra-dermal injection of botulinum toxin and normal saline serum (NSS) in the treatment of large facial pores. **Methods:** The study included 25 people who referred to the skin clinic of Imam Khomeini Hospital in Ahvaz from June 2021 to January 2022 for the treatment of large facial skin pores. Randomly, some subjects were injected with botulinum toxin at ten points, and each point was equivalent to 2.5 units of Masport (500 units vial of Masport diluted with 10 ml of NSS). Some other people were injected with 0.05 ml of NSS by intra-dermal injection at ten points. Finally, the data were analyzed using SPSS-Ver. 22 software. **Results:** Based on optical coherence tomography results, it was determined that the diameter of facial pores decreased significantly ($P = 0.011$). Dermoscopy showed a significant decrease in the average size of facial pores ($P < 0.011$), and also, the pore score decreased significantly ($P = 0.021$). In addition, the results showed that the size of skin pores and facial fat on both sides of the face did not decrease significantly from the patients' point of view ($P = 0.71$). **Conclusion:** Based on the results of the present study, it can be concluded that intra-dermal injection of botulinum toxin is an effective and safe method to control facial pores, which showed acceptable results after 3 months.

Keywords: Botulinum toxin, intra-dermal injection, normal saline, skin pores

Introduction

The skin pore (SP) is a visible topographical feature on the surface of the skin and is generally referred to as the enlarged opening of the follicles of the pilosebaceous units of the facial pore (wider than 0.02 mm^2).[1] Facial skin pores are not fixed and are dynamic structures.[2] These pores are benign skin defects with depressions visible from the surface of the facial skin (golf ball appearance), relatively large in size (250–500 micrometres) and visible with a spherical appearance.[3] They are cosmetic problems that are not considered a disease, but their psychological effects affect a person's feelings and self-confidence.[4]

Facial SP is usually seen on the skin of the nose and cheek, and the appearance of SP varies among different people.[2] The density of these pores in the chin is between 10 and 90 cm^2.[3]

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This defect is mainly related to the race and has less relation to the age factor. The presence of facial pores in the Asian race is the lowest, while the American and African races have the largest size of pores compared to other racial groups.[4,5]

Many factors such as sex, genetics, aging, ultraviolet rays, pimples, and seborrhea also affect the formation of SP pores.[2] Among these factors, excessive sebum production is associated with enlarged facial pores and shiny, oily skin.[6] When the facial skin is oily and shiny, it may be associated with large pores, follicles, sebaceous glands, and comedones. The sebum secretion rate decreases with age, and after reaching the maximum amount of sebum production at around 20 years of age, sebum secretion continuously decreases in men and women throughout life.[2] In addition, environmental factors such as season, relative humidity, temperature, and hormonal factors such as androgens also affect sebum secretion.[7]

Hormonal fluctuations, including serum estradiol concentration during menstruation, affect skin quality, pore diameter, skin colour, and moisture. In women aged 40 to 50 years, low estradiol levels lead to good skin appearance, a decrease in moisture, and a decrease in the diameter of skin pores.[8] An increase in androgen levels has a significant effect on the proliferation of sebocytes and sebum production. When the composition and amount of food change significantly, it may cause a change in sebum secretion.[9] Oily skin is the main complaint of patients who go to skin beauty clinics for skin evaluation, but the existing treatments are not satisfactory.[10]

As a part of the face, the so-called "T zone", including the forehead, nose, and chin, has higher sebum production than other areas due to the higher density of fat follicles in the face (2300–900 cm).[11] In adults, the average production of sebum is 1 mg/10 cm^2 every 3 hours. When sebum production exceeds 1.5 mg, it leads to oily skin, acne, large pores, and seborrheic dermatitis.[9,12,13] Excessive production of sebum creates facial conditions with large pores and shiny appearance and pus-like feeling associated with acne.[11,14] Excessive sebum production may be associated with psychological and social side effects of acne, enlarged pores, and skin shine, which can lead to low self-esteem, depression, and distress.[9,12,13]

Laser, isotretinoin, chemical peels, retinoids, and other topical treatments have all been used to treat oily skin and enlarged pores, each with varying levels of effectiveness.[1,6,15] In addition, injections of hyaluronic acid and 10-hydroxysteric acid (HSA) can also improve the appearance of the skin, reduce the size of the pores, and enhance the radiance of the skin.[16,17]

Observations and reports of patients with tighter pores and a smoother skin after botulinum toxin injections have fueled speculation that botulinum toxin may be an effective treatment for oily skin and enlarged pores.[6] Intra-muscular injections of botulinum toxin have been used to treat glabella lines, crow's feet lines, muscle spasms, cervical dystonia, and migraine control. Intra-dermal injections have also been used to treat hyperhidrosis in the armpits, palms, and soles of the feet and to tighten the skin of the face as well as to treat Raynaud's phenomenon and finger ulcers in patients with systemic sclerosis.[18-23]

The use of botulinum toxin A (BTXA) can reduce the intensity of tensile forces during the wound healing process and lead to better and early maturation of new collagen. The scar appearance in the area treated with BTXA is better than the area without treatment with that substance.[24] Less acne was observed in people who used BTXA to treat skin wrinkles.[6,9] Based on previous research results, BTXA injection significantly reduces sebum production at the injection site and around the injection site, but higher injection doses do not significantly improve the effectiveness of the toxin.[9] The results of previous studies show that intra-dermal injection of BTXA is effective for treating erythema, flushing, rosacea, and skin rejuvenation.[20,25] The findings of previous studies show that the size of skin pores and sebum after intra-dermal injection of BTXA in the area of cheeks and forehead has decreased.[6,9,11] In addition, the results of previous studies show that BTXA injection caused neurological adjustment in sweat and fat glands, reducing their production and adjusting the size of blood vessels and reducing facial pores.[3]

Current treatment methods have been used to treat large facial skin pores, which include topical retinoids, chemical peels, and laser devices, which have not been very satisfactory. The main purpose of this study was to evaluate the effect of BTXA on reducing sebum secretion and subsequently reducing the size of facial skin pores and comparing it with the injection of normal saline serum (NSS) as a control group

Material and Methods

Design

The current research is a double-blind clinical trial that was conducted from June 2021 to January 2022 at Imam Khomeini Hospital of Ahvaz, affiliated to the Faculty of Medicine of Ahvaz University of Medical Sciences, Iran. The study population included patients who had referred to the dermatology clinic of Imam Khomeini Hospital in Ahvaz, Iran, for the treatment of large facial pores and were willing to participate in the study.

Sampling

Using the results obtained from the study of Sayed *et al.* (2020),[15] the accuracy (d) and standard deviation (S.D) for the difference between before and after treatment with intra-dermal botulinum toxin were considered equal to 0.68 and -0.4, respectively. Considering the probability of type 1 error equal to 0.05 and the study power equal to 90%, finally, the sample size was estimated to be 25 people by equation (1).

$$n = \frac{s_d^2 \left(z_{1-\frac{\alpha}{2}} + z_{1-\beta}\right)^2}{d^2} \quad (1)$$

In the following, one patient withdrew from the study due to facial paralysis and four patients due to the spread of the

coronavirus and personal issues. For this purpose, 20 patients with large facial pores who visited the skin clinic of Imam Khomeini Hospital in Ahvaz and were eligible for the study were included in this research. Therefore, this study was conducted on 20 patients, 16 women (80%) and 4 men (20%).

Inclusion and exclusion criteria

The presence of large facial skin pores and an age over 18 years were among the inclusion criteria. The most important criteria for exclusion from the study included pregnant mothers, nursing mothers, an age less than 18 years, active disease or infection on the facial skin, simultaneous use of other treatment methods for the treatment of facial pores, history of allergy to the studied drugs, suffering from neurological diseases, use of aminoglycoside drugs, and history of skin keloid formation.

Study implementation

Written consent was obtained from all patients after providing necessary explanations. Patients were included in the study in the first visit after taking patient history and physical examination if they met the necessary entry and exit criteria. A questionnaire was given to the selected patients to record the demographic characteristics of the patients, including age, sex, family history of open facial pores, history of previous treatments, location of the lesion, history of skin and non-skin diseases, and medications. First, from both types of patients, with a Galaxy s21 mobile phone camera (Sumsung, KOREA) and a Handyscope dermoscope (Photofinder, Germany) as well as optical coherence tomography (OCT) (Heidelberg Engineering GmbH Germany) photographs were taken.

Patients entered the study after completing the consent form and a skin-related questionnaire, and after taking photographs with a camera, dermoscope, and OCT device, botulinum toxin was randomly diluted on one side of the face and NSS was injected intra-dermally on the other side. Three months later, photographs were taken again with a camera, dermoscope, and OCT device, and questionnaires were collected from the patients.

In the following, ten points on each side of the species were marked at a distance of 1 cm. Each 500-unit vial of Masport (Masun Daro-Alborz, Iran) was diluted with 10 ml of normal saline, and 0.05 ml (2.5 units of Masport) with a 30G insulin syringe (AVA, Iran) in one cheek (randomly) was injected. On the opposite side, 10 points were marked at a distance of 1 cm and 0.05 ml of NSS was injected. It should be noted that the patient and the therapist are blind and do not know how to assign the type of treatment to the left and right cheeks.[3]

Patients were advised to use only sunscreen during the treatment period and not to use exfoliating creams. In order to randomize the type of treatment assigned to the left and right sides of the patients' face, two treatment modes including AB (treatment A for the left side and B for the right side) and BA (treatment B for the left side and A for the right side) were considered. By assigning random numbers from the random number table to patients, if an odd number was obtained, AB treatment was assigned to the patient, and if an even number was observed, BA treatment was considered for the patient. This process continued until the number of AB and BA treatments became the same. In other words, according to the sample size (25 people), whenever the frequency of one of the two methods reached 13, another method was considered for the rest of the patients. The present study was a double-blinded study so that the patient and the therapist were not aware of how to assign the type of treatment to the left and right sides of the cheek.

Two weeks and three months after the injection, the patients were visited again and possible complications were recorded. In addition, during these two visits, the patients' faces were photographed again, and in the third month's visit, the aforementioned questionnaire was filled again by the patients. Finally, the level of patient satisfaction based on poor, average, good, and excellent was recorded in the questionnaire. Also, the photos taken were classified and the diameter of the pores was measured by computer.

The images obtained from dermoscopy of the skin of the volunteers' cheeks were divided into four categories based on the clarity of the facial skin pores, including unknown, known, enlarged, and with black heads.[3] In addition, to further emphasize the evaluation results, the findings of dermoscopy were evaluated by three dermatologists.

Study analysis

The results of this study were described and analyzed by SPSS-Ver. 23. Descriptive parameters were used to describe the data. In addition, in order to analyze the data, especially to compare the average results of related groups (before the intervention, 2 weeks and 3 months after the intervention), the corresponding statistical test was used. Two-way repeated measures ANOVA was used for quantitative response, and paired *t*-test was used for ordinal response at a significance level of $\alpha = 0.05$.

Results

The results of this study showed that the number of men and women participating in the study was 16 (80%) and 4 (20%), respectively. Also, the average age of the participants in the study was 34.95 ± 6.44 years. The frequency of selected patients in terms of the size of facial pores based on the classification of "invisible", "visible", "large", and "black head" was 0 (0%), 3 (15%), 8 (40%), and 9 (45%), respectively [Table 1].

The mean difference of facial skin pores in the study groups at different times of the intervention is presented in Table 1. In addition, the mean difference of facial skin pores in the study groups at different times of the intervention is shown in Table 2.

The findings of Tables 2 and 3 showed that the difference between the before the intervention and 2 weeks after the

Table 1: The demographic characteristics of study participants

Variables	Value
Age (year)	6.44±34.95
Frequency based on sex	
Man	16 (80%)
Woman	4 (20%)
Face pore size	
Invisible	0 (0%)
Visible	3 (15%)
Large	8 (40%)
Blackhead pores	9 (45%)

Table 2: The mean difference of facial skin pores in the study groups at different times of the intervention

Study group	Intervention time (week)	Number	Mean difference	Standard deviation (S.D)
Botulinum toxin (BTX)	0 and 2	20	48.5	17.76
	0 and 12	20	35.45	19.42
	2 and 12	20	-13.05	10.03
Normal saline serum (NSS)	0 and 2	20	23.5	12.81
	0 and 12	20	8.85	9.65
	2 and 12	20	-14.65	12.90

Table 3: The mean difference of facial skin pores after treatment by botulinum toxin and normal saline serum

Study group	Intervention time (week)	Number	Mean difference±S.D	*P*
BTX-NSS	0 and 2	20	25.01±12.92	<0.001
BTX-NSS	0 and 12	20	26.06±22.38	<0.001
BTX-NSS	2 and 12	20	1.60±15.51	<0.001

intervention as well as the difference between the before the intervention and 3 months after the intervention, in terms of the average diameter of the skin pores, in the two treatment groups was significantly different. The maximum reduction in the size of facial skin pores was 2 weeks after the injection, and over time, this diameter became closer to the initial value.

Table 4 shows the level of satisfaction of patients 3 months after treatment intervention in two treatment groups (BTX and NSS). Based on the results, the satisfaction level of patients in the BTX treatment group was higher than that of the NSS group, but this difference was not statistically significant ($P = 0.71$). In Figure 1, the facial image in terms of skin pores before and after treatment by BTX and NSS is shown. In addition, the classification of skin pores based on dermoscopy is presented in Figure 2.

Discussion

The results showed that the size of facial pores on the side treated with BTX compared to the side treated with NSS, 3 months after treatment, was significantly smaller. In addition, based on the obtained results, the level of patient satisfaction

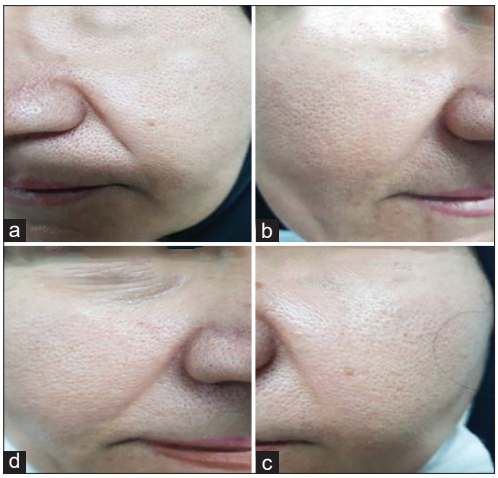

Figure 1: Facial image before therapeutic intervention in left and right cheeks (a and b), treatment with NSS (c), and treatment with BTX (d)

in the BTX treatment group was higher than that in the NSS group, but this difference was not statistically significant. The effect of intra-dermal BTX in the management of facial pores can be explained by several hypotheses. Reducing the activity of the sebaceous glands logically leads to an improvement in seborrhea from a clinical point of view, thereby reducing the size of the pores. Additionally, recent studies have shown that BTX increases collagen production,[12] which may further improve the facial pore size.

Percutaneous acupuncture itself causes multiple microbruises in the skin, which in turn causes some complexation of growth factors and ultimately leads to collagen production,[11,13,14] with OCT measurements on both sides of the face (with and without BTX); this fact is shown in the present study.

In contrast to the results of the present study, the findings of Sapra *et al.* (2017)[26] showed no improvement in pore management using intradermal BTXA. This discrepancy may be due to the fact that the mentioned study included a small sample size and was also only evaluated based on clinical photographs.

The improvement on the NSS-treated side at the 3-month assessment was lower than on the BTX side, but there was a partial improvement compared to before treatment, which could be explained by the acupuncture action, as mentioned earlier. In addition, it is possible to say that NSS itself may reduce sebum secretion instead of reducing production through oedema, pore size, and even increased skin thickness caused by normal saline.[19] This oedema can block the ducts and thus reduce sebum production. Ultimately, this causes the pore size to decrease. The short duration of this effect, as documented in the present study, provides evidence for the speculation that it is an oedema-dependent response following NSS injection. Continued improvement at the 3-month assessment demonstrated the true value of BTXA intra-dermal injection, resulting in greater patient satisfaction on the BTXA-treated side than on the NSS-treated side.

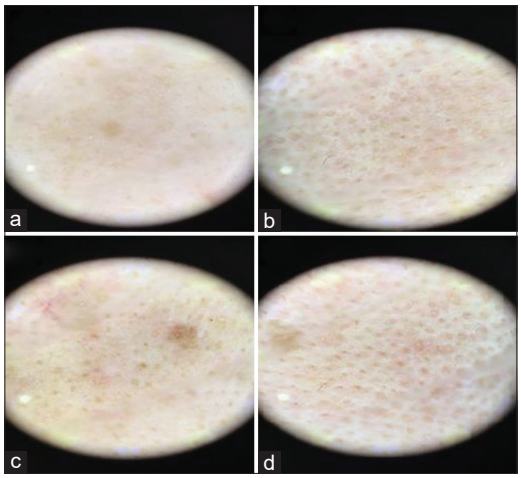

Figure 2: Classification of skin pores based on dermoscopy (a: invisible pore; b: visible pore; c: large pore; d: pore with black head)

Table 4: The level of patient satisfaction at the end of the treatment period (3 months after the intervention) in the two treatment groups

Satisfaction level	Study group		*P*
	BTX	NSS	
Weak	0	1	0.71
Medium	11	15	
Good	7	4	
Excellent	2	0	

Based on the results of the present study, the main concern of the treated patients was the durability of the obtained output because short-term improvement occurred for both groups, especially in the group receiving BTXA. In addition, the negative and significant correlation between pore size and patient satisfaction indicated the patient's high concern for facial pores instead of oily faces. The results of Rose and Goldberg's study (2013) showed that intra-dermal injection of BTXA reduces sebum secretion through a neuromodulatory effect on pili dilator muscles and local muscarinic receptors in the sebaceous gland.[6] In addition, relaxation of the arcuate pili muscle may also help reduce the facial pore size.[11]

In a study by Ren *et al.* (2022)[27] performed on 75 patients, the efficacy and side effects of fractional microneedle radiofrequency (FMR) for enlarged pores in different areas of the face were retrospectively analyzed. The rate of moderate to excellent improvement in patients with large skin pores for the nose, forehead, and cheek after the first session was 13.8, 8.9, and 11.1%, respectively, and the improvement rate increased with the increase in the number of treatment sessions. Although the methodology of the aforementioned study is different from the results of the present study, the findings confirm that FMR is safe and effective in improving facial enlarged pores. In other words, the application of FMR is associated with the improvement of the large pores of the nasal skin, which indicates the effectiveness of this type of treatment and is consistent with the results of the present study. Vachiramon *et al.* (2021)[28] conducted a study titled Combined Study of Microfocused Ultrasound and Hyaluronic Acid Dermal Filler in the Treatment of Large Facial Pores in Asians. The findings of the mentioned study showed that the average volume of the pores on both sides of the face decreased significantly compared to before the intervention, which was the lowest average in 4 months after the treatment. The results of the study of Shirshakova *et al.* (2021)[29] showed that BTXA for the treatment of oily facial seborrhea, enlarged pores, and post-acne symptom complex resulted in 4% increase in skin moisture index and 7% decrease in porosity during treatment. Sayed *et al.* (2019)[15] in Egypt injected BTXA intra-dermally on one side of the cheek in 20 people who suffered from large facial pores, and then NSS was injected intra-dermally on the cheek of the opposite side of the samples. The size of facial skin pores was measured at the beginning of the study and 1 month and 4 months later through a dermoscope and OCT device. The results of the aforementioned study showed that a significant decrease in the diameter of the pores was observed, which was consistent with the results of the present study.

Kim *et al.*[19] (2019) in South Korea randomly divided 24 patients with mild to moderate facial erythema into two groups. In the first group, BTXA was injected intra-dermally, and in the second group, NSS was injected into the cheeks of the patients. Then at the beginning of the study, 2, 4, 8, and 12 weeks after the treatment, the amount of sebum secretion, skin moisture, Clinician Erythema Assessment (CEA) score, erythema index, Global Aesthetic Improvement Scale (GAIS) score, and trans epidermal water loss (TEWL) were measured; all of them showed significant improvement, except for sebum secretion and TEWL. The results obtained from the aforementioned study were consistent with the results of the present study.[22]

Shuo *et al.* (2019) conducted a review study in China and concluded that in most studies, intra-dermal injection of BTXA leads to a decrease in the size of skin pores and a decrease in sebum secretion, which causes high satisfaction and no significant side effects. These findings are consistent with the results of the present study.[9]

The main limitation of the current study can be its low sample size because the results cannot be generalised to the entire society. Also, the findings of the present study showed that after 3 months, the rate of improvement in both groups (BTXA and NSS) was higher than at the beginning of the study. In order to accept the aforementioned results, it is necessary to conduct a study with a longer follow-up period, a higher sample size, and different gender groups because this methodology can also include different results. Also, the OCT device is a specialised ophthalmic device, and the use of devices that evaluate the patients' skin in a specialised way will definitely have more valuable results.

Conclusion

Based on the results of the present study, it can be concluded that intra-dermal injection of botulinum toxin A (BTXA) is an

effective and safe method for controlling facial skin pores, which gave acceptable results after 3 months. In addition, the results of the study showed that the highest amount of its effectiveness was at the beginning of the injection, and its effectiveness decreased over time. Based on the results, intra-dermal injection of NSS also had an acceptable effect in reducing the diameter of facial skin pores. The results of the present study showed that according to the patients' point of view, intra-dermal injection of BTXA caused a relative reduction in skin fat (about 40%) and a reduction in facial erythema (about 30%).

Authors' contribution

N. P. design and preparation of educational content S.A. monitoring the implementation of the plan. A.M., and M.S. conducting research and data analysis.

Ethical approval

The study protocol was approved by the Research Ethics Committees of Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran. (Ethic code: IR.AJUMS.HGOLESTAN.REC.1399.173). The IRCT registration number of this study was IRCT20210321050754N1.

Informed consent

This study was conducted with the informed consent of the participants.

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Conflicts of interest

There are no conflicts of interest.

References

1. Lee SJ, Seok J, Jeong SY, Park KY, Li K, Seo SJ. Facial pores: Definition, causes, and treatment options. J Dermatol Surg 2016;42:277-85.
2. Lee SJ, Seok J, Jeong SY, Park KY, Li K, Seo SJ. Facial pores: Definition, causes, and treatment options. J Dermatol Surg 2016;42:277-85.
3. Shaiek A, Flament F, François G, Lefebvre-Descamps V, Barla C, Vicic M, *et al.* A new tool to quantify the geometrical characteristics of facial skin pores. Changes with age and a making-up procedure in Caucasian women. Skin Res Technol 2017;23:249-57.
4. Jang SI, Kim EJ, Lee HK. A method of evaluating facial pores using optical 2D images and analysis of age-dependent changes in facial pores in Koreans. Skin Res Technol 2018;24:304-8.
5. Jung HJ, Ahn JY, Lee JI, Bae JY, Kim HL, Suh HY, *et al.* Analysis of the number of enlarged pores according to site, age, and sex. Skin Res Technol 2018;24:367-70.
6. Rose AE, Goldberg DJ. Safety and efficacy of intradermal injection of botulinum toxin for the treatment of oily skin. J Dermatol Surg 2013;39:443-8.
7. Dissanayake B, Miyamoto K, Purwar A, Chye R, Matsubara A. New image analysis tool for facial pore characterization and assessment. Skin Res Technol 2019;25:631-8.
8. Jablonska I, Mielicki W. Analysis of the effect of serum estradiol concentration on facial skin moisture, pore width, discoloration and smoothness in 16-to 50-year-old women at the 5th and 25th days of the menstrual cycle. Skin Pharmacol Appl Skin Physiol 2019;32:125-31.
9. Shuo L, Ting Y, KeLun W, Rui Z, Rui Z, Hang W. Efficacy and possible mechanisms of botulinum toxin treatment of oily skin. J Cosmet Dermatol 2019;18:451-7.
10. Khan H, Akhtar N, Ali A. Assessment of combined ascorbyl palmitate (AP) and sodium ascorbyl phosphate (SAP) on facial skin sebum control in female healthy volunteers. Curr Drug Discov Technol 2017;67:52-8.
11. Min P, Xi W, Grassetti L, Trisliana Perdanasari A, Torresetti M, Feng S, *et al.* Sebum production alteration after botulinum toxin type A injections for the treatment of forehead rhytides: A prospective randomized double-blind dose-comparative clinical investigation. Aesthet Surg J 2015;35:600-10.
12. Wu Y, Niu Y, Zhong S, Liu H, Zhen Y, Saint-Leger D, *et al.* A preliminary investigation of the impact of oily skin on quality of life and concordance of self-perceived skin oiliness and skin surface lipids (sebum). Int J Cosmet Sci 2013;35:442-7.
13. Arbuckle R, Atkinson MJ, Clark M, Abetz L, Lohs J, Kuhagen I, *et al.* Patient experiences with oily skin: The qualitative development of content for two new patient reported outcome questionnaires. Health Qual Life Outcomes 2008;6:80.
14. Weber N, Schwabe K, Schempp CM, Wölfle U. Effect of a botanical cleansing lotion on skin sebum and erythema of the face: A randomized controlled blinded half-side comparison. J Cosmet Dermatol 2019;18:821-6.
15. Sayed KS, Hegazy R, Gawdat HI, Abdel Hay RM, Ahmed MM, Mohammed FN, *et al.* The efficacy of intradermal injections of botulinum toxin in the management of enlarged facial pores and seborrhea: A split face-controlled study. J Dermatolog Treat 2021;32:771-7.
16. Qian W, Zhang YK, Hou Y, Lyu W, Cao Q, Li YQ, *et al.* Effect analysis of intradermal hyaluronic acid injection to treat enlarged facial pores. J Cosmet Dermatol 2018;17:596-9.
17. Schütz R, Rawlings AV, Wandeler E, Jackson E, Trevisan S, Monneuse JM, *et al.* Bio-derived hydroxystearic acid ameliorates skin age spots and conspicuous pores. Int J Cosmet Sci 2019;41:240-56.
18. Hexsel D, Cartier H, Hedén P, Delmar H, Bergentz P, Camozzato F, *et al.* Efficacy, safety, and subject satisfaction after AbobotulinumtoxinA treatment of upper facial lines. J Dermatol Surg 2018;44:1555-64.
19. Kim MJ, Kim JH, Cheon HI, Hur MS, Han SH, Lee YW, *et al.* Assessment of skin physiology change and safety after intradermal injections with botulinum toxin: A randomized, double-blind, placebo-controlled, split-face pilot study in rosacea patients with facial erythema. J Dermatol Surg 2019;45:1155-62.
20. Verma R, Klein G, Xu Y, Rafailovich M, Fernandez JJ, Khan SU, *et al.* Digital image speckle correlation to optimize botulinum toxin type A injection: A prospective, randomized, crossover trial. Plast Reconstr Surg 2019;143:1614-8.
21. Cavallini M, Papagni M, Gazzola R. An objective method to assess the improvements of skin texture roughness after

botulinum toxin type a treatment of crow's feet. Skin Res Technol 2019;25:54-9.

22. Ballard TN, Vorisek MK, Few JW. Impact of botulinum toxin type A treatment of the glabella and Crow's feet on static forehead rhytides. J Dermatol Surg 2019;45:167-9.
23. Sirithanabadeekul P, Lapsomboonsiri S, Rungjang A, Thanasarnaksorn W. Split face comparison between common concentration vs double dilution of intradermal abobotulinum toxin type A (Dysport) injection for facial lifting in Asians. J Cosmet Dermatol 2018;17:355-60.
24. Padulla GA, Bagatin E, Hirata SH, Yarak S. Effect of botulinum toxin type A on the healing of facial skin biopsies-series of cases. An Bras Dermatol 2018;93:610.
25. Choi JE, Werbel T, Wang Z, Wu CC, Yaksh TL, Di Nardo A. Botulinum toxin blocks mast cells and prevents rosacea like inflammation. J Dermatol Sci 2019;93:58-64.
26. Sapra P, Demay S, Sapra S, Khanna J, Mraud K, Bonadonna J. A single-blind, split-face, randomized, pilot study comparing the effects of intradermal and intramuscular injection of two commercially available botulinum toxin a formula to reduce signs of facial aging. J Clin Aesthet Dermatol 2017;10:34.
27. Ren K, Liu H, Li B, Zhou B. Fractional microneedle radiofrequency treatment for enlarged facial pores: A real-world retrospective observational study on 75 patients. J Cosmetic Dermatol 2022;21:6742-53.
28. Vachiramon V, Namasondhi A, Anuntrangsee T, Kositkuljorn C, Jurairattanaporn N. A study of combined microfocused ultrasound and hyaluronic acid dermal filler in the treatment of enlarged facial pores in Asians. J Cosmetic Dermatol 2021;20:3467-74.
29. Shirshakova M, Morozova E, Sokolova D, Pervykh S, Smirnova L. 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. Int J Dermatol 2021;60:1232-41.