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Unparallel improvement patterns of dynamic wrinkles and skin quality after botulinum toxin type A treatment on the upper face

Yixin Sun[1] | **Yunzhu Li**[1] | **Yixuan Zhang**[1] | **Ruijia Dong**[2] | **Xinze Lan**[3] | **Mengyuan Zhang**[1] | **Nanze Yu**[1] | **Xiao Long**[1]

[1]Department of Plastic Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

[2]Department of Plastic Surgery, Beijing Tsinghua Changgung Hospital, Tsinghua University, Beijing, China

[3]School of Computing, National University of Singapore, Singapore, Singapore

Correspondence
Nanze Yu and Xiao Long, Department of Plastic Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, No.1, Shuaifuyuan, Dongcheng District, Beijing 100005, China.
Email: yunanze@pumch.cn; pumclongxiao@126.com

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Abstract

Background: Botulinum toxin type A (BoNT-A) can not only reduce the dynamic wrinkles but also improve the skin quality. This study aims to quantitaively and comprehensively assess the improvement of dynamic wrinkles and skin quality following BoNT-A treatment on the upper face.

Methods: Patients were recruited to receive BoNT-A treatment of the glabellar, frontal, and lateral periorbital wrinkles. Antera 3D camera was used to evaluate the skin quality and dynamic wrinkle severity. Follow-up visits were at 1 week, 1 month, 3 months, and 6 months after treatment. Different filters were utilized to quantitatively detect the severity of fine wrinkles (FWS), the volume of pores (PV), the roughness of skin texture (STR), and the severity of dynamic wrinkles (DWS).

Results: Twenty-four participants (average 30.5 $\pm$ 7.2 years) were recruited. The significant improvement of PV, FWS, and STR in different areas usually maintained from 1 to 6 months after injections but of DWS only existed within 3 months. For each area, the improvement rates of FWS, PV, and STR peaked at 3 months or 6 months after treatment while the maximal improvement of DWS was observed at 1 month posttreatment.

Conclusion: After BoNT-A treatment for dynamic wrinkles on the upper face, the skin quality of target regions can also be ameliorated. The improvement of skin quality and dynamic wrinkles presented unparallel patterns. The former is with a slower onset but longer duration while the latter exhibits a more rapid onset but shorter duration.

KEYWORDS
botulinum toxin type A, fine wrinkles, pores, skin quality

Yixin Sun, Yunzhu Li, and Yixuan Zhang authors contributed equally to this work.

1 | INTRODUCTION

Botulinum toxin type A (BoNT-A) is a neurotoxin that blocks the release of acetylcholine at neuromuscular junctions by cleaving synaptosomal-associated protein 25,[1] inducing reversible relaxation of facial muscles.[2] BoNT-A injections are frequently administered into the subcutaneous or intramuscular layers to alleviate dynamic wrinkles.[3] However, many patients and doctors have observed that BoNT-A's effects may go beyond its intended short-term outcome on muscular activity during clinical practice.[4] Increasing evidence demonstrates progressive improvements in skin quality after regular treatments with BoNT-A,[5,6] which suggests the production of sebum and skin remodeling may be also regulated by BoNT-A.

Efficacy evaluation after BoNT-A treatment can be classified as subjective and objective methods. Numerous rating scales, such as the Facial Wrinkle Scale[5] and the Wrinkle Severity Rating Scale,[7] are examples of subjective approaches. The primary drawback of the subjective scales is that they are prone to subjective bias while scoring. For assessing the change of skin quality, the grading scales are too imprecise to detect the subtle difference. The newly developed objective evaluation such as various three-dimensional (3D) devices like Antera and Vectra,[8] fills in the gaps left by subjective evaluation. These equipments can quantitatively and objectively measure the wrinkle severity and topographical characteristics relating to the skin quality, like pores and fine lines,[8] enabling the accurate efficacy assessment.

Few attempts have been made to comprehensively and quantitatively capture the skin change after BoNT-A treatments with an objective device. This study aims to assess the improvement of dynamic wrinkles and skin quality following BoNT-A treatment on the upper face with Antera 3D camera and compare the onset and duration of the two different effects.

2 | METHODS

2.1 | Study design and patients

This prospective study was approved by the ethics committee of Peking Union Medical College Hospital (SK-1556) and registered on Chinese Clinical Trial Registry (ChiCTR2100046880). All participants signed written consent. Patients were eligible if they were healthy adults aged 18–65 years, with moderate or severe dynamic forehead, glabellar, and lateral periorbital wrinkles and without neuromodulator or filler injections in the previous year. The exclusion criteria include visible scars and infection in the upper face, pregnancy, lactation, and hypersensitivity to BoNT-A.

2.2 | Injection technique

All patients received Botox (Allergan, USA) injections. One hundred units of BoNT-A were reconstituted with 2.5 ml of 0.9% sterile physiologic saline. Compound lidocaine cream (Tongfang Pharm. Group, Beijing, China) was applied to relieve pain 30 min before treatment. For the forehead wrinkles, injections were administrated subcutaneously in two rows with 0.5U on each site. Six sites and 7 sites were selected in the upper row and the lower row, respectively. The lower row was 2 cm above the eyebrow to avoid brow ptosis. For the glabellar wrinkles, the medication was delivered to the periosteum at the origin of the corrugator supercilii and subcutaneously at its insertion with 4 U on each site. An additional injection with 2 U was performed in the center of glabellar area to block the procerus. For the lateral periorbital lines, injections were performed subcutaneously at three sites distributing around the lateral canthus evenly with 2 U on each site (Figure 1). All injections were administrated by an experienced plastic surgeon (Y.L.) with 30G needles, 1.3 cm in length (Becton Dickinson Labware, NJ, USA).

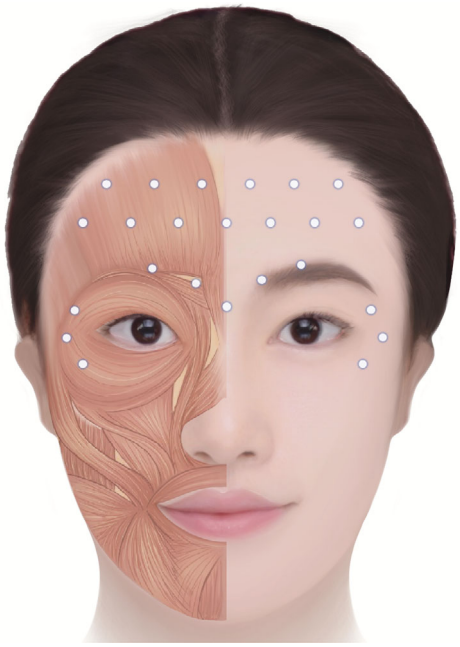

FIGURE 1 The distribution of injection sites for treating frontal, glabellar, and lateral periorbital wrinkles. Thirteen sites were chosen to block the frontalis with 0.5 U on each site in the frontal region, distributed evenly over two rows. In the glabellar area, the botulinum toxin type A was delivered to the origin and insertion of the corrugator supercilii with 4 U on each site. An additional injection of 2 U was performed in the center of the glabellar area to block the procerus. In the lateral periorbital area, injections were administrated at three sites around the lateral canthus with 2 U on each site.

2.3 | Outcome measurement

Antera 3D camera (Miravex, Dublin, Ireland) was utilized to assess the skin quality and dynamic wrinkle severity before treatment and at 1 week, 1 month, 3 months and 6 months after treatment. Four areas on the face, including the mid-forehead, glabellum and bilateral lateral canthus, were captured three times at rest and maximum muscle activity. Three filters including wrinkle-small, pore-small and skin texture-small were used to quantitatively detect the severity of fine

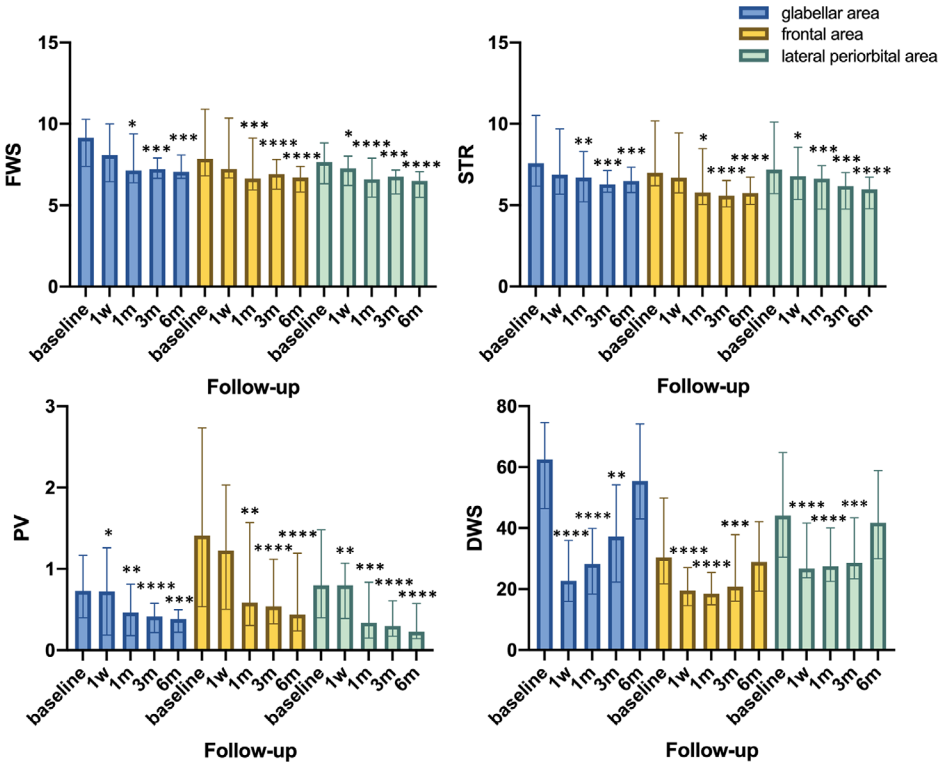

FIGURE 2 The value of FWS (A), PV (B), STR (C), and DWS (D) at each follow-up visit. Blue color: glabellar area, yellow color: the frontal area, green color: for the periorbital area. DWS, dynamic wrinkle severity; FWS, fine wrinkle severity; PV, pore volume; STR, skin texture roughness. The symbol of " * " represents for a significant difference from the baseline. $^{****}p < 0.0001$; $^{***}p < 0.001$; $^{**}p < 0.01$; $^{*}p < 0.05$.

wrinkles (FWS), the volume of pores (PV), and the roughness of skin texture (STR) at rest respectively. The filter called wrinkle-medium was used to quantitatively detect the severity of dynamic wrinkles (DWS) at maximum muscle activity. Complications were also recorded during follow-ups.

2.4 | Statistical analysis

The Shapiro-Wilk test was performed to detect the normality of the collected data. FWS, PV, and STR were expressed as median (interquartile range). Wilcoxon matched-pairs signed rank test was performed to detect the difference. An index called the improvement rate was introduced to compare the change rates of different parameters with time. The improvement rate was defined as (baseline- follow-up)/baseline * 100%. $p < 0.05$ was considered statistically significant. All the data were analyzed by GraphPad Prism software version 9.0 for Mac.

3 | RESULTS

3.1 | Baseline characteristics

24 participants aged 21–44 (average 30.5 ± 7.2 years) were enrolled in the study, including 5 males and 19 females. All the participants completed the follow-up visits. The data were gathered between April 2021 and January 2022.

3.2 | FWS

FWS first showed significant improvement in all three areas 1 month after injection (the glabellar area: $p = 0.0004$; the frontal area: $p = 0.0105$; the periorbital area: $p < 0.0001$). The significant improvement was maintained from 1 month to 6 months after BoNT-A treatment (Figure 2A). The representative cases are presented in Figure 3.

3.3 | PV

For the frontal area, PV was improved significantly at 1 month ($p = 0.0138$) posttreatment and remained stable for the following 5 months. Regarding the glabellar and periorbital areas, significant improvement of PV was first observed at 1 week (the frontal area: $p = 0.0014$; the periorbital area: $p = 0.0003$) and this pore-shrinking effect also persisted for another 5 months (Figure 2B). The representative cases were presented in Figure 4.

3.4 | STR

For the glabellar and frontal areas, significant improvement of STR was first noticed at 1 month (the glabellar area: $p = 0.0011$; the frontal area: $p = 0.0211$), and it persisted for the subsequent 5 months. For the lateral periorbital area, the improvement of STR became

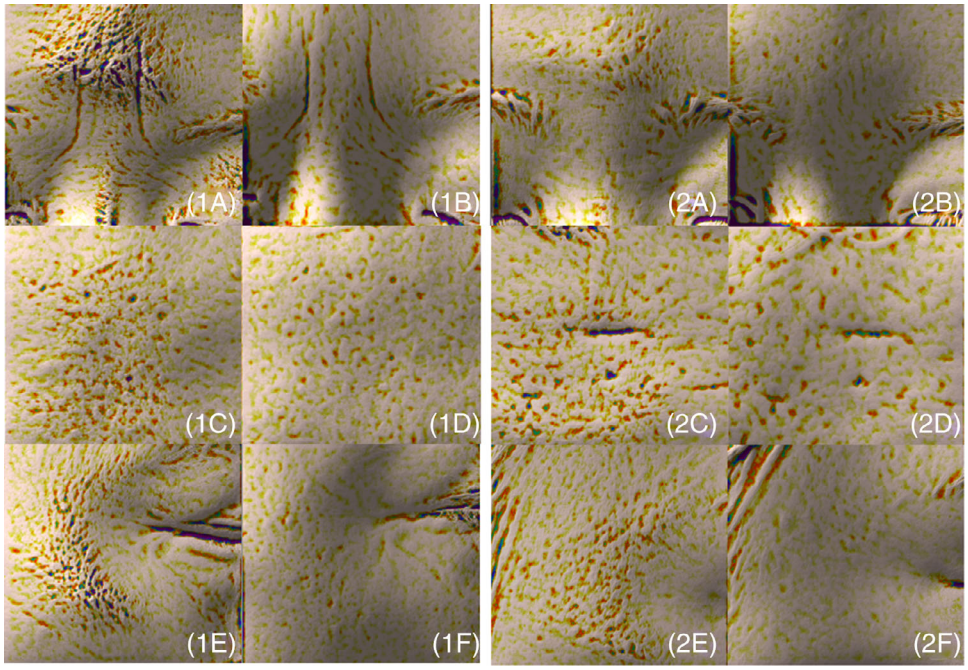

FIGURE 3 3D photographs with "wrinkle-small" filter showing the fine wrinkles. The glabellar area (1A), frontal area (1C) and periorbital area (1E) of a 38-year-old female at baseline. The glabellar area (1B), frontal area (1D) and periorbital area (1F) of the 38-year-old female at 3 months after treatment. The glabellar area (2A), frontal area (2C), and periorbital area (2E) of a 32-year-old female at baseline. The glabellar area (2B), frontal area (2D), and periorbital area (2F) of the 32-year-old female at 3 months after BoNT-A treatment.

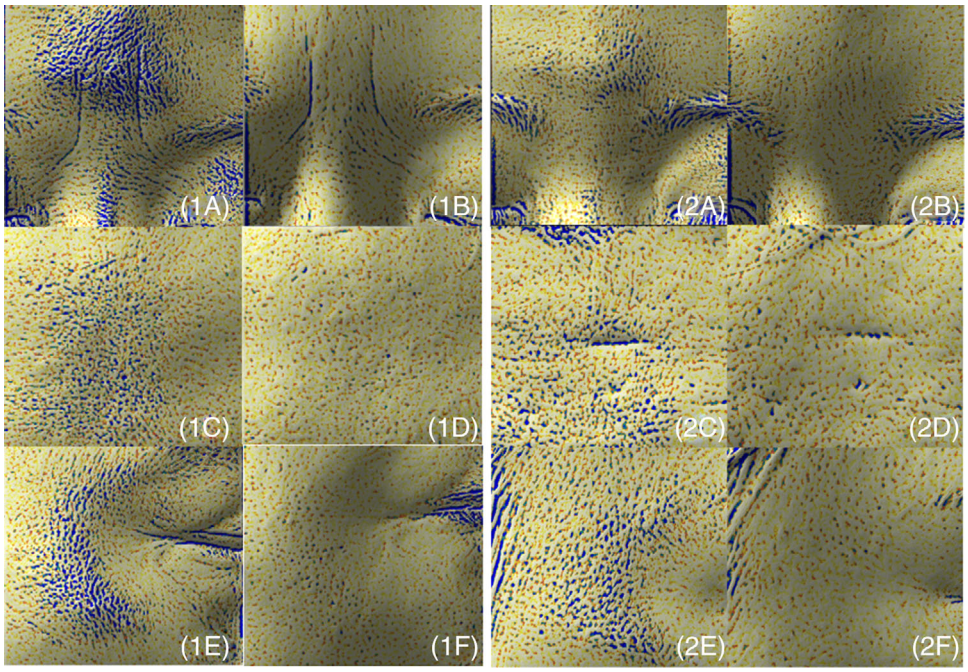

FIGURE 4 3D photographs with "pore-small" filter showing the pores. The glabellar area (1A), frontal area (1C) and periorbital area (1E) of a 38-year-old female at baseline; the glabellar area (1B), frontal area (1D) and periorbital area (1F) of the 38-year-old female at 3 months after BoNT-A treatment. The glabellar area (2A), frontal area (2C) and periorbital area (2E) of a 32-year-old female at baseline; the glabellar area (2B), frontal area (2D), and periorbital area (2F) of the 32-year-old female at 3 months after BoNT-A treatment.

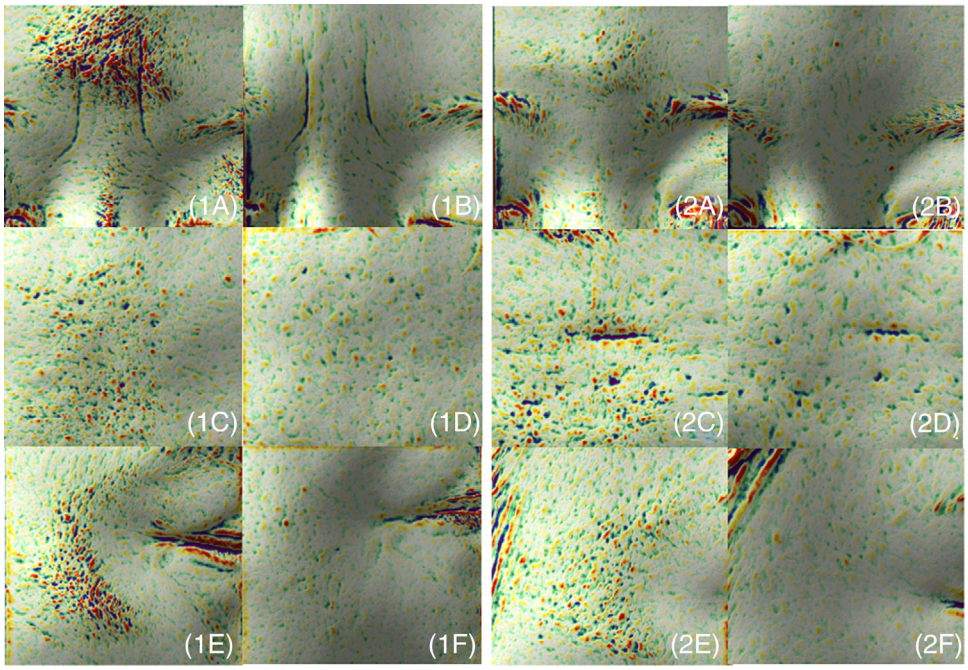

FIGURE 5 3D photographs with "skin texture-small" filter showing the skin texture. The glabellar area (1A), frontal area (1C) and periorbital area (1E) of a 38-year-old female at baseline. The glabellar area (1B), frontal area (1D) and periorbital area (1F) of the 38-year-old female at 3 months after BoNT-A treatment; the glabellar area (2A), frontal area (2C) and periorbital area (2E) of a 32-year-old female at baseline. The glabellar area (2B), frontal area (2D), and periorbital area (2F) of the 32-year-old female at 3 months after BoNT-A treatment.

statistically significant at the first follow-up visit (1 week after treatment; $p = 0.0395$), and the difference was sustained at 6 months after injection (Figure 2C). The representative cases are presented in Figure 5.

3.5 | DWS

Significant improvement was observed in each of the three areas at 1 week (the glabellar area: $p = 0.0004$; the frontal area: $p = 0.0105$; the periorbital area: $p < 0.0001$) after injection. The difference gradually diminished and fell below significance after 3 months but still existed at 6 months postinjection (Figure 2D).

3.6 | The improvement rates

For the glabellar area, the improvement rates of FWS, PV, and STR peaked at 3 months (15.7% [21.3%]), 3 months (46% [55.3%]), and 6 months(12.18% [17.7%]) respectively, whereas the improvement rate of DWS peaked at 1 week (82.54% [35.31%]) after injection and then declined over time (Figure 6A).

For the frontal area, the skin quality was steadily improved after injection with the greatest improvement observed at 6 months posttreatment for FWS (18.52% [19.1%]), PV (39.77% [66.5%]), and STR (23.01% [23.9%]). On the contrary, the median improvement rate of DWS reached the maximum at 1 week (63.43% [38.0%]) after injection and declined to 10.22% (89.6%) at 6 months (Figure 6B).

For the lateral periorbital area, the change patterns of DWS and parameters related to the skin quality were analogical to those of the frontal area. The maximal improvement rates were observed at 3 months for FWS(14.30% [18.4%]), and at 6 months for PV (64.06% [43.3%]) and STR (19.91% [28.6%]), but the maximum improvement rate of DWS (48.06% [51.4%]) was observed at just 1 week posttreatment (Figure 6C).

3.7 | Complications

Three patients (12.5%) reported mild bruises in the injection area which resolved spontaneously in 2 weeks. No severe complications like diplopia, ptosis, and headache were recorded.

4 | DISCUSSION

Numerous investigations have proven the outstanding efficiency of BoNT-A in treating various dynamic wrinkles. Microbotulinum, a novel injection technique of BoNT-A, exhibited exceptional efficacy in improving the appearance of skin, such as treating facial erythema,[9] oily skin,[10] and acne.[11] The injection layers of conventional wrinkle treatment and Microbotulinum are different, the former delivering the medication into the subcutaneous or intramuscular layer and the latter into the intradermal layer.[12,13] In clinical settings, the improvement of skin quality can also be observed after conventional wrinkle treatment, but it has not been well documented. Studies exploring the onset

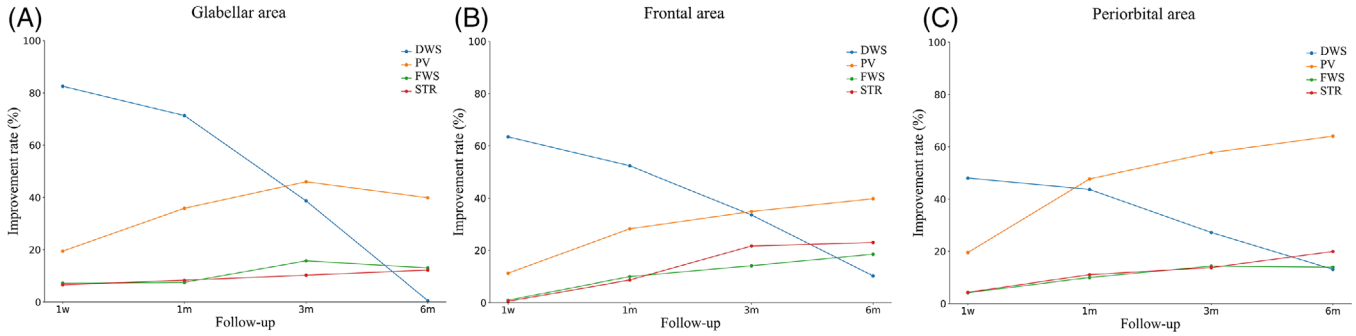

FIGURE 6 Improvement rates of FWS, PV, STR, and DWS in the glabellar area (A), the frontal area (B), the periorbital area (C). DWS, dynamic wrinkle severity; FWS, fine wrinkle severity; PV, pore volume; STR, skin texture roughness.

and durability of BoNT-A's effectiveness on dynamic wrinkles and skin quality are lacking as well. Our study has demonstrated long-lasting improvement in several attributes relating to skin quality following conventional wrinkle treatment on the upper face through objective and quantitative assessment. The improvement rates of dynamic wrinkles peaked at 1 week after treatment and gradually decreased over time, whereas the improvement rates of parameters relating to skin quality continued to rise over time, displaying unparallel improvement patterns.

The median improvement rate of PV was found to be remarkably high. Pores detected by Anetra 3D camera in this study are apertures of pilosebaceous follicles, which shrink when sebum secretion is reduced and local skin elasticity is increased.[11,14] Multiple mechanisms are involved in the pore-shrinkage effect induced by BoNT-A. First, it may reduce sebum production by preventing cholinergic signals from reaching sebaceous glands. By interacting with the alpha 7 nicotinic acetylcholine receptor(α7nAChR) of sebocytes, acetylcholine indirectly activated MAPK/ERK pathway,[15] upregulating sebum secretion in a dose-dependent manner. The BoNT-A inhibits the release of acetylcholine, which blocks the pathway and prevents the production of sebum. Second, BONT-A may reduce sebum excretion by suppressing the contraction of the arrector pili muscle, a smooth muscle controlled by a small amount of cholinergic nerve.[16] The arrector pili muscle contracts, compressing the acini of the sebaceous gland, causing sebaceous fluids to be expelled.[17] Less sebum is excreted because BoNT-A partially denervates the arrector pili muscle. Finally, BoNT-A may improve skin elasticity and then minify facial pores by blocking the interaction between acetylcholine and α7nAChR[18] and alpha 3 nicotinic acetylcholine receptor (α3nAChR),[19] which is involved in tissue remodeling. This process may also be responsible for the decrease in fine wrinkles that was seen after BoNT-A treatment. Since the rigidification of the stratum corneum and thinning of the dermal layer are related to the development of fine wrinkles,[20] BoNT-A regulated collagen homeostasis and enhanced skin elasticity, leading to the smoothing of skin[18,19] (Figure 7).

Interestingly, the improvement patterns of dynamic wrinkles and skin quality after treatment are not parallel. The two differ in that the former has a rapid onset and short duration but the latter has a sluggish onset but protracted duration, which shows that the underlying

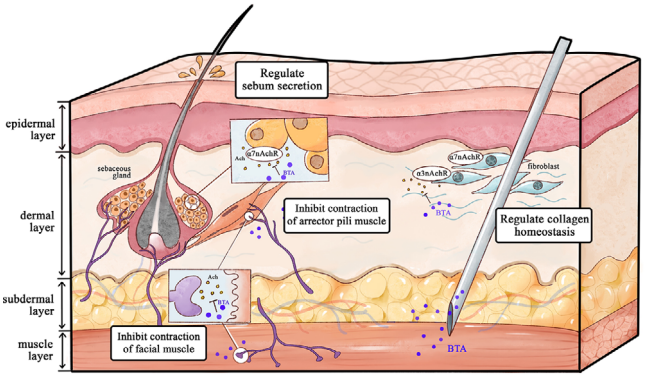

FIGURE 7 The possible mechanism of improving skin quality and reducing wrinkles by botulinum toxin type A(BoNT-A). BoNT-A diffuses to the dermal and musle layer after subdermal injection. It affects the interaction between acetylcholine(Ach) and its receptors (alpha 3 nicotinic acetylcholine receptor, α3nAChR; alpha 7 nicotinic acetylcholine receptor, α7nAChR) in sebocyte and fibrblast to regulate sebum secretion and collagen homeostasis. Besides, BoNT-A inhibits the release of acetylcholine at the neuromuscular junction and then blocks the contraction of facial muscle as well as the arrector pili muscle.

mechanisms for reducing dynamic wrinkles and improving skin quality are distinct. BoNT-A paralyzes the facial muscles by forming an irreversible bond with the synaptic membrane and blocking the neuronal pulse. The neuronal transmission is blocked once the previously stored acetylcholine is completely removed, which explains the quick onset (within 1 week in our findings).[21] According to earlier studies and our results, the paralyzing effect can endure for 3–6 months.[22] During this period, new axons are generated to replace the dysfunctional ones, gradually restoring the muscles' strength.[23] However, nonneuronal cholinergic pathways, including neuroendocrine activities and consequent metabolic reactions, are the principal method that BoNT-A influences skin quality. Although it may begin slowly, the procedure ultimately takes longer. For instance, the synthesis of collagen and remodeling of skin elasticity take time but result in a longer-lasting reduction of fine wrinkles. Regarding the shrinkage of pores, BoNT-A reduces the production of sebum and the number of sebocytes and

hair follicles,[24] which normally take months to recover from, explaining why the improvement of pores persisted over 6 months (Figure 7).

Our study had some limitations. First, only a small population with a limited study period was investigated. A larger sample size with more intensive and long-term follow-up visits may demonstrate a more comprehensive view of the improvement patterns after treatment. Second, subpopulation analysis was not performed. For further studies, patients can be classified into different subgroups according to their age, sex, and other factors, which may contribute to the pharmacodynamics of BoNT-A. Third, basic experiment verification was not conducted. Further molecular, cellular, and animal experiment can be conducted to explore the specific mechanisms of skin quality improvement after BoNT-A injection.

5 | CONCLUSION

With objective assessment, the reduction of dynamic wrinkles as well as the improvement of skin quality was observed after BoNT-A treatment. Unparallel improvement patterns of dynamic wrinkles and skin quality were presented. The former presents a slower onset but longer duration while the latter exhibits a more rapid onset but relatively shorter duration. The findings of this study provided new insights for facial BoNT-A treatment.

5.1 | Ethical approval and consent to participate

This study conformed to the 1975 Declaration of Helsinki ethical principles and was approved by Peking Union Medical College Hospital (number: S-K1556). All participants signed the written consent.

ACKNOWLEDGMENTS

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author (N.Y.).

REFERENCES

1. Eleopra R, Tugnoli V, Rossetto O, De Grandis D, Montecucco C. Different time courses of recovery after poisoning with botulinum neurotoxin serotypes A and E in humans. *Neurosci Lett*. 1998;256(3):135-138.
2. Satriyasa BK. Botulinum toxin (Botox) A for reducing the appearance of facial wrinkles: a literature review of clinical use and pharmacological aspect. *Clin Cosmet Investig Dermatol*. 2019;12:223-228.
3. Ascher B, Klap P, Marion MH, Chanteloub F. Botulinum toxin in the treatment of frontoglabellar and periorbital wrinkles. An initial study. *Ann Chir Plast Esthet*. 1995;40(1):67-76. (in French)
4. Humphrey S, Jacky B, Gallagher CJ. Preventive, cumulative effects of botulinum toxin type A in facial aesthetics. *Dermatol Surg*. 2017;43 Suppl 3:S244-5251.
5. Carruthers A, Carruthers J, Fagien S, Lei X, Kolodziejczyk J, Brin MF. Repeated onabotulinum toxin A treatment of glabellar lines at rest over three treatment cycles. *Dermatol Surg*. 2016;42(9):1094-1101.
6. Rivkin A, Binder WJ. Long-term effects of onabotulinumtoxin A on facial lines: a 19-year experience of identical twins. *Dermatol Surg*. 2015;41 Suppl 1:S64-566.
7. Qiao J, Jia QN, Jin HZ, et al. Long-term follow-up of longevity and diffusion pattern of hyaluronic acid in nasolabial fold correction through high-frequency ultrasound. *Plast Reconstr Surg*. 2019;144(2):189e-196e.
8. Linming F, Wei H, Anqi L, et al. Comparison of two skin imaging analysis instruments: the VISIA(®) from Canfield vs the ANTERA 3D(®) CS from Miravex. *Skin Res Technol*. 2018;24:3-8.
9. Eshghi G, Khezrian L, Alirezaei P. Botulinum toxin A in treatment of facial flushing. *Acta Med Iran*. 2016;54(7):454-457.
10. 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(10):1232-1241.
11. Kim BY, Choi JW, Park KC, Youn SW. Sebum, acne, skin elasticity, and gender difference - which is the major influencing factor for facial pores? *Skin Res Technol*. 2013;19(1):e45-53.
12. Rzany B, Ascher B, Fratila A, Monheit GD, Talarico S, Sterry W. Efficacy and safety of 3- and 5-injection patterns (30 and 50 U) of botulinum toxin A (Dysport) for the treatment of wrinkles in the glabella and the central forehead region. *Arch Dermatol*. 2006;142(3):320-326.
13. Wu WTL. Microbotox of the lower face and neck: evolution of a personal technique and its clinical effects. *Plast Reconstr Surg*. 2015;136(5 Suppl):92S-100S.
14. Roh M, Han M, Kim D, Chung K. Sebum output as a factor contributing to the size of facial pores. *Br J Dermatol*. 2006;155(5):890-894.
15. Li ZJ, Park SB, Sohn KC, et al. Regulation of lipid production by acetylcholine signalling in human sebaceous glands. *J Dermatol Sci*. 2013;72(2):116-122.
16. Donadio V, Incensi A, Vacchiano V, Infante R, Magnani M, Liguori R. The autonomic innervation of hairy skin in humans: an in vivo confocal study. *Sci Rep*. 2019;9(1):16982.
17. Song WC, Hu KS, Kim HJ, Koh KS. A study of the secretion mechanism of the sebaceous gland using three-dimensional reconstruction to examine the morphological relationship between the sebaceous gland and the arrector pili muscle in the follicular unit. *Br J Dermatol*. 2007;157(2):325-330.
18. Stegemann A, Raker V, Del Rey A, Steinbrink K, Böhm M. Expression of the α7 nicotinic acetylcholine receptor is critically required for the antifibrotic effect of PHA-543613 on skin fibrosis. *Neuroendocrinology*. 2022;112(5):446-456.
19. Arredondo J, Hall LL, Ndoye A, et al. Central role of fibroblast alpha3 nicotinic acetylcholine receptor in mediating cutaneous effects of nicotine. *Lab Invest*. 2003;83(2):207-225.
20. Batisse D, Bazin R, Baldeweck T, Querleux B, Lévêque JL. Influence of age on the wrinkling capacities of skin. *Skin Res Technol*. 2002;8(3):148-154.
21. Kattimani V, Tiwari RVC, Gufran K, Wasan B, Shilpa PH, Khader AA. Botulinum toxin application in facial esthetics and recent treatment indications (2013-2018). *J Int Soc Prev Community Dent*. 2019;9(2):99-105.

22. Nestor M, Cohen JL, Landau M, et al. Onset and duration of abobotulinumtoxin A for aesthetic use in the upper face: a systematic literature review. *J Clin Aesthet Dermatol*. 2020;13(12):E56-83.
23. Niamtu J 3rd. Aesthetic uses of botulinum toxin A. *J Oral Maxillofac Surg*. 1999;57(10):1228-1233.
24. Kucukkaya D, Irkoren S, Ozkan S, Sivrioglu N. The effects of botulinum toxin A on the wound and skin graft contraction. *J Craniofac Surg*. 2014;25(5):1908-1911.

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