

Clinical Observation of Botulinum Toxin Type A Combined with Nanofat in Facial Rejuvenation Treatment

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Abstract: *Objective:* To investigate the efficacy of botulinum toxin type A combined with nanofat in the treatment of facial rejuvenation. *Methods:* from January 2020 to January 2021, 20 patients with facial wrinkles in our hospital (The First Affiliated Hospital of Dalian Medical University) were treated with botulinum toxin type A combined with nanofat, and the effect, duration and complications were observed. *Results:* After 1, 3 and 6 months of injection, the effective rates were 90%, 75% and 40%, respectively; there was no occurrence of postoperative infection, fat mass, granuloma, and other adverse reactions. *Conclusion:* Botulinum toxin type A combined with nanofat filling has a clear therapeutic effect in the facial rejuvenation treatment, and can improve the skin texture while improving wrinkles, which is worthy of further popularization and application in clinic.

Keywords: Botulinum toxin type A; Nanofat; Facial rejuvenation

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1. Introduction

Facial rejuvenation is pursued by more and more beauty seekers, which makes it one of the directions of plastic surgeons' exploration and research. Facial wrinkle is one of the manifestations of facial aging. It is a clinical manifestation caused by the increase of free radicals in the skin caused by various factors, which destroys the active substances of normal cells and the normal physiological function of collagen ^[1]. Botulinum toxin type A is a neurotoxin, which can play the role of muscle paralysis for a short time by injection, to remove facial wrinkles; the concept of nanofat, was first proposed by Professor Patrick Tonnard ^[2] from Belgium in 2013. It reconstructs the internal structure of the affected skin through the enriched pluripotent differentiated stem cells in nanofat, to improve the skin texture and surface fine lines, and finally achieve the effect of rejuvenation. Our hospital (The First Affiliated Hospital of Dalian Medical University) combined botulinum toxin type A and nanofat injection for facial rejuvenation treatment, and achieved good results, which are reported as follows.

2. Materials and methods

2.1. Clinical data

Methods: 20 female patients with facial wrinkles in our hospital from January 2020 to January 2021, aged between 35 and 55 years, were selected, including 5 patients with frontal lines group, 6 patients with crow's

feet, 3 patients with perioral lines, and 6 patients with mixed wrinkles. The patients were graded according to the severity of wrinkles: Grade I, mild, no wrinkles in static state, only continuous skin lines, and small wrinkles in dynamic state; Grade II, moderate, visible in static state and skin fold lines and fine facial wrinkles, obvious in dynamic state; Grade III, severe, deep wrinkles can be seen in static state, facial wrinkles are clear, and more obvious in dynamic state; Grade IV, extremely severe, with significant wrinkles and deep and long folds in static state, and obvious wrinkles can still be seen when the skin is stretched. We selected patients of Grade II to III.

2.2. Treatment methods

2.2.1. Materials and equipment

Hengli botulinum toxin type A lyophilized preparation (100u/ piece) produced by Lanzhou Institute of Biological Products, China; 20ml thread syringe (kantley), nanofat emulsifier (as shown in **Figure 1**).



Figure 1. Nanofat treatment connector

2.2.2. Injection method

The patients signed a consent form, the liposuction site and the site to be treated were marked with a scribe pen, and an aseptic towel was placed onto the area. Local swelling anesthesia (400 mg lidocaine + 0.5 mg epinephrine hydrochloride injection + 250mg sodium bicarbonate injection mixed with 500ml normal saline) was injected into the liposuction site. The liposuction tube was connected with 20ml threaded syringe for low negative pressure manual suction from the fat dense parts of the patients such as the thigh, or the lateral or lower abdomen. After liposuction, the patient was instructed to stand for 10 min. It was found that the bottom layer was a mixture of reddish swelling liquid and bloody liquid, the middle layer was a connective tissue layer with high density, and the top layer was adipose tissue (as shown in **Figure 2**). The bottom and middle layers were removed, the remaining top layer adipose tissue was filtered. Two 20ml threaded syringes were connected with a converter connector, quickly and repeatedly inject for 30 times. Then, mechanical emulsification treatment was carried out, and the liquid was filtered again with a 0.5 mm aperture filter screen. The obtained fat emulsion is nanofat (as shown in **Figure 3**). A 1 ml syringe (produced by BD company in the United States) was used to extract the nanofat, and a 27 g injected needle was connected as a standby.



Figure 2. Stratification of the fat after resting



Figure 3. Nanofat production process

100u botulinum toxin type A was dissolved in 2.5 ml normal saline. A 1ml syringe (the same as above) was connected to a 30 g injection needle and injected vertically into the subcutaneous muscle layer at the wrinkles. The injection points were evenly selected. The frontal line group was injected at an interval of 2 cm, the crow's feet group and the perioral line group were injected at an interval of 1.5 cm, and the injection volume at each point was 0.1 ml. Generally, the injection volume should be appropriately increased or reduced according to the actual situation of the patient.

The prepared nanofat was injected into the deep fan-shaped dermis at the wrinkles of the patient until the skin color turned yellow. The injection should be gentle, and attention should be paid to avoid puncturing blood vessels and avoid seroma. The yellow color of the skin usually disappears spontaneously after several hours of injection.

3. Results

The photos before and after treatment were compared with static and dynamic facial expressions. The photos were taken by a fixed photographer and shooting conditions, and the photos were scored by a physician. The therapeutic effect was determined according to the grading, that is, the static pre and post difference + the dynamic pre and post difference ≥ 2 is considered significantly effective, ≥ 1 was considered effective, and 0 was considered invalid. The curative effect was observed at 1, 3, and 6 months after injection, and the significant efficiency was 90%, 75%, and 40%, respectively; No postoperative infection, fat mass, granuloma and other adverse reactions occurred (**Table 1**).

Table 1. Analysis of the number of cases with curative effect after 1, 3, 6 months of treatment

	1 month	3 months	6 months
Markedly effective	18	15	8
Effective	1	3	8
Invalid	1	2	4

4. Discussion

Botulinum toxin type A is a high molecular weight protein neurotoxin, which has been widely used in clinics. It reduces or eliminates wrinkles by acting on cholinergic motor nerve terminals, inhibiting the release of acetylcholine from presynaptic membrane, leading to muscle relaxation and paralysis ^[3].

The concept of nanofat may become a milestone in the development of autologous fat transplantation, allowing new development direction for autologous fat in the field of non-structural transplantation. Tonnard et al. isolated and cultured nanofat to obtain SVF (stromal vascular component) cells, the number

of which is about 2/3 of the same volume of granular fat, while the main stem cells of SVF are ADSCs (adipose derived mesenchymal stem cells), indicating that there are still many ADSCs in nanofat, and the dryness of these mesenchymal stem cells is confirmed by CD34+ detection and differentiation induction. Several wound healing studies have shown that ADSCs and cytokines secreted by ADSCs in adipose tissue can promote fibroblast proliferation, increase collagen synthesis, antioxidant, and other effects [4]. Through follow-up of patients with traditional fat transplantation, we found that their skin wrinkles decreased, elasticity increased, pores narrowed, and their skin color was uniform at the fat transplantation site, which was caused by the differentiation of ADSCs into different tissue cells, thus promoting tissue repair and function improvement [5]. Tamburino et al. [6] reported in January 2016 that 20 ml of nano fat was injected into the skin near the vaginal orifice and clitoris a female patient with atrophic sclerosing lichen vulvae. The 10-month follow-up showed that the lesion skin texture and labia magna morphology were significantly restored, which was due to the skin regeneration promoting ability of stem cells in nanofat. Huang et al. [7] proved that nanofat can promote collagen production, microvessel density increase and epidermal cell proliferation in the dermis, thereby improving skin aging through experimental research on nanofat improving the texture of photoaging skin in nude mice in August 2016. In 2019, Cao et al. [8] also achieved remarkable results by improving the treatment of facial scars with nano fat transplantation. Nanofat is a compact stem cell bundle with regeneration and tissue remodeling potential, which has potential in translational and regenerative medicine [9].

Our hospital improved facial aging through the combined injection of botulinum toxin type A and nano fat, and the effect was clear. It can not only reduce or eliminate facial wrinkles, but also improve the texture of the skin, enhance the color and elasticity of the face. The combined application of botulinum toxin A and nanofat can increase the precision and stability of the injection site, with more lasting clinical effects. It has a broad development prospect in cosmetic surgery. Autologous fat transplantation fully considers individual genetics, race and facial fat density and distribution, and has rich materials, low rejection rate and good biocompatibility, which has a positive effect on improving facial disease defects or aging of patients [10].

However, there are also shortcomings. It can be seen from **Table 1** that the effective rate gradually declines over time. This means that repeated injections are needed for this treatment to maintain a stable effect. Hence, further studies need to be on the effective duration of the combination of the two in facial rejuvenation treatment.

Disclosure statement

The authors declare no conflict of interest.

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