Comparison of single-point injection of 50 units of abobotulinum toxin A in the procerus muscle versus five-point injection methods in the treatment of glabellar lines

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Background: Injectable neuromodulators are commonly used in facial aesthetic procedures, particularly for treating glabellar wrinkles. The five-point injection technique is widely utilized; however, the effectiveness of a single injection into the procerus muscle has not yet been evaluated. This study aimed to compare the efficacy of a single-point injection of 50 units of abobotulinum toxin A into the procerus muscle with that of the five-point injection technique using the same dose for treating glabellar lines.

Methods: Eleven patients received a single injection of 50 units of abobotulinum toxin A into the procerus muscle, while nine patients received a total of 50 units divided equally across five injection sites. For patients requiring a touch-up injection at week two, five to ten units of abobotulinum toxin A were administered. The evaluation of results was based on measuring the distance between the medial eyebrow heads at baseline, week two and week four. Changes in this distance before and after the procedure were then analyzed.

Results: Repeated measures ANOVA indicated a significant change in the distance between the medial eyebrow heads from baseline through week four for both techniques ($P = 0.03$ and $P < 0.01$ for the five-point and single-point injection techniques, respectively). However, there was no significant difference between the two techniques at week two and week four ($P = 0.91$ and $P = 0.72$, respectively).

Conclusion: The efficacy of the single-point injection method in treating frown lines is comparable to that of five-point injection method.

Keywords: Botulinum toxin type A, procerus muscle, single-point injection technique, five-point injection technique, glabellar line

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What is already known on the subject?

- The efficacy and safety of the five-point botulinum toxin injection technique for treating glabellar lines have been well documented and widely accepted.

The study's main messages:

- A single-point injection of 50 units of

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abobotulinum toxin A into the procerus muscle is an effective treatment for glabellar lines, demonstrating results comparable to that of five-point injection technique.

INTRODUCTION

The treatment of glabellar wrinkles has gained popularity as a cosmetic procedure in recent decades. These wrinkles are primarily caused by the hyperactivity of the depressor glabellar muscle complex, particularly the procerus and corrugator muscles. Since its FDA approval in 2002, botulinum toxin type A injections have emerged as the most popular technique for treating facial aging, especially glabellar lines [1].

Although the original objective of botulinum toxin type A treatment was to paralyze the target muscles, the current focus has shifted toward modulating muscular activity. Additionally, there is a trend toward using lower doses and extending the intervals between injections [2].

In 1996, Jean and Alastair Carruthers introduced a five-injection point technique for treating glabellar lines. This method involved two injections in the superomedial and inferomedial parts of the corrugator muscles, along with one injection in the procerus muscle [3].

In 2002, a multicenter, double-blind, randomized, placebo-controlled study evaluated the efficacy and safety of botulinum toxin type A using a different five-point injection technique. This method involved two injections in the body and tail of the corrugator muscles and a single injection in the procerus muscle [4]. Another approach, proposed by Rzany *et al.*, utilized a three-point injection technique, with one injection in the belly of each corrugator muscle and one in the procerus muscle [5]. Additionally, Olver suggested a technique involving only one injection in each corrugator muscle, without targeting the procerus. This approach is based on the premise that sufficient diffusion occurs from the corrugator muscles to the procerus, making direct injection unnecessary [6].

The procerus is a small, fasciculate muscle continuous with the medial side of the frontalis [6]. To date, no studies have evaluated the effects of a single injection of botulinum toxin type A into the procerus for the treatment of glabellar wrinkles. The diffusion of botulinum toxin type A is a well-documented, dose-dependent phenomenon and is a critical factor in this research. In this study, we administered a single dose of 50 units of abobotulinum toxin A into the procerus muscle and compared its effects to the method of a total of 50 units of abobotulinum toxin A delivered using the five-point injection technique (10 units at each point).

METHODS

In this study, patients aged 20 to 55 years seeking treatment for glabellar lines were selected based on a criterion of more than a 5 mm decrease in the distance between the medial heads of the eyebrows during maximal contraction compared to their resting position. A total of twenty patients (18 women and 2 men) were recruited. Eligibility criteria included the absence of neurological or neuromuscular diseases (e.g., myasthenia gravis), autoimmune disorders, a history of botulinum toxin treatment within the past six months, or any condition that could adversely affect patient participation.

The distance between the eyebrows logically increases following a botulinum toxin injection due to muscle relaxation. Therefore, we measured the distance between the eyebrow heads before and after the injection, and subsequently analyzed the changes in distance resulting from the procedure.

The patients were treated with abobotulinum toxin A (Dysport, Ipsen, Berkshire, England). Each vial contained 500 U of abobotulinum toxin A and was reconstituted with 2.5 mL of 0.9% sterile saline solution, resulting in a final dilution of 200 U/mL. Each patient received a total injection volume of 0.25 mL (a total dose of 50 units of abobotulinum toxin A). Nine patients (eight women and one man) were treated using the five-point injection technique, while eleven patients (ten women and one man) underwent a single-point injection treatment. Patients in the single-point injection group received 50 units of abobotulinum toxin A in the procerus muscle (Figure 1A). Those treated with the five-point injection technique received a total of 50 units of abobotulinum toxin A distributed across five points (10 units per point) (Figure 1B). Participants were instructed not to apply pressure to the injection sites. Follow-up sessions were scheduled at the end of the weeks two and four post-injection, which correspond to the peak effect of abobotulinum toxin A [3,7].

A B

Figure 1. Injection techniques: (A) Single injection of 50 units of abobotulinum toxin A into the procerus muscle; (B) Five-point injection of 10 units of abobotulinum toxin A at each point.

Five to ten units of abobotulinum toxin A were administered to patients requiring a touch-up injection at week two.

Statistical analysis

R software version 3.6.0 (R Core Team, 2017; R: A language and environment for statistical computing, R Foundation for Statistical Computing, Vienna, Austria. URL: https://www.R-project.org/) was used for statistical analysis. Repeated measures ANOVA was used to detect any significant changes in the distance between the medial eyebrow heads across sessions for each injection technique. The Wilcoxon rank-sum test was used to assess differences in the changes in the distance between the medial eyebrow heads. For all tests, the alpha level was set at 0.05 to determine statistical significance.

Ethical considerations

The study was conducted in 2017 in accordance with the principles outlined in the Declaration of Helsinki (1975) and received approval from the Ethics Committee of the Skin Research Center at Shahid Beheshti University of Medical Sciences in Tehran, Iran. All participants provided written informed consent.

RESULTS

A total of 20 patients were treated and successfully completed the follow-up sessions at weeks two and 4, with nine patients in the five-point injection group and 11 patients in the single-injection group. Notably, each group included only one male patient, which led us to refrain from analyzing or adjusting the results based on sex. The mean and standard deviation (SD) of the distance between the medial heads of the eyebrows during both maximal contraction and rest are detailed in Table 1.

In the five-point injection method, repeated measures ANOVA revealed a statistically significant difference at rest among the measurements taken at baseline, week two, and week four ($F = 4.52$, $P = 0.03$). At maximal contraction, a statistically significant change was observed across the three

Table 1. Measurements at three different time points for two groups at rest and during maximal contraction

	Distance between the medial eyebrow heads, mean (SD), mm	
	Five-point injection (50 units) (n = 9)	Single-point injection (50 units) (n = 11)
Rest		
Baseline	22.3 (3.1)	21.9 (2.9)
Week 2	22.8 (3.3)	22.4 (3.2)
Week 4	22.7 (3.3)	22.4 (3.1)
Maximal contraction		
Baseline	17.1 (2.3)	16.7 (2.3)
Week 2	20.7 (2.9)	20.4 (2.6)
Week 4	21.1 (2.9)	20.9 (2.7)

sessions (F = 78.52, $P < 0.01$). The most significant changes occurred from baseline to week two ($P < 0.01$ for both rest and maximal contraction).

In the 50 units single-point injection method, a statistically significant difference was found among the three measurements at rest (F = 8.85, $P < 0.01$). Similarly, at maximal contraction, a statistically significant change was observed among the three sessions' measurements (F = 118, $P < 0.01$). The most significant changes occurred from baseline to week two ($P < 0.01$ for both rest and maximal contraction).

There was no statistically significant difference between the two techniques in the distance of the medial eyebrow heads at week two ($P = 0.73$) and week four ($P = 0.91$). Additionally, the changes from baseline to week two and from baseline to week four did not demonstrate any significant differences between the two techniques ($P = 0.91$ and $P = 0.72$, respectively) (Figure 2).

The efficacy of a single-point injection of 50 units of abobotulinum toxin A into the procerus muscle, as well as a five-point injection totaling 50 units of the same toxin, and the changes observed during follow-up are shown in Figures 3 and 4, respectively.

DISCUSSION

Our study compared the efficacy of a single-point injection of 50 units of abobotulinum toxin A into the procerus muscle with a five-point injection totaling 50 units of the same toxin. We found no significant difference in treatment efficacy between the two groups. Additionally, no ptosis or other adverse effects were observed in either group.

Over the past two decades, botulinum toxin type A injections have been used to treat glabellar lines [1,3,8,9]. The five-point injection method is the most commonly used technique among aestheticians and physicians [1,4,8]. However, several alternative injection techniques have also been proposed and have demonstrated successful outcomes [3,5,6,10,11].

The efficacy and safety of the five-point injection technique for treating glabellar lines are well documented and widely accepted. This technique involves injecting one point into the procerus muscle and two points into each corrugator muscle, with a consensus recommendation of administering 10 units at each injection site, totaling 50 units [1,2,4].

We aimed to compare our technique with the established glabellar treatment method. Effectively

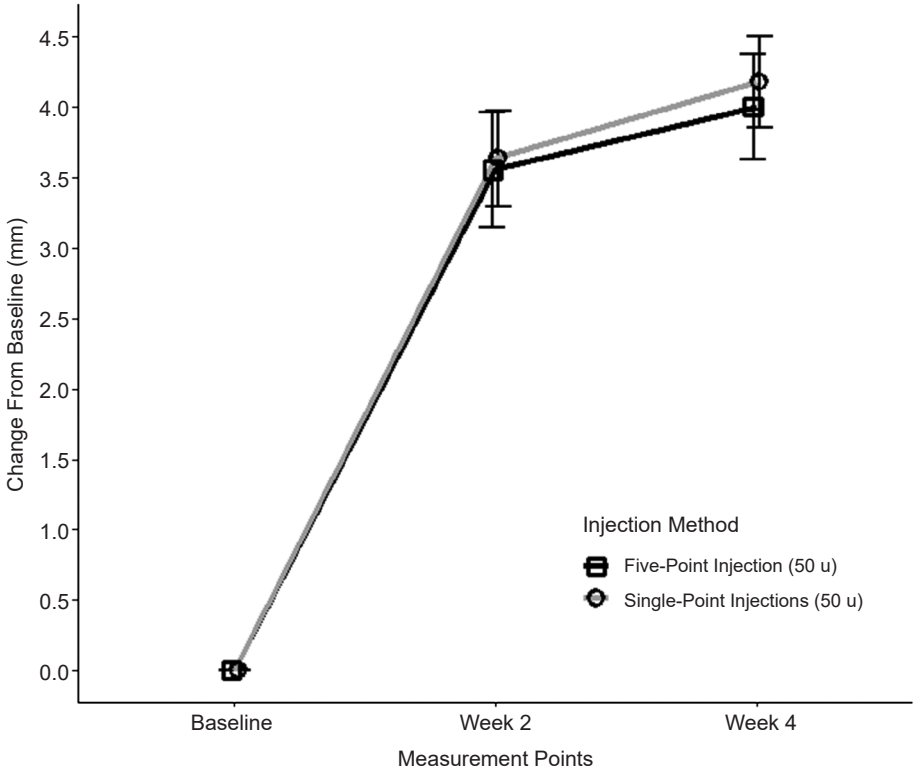

Figure 2. Changes in the distance between the medial eyebrow heads from baseline through weeks two and four.

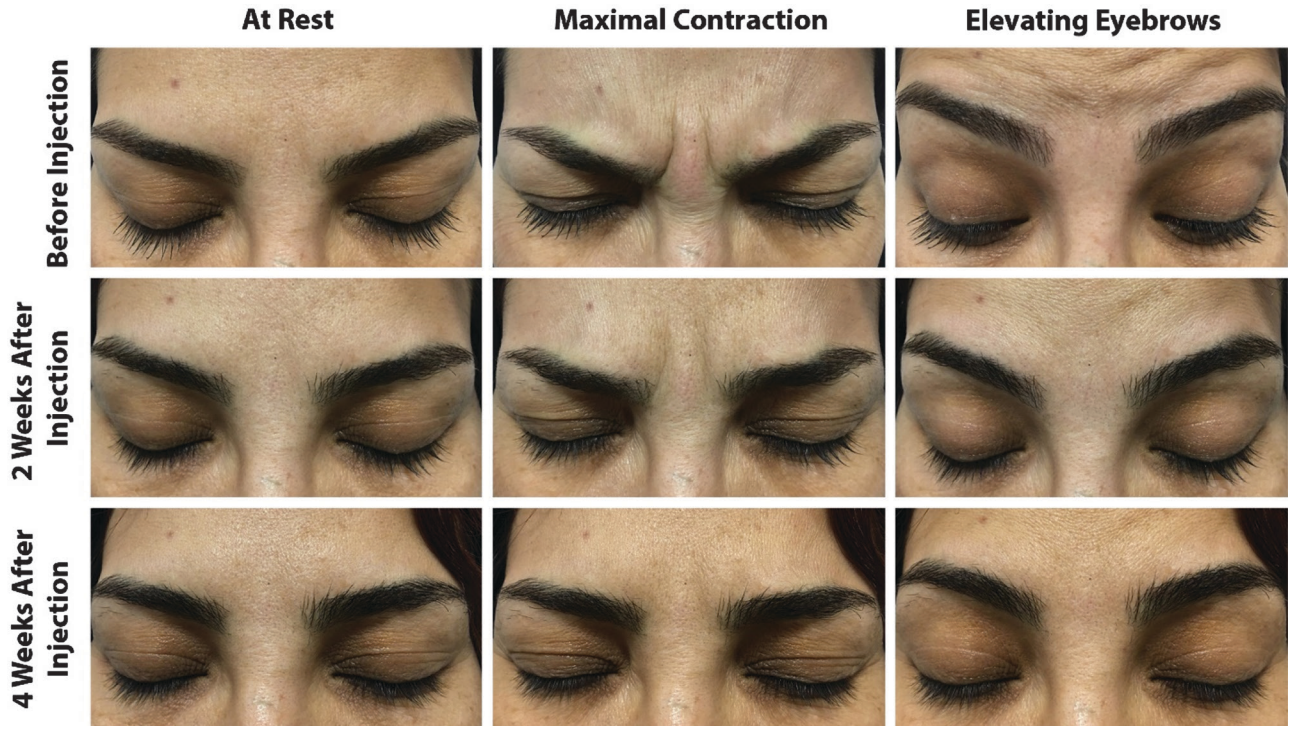

Figure 3. Single-point injection and changes during follow-up. Photographs were taken before the injection, and at two and four weeks post-injection. The patient was photographed at rest, during maximal contraction (frowning), and while raising the eyebrows.

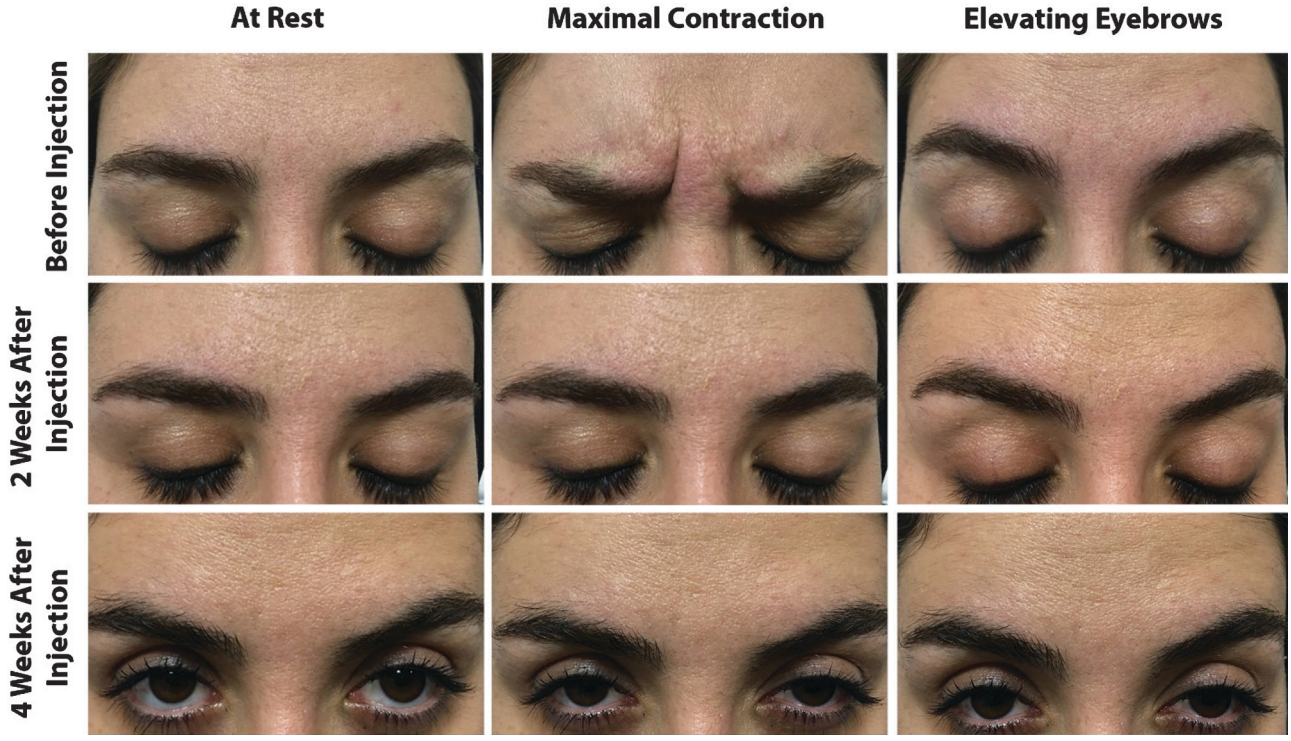

Figure 4. Five-point injection and changes during follow-up. Photographs were taken before the injection, and at two and four weeks post-injection. The patient was photographed at rest, during maximal contraction (frowning), and while elevating the eyebrows.

treating glabellar lines requires blocking the neuromuscular junctions of the glabellar muscles, and our technique successfully achieved this goal. The diffusion of toxins from the procerus muscle into

the corrugator muscle contributes to this effect [8,13-15]. Additionally, the single-point injection technique provides a natural appearance, is suitable for various professions, and minimizes discomfort. Notably, the reduced risk of ptosis is a significant advantage of this treatment.

CONCLUSION

A single-point injection of 50 units of abobotulinum toxin A into the procerus muscle is an effective treatment for glabellar lines, demonstrating results comparable to the five-point injection technique. However, further studies with larger sample sizes and longer follow-up periods are needed to confirm these findings.

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None.

Authors' contributions

FG designed and performed the research and wrote the article. **SG** contributed to patient selection and recorded the results. **AS** contributed to patient selection. **SH** and **GM** contributed to editing the article.

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