

The Efficacy of Botulinum Toxin A Injection for Gastrocnemius Hypertrophy: A Prospective, Randomized, Double-blinded Controlled Trial

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Background: Many individuals hold an interest in aesthetic appeal, with one aspect of physical attractiveness being the alluring contour of the lower leg. Utilizing botulinum toxin A (BTX-A) injections offers several advantages, including a short procedure time, low pain, and a speedy recovery. With a demand for high-level evidence regarding the effectiveness of BTX-A injections for correction of lower leg contour, we evaluated the safety and efficacy of BTX-A injection for improvement of gastrocnemius muscle hypertrophy.

Methods: We conducted a prospective, randomized, and controlled clinical trial to evaluate whether the injection of BTX-A into the gastrocnemius muscle could decrease muscular hypertrophy. The patients were randomized into a low-dose injection (60 units) group and a high-dose injection group (100 units) for each leg. Demographics, clinical outcome, and satisfaction score were compared between the two groups.

Results: A total of 20 patients and 40 legs were enrolled in this study. Clinical and surgical demographics were similar between the two groups. BTX-A injection showed a significant decrease in the circumference of the calf after 8 weeks (preinjection: 36.35 ± 0.63 cm versus postinjection: 35.87 ± 0.61 cm; $P = 0.03$). However, no significant difference was observed between the low- and the high-dose group (-0.52 ± 0.74 cm versus -0.44 ± 1.04 cm, $P = 0.78$).

Conclusions: BTX-A injection can be a good noninvasive method for the correction of hypertrophic gastrocnemius muscles. This study supports the use of BTX-A injections in patients unsatisfied with lower leg hypertrophy. (*Plast Reconstr Surg Glob Open* 2024; 12:e5813; doi: [10.1097/GOX.0000000000005813](https://doi.org/10.1097/GOX.0000000000005813); Published online 20 May 2024.)

INTRODUCTION

Aesthetics hold great importance for many individuals, and an appealing lower leg contour is regarded as a significant aspect of being physically attractive. In the past, invasive and surgical operations including liposuction and radiofrequency therapy were performed to correct the contours of the calf muscles. Surgical excision of

the gastrocnemius muscle, which is a major muscle determining the shape and size of the calf, was successfully performed, and the calf contour was corrected.^{1,2} However, it showed unstable walking and running as a result of the follow-up period.³ Liposuction was not recommended as a suitable method because it was the gastrocnemius rather than subcutaneous fat by which the shape and size of the lower leg were determined. Radiofrequency therapy was deemed an unsuitable method due to resulting fibrosis and the inability to contract muscles that followed.⁴

Botulinum toxin A (BTX-A) is a neurotoxic protein produced by *Clostridium botulinum*, a Gram-positive anaerobic bacterium. It inhibits the secretion of the neurotransmitter acetylcholine at the nerve-muscle junction, resulting in muscle paralysis. The BTX-A injection method has many advantages, such as short procedure time, low pain, and a quick return to daily life after the procedure. Therefore, it has been widely used for aesthetic procedures. To et al⁵ reported the effect of BTX-A injection on hypertrophic

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masseteric muscle in a prospective study. Some studies reported on the effects and advantages of BTX-A injection for the correction of gastrocnemius muscle hypertrophy as a noninvasive treatment.⁶⁻¹⁴ However, there was no prospective, randomized control study to prove the effectiveness of BTX-A injection for correction of lower leg contour.

Given the need for high-level evidence on the effectiveness of BTX-A injection for correction of lower leg contour, we conducted a prospective, double-blinded, randomized controlled trial to evaluate the safety and efficacy of BTX-A injection for improvement of gastrocnemius muscle hypertrophy.

MATERIALS AND METHODS

This was a prospective, randomized controlled clinical trial that included adult patients between 20 and 60 years of age who wanted to correct the contour of calf hypertrophy. There was no other compensation for participation. Exclusion criteria included the following: (1) a history of medical conditions affecting neuromuscular function; (2) history of BTX-A injection within 6 months; (3) any history of disease or treatment involving the gastrocnemius within 6 months; and (4) history of allergy to investigational drugs. Patients were prospectively randomized to a low-dose group (60 units) or high-dose (100 units) group. They were treated with BTX-A (Botulax, Hugel, Co., South Korea), which has been approved by the Korean Food and Drug Administration and is commercially available. This study was approved by the institutional review board at Asan Medical Center (institutional review board number S2021-1715) and registered in the Clinical Research Information Service (registry number KCT0008039). Signed informed consent was obtained from all patients.

BOTULINUM TOXIN A INJECTION

To prepare the BTX-A solution, two vials, each containing 100 units, were dissolved in 10 mL of normal saline. A half-inch long 24 gauge needle was used for the injection. The BTX-A investigation group was divided depending on BTX-A dose arm I (low-dose injection; 60 units) and arm II (high-dose injection; 100 units). Before injection, the test drug was diluted and a syringe was filled by a designated dilution manager. They prepared three units of 0.3 mL per point for the low-dose group, and five units of 0.5 mL per point for the high-dose group. The dilution manager did not inform the researcher in charge of injection and evaluation. The patients raised the heel to check the thickest part of the calf. The researcher injected 20 points at the thickest part (Figs. 1 and 2).

EVALUATION OF EFFICACY ANALYSIS

Before and 8 weeks after the injection, the researcher measured the circumference of the calf at the thickest part as the heel was raised. The difference in circumference

Takeaways

Question: Can we expect cosmetic improvement in gastrocnemius hypertrophy using botulinum toxin?

Findings: We demonstrated a significant circumference reduction. BTX-A injection showed a significant decrease in calf circumference after 8 weeks (preinjection: 36.35 ± 0.63 cm versus postinjection: 35.87 ± 0.61 cm; $P = 0.03$).

Meaning: BTX-A injections can be a good noninvasive method for the correction of hypertrophic gastrocnemius muscles.

and difference ratio was compared with the initial length in both groups. Complications such as walking and running discomfort were analyzed. Additionally, the researcher evaluated the participants' satisfaction score. To calculate the satisfaction score, values were divided into five categories: 1 = "dissatisfied," 2 = "somewhat dissatisfied," 3 = "indifferent," 4 = "somewhat satisfied," and 5 = "satisfied."

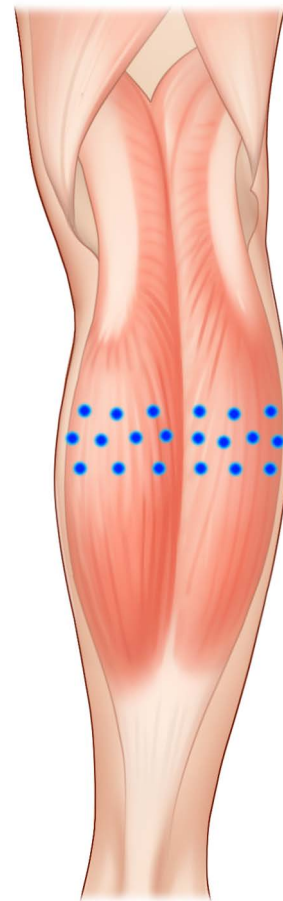


Fig. 1. The BTX-A was injected on the thickest part while raising the heel.

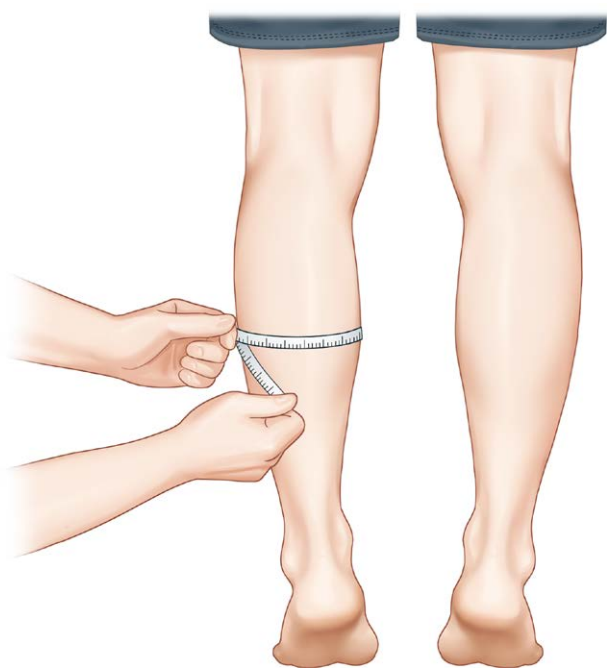


Fig. 2. The circumference of the calf at the thickest part were measured before and 8 weeks after injection.

STATISTICAL ANALYSIS

Categorical variables were presented using absolute frequencies and percentages, and they were compared using the chi-square test or Fisher exact test. Continuous variables were presented as means with SDs, and they were compared using a Wilcoxon signed rank test or the Mann–Whitney U test, with a normality test. Statistical significance was defined as a *P* value of less than 0.05. All data analyses were performed using IBM SPSS Statistics version 21 (IBM, Armonk, N.Y.).

RESULTS

A total of 20 patients and 40 legs were enrolled in this study. The mean age of the patients was 35.3 ± 9.72 years (range: 21–51 y). Patients were divided into the two groups: the low-dose group (60 units; *n* = 10, 50%) and the high-dose group (100 units; *n* = 10, 50%). The mean age was 38.6 ± 10.63 years (range: 23–51 y) in the low-dose

group, and 31.7 ± 8.51 years (range: 21–44 y) in the high-dose group without significant difference (*P* = 0.25). No complications were observed with the BTX-A injection in any of the patients.

BTX-A injection showed a significant decrease in calf circumference after 8 weeks (preinjection: 36.35 ± 0.63 cm versus postinjection: 35.87 ± 0.61 cm; *P* = 0.03). However, no significant difference was observed in the change of circumference of the calf between the low- and the high-dose groups (-0.52 ± 0.74 cm versus -0.44 ± 1.04 cm, *P* = 0.78). Furthermore, no significant difference was observed in the ratio of circumference difference between both groups ($-1.46 \pm 2.17\%$ versus $-1.10 \pm 2.88\%$, *P* = 0.64). However, the high-dose group (4.5 ± 0.97 , range: 3–5) showed a higher satisfaction score than the low-dose group (3.9 ± 0.68 , range: 2–5) without a significant difference (*P* = 0.17; Tables 1 and 2; Figs. 3 and 4).

DISCUSSION

The gastrocnemius, commonly known as the calf muscle, is located in the back of the lower leg. It is responsible for flexing the foot and bending the knee. An enlarged lower leg is mainly determined by the size and shape of this gastrocnemius muscle. Von Szalay et al¹⁵ reported that maximal female calf circumference ranged between 33 and 36 cm. Tsai et al¹⁶ performed a scientific study describing criteria for the ideal female leg. They reported the average maximal circumference was 32 cm (range: 29–35 cm).¹⁶ In the past, there were some studies about surgical treatment for reducing calf hypertrophy. However, it showed invasive procedures and complications.^{1,2,17} BTX-A is a neurotoxin that is best known for its cosmetic use in reducing wrinkles and fine lines. However, it has several medical uses as well, including the treatment of spasms and tightness in the gastrocnemius muscle. Gastrocnemius is often a target for BTX-A injections. They are mainly used to treat diseases related to walking, muscle spasticity, and sports injury. When the muscle is overactive, it can cause spasms and tightness, leading to discomfort, pain, and difficulty with walking. Filippetti et al¹⁸ reported that BTX-A injections of the gastrocnemius were effective in improving foot walking patterns in children with walking problems. Santamato et al¹⁹ reported that BTX-A injection was effective in relieving chronic to poststroke spasticity of gastrocnemius muscle

Table 1. Clinical Outcome of BTX-A Injection

Variable	Age (y)	Preinjection (cm)	Postinjection (cm)	<i>P</i>
BTX-A injection (<i>n</i> = 40)	35.3 ± 9.72 (21–51)	36.35 ± 0.63	35.87 ± 0.61	0.03
60 units (<i>n</i> = 20)	38.6 ± 10.63 (23–51)	36.03 ± 2.53	35.38 ± 2.34	0.62
100 units (<i>n</i> = 20)	31.7 ± 8.51 (21–44)	36.67 ± 5.05	36.45 ± 4.91	0.35

Table 2. Comparison between Low- and High-dose Groups

Variable	60 Units (<i>n</i> = 20)	100 Units (<i>n</i> = 20)	<i>P</i>
Circumference difference (cm)	-0.52 ± 0.74	-0.44 ± 1.04	0.78
Difference percentage (%)	-1.46 ± 2.17	-1.10 ± 2.88	0.64
Satisfaction score	3.9 ± 0.68	4.5 ± 0.97	0.17



Fig. 3. A 31-year-old woman was injected with 60 units of BTX-A on the thickest part of both gastrocnemius muscles. A, Preoperative appearance. B, Reduction of calf circumference was found after 8 weeks.

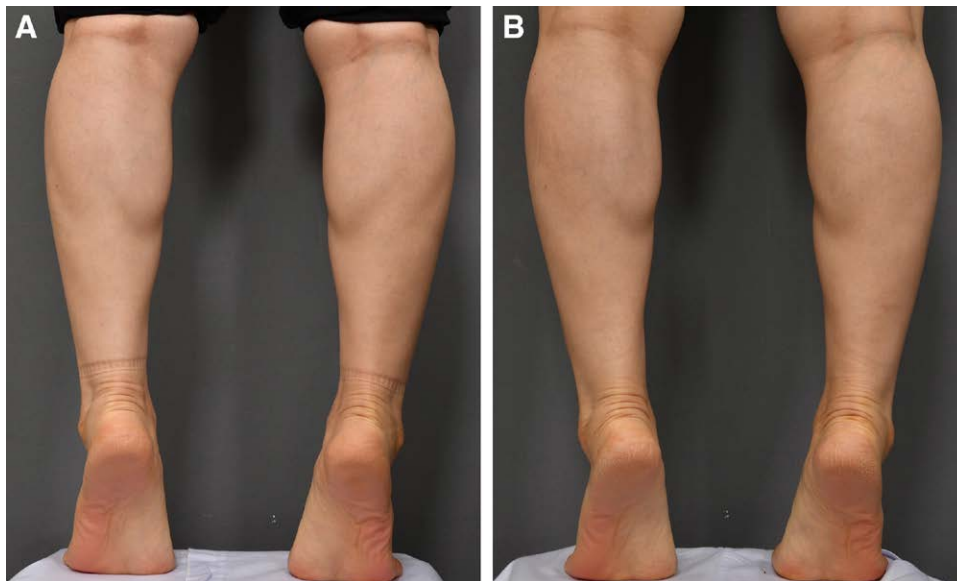


Fig. 4. A 41-year-old woman was injected with 100 units of BTX-A on the thickest part of both gastrocnemius muscles. A, Preoperative appearance. B, Reduction of calf circumference was found after 8 weeks.

tension, thereby achieving pain relief. Also, Koog and Min²⁰ reviewed the effects of BTX-A on the gastrocnemius in children with cerebral palsy. BTX-A injections on the gastrocnemius have been performed for a variety of reasons, and research continues to determine what benefits these treatments offer to patients.

In recent years, as interest in leg contour correction for beauty has increased, some patients have sought BTX-A injections. There are relatively few studies on the use of BTX-A injections for gastrocnemius for cosmetic purposes. Lee et al⁶ first reported the use of BTX-A injection for the treatment of gastrocnemius hypertrophy in 2004. They found that the BTX-A injection for correction of the enlarged medial

gastrocnemius muscle to be without functional disabilities.⁶ Oh et al¹⁰ reported volume reduction on three-dimensional computed tomography after BTX-A injection in hypertrophic gastrocnemius. However, the use of BTX-A injection for gastrocnemius for these cosmetic purposes is still at an early stage of research, and further research with high-evidence is needed. Also, there was no study about a definite recommended dose for an effective but safe injection for the correction of gastrocnemius hypertrophy.

In our study, we found significant circumference reduction in the hypertrophic calf after 8 weeks without any complications. Suh et al¹⁴ reported 6 months duration of its effectiveness on circumference reduction. Although

not significant in the patient satisfaction survey, satisfaction seemed to be higher in the 100 units group. However, there was no significant difference in the circumference reduction between 60 and 100 units. Cheng et al⁸ reviewed the literature about BTX-A injections for leg contouring in East Asians. In this systematic review, BTX-A ranging from 72 to 360 units improved the circumference of the lower leg. However, BTX-A injection more than 100 units showed some complications, including ecchymosis around injection sites, myalgia, and cramps.⁸ In this study, we found that 60 units of BTX-A injection showed a significant correction of gastrocnemius hypertrophy. This is a meaningful study indicating that the calf circumference could be corrected with a smaller dose compared with previous studies. However, because the patients' muscle volume or size is not considered for the dose, further research is needed on the threshold dose according to the patients' muscle size.

The major strength of this study is the high level of evidence from this prospective, double-blinded, randomized controlled trial design. However, there were a few limitations. A small number of participants were enrolled in one center during short follow-up period. Additionally, there are limitations in comparing the contour with objective indicators, so it was determined that the treatment was effective in reducing the circumference. Although the circumference was the most objective value for measurement, the change was more minimal than that of a surgical procedure. Also, comparison of effects and complications between doses was important, but only two groups were compared in this study. There may be differences according to the amount of muscle, and the variation of the injection site has not been accurately analyzed. Therefore, further research, including a large sample size and a variety of groups during a longer period, will improve the level of clinical evidence for using BTX-A on gastrocnemius in the future.

CONCLUSIONS

BTX-A injections can be a good noninvasive method for the correction of hypertrophic gastrocnemius muscles. We demonstrated a significant circumference reduction and effective dose of BTX-A through a prospective, double-blinded, randomized controlled clinical trial. This study supports the use of BTX-A injection in patients unsatisfied with lower leg hypertrophy. The patients were highly satisfied with improved lower leg contour after BTX-A injection.

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DISCLOSURES

Prof. Han reports being funded by the Hugel Co., to conduct clinical trials. The other authors have no financial interest to declare.

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