The Change of Maximum Bite-force after Botulinum Toxin Type A Injection for Treating Masseteric Hypertrophy

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감사의 글

이 논문이 완성되기까지 따뜻한 배려와 함께 세심한 지도와 격려를 아끼지 않으신 최종훈 교수님께 먼저 깊은 감사를 드립니다. 또한, 성형외과 전문의로 바쁜 와중에도 기꺼이 함께 연구에 참여해 주신 안기영 원장님께도 고마움을 전합니다.

이 책이 발간 될 즈음, 20년만에 부모님, 두 동생, 나의 가족이 미국에서 다시 만날 수 있도록 허락해주신 하나님께 이 작은 결실을 드립니다.

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Abstract

The Change of Maximum Bite Force after Botulinum Toxin Type A Injection for Treating Masseteric Hypertrophy

A botulinum toxin type A (BTX-A) injection into the masseter muscle has been used as a noninvasive treatment for masseteric hypertrophy. However, muscle atrophy inevitably causes a change of bite force. The aim of this study was to evaluate the change in the maximum bite force after a BTX-A injection for the treatment of masseteric hypertrophy. Seven patients who had presented for treatment of masseteric hypertrophy participated in this study. Twenty-five units of BTX-A was injected into each masseter muscle, 50units in total, at two to five points at the prominent portions of the mandibular angle. The bite-force measurement apparatus included a digital multimeter and a bite-force transducer. The maximum bite force between the maxillary and mandibular first molars was measured before injection and at 2, 4, 8 and 12 weeks after the injection.

The difference in maximum bite force between the preinjection and 2-, 4-, 8-week postinjection time points was statistically significant. However, there was no such difference between the preinjection and 12-week postinjection values($p<0.05$).

The maximum bite force was significantly reduced after injection of BTX-A for the treatment of masseteric hypertrophy. However, it gradually recovered by 12 weeks.

KEY WORDS: Botulinum toxin type A (BTX-A); masseter muscle hypertrophy; maximum bite-force.

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1. Introduction

The perception of beauty in Asians is different from that of Caucasians. Asian women tend to prefer oval or almond-shaped faces and dislike a square jaw, which they believe gives them a masculine image. The cause of a square jaw might be overgrowth of the mandible, masseteric hypertrophy, or fat accumulation. Among them, masseteric hypertrophy is known as the asymptomatic enlargement of the masseter muscle and is commonly associated with abnormal habits such as nocturnal bruxism and daytime clenching.

The treatment usually involves a surgical resection of a portion of the mandibular angle or masseter muscle. Recently, there have been some reports showing that a Botulinum toxin type A(BTX-A) injection into the masseter muscle can be used as an alternative noninvasive treatment for masseteric hypertrophy.[1-5] These studies have revealed atrophy of the hypertrophic muscles after a BTX-A injection using clinical photographs, ultrasound, electromyography and computed tomography.[4-10] To et al. evaluated the effects of BTX-A on masseteric hypertrophy using ultrasound and electromyography. All five patients in their study showed good responses, with a maximum effect of a 31 percent reduction in muscle bulk 3 months after treatment[5]. Park et al. reported serial measurements of the thickness of the masseter muscle using ultrasound and computed tomography before the injection and at 1 and 3 months thereafter.[9] They reported the long-term clinical effects and the degree of patient satisfaction, and monitored any potential side effect during a 4- to 10-month follow-up period. Kim et al. evaluated the effects of two different doses of BTX-A on the thickness and cross-sectional area using computed tomography and electromyography to determine the changes in the masseter muscle.[11]

The mechanisms involved in the treatment of masseteric hypertrophy with a BTX-A injection are somewhat different from those for treating facial hyperkinetic wrinkles.[12] An intramuscular injection of BTX-A leads to temporary partial denervation at the area of the neuromuscular synapses and eventually causes muscle atrophy. However, there are few reports showing a change in the bite force after BTX-A injection for masseteric hypertrophy. The aim of this study was to evaluate the change in the maximum bite force after BTX-A injection for treating masseteric hypertrophy.

2. Materials and Methods

A total of seven female patients who had presented for treatment of masseteric hypertrophy at two medical centers were enrolled in this study. The mean age was 28.4 years(range, 22 to 42 years).

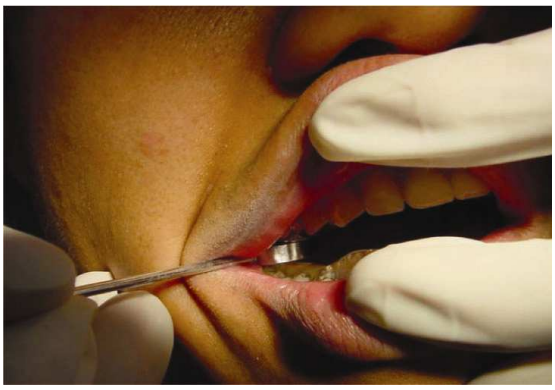
BTX-A(Lanzhou Institute of Biological Products, Lanzhou, China) was a freeze-dried powder of 100 units, and was reconstituted to a concentration of 5 units/0.1㎖ with 2 ㎖ of normal saline. By palpation of the masseter muscles, 25 units was injected into each side, 50 units in total, at two to five points at the prominent portions of the mandibular angle.

Intraoral stents were made individually for each patient before the injection to measure the stable maximum bite force on a flat surface. The bite-force measurement apparatus included a digital multimeter (MPM-3000; Nihon Koudenshi Co., Tokyo, Japan), and a bite-force transducer with a 17-㎜-diameter plate at the end, and a block, 1 ㎜ high and 3 ㎜ in diameter, located at the center. The block was placed on the occlusal surface of the first molar. The subject was then asked to bite on the block as hard as possible, and the maximum digital readouts were measured and displayed in kilograms per centimeter squared. The maximum bite force between the maxillary and mandibular first molars was measured before the injection and at 2, 4, 8, and 12 weeks after injection (Fig 1). An analysis of variance test was carried out to evaluate the influence of the different side (right and left) of BTX-A on each masseter muscles. As a result of the paired *t* test of both masseter muscles, the *p* value was not found to be significant. Therefore, the number of samples was doubled by pooling. The data was analyzed using SAS version 8.1 (SAS institute, Inc., Cary, N.C.).

A .The upper and lower stents.

B. Intraoral view of the stents.

C. Bite-force measuring machine(MPM 3000).



D. Measuring bite force on the first molar.

Fig 1. Bite-force measuring method.

3. Results

Mean values of bite forces of maximum voluntary clenching at each point are shown in Figure 2. There was an approximately 40 percent decrease in the mean maximum bite force at 2 weeks compared with that before the injection. The maximum bite forces recovered gradually after 4 weeks and remained 20 percent lower at 12 weeks than that measured before the injection. The difference between the maximum bite forces befoere injection and at 2, 4, 8 weeks after injection was statistically significant. However, there was no such difference between the preinjection and 12-week postinjection values ($p < 0.05$) (Table 1).

Time Point	Mean(kg/cm^2)	SD(kg/cm^2)	*p*
Before injection	51.0	13.0	-
After injection			
2 week	30.7	11.6	0.0004*
4 week	33.6	12.7	0.0008*
8 week	36.4	16.3	0.0264*
12 week	41.4	16.6	0.0884

Table 1. Mean of bite forces of maximum voluntary clenching at each point . (n=14)

* $p < 0.05$.

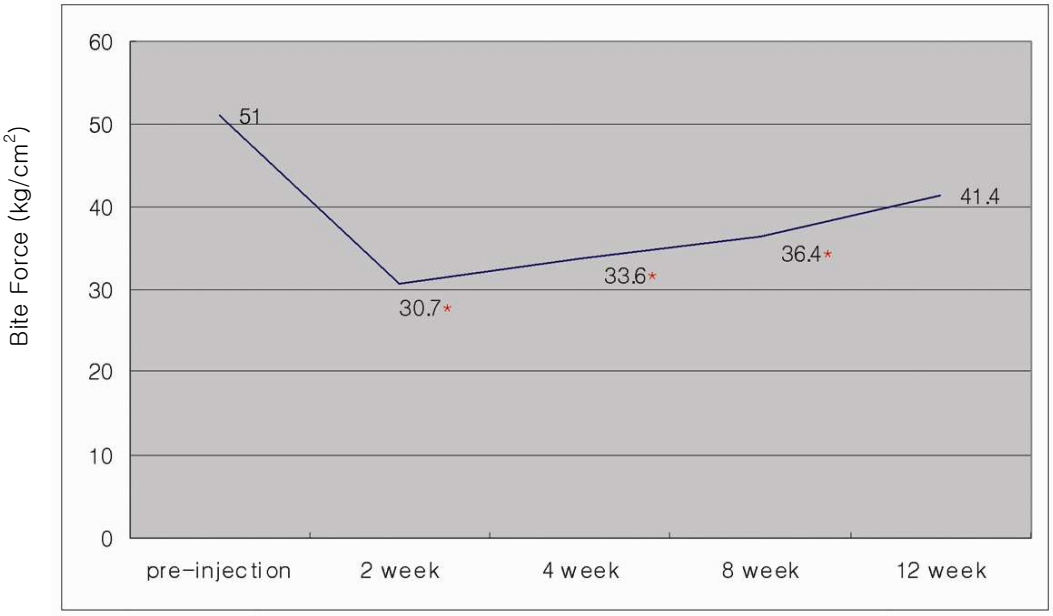


Fig 2. Mean of bite forces of maximum voluntary clenching at each point (in kilograms per centimeter squared; n = 14; * $p < 0.05$). There was an approximately 40 percent decrease in the bite force at 2 weeks after injection compared with that observed before injection, and there were statistically significant differences between the bite force measured before injection and that measured at 2, 4, and 8 weeks after injection. However, there was no significant difference between the preinjection and 12-week postinjection values.

4. Discussion

In the case of contouring the lower face, the mechanisms for treating masseteric hypertrophy with BTX-A are somewhat different from those for treating facial hyperkinetic wrinkles such as crow's feet and wrinkles on the glabellar and forehead area.[12] The main effect of BTX-A is the temporary effect of muscle atrophy, followed by chemodenervation caused by an acetylcholine blockade at the neuromuscular junction by the toxin. In animal experiments,[13] the muscle fibers begin to show atrophy histologically within 10 to 14 days after the injection. This atrophy continues to develop over a 4- to 6-week period. It should be noted that there is not only fiber atrophy, as indicated by the generalized reduction in the fiber diameter, but also large variations in the fiber size. Fiber atrophy is a reversible phenomenon, and usually recovers within 4 to 6 months. Seventeen orbicularis oculi muscle specimens taken from patients during ptosis and myectomy surgery were evaluated for their cholinesterase staining characteristics and fiber variability. Diffuse cholinesterase activity was observed, beginning at weeks 3 to 4, which was maintained for 3 to 4 months after the injection. In all patients studied, the staining pattern was similar to that observed in the control subjects after 6 months.[14]

The dosages used for masseter muscle were generally 25 to 30 units of BTX-A .[3-5,8] The side effects of a BTX-A injection for masseteric hypertrophy, such as change in bite force, speech disturbance, muscle pain, facial asymmetry and prominent zygoma, have been reported.[8,11,15] Among them, the change in bite force is an inevitable side effect of muscle atrophy even though it is generally temporary.

The bite force is a force generated by occlusal contact between the opposing teeth and is also called the occlusal force. A number of appliances for measuring the bite force have been reported. These include a strain gauge transducer, biting fork, and bite force dynamometers. The bite-force varies from individual to individual, and males subjects generally have a larger bite force than female subjects.[16] It has also

been reported that the maximum bite force applied to a molar is several times stronger than that applied to an incisor. It was reported that the maximum bite force applied to the first molar ranged from 91 to 198 pounds (41.3 to 89.8 ㎏/㎠), whereas the maximum force applied to the central incisors ranged from 29 to 51 pounds (13.2 to 23.1㎏/㎠).[17] A bite force study using this MPM-3000 apparatus reported that the mean maximum bite force of 9-year-old girls was 27 ± 4.4 ㎏/㎠.[18]

In this study, the average maximum bite force of the first molar before the injection was 51㎏/㎠ and there was no difference between the right and left sides. There was an approximately 40 percent decrease in the mean maximum bite force at 2 weeks compared with that recorded before injection. The bite force was restored to its preinjection value by 12 weeks after the injection($p < 0.05$). Because of weakened muscle strength by atrophic change, some patients complained of masticatory difficulties in chewing hard food (but not when on a soft diet).

This study has some limitations. There were only seven patients, all of whom were female, and only the bite force of the molar was measured. Therefore, a further prospective long-term study covering a large number of subjects from both genders with measurements of the bite force of the whole teeth should be carried out to fully estimate the change in the bite force after a BTX-A injection and determine its potential effects on patients with masseteric hypertrophy.

5. Conclusion

The maximum bite force was significantly reduced after injection of BTX-A for treatment of masseteric hypertrophy. However it gradually recovered by 12 weeks.

6. References

1. Smyth AG. Botulinum toxin treatment of bilateral masseteric hypertrophy. *Br J Oral Maxillofac Surg* 1994; 32: 29-33.

2. Moore AP, Wood GD. The medical management of masseteric hypertrophy with botulinum toxin type A. *Br J Oral Maxillofac Surg* 1994; 32: 26-28.

3. Mandel L, Tharakan M. Treatment of unilateral masseteric hypertrophy with botulinum toxin: case report. *J Oral Maxillofac Surg* 1999; 57: 1017-1019.

4. von Lindern JJ, Niederhagen B, Appel T, Berge S, Reich RH. Type A botulinum toxin for the treatment of hypertrophy of the masseter and temporal muscles: an alternative treatment. *Plast Reconstr Surg* 2001; 107: 327-332.

5. To EW, Ahuja AT, Ho WS, King WW, Wong WK, Pang PC, Hui AC. A prospective study of the effect of botulinum toxin A on masseteric muscle hypertrophy with ultrasonographic and electromyographic measurement. *Br J Plast Surg* 2001; 54: 197-200.

6. Choe SW, Cho WI, Lee CK, Seo SJ. Effects of botulinum toxin type A on contouring of the lower face. *Dermatol Surg* 2005; 31: 502-507; discussion 507-508.

7. Kim NH, Chung JH, Park RH, Park JB. The use of botulinum toxin type A in aesthetic mandibular contouring. *Plast Reconstr Surg* 2005; 115: 919-930.

8. Kim HJ, Yum KW, Lee SS, Heo MS, Seo K. Effects of botulinum toxin type A on bilateral masseteric hypertrophy evaluated with computed tomographic measurement. *Dermatol Surg* 2003; 29: 484-489.

9. Park MY, Ahn KY, Jung DS. Botulinum toxin type A treatment for contouring of the lower face. *Dermatol Surg* 2003; 29: 477-483; discussion 483.

10. Borodic GE, Ferrante R, Pearce LB, Smith K. Histologic assessment of dose-related diffusion and muscle fiber response after therapeutic botulinum A toxin injections. *Mov Disord* 1994; 9: 31-39.

11. Kim JH, Shin JH, Kim CY, Kim ST. Effects of two different units of BTX-A evaluated by computed tomographic and electromyographic measurements of human masseter muscle. *Plast Reconst Surg* 2007; 119: 711-717.

12. Ahn KY, Park MY, Park DH, Han DG. Botulinum toxin A for the treatment of facial hyperkinetic wrinkle lines in Koreans. *Plast Reconstr Surg* 2000; 105: 778-784.

13. Borodic GE, Ferrante RJ, Pearce LB. Pharmacology and histology of the therapeutic application of botulinum toxin. In: Jankovic J, Hallett M (Eds.), *Therapy with Botulinum Toxin*, New York: Mancel Dekky, 1994. 119.

14. Borodic GE, Ferrante R. Effects of repeated botulinum toxin injections on orbicularis oculi muscle. *J Clin Neuro Ophthalmol* 1992; 12: 121-127.

15. Oshima M, Middlebrook JL, Atassi MZ. Antibodies and T cells against synthetic peptides of the C-terminal domain (Hc) of botulinum neurotoxin type A and their cross-reaction with Hc. *Immunol Lett* 1998; 60: 7-12.

16. Brekhus PH, Armstrong WD, Simon WJ. Stimulation of the muscles of mastication. *J Dent Res* 1941; 20: 87-92.

17. Howell AH, Manly RS. An electronic strain gauge for measuring oral forces. *J Dent Res* 1948; 27: 705-712.

18. Maki T, Nishioka A, Morimoto A, Naito M, Kimura M. A study on the measurement of occlusal force and masticary efficiency in school age Japanese children. *Int J Paediatr Dent* 2001; 11: 281-285.

국문요약

교근에 보툴리눔 A 형 독소 주사 후 최대 교합력의 변화

연세대학교 대학원 치의학과

김 성 택

<지도 **최 종 훈** 교수>

교근에의 보툴리눔 A형 독소(BTX-A) 주사는 교근 비대 환자에 대한 비침습적인 치료로 사용되어 왔다. 하지만 이에 의한 근육의 위축은 필연적인 교합력의 변화를 동반하게 된다. 본 연구의 목적은 교근비대의 치료를 위한 BTX-A 주사 후 최대 교합력의 변화를 평가하는 것이다. 교근비대를 나타내는 총 7명의 환자가 실험대상으로 참여하였으며, 편측 교근 당 25U씩 총 50U의 BTX-A를 양측 하악각 부위의 최대 풍융부에 2개에서 5개의 자입점을 통하여 분할 주입하였다. 교합력을 측정하는 기구로 계수형 전압계(digital multimeter)와 교합력변환기를 이용하여 시행하였다. 상악 제1대구치와 하악 제1대구치간의 최대 교합력을 측정하였으며, 주입 전, 주입 후 2주, 4주, 8주 및 12주 경과 후에 측정하였다.

주입 전과 주입 후 2주, 4주, 8주 경과 후의 최대 교합력은 유의할만한 차이를 나타냈다. 하지만 주입 후 12주 경과 후에는 술전과 유의할만한 차이를 나타내지 않았다($P<0.05$).

연구 결과, 교근비대 치료를 위한 BTX-A 주입 후, 최대 교합력은 유의할만한 감소를 보이지만, 약 12주에 걸쳐 점차 회복되는 것으로 사료된다.

핵심되는 말: 보툴리눔 A 형 독소(BTX-A); 교근비대; 최대 교합력