Effects of different units of Botulinum toxin type A (BTX-A) on the computed tomographic and electromyographic measurements of human masseter muscle

연세대학교 대학원

치의학과

김 재 홍

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이 논문을 박사 학위논문으로 제출함

2005년 6월 일

연세대학교 대학원

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김 재 홍

김재홍의 박사 학위논문을 인준함

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감사의 글

여전히 부족한 면도 많고 아직도 배워야 할 것이 끝도 없지만 하나의 결실을 맺을 수 있게 된 것에 대하여 모든 분들께 감사를 드립니다. 이러한 과실이 끝이 아닌 새로운 시작으로 나아가는 또 하나의 받침대의 역할을 할 수 있도록 스스로에 대한 끊임없는 채찍이 필요하리라 생각됩니다. 특히, 이러한 값진 기회를 통하여 치의학 분야에서는 아직은 상대적으로 미개척 분야에 관한 나름대로의 지견을 얻게 된 것에 대하여 나름대로의 자긍심과 함께 자신감을 가지게 된 것은 큰 수확이라 하지 않을 수 없습니다.

먼저 이 논문을 완성하기까지 시종일관 끊임없는 관심과 사랑을 베풀어 주신 김종열 교수님과 윤창륙 교수님, 최종훈 교수님, 그리고 신경진 교수님께 감사의 말씀을 드리고 싶습니다. 그리고, 심사위원으로서, 한편으로는 동기로서 항상 아낌없는 조언을 준 안형준 교수님께도 감사의 마음을 전하고 싶습니다. 더불어 이 논문의 세세한 부분을 이끌어주시고 방향 설정에 많은 도움을 주신 김성택 교수님께도 감사의 말씀을 드리고 싶습니다. 또한, 논문의 시작부터 완성에 이르기까지 작은 부분까지 항상 챙겨주고 도움을 주었던 유지원 선생님과 지금은 공중보건의 생활을 하고 있는 김기서 선생님, 그리고 바쁜 전공의 과정 중 시간을 쪼개가면서 열심히 도움을 준 신준한 선생님, 강승철 선생님, 그리고 강진규 선생님과 그 외 모든 구강내과 의국원 선생님들에게도 감사의 마음을 전하고 싶습니다. 그리고, 좀 더 효율적인 결과를 얻을 수 있도록 여러 가지 면에서 항상 도움을 주신 통계학 임아경 선생님께도 감사의 말씀을 드립니다.

또한, 영원히 갚을 수 없는 사랑과 지원을 항상 해주신 아버님과 어머님께 형용할 수 없는 감사의 말씀을 드리며 이 논문을 바칩니다. 또한, 자식 대하시듯이 언제나 걱정과 사랑을 주신 장인어른, 그리고 장모님께도 한없는 감사의 말씀을 드리고 싶

습니다. 그리고, 결혼 9년째 동안 한결같은 마음을 간직해 준, 그리고 지난 **2**년 동안의 미국 유학생활을 어려움 없이 무사히 끝마칠 수 있도록 든든한 동반자가 되어준 아내에게도 한없는 감사의 마음을 전하고 싶습니다. 그리고, 무척이나 장난꾸러기이지만 한편으로 듬직함을 주는 성헌이, 그리고 새로운 생명에 대한 기쁨과 함께 언제나 웃음을 피어주는 병헌이와 함께 이 작은 기쁨을 함께 하고 싶습니다. 마지막으로 **200**3년 **6**월 미국 앤아버 생활의 시작부터 한국으로 떠나올 때까지 작은 부분에 이르기까지 도움을 주시고 저희 가족을 항상 생각하면서 기도해 주신 손우성 선생님, 오태주 선생님, 이동호 선생님, 그리고 변호영 선생님을 비롯한 모든 치과대학 선생님들, 목사님을 비롯한 모든 한인성서교회 가족분들, 그리고 그 외 앤아버 생활의 크고 작은 기쁨을 함께 한 모든 분들과도 이 기쁨을 나누고 싶습니다.

2005년 **6**월

김 재 홍

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ABSTRACT

Effects of different units of Botulinum toxin type A (BTX-A) on the computed tomographic and electromyographic measurements of human masseter muscle

Masseteric hypertrophy is recognized as an asymptomatic enlargement of one or both masseter muscles. Its etiology includes abnormal habits such as bruxism and clenching, changes in the proprioceptors, or a disturbance in the neurotransmitter balance. However, there has been some controversy. Treatment has concentrated on conservative therapy such as occlusal splints and muscle relaxants, and surgery. Botulinum neurotoxin (BTX) is known to be one of the most toxic naturally-occurring substances. On the other hand, the therapeutic use of BTX is generally safe and well-tolerated. There are a few reports showing that a BTX type A (BTX-A) injection into the masseter muscle can be alternatively used as a non-invasive treatment for masseteric hypertrophy. However, there is a paucity of controlled clinical studies involving objective and quantitative evaluation. Moreover, there are no reports comparing the effect of different BTX-A doses on masseteric hypertrophy. In this study, in order to evaluate the effects of two different BTX-A doses on masseteric atrophy, along with the changes in the electromyographic (EMG) values in the masseter muscle, 25 units

of BTX-A were injected bilaterally in the masseter muscle of 16 subjects, and 35 units were injected bilaterally in the remaining 16. The thickness and cross-sectional area of the masseter muscle were measured at each 3 position before and 12 weeks after the injection using computed tomography (CT). The EMG changes in the masseter muscle during maximum voluntary clenching were also evaluated before and 2, 4, 12, and 24 weeks after the injection. The differences in the results were statistically analyzed. The results are summarized as follows:

1. Statistically significant differences between the pre- and post-injection in both 25 units and 35 units of BTX-A were observed when the dimension and EMG values of the masseter muscle were evaluated ($P<0.01$).

2. There was no significant difference between the 25 units and 35 units of BTX-A in the dimension and EMG values of the masseter muscle.

3. The less reduction of the thickness and cross-sectional area of the masseter muscle was found at the farther site from the injection point ($P<0.01$).

4. Several mild side effects were reported, which were all temporary and localized.

From the results above, we can suggest that BTX-A is effective in treating the hypertrophy of the masseter muscle, but the dose of the toxin is not associated with its effectiveness within the limits of this study. However, a longer

follow-up will be needed to determine the lowest units of BTX-A for obtaining the most desirable clinical effects, and to decide the frequency of injections for sustaining the optimal efficacy.

Key Words : **Botulinum toxin type A (BTX-A), masseter muscle, computed tomography (CT), electromyographic (EMG) changes**

Effects of different units of Botulinum toxin type A (BTX-A) on the computed tomographic and electromyographic measurements of human masseter muscle

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Ⅰ. Introduction

Masseteric hypertrophy is recognized as an asymptomatic enlargement of one or both masseter muscles. This phenomenon was first described by Legg (1880). Gurney (1947) suggested that masseteric hypertrophy is commonly associated with abnormal habits such as bruxism and clenching. Changes in the proprioceptors (Beckers, 1977) and a disturbance in the neurotransmitter balance between dopamine and acetylcholine (Nishioka & Montgomer, 1988) have also

been touted as possible causes. However, there has been some controversy regarding its etiology.

Treatment has concentrated on conservative therapy and surgery. Surgical therapy usually involves a partial surgical resection of the masseter muscle and a modeling ostectomy in the region of the masseteric tuberosity. In the conservative therapeutic approach, an attempt was made to reduce the muscular hyperactivity using occlusal splints or the systemic administration of muscle relaxants. Bertram *et al.* (2001) revealed a significant decrease in the local asymmetry of the masseter muscle associated with splint therapy, and splints are known to have a site-specific effect in reducing the local maximum clenching-related asymmetry of the masseter muscle (Bertram *et al.*, 2002).

Initial interest in the botulinum neurotoxin (BTX) focused on the potentially lethal food-borne botulism produced by the ingestion of adulterated foods. This neurotoxin is known to be one of the most toxic naturally-occurring substances. BTX is composed of a 100-kd heavy chain and a 50-kd light chain joined by disulfide bonds. Seven serotypes (Type A, B, C1, D, E, F and G), each of which has its own specific site of action, that are produced by Gram-positive and anaerobic *Clostridium botulinum*, exert their paralytic effect by inhibiting the release of acetylcholine at the neuromuscular junction. This process of enzymatic action involves 4 steps: Binding, internalization, membrane translocation, and protease activity (Pellizzari *et al.*, 1999) Binding specifically and irreversibly occurs to the peripheral cholinergic nerve terminals. The toxin molecules then undergo receptor-mediated endocytosis. The light chain translocates to the cytoplasmic side of the endosome, and acts as a zinc-dependent protease that cleaves the proteins involved in the exocytosis of acetylcholine, thereby

preventing the release of neurotransmitters and rendering the nerve terminals nonfunctional (Pearce *et al.*, 1997).

The therapeutic use of BTX is generally safe and well tolerated. The potential medical applications of BTX-A were first recognized when a local injection of minute doses was used to selectively inactivate the muscle spasticity in strabismus (Scott, 1980). The success of this and a series of clinical studies led to the Food and Drug Administration (FDA) approval in 1989 for ophthalmologic and neurologic uses. The therapeutic benefits derived from a local injection of BTX preparations are based on the site-specific delivery and the fact that these compounds have a high affinity for uptake by cholinergic neurons. This results in temporary chemodenervation, which is effective for both striated muscles and eccrine glands (Klein, 2003). BTX therapy has also been reported to alleviate the pain associated with various conditions. Reports of BTX-A for the reduction of primary pain include a tension-type headache (Wheeler, 1998), chronic whiplash-associated neck pain (Freund & Schwart, 2000), myofascial pain (Acquadro & Borodi, 1994; Cheshire *et al.*, 1994), and migraine headache prophylaxis (Silberstein *et al.*, 2000)

The electromyographic (EMG) activity has been used as one of the most common diagnostic measurements in dentistry since the report by Moyer (1949). Its use is based on the assumption that various pathological or dysfunctional conditions can be discerned from the records of the EMG activity of the muscles (Mohl *et al.*, 1961). In addition, records of the EMG activity before and after therapeutic interventions have been used to document the changes in the muscle function (Ramfjord, 1961). There are many reports of basic research and clinical studies evaluating the applicability of EMG. Kawazoe *et al.* (1979) evaluated the

relationship between the EMG activity and the biting force in the masticatory muscles. Manns *et al.* (1983) used occlusal splints constructed at 3 different vertical heights to study the EMG influence of the vertical dimension in the treatment of myofascial pain dysfunction syndrome, and Ingervall *et al.* (1982) examined the EMG activities of the masseter and temporal muscles before and after the elimination of the occlusal interference in the balancing side. However, several deficiencies limit the interpretation of the results of these clinical trials. These include: The lack of adequate control groups, the lack of studies on the reliability and validity of the methods, and the variability in both the normal and patient groups. Therefore, there is a need for well-controlled clinical studies.

There are a few reports showing that a BTX-A injection into the masseter muscle can be alternatively used as a non-invasive treatment for masseteric hypertrophy. Atrophy of the hypertrophic muscles was noted in clinical photographs (Moore & Wood, 1994; Smyth 1994; von Lindern *et al.*, 2001), and the reduction in the EMG potential was also reported 4 weeks after the injection in one of the patients (Smyth, 1994). Recently, favorable responses were also revealed using ultrasound, EMG and/or computed tomography (Kim *et al.*, 2003; Park *et al.*, 2003; To *et al.*, 2001). However, there is a paucity of controlled clinical studies involving objective and quantitative evaluation. Moreover, there are no reports comparing the effect of different BTX-A doses on masseteric hypertrophy.

The aim of this study was to evaluate the effects of two different BTX-A doses on masseteric atrophy, along with the changes in the EMG values in the masseter muscle so that we can determine the optimal units of BTX-A for obtaining the most desirable clinical effects.

Ⅱ. Material and Methods

1. Subjects

This study was performed in accordance with the 1975 Declaration of Helsinki. Before admission to the study, a signed written consent form was obtained from each volunteer comprised of dental students and staffs at the College of Dentistry, Yonsei University, Seoul, Korea after the nature and the established use of BTX-A as well as its potential side effects had been fully explained. They were also free to withdraw from the experiment at any time. After screening for TMJ and orofacial pain examination, a total of 32 volunteers, aged 22 to 35 years (mean age of 26.1 years, 14 males and 18 females), were enrolled in this study. The exclusion criteria for this study included pregnancy, a history of drug allergy or any other serious medical illnesses. 29 out of 32 (90.6%) subjects reported tenderness to palpation on the masseter muscle, 30 (93.8%) had parafunctional habits, and 14 (43.8%) had unilateral chewing habits, who showed a preference for chewing on the right side. The volunteers were divided into 2 groups depending on the number of units of BTX-A injected in the masseter muscle; The 25U group (volunteers who were given 25 units of the toxin bilaterally), and the 35U group (volunteers who were given 35 units of the toxin bilaterally).

2. Methods

A. Injection of the BTX-A into the masseter muscle

The BTX-A (BTXA®, Lanzhou Institute of Biological Products, China) was supplied as a freeze-dried powder of 100U and was reconstituted with 1㎖ of sterile saline to a concentration of 10U/0.1㎖. The reconstituted drug was used immediately, and any surplus was discarded because the drug must be used within 1 hour of reconstitution. A total of 25U or 35U of the toxin per side was injected percutaneously using a 1㎖-syringe with a 26-gauge, and a ½-inch needle. The toxin was double-blindedly injected into two points, which were located at a distance of 1㎝ from each other, at the center of the lower ⅓ of the masseter muscle, that is, 1㎝ above the inferior border of the mandible.

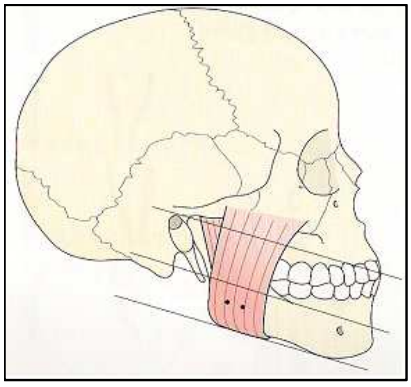

Fig 1. Points of the BTX-A injection

B. Computed tomographic (CT) measurements of the thickness and cross-sectional area of the masseter muscle

With respect to the thickness and cross-sectional area of the masseter muscle, computed tomographic (CT) measurements were performed before and 12 weeks after the injection. The CT scans were taken from the most inferior border of the mandible up to the condylar areas. The CT examinations were carried out using a CT HiSpeed Advantage (GE Medical System, Milwaukee, USA), and the images were obtained under the conditions of a soft tissue algorithm, 512×512 matrix, 120kV, and 200mA. Five-millimeter contiguous axial scanning was performed parallel to the inferior border of the mandible with the subjects in the rest position. Images from the CT scans were reconstructed using V-Works 4.0™ (Cybermed Inc., Seoul, Korea) software after transmitting them into a personal computer. The thickness and cross-sectional area from the 3 reference points on both sides of the masseter muscle were measured using the V-Works 4.0™ program. Position 1 was located at 10㎜, position 2 at 20㎜, and position 3 at 40 ㎜ above the inferior border of the mandible (Fig 1). The thickness was determined to be the distance from the most protuberant point of the muscle to the bone surface. The measurements were carried out 5 times by one investigator, and were averaged for further analyses.

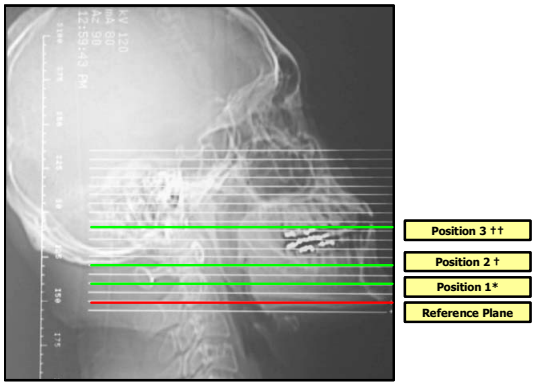

Fig 2. Selection of the measurement positions

*10mm above the inferior border of the mandible
+20mm above the inferior border of the mandible
++40mm above the inferior border of the mandible

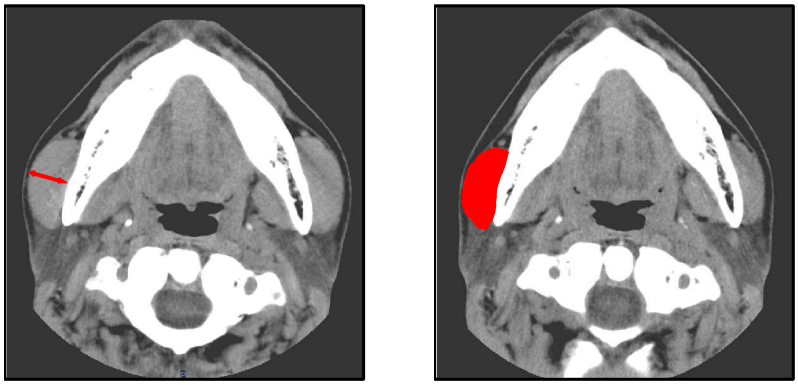

Fig 3. Computed tomographic measurements of the thickness and cross-sectional area of the masster muscle

C. Electromyographic (EMG) measurements of the masseter muscle

Electromyography (EMG) was performed using a BioPak system (BioResearch Inc., Milwaukee, USA) before and 2, 4, 12, and 24 weeks after the injection. The data was taken from the masseter muscle during the maximum voluntary clenching.

D. Statistical analysis

Statistical analyses were performed to examine the effects of BTX-A on the reduction in the thickness, cross-sectional area, and EMG measurements of the masseter muscle using a paired *t* test. An ANOVA test was also carried out to evaluate the influence of two different units of BTX-A on each parameter. SAS Version 8.1 Windows Statistics Program (SAS Institute, USA) was used for statistical analyses. A P value of <0.01 was considered statistically significant.

Ⅲ. Results

1. Computed tomographic measurements of the thickness and cross-sectional area of the masseter muscle

A statistically significant difference was observed between the results of the pre-injection and 12-week post-injection at the positions of 1, 2, and 3, with regard to the thickness and cross-sectional area of the masseter muscle in both groups (P<0.01). There were significant differences in the thickness and cross-sectional area between positions 1 and 3, and positions 2 and 3 in both groups (P<0.01), but there was no difference between positions 1 and 2 at the 12-week post-injection. No statistically significant differences were observed at positions of 1, 2, and 3 between the two groups at 12-week post-injection (Table 1, and Fig 2 and 3).

Table 1. Mean % decrease in the thickness and cross-sectional area of the masseter muscle at 12-week post-injection compared to those of pre-injection in each position of the 25U and 35U BTX-A group

	Position	25U (n=32)	35U (n=32)
Thickness	1	24.9%	30.7%
	2	18.2%	20.4%
	3	5.7%	6.6%
Cross-sectional Area	1	31.4%	36.4%
	2	26.1%	29.0%
	3	10.5%	8.9%

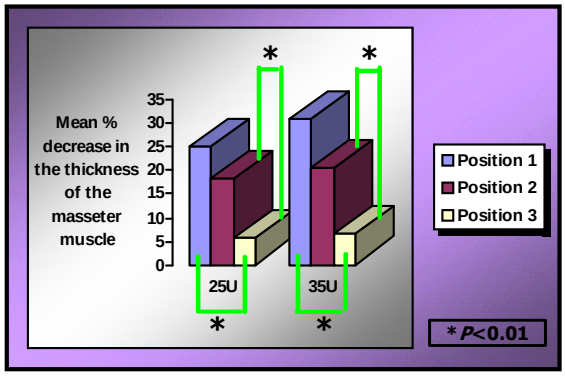

Fig 4. Mean % decrease in the thickness of the masseter muscle at 12-week post-injection compared to that of pre-injection in each position of the 25U and 35U BTX-A group

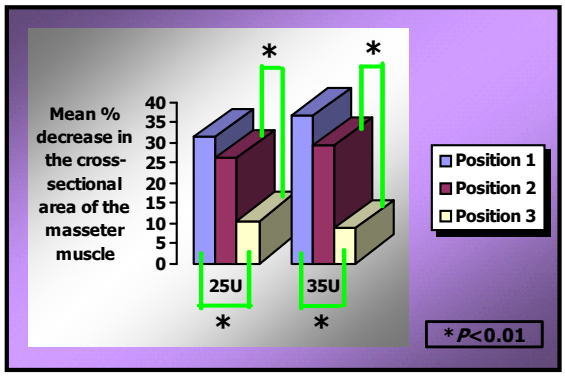

Fig 5. Mean % decrease in the cross-sectional area of masseter muscle at 12-week post-injection compared to that of pre-injection in each position of the 25U and 35U BTX-A group

2. Electromyographic (EMG) measurements of the masseter muscle

The electromyographic (EMG) results showed higher percentage decrease of the values in the 25U group at all the follow-up periods after the injection, but there was no statistically significant difference between the 2 groups. At 24 weeks after the injection, there was a 56.2% of recovery in the EMG values in the 25U group compared to 71.3% in the 35U group, based on the measurements at the baseline (Table 2 and Fig 4).

Table 2. Mean % decrease in the EMG values of the masseter muscle at 2-, 4-, 8-, 12-, and 24-week post-injections compared to those of pre-injection in the 25U and 35U BTX-A group

	25U (n=32)	35U (n=32)
2 weeks	73.6%	71.8%
4 weeks	74.5%	69.5%
8 weeks	71.5%	61.0%
12 weeks	55.0%	46.9%
24 weeks	43.8%	28.7%

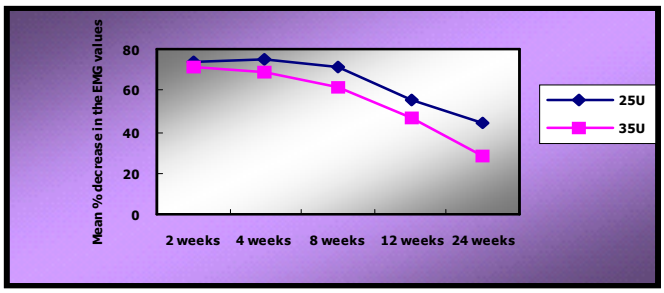

Fig 6. Mean % decrease in the EMG values of the masseter muscle at 2-, 4-, 8-, 12-, and 24-week post-injections compared to those of pre-injection in the 25U and 35U BTX-A group

3. Side effects of the BTX-A injection

There were no major local or systemic complications associated with the BTX-A injection. However, mild side effects were observed, all of which were temporary and localized. Out of the 16 subjects given 25U of the toxin, 3 subjects reported headache, 1 subject swelling and 3 subjects pain in the area of the injection, and 4 showed muscle weakness. In the 35U group, headache was observed in 2 subjects, bruise in 1 subject, pain in 2 subjects, muscle weakness in 4, and a dry mouth in 1. There were no differences in the incidence of the side effects between the 25U and 35U group (Table 3).

Table 3. **Side effects of the BTX-A injection (Pleural response)**

	Bruise	**Dry Mouth**	**Headache**	**Pain at Injection Site**	**Swelling**	**Muscle Weakness**	**Worsening of Parafunctional Habits**	**Total Side Effects**
25U (n=16)	**0**	**0**	3	3	1	4	1	12
35U (n=16)	1	1	**2**	**2**	**0**	4	**0**	10

Ⅳ. Discussion

The effect of BTX is dependent on the location, concentration, and volume of the solution injected. In an attempt to examine the relationship between the dose, volume, and targeted muscles, Borodic *et al.* (1994) reported that the size of the denervation field is determined by the dose and volume. In addition, Shaari and Sanders (1993) reported that the dose was a stronger predictor of the area of paralysis than the volume. In order to achieve the maximum dose response and to minimize the side effects, clinicians should use the most effective dose at the smallest volume. In this study, it was shown that 25 units of BTX-A was still effective, thereby making it necessary to assess this toxin dosage. In other words, the relative response according to the volume of the toxin was not determined.

BTX preparations administered at higher doses are likely to have less-favorable safety profiles. In this study, 25 or 35 units was not categorized within the poor safety profiles because the side effects encountered were mild and localized. The most common adverse effects were the weakness of the treated muscle, and local diffusion of the neurotoxin from the injection site causing unwanted weakness in the adjacent muscles as this study revealed that the muscle weakness was a relatively more common side effect in both groups. The long-term effects of BTX might include local changes in the muscle fiber size and EMG abnormalities, and cause reversible denervation atrophy in the muscles injected (Borodic & Ferrante, 1992). One unusual dose-related adverse effect, a dry mouth, was reported in patients with cervical dystonia who were treated with BTX-B that escaped from the injected muscle and reached the salivary gland through systemic distribution

(Lew *et al.*, 1997). It was found that one patient receiving 35 units of BTX-A had a slight and transient dry mouth. Therefore, it is strongly recommended that a detailed explanation of the possible adverse reactions be given to patients prior to treatment.

High doses and frequent injections of BTX have been associated with neutralizing antibody formation (Atassi & Oshima, 1999). However, in this study, no laboratory tests were performed to detect the presence of these antibodies. Therefore, it cannot be determined whether the subjects had hypersensitivity to BTX-A. The incidence of antibody formation with type A for the treatment of cervical dystonia has been < 5% (Greene *et al.*, 1994). Once the formation of neutralizing antibodies is identified, the type of BTX used needs to be changed. Otherwise, the effects of BTX may be short-term lived, and patients would require injections more often to maintain the desired efficacy. However, an additional concern with the development of antibodies is the possibility of serum cross-reactivity among the BTX serotypes (Oshima *et al.*, 1998). In order to minimize antibody resistance, a clinician should use the smallest possible effective dose, use treatment intervals of, at least, 3 months, and avoid booster injections (Greene *et al.*, 1994).

To *et al.* (2001) evaluated the effects of BTX-A on masseteric muscle hypertrophy using ultrasound and EMG. All 5 patients showed a good response with a maximum effect of a 31% reduction in the muscle bulk seen 3 months after treatment. However, this effect may be temporary and the main problem of this study seems that ultrasonography resulted in less reliability due to the variability in the probing forces. Kim *et al.* (2003) evaluated the effects of BTX-A on masseteric hypertrophy using CT. Nine out of 11 subjects showed a mean

reduction of approximately 22% in the masseteric muscle volume. Park *et al.* (2003) attempted a quantitative analysis of the reduction in masseter muscle hypertrophy after Botox® injection, using ultrasound and CT. The thickness on both sides of the masseter muscle was gradually reduced during the first 3 months. They used the F-H plane as a reference to obtain 10㎜ contiguous axial scans, in which the F-H plane was not aligned perpendicular to the muscle fibers and a 10㎜ contiguous scan was not the appropriate serial section in obtaining the precise data, resulting in an increased error in the measurements. The less reduction of the muscle thickness was found at the farther site from the injection point. Therefore, if there is a wide range of muscle hypertrophy, injections might be required at a distance of, at least, 2㎝. However, the problem of this study was that the point of injection did not always coincide with the position 1 (Fig 1). In addition, it was also found that the 35U group had a higher percentage decrease in the thickness and cross-sectional area of the masseter muscle at all positions other than the cross-sectional area of position 3. However, there were no significant differences between both groups regarding these 2 parameters.

Basically, the restoration of the neuromuscular function follows axon terminal sprouting (Brin, 2000). The primary BTX-A-intoxicated nerve terminals are incapable of neurotransmitter exocytosis and produce sprouts that eventually demonstrate exocytosis. However, these original BTX-A-intoxicated terminals resume exocytosis, and the sprouts regress to return the neuromuscular junction to its original state (de Paiva *et al.*, 1999). In this study, there was a statistically evident trend in the % decrease in the EMG values of both groups at all the follow-ups compared to those of pre-injection, but there was no significant

difference between the two groups. Furthermore, all the EMG values were recovered reaching the baseline measurements irrespective of the toxin doses, but the 35U group showed more recovery at all the follow-up periods than the 25U group although a significant difference was not noted.

EMG guidance has proven to be helpful in precisely placing BTX. This allows a clinician to locate the deep and small muscles that are impossible to palpate and allows the localization of the most active areas of the larger muscles (Blitzer & Sulica, 2001). It has been suggested that the addition of EMG can reduce the variability of successive injections, if needed, as well as maximize the effect of each treatment by placing the toxin close to its site of action at the motor end plates. In addition, there is a need for the use of an extraoral head splint, which allows subjects to constantly pose the same position when it comes to scanning the masseter muscle through CT. Moreover, it should be taken into consideration to perform one-millimeter contiguous axial scannings in order to measure the changes in the muscle dimension more precisely. However, it causes the patients to be exposed to more radiation. It is also possible to obtain more objective data if the subjects initially have similar masseter muscle volumes.

Within the limits of this study, Botulinum toxin type A (BTX-A) was effective in treating the hypertrophy of the masseter muscle, but the dose of the toxin was not associated with its effectiveness. However, a longer follow-up will be needed to determine the lowest units of BTX-A for obtaining the most desirable clinical effects, and to decide the frequency of injections for sustaining the optimal efficacy.

Ⅴ. Conclusion

In order to evaluate the effects of two different BTX-A doses on masseteric atrophy, along with the changes in the electromyographic (EMG) values in the masseter muscle, 25 units of BTX-A were injected bilaterally in the masseter muscles of 16 subjects, and 35 units were injected bilaterally in the remaining 16. The thickness and cross-sectional area of the masseter muscle were measured at each 3 position before and 12 weeks after the injection using computed tomography (CT). The EMG changes in the masseter muscle during maximum voluntary clenching were also evaluated before and 2, 4, 12, and 24 weeks after the injection. The differences in the results were statistically analyzed. The results are summarized as follows:

1. Statistically significant differences between the pre- and post-injection in both 25 units and 35 units of BTX-A were observed when the dimension and EMG values of the masseter muscle were evaluated (P<0.01).

2. There was no significant difference between the 25 units and 35 units of BTX-A in the dimension and EMG values of the masseter muscle.

3. The less reduction of the thickness and cross-sectional area of the masseter muscle was found at the farther site from the injection point (P<0.01).

4. Several mild side effects were reported, which were all temporary and

localized.

From the results above, we can suggest that BTX-A is effective in treating the hypertrophy of the masseter muscle, but the dose of the toxin is not associated with its effectiveness within the limits of this study. However, a longer follow-up will be needed to determine the lowest units of BTX-A for obtaining the most desirable clinical effects, and to decide the frequency of injections for sustaining the optimal efficacy.

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국 문 요 약

A형 보툴리눔 독소의 단위용량에 따른 전산화 단층촬영을 이용한 교근 크기 및 근전도에 미치는 효과

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김 재 홍

교근 비대증은 편측 또는 양측 교근의 무증상 비대로 정의된다. 이의 원인으로 이갈이 및 이악물기와 같은 비정상적 습관, 고유수용기의 변화 또는 신경전달물질의 균형 장애 등이 제시되고 있으며, 치료방법으로 교합장치 또는 근육 이완제와 같은 보존적 요법 및 수술 등이 시행되고 있다. 한편, 국소주사를 통한 보툴리눔 독소의 사용이 교근 비대증의 치료를 위한 보존적 치료방법으로 소개되고 있다. 이러한 보툴리눔 신경독소는 자연에 존재하는 독성이 강한 물질 중 하나로 알려져 있지만, 치료목적으로 사용되는 보툴리눔 독소의 경우 일반적으로 안전한 것으로 입증되고 있다. 하지만, 이에 대한 객관적이고 정량적인 평가를 통한 대조 임상연구가 부족한 실정이다. 또한, 교근 비대증에 대한 서로 다른 용량의 독소효과에 대한 비교, 평가는 전무한 실정이다. 본 연구에서는 교근 위축에 대한 두 가지 서로 다른 용량의 독소 효과 및 교근의 근전도 수치를 평가하기 위하여 **16**명의 대상자에게는 **25**단위의 독소를, 나머지 **16**명에게는 **35**단위의 독소를 각각 양측 교근에 주사하였다. 술전 및 술후 **12**주에 전산화 단층촬영을 이용하여 각각 세 가지 서로 다른 위치에서 교근의 두께 및 단면적을 측정하였다. 또한, 술전 및 술후 **2**, **4**, **12** 및 **24**주에 최대 수의성 이악물기 동안 교근의 근전도 변화를 분석, 평가한 후 다음과 같은 결과를 얻었다.

1. 교근의 크기 및 근전도 평가 시 **25**단위 및 **35**단위 모두 술전 및 술후 결과 사이에 유의성 있는 차이를 보였다 **(*P*<0.01)**.

2. 교근의 크기 및 근전도 평가 시 **25**단위 및 **35**단위 결과 사이에 유의성 있는 차이는 보이지 않았다.

3. 주사부위로부터 멀리 떨어질수록 교근 두께 및 단면적의 감소효과가 줄어들었다 **(*P*<0.01)**.

4. 술후 경미한 부작용이 관찰되었으나, 모두 일시적이고 또한 국소적인 부작용이었다.

이상의 결과로부터 **A**형 보툴리눔 독소는 교근비대증의 치료에 효과적인 것으로 판단된다. 하지만, 보툴리눔 독소의 용량에 따른 차이는 보이지 않았다. 한편, 최대의 임상적 효과를 얻기 위한 최소용량 및 독소의 적절한 효능 유지를 위한 주사빈도를 결정하기 위하여 좀더 장기간에 걸친 연구가 필요할 것으로 사료된다.

핵심되는 말 : **A**형 보툴리눔 독소, 교근, 전산화 단층촬영, 근전도 변화