



Management of myofacial pain associated with severe bruxism with type A botulinum toxin (lantox): a twelve month follow-up

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ABSTRACT

Numerous treatment alternatives have been suggested for the management of bruxism and myofascial pain with variable results, including the local application of botulinum toxin; however few studies have been reported and with limited sample size. The objective of this study was to evaluate the clinical efficiency of botulinum toxin type A for the treatment of patients with myofascial pain associated with severe bruxism. An interventional, blind, longitudinal twelve month study was carried out; sample size consisted of forty patients with a diagnosis of myofascial pain associated with severe bruxism on whom botulinum toxin type A was applied; patients were evaluated prior to application at 3, 6, 9 and 12 months and variables including age, sex, spontaneous and provoked pain, mandibular opening, mandibular deviation and presence of joint noises were considered. 77.7% of the sample consisted of women with an average age of 33.56 ± 12.17 years old. 80.5% reported improvement for both spontaneous and provoked pain during treatment, out of which 51.7% presented increased pain 3 and 6 months, 13.7% increased pain between 6 and 9 months and 3.4% between 9 and 12 months. Application of botulinum toxin type A is a safe and effective treatment for myofascial pain associated with severe bruxism and its therapeutic effect requires new applications every three to six months for its effectiveness to persist.

Keywords: Botulinum toxin, myofascial pain, bruxism, lantox.

INTRODUCTION

Stress is the result of the interaction between the individual and a threatening environment that endangers his security and produces physical, symptomatic and emotional manifestations that could lead to death (Rodríguez et al., 1998, Ash and Ramfjord, 1996).

One of the most common somatic manifestations of stress is bruxism. This pathology is defined as movement alteration of the masticatory system, characterized by crunching and grinding of teeth during sleep or alertness which affects the stomatognathic system causing

damage, sometimes irreversible, on anatomic structures such as the TMJ, teeth and muscle tissue among others (Okeson, 1985; Okeson, 1996). This can affect the entire population, including children; its prevalence is varied and ranges between 5% and 96% in adults and 6% and 68% in adolescents and children. It is more common in women than men and in younger individuals between 24 and 40 years old (Chung et al., 2000).

Symptomatic manifestations of bruxism can vary and include dental wear facets, pain of masticatory and facial

muscles, headaches, TMJ pain and earache among others. These group of symptoms is defined as myofascial pain.

Myofascial pain of masticatory muscles has a high epidemiological prevalence which affects between 38% and 75% of patients with signs and symptoms of temporomandibular disorders (List and Dworkin, 1996).

Numerous etiological theories of bruxism have been suggested including malocclusions, muscle alterations, TMJ disorders and psychological factors, none of which have been confirmed or rebutted given its multifactorial nature (Attanasio, 1997; Casassus et al., 2007). During recent years most reports have focused on physiopathological factors which reveals a tendency in bruxism research to approach the problem from a biomedical-bio-psychological perspective which is not concentrated only on occlusion (Lobbezoo et al., 2006).

Currently, there is great controversy regarding which is the most adequate treatment for bruxism. Part of the discussion is based on the confusion regarding etiopathogenesis, characteristics and diagnostic criteria.

Multiple therapies have been reported for the treatment of bruxism with varied results such as occlusal splints (Raphael and Marbach, 2001), physical means, physical therapy (Nikolakis et al., 2002), psychological therapy (Laat et al., 2003), selective grinding, pharmacotherapy (Dionne, 2000), and anti-stress activities. In certain cases, conventional treatment does not provide enough control for severe bruxism which requires alternative treatments that can offer better results or compliment conventional ones. The objective of the different methods is to produce muscle relaxation and various alternatives have been introduced in order to reach this goal.

Type A botulinum toxin is the safest, most potent and effective biological toxin (Jankovic et al., 1990; Jankovic and Brin, 1991) which is widely used since 1980 to treat multiple pathologies associated with muscle hyperactivity. (Kessler and Benecke, 1997) Neurologists and physicians who work with physical rehabilitation use it as the treatment choice for neuromuscular alterations such as dystonias and spasticity of both children and adults. More recently other applications of great benefit have been reported such as treatment of facial expression lines (wrinkles), sialorrhea in infantile cerebral palsy and Parkinson's disease, bruxism and different types of myofascial and joint-muscle pain (Acquadro and Borodic, 2005; Aguilar-Rebolledo, 2005).

Botulinum toxin type A is a bacterial neuro-toxin cultivated from *Clostridium Botulinum* which binds to the nerve ending of motor plates and blocks the liberation of acetylcholine, which produces a temporary (1 to 6 month) functional chemical denervation of the muscle which limits its activity (Pidcock et al., 2002).

Seven types of botulinum toxins with different antigenic composition have been identified which includes type A,B,C,D,E,F and G, with type A being the

most utilized commercially and therapeutically. Its maximum recommended dose is between 300 and 400 units per session and no more than 400 units during a three month period. Doses can vary however depending on size of the objective muscle, intensity of contraction and other factors such as muscle response to initial treatment with the toxin. Until the moment, no reports of anaphylactic reactions or deaths caused by the toxin have been reported (Brin, 1997).

Lantox is a botulinum toxin type A, produced by Lanzhou Biological Products (LIBP) in China. Each ampoule contains 100 U or 50 U of the toxin, 5 mg of gelatin, 25 mg of dextran and 25 mg of sucrose.

Studies have reported satisfactory results on patients with bruxism with the use of botulinum toxin type A, which is safe, effective and conservative option with minimal adverse effects when used by trained professionals. Despite these reports, there are few studies on limited numbers of patients which have evaluated its effectiveness patients with bruxism, TMJ disorders and hypertrophy of masticatory muscles in our population. Therefore the purpose of this study is to evaluate its long term effectiveness in a group of patients with myofascial pain associated with severe bruxism.

MATERIALS AND METHODS

This is was a longitudinal, interventional, blind pre-experimental study in which individuals served as their own controls at three, six, nine and twelve month intervals.

Forty patients were included initially out of which four were removed due to presence of exclusion criteria thus leaving a final sample of 36 patients which met all the inclusion criteria which were evaluated at three, six, nine, and twelve month intervals. Patients which presented myofascial pain of masticatory muscles associated with severe bruxism were followed at the Oral and Maxillofacial Surgery Clinic at CES University in Medellin, Colombia. Inclusion criteria were as follows:

- Patients older than 18 years of age in good health condition without presence of dental care or periodontal disease and who presented a stable occlusion and presented bruxism marked by dental wear facets or shiny areas on restorations, a history of clenching of at least 5 days and/or nights per week, a sense of tiredness or muscle fatigue in the mornings, spontaneous and/or provoked pain of masticatory muscles, tooth grinding during the last three months reported by family members or spouse.
- Patients who had received unsuccessful treatment for bruxism
- Decreased mandibular opening of up to 30 mms.
- Patients with crepitus or click type joint noises which met the other inclusion criteria.

Exclusion criteria were:

- Pregnant women
- Patients undergoing treatment for bruxism with drugs or splints during the last month.
- Patients with a clinical diagnosis of non-reducing unilateral or bilateral disc displacement
- History of luxations or TMJ blockages during the last 12 months

A clinical evaluation of each patient was completed prior to the application of the botulinum toxin. Information regarding each one of the studied variables which included age, sex, and spontaneous pain according to a VAS scale (0-10), mandibular opening, mandibular deviation and presence of joint noises were recorded in a previously designed chart. Informed consent was obtained from each of the participants.

Application of 15 units (U) of botulinum toxin type A - LANTOX[®] was performed with the patient sitting in an upright position in three sites of the masseter muscle: insertion, mid area and origin for a total of 150 U per patient. The toxin was distributed in 10 infiltration sites (5 per side).

One of the authors applied the toxin while the other one completed the initial and further evaluations at 3, 6, 9 and 12 months. A statistician compared the information from the five established periods for each one of the variables and performed the corresponding statistical analysis (ANOVA for repeated post-hoc samples with the Bonferroni test). None of the authors had access to the information obtained by others in order to guarantee the double blind nature of the study. Both authors were previously trained and standardized for both the application of the toxin as for the completion of evaluations.

This study was classified as a study *with a Higher than Minimal Risk* according to article 11 of Resolution N^o 008430 de 1993 of the National Ministry of Social Protection given that it was a pharmaceutical investigation. According to article 49 which emphasizes therapeutic studies on human beings which seek to modify known effects it is important to clarify that this Project did not intend to modify the effect of the botulinum toxin which is well known, but to take advantage of its benefits in order to apply it to temporal and masseter muscles as described above. This study was approved by the Institutional Review Board at CES University according to resolution approved on April 18, 2008.

Statistical Analysis

Evaluation of spontaneous pain, provoked pain, mandibular opening and mandibular deviation were compared with respect to evaluation times (initial, three, six, nine and twelve months) with an ANOVA test for repeated samples. Statistically significant differences

were observed between different evaluation times for spontaneous and provoked pain with P values <0.000. A post-hoc analysis with the Bonferroni test was applied afterwards to determine differences between evaluation times.

RESULTS

The sample of thirty six patients met the inclusion criteria, consistent of 28 females (77.7%) and 8 males (22%). Age ranged between 18 and 59 years with an average of 33.56 ± 12.17 years.

Significant differences were observed between the initial evaluation and those made at 3,6,9 and 12 months as well as between the evaluation at completed at 3 months and those at 6,9 and 12 months. No significant differences were observed however between evaluations at 6, 9 and 12 months for spontaneous or provoked pain (Table 1, Table 2, Graph 1). There no differences observed either for mandibular opening and mandibular deviation for any of the of the evaluation times.

Spontaneous pain prior to the application of the botulinum toxin presented an average VAS score of 6.0 ± 1.7 with an average decrease of pain to 2.4 ± 1.6 at three months, 3.5 ± 2.0 at 6 months and average values of 4.1 ± 2.0 at 9 and 12 months. 7 patients (19.4%) did not present any improvement in spontaneous symptomatology after application of the toxin.

Provoked pain prior to the application of the botulinum toxin presented an average VAS score of 4.7 ± 2.4 which decreased to 2.2 ± 1.6 at three months, 3.3 ± 2.1 at 6 months, 4.1 ± 2.1 at 9 months and 4.2 ± 2.3 at 12 months. 7 patients (19.4%) did not present any improvement in provoked symptomatology after application of the toxin.

Average values for mandibular opening were 41.3 ± 3.7 mm prior to the application of the toxin, $41.4 \text{ mm} \pm 2.0 \text{ mm}$ three months after the application, $40.9 \text{ mm} \pm 1.9 \text{ mm}$ at 6 months, $40.7 \text{ mm} \pm 1.6 \text{ mm}$ at 9 months and $40.5 \text{ mm} \pm 1.6 \text{ mm}$ at 12 months; 2 patients (5.5%) increased their opening 7 mms after the application from an initial opening of 30 and 32 mm respectively which persisted throughout the twelve months; 2 patients (5.5%) presented decreased openings after application of the toxin 4 and 3 mm respectively to a final value of 40 mm which persisted until the final evaluation, and which did not present any clinical relevance.

Mandibular deviation prior to the application was 0.6 ± 0.8 mm and remained stable without any variation during post-application evaluations at 3, 6, 9 and 12 months.

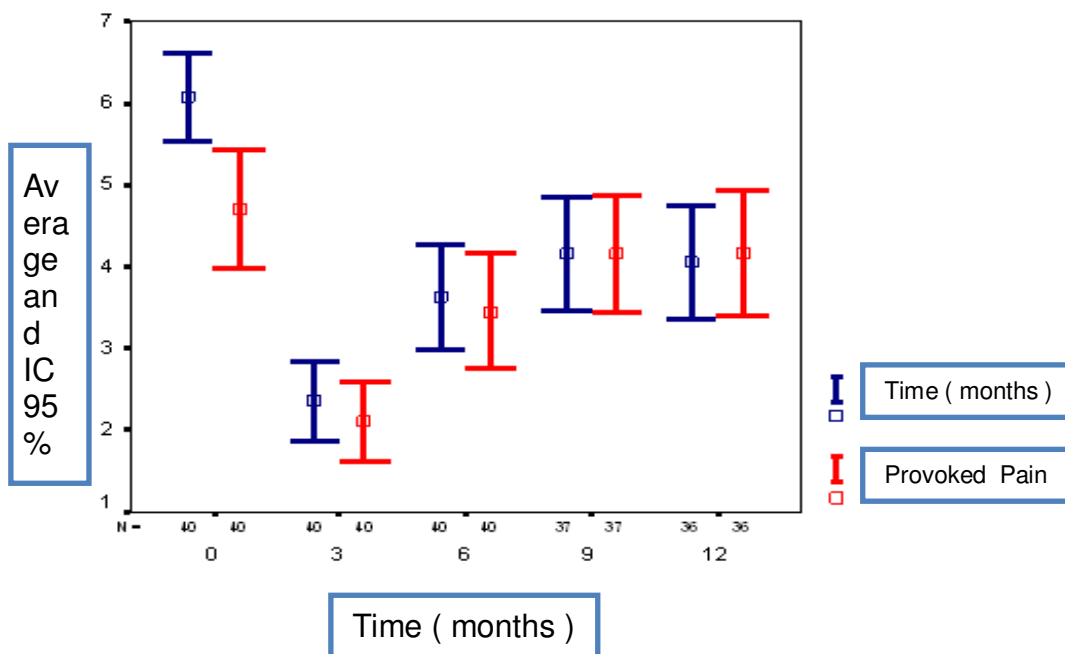
Eleven patients (30.55%) presented joint noises prior to the application of the toxin which persisted after its application during all evaluation times at 3,6,9 and 12 months.

Table 1. Average distribution of spontaneous and provoked pain in time in patients with myofascial pain associated with bruxism

	Spontaneous Pain	Provoked Pain	Mandibular Opening	Mandibular Deviation
Time (months)	$\bar{X} \pm D.E.$	$\bar{X} \pm D.E.$	$\bar{X} \pm D.E.$	$\bar{X} \pm D.E.$
0	6.0±1.7	4.7±2.4	41.3±3.7	0.6±0.8
3	2.4±1.6	2.2±1.6	41.4±2.0	0.6±0.8
6	3.5±2.0	3.3±2.1	40.9±1.9	0.6±0.8
9	4.1±2.0	4.1±2.1	40.7±1.6	0.6±0.8
12	4.1±2.0	4.2±2.3	40.5±1.6	0.6±0.8

Table 2. Comparison of time and clinical manifestations associated with bruxism (p values) after botulinum toxin Type A Lantox

	P Value for the Bonferroni Test			
0 vs 3	.000	.000	1.000	1.000
0 vs 6	.000	.011	1.000	1.000
0 vs 9	.001	.837	1.000	1.000
0 vs 12	.001	1.000	1.000	1.000
3 vs 6	.012	.016	.693	1.000
3 vs 9	.001	.000	.076	1.000
3 vs 12	.001	.000	.007	1.000
6 vs 9	.528	.048	1.000	-----
6 vs 12	.719	.047	.453	1.000
9 vs 12	1.00	1.000	.831	1.000



Graph 1. Average distribution of pain in patients at the time Myofascial pain associated with bruxism

DISCUSSION

Literature reports support the use of type A botulinum toxin for the treatment of different entities that affect the maxillofacial complex which includes TMJ disorders (Freund et al., 2000), recurring TMJ luxations (Daelen et al., 1997; Daelen et al., 1998), hypertrophy of masseter muscles (Mandel and Tharakan, 1999; Smyth, 1994; Schwartz and Freund, 2002), hemi-facial spasms (Surya, 2000), masticatory muscle dysfunction, cervico-facial dystonias (Lindern, 2001), salivary gland pathologies (Ellis et al., 2000), myalgias of masticatory muscles (Fross, 2000), and severe bruxism (Erdal et al., 2000; Chikhani et al., 2003; Lindern et al., 2003) among others (Umstadt, 2002; Roser et al., 1998).

The results of this study revealed a reduction of four points on the VAS scores for spontaneous pain, when comparing the initial examination (6.0 ± 1.7) with the three month follow-up (2.4 ± 1.6); a reduction of 2.5 points, when comparing with six month evaluation (3.5 ± 1.6) and during the corresponding evaluations at nine and twelve months values indicated a significant increase (4.1 ± 2.0 with respect to the three and six month evaluations although still lower than the initial scores).

With regards to provoked pain a similar behavior to spontaneous pain was observed when comparing with the initial VAS score (4.7 ± 2.4); A decrease of three points was observed at the three month evaluation (2.2 ± 1.6) and a two point reduction at six months (3.3 ± 2.1); Evaluations at nine and twelve months did not reveal significant reductions in VAS scores and with spontaneous pain show a trend to return towards initial values, indicating the decreased therapeutic effect and the need for a new application.

These results are comparable with those published by Freund et al in 2000 who reported an initial average VAS score of 8 with a three point reduction during an eight week period. Fross in 2000 reported an initial score of 8 and a reduction of two points during a 10 week period. Luca et al in 2008 reported an initial VAS score of 6.2 which decreased 2.6 points to 3.6 during a six month period for provoked pain and an initial VAS score of 5 which decreased 1.4 points to 3.6 during the same period of time for spontaneous pain.

In this study, improvement of pain symptoms of masticatory muscles was 80.5% which is comparable with those of Vonlindern in 2001 who reported an improvement of 80%. Niamtu in 2003 reported an improvement of 79% of masticatory muscle symptomatology. However, in a later report, Vonlindern in 2003 observed an improvement of over 90% similar to the one reported by Ortiz et al in 2004 of 95.2%.

Freund et al reported an improvement of 5 mm in mandibular opening from 29.5 mm up to 34.5 mm during an 8 week period coinciding with those reported by Luca et al in 2008 who found an increase of 2 mm from an initial value of 46.30 mm to 48.40 mm six months later.

The results of this study did not indicate significant changes in mandibular opening at any of the times evaluated with initial values of 41.3 ± 3.7 and final values of 40.5 ± 1.6 mm.

During the course of the study no adverse effects were observed after the application of botulinum toxin type A, demonstrating its clinical use is safe and practical (Freund et al., 1999).

CONCLUSION

The application of botulinum toxin type A, constitute an innovative, adequate and efficient method for the treatment of myofascial pain associated with chronic bruxism. Its therapeutic effect requires a new application between every three to six months in order to have a continued clinical effect.

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