Int. J. Oral Maxillofac. Surg. 2013; 42: 759–764
http://dx.doi.org/10.1016/j.ijom.2013.02.009, available online at http://www.sciencedirect.com

International Journal of Oral & Maxillofacial Surgery

Clinical Paper
TMJ Disorders

Botulinum toxin injection for management of temporomandibular joint clicking

A. S. Emara[1], M. I. Faramawey[1], M. A. Hassaan[2], M. M. Hakam[1]
[1]Oral and Maxillofacial Surgery Department, Faculty of Oral and Dental Medicine, Cairo University, Cairo, Egypt; [2]Radiodiagnosis Department, Faculty of Medicine, Cairo University, Cairo, Egypt

A. S. Emara, M. I. Faramawey, M. A. Hassaan, M. M. Hakam: Botulinum toxin injection for management of temporomandibular joint clicking. Int. J. Oral Maxillofac. Surg. 2013; 42: 759–764.

Abstract. The aim of the present study was to investigate the effect of botulinum toxin type A (BTX-A) injection in the lateral pterygoid (LP) muscle on temporomandibular joint (TMJ) clicking. The study enrolled seven patients with a total of 11 joints; all patients were stage I or II of Wilke's staging for internal derangement. BTX-A was injected in the ipsilateral LP muscle with electromyogram (EMG) guidance and the subjects were assessed for 4 months. Maximum inter-incisal opening, range of lateral movement, and the presence of a click were recorded throughout the follow-up period, and magnetic resonance imaging (MRI) was ordered at the end of the 4 months. The results showed that the decrease in inter-incisal opening and side to side movement immediately postoperative was statistically significant, while the difference by the end of the follow-up period was insignificant. MRI showed a marked improvement in disc position postoperatively. It may be concluded that BTX injection in the LP muscle leads to the disappearance of joint clicking clinically and a significant improvement in disc position as shown on MRI.

Key words: temporomandibular joint; click; BOTOX; MRI.

Accepted for publication 18 February 2013
Available online 26 March 2013

Temporomandibular disorders (TMD) is a collective term used for a number of clinical problems that involve the masticatory muscles, temporomandibular joint (TMJ), and/or associated structures.[1] Anterior disc displacement (ADD) is one of the major findings in TMDs, as well as the most common cause of TMJ sounds.[2] Currently followed treatment regimens for disc displacement include splint therapy, therapeutic exercises, and surgery. Often, the joint clicking does not change considerably with conservative treatment.[2,3]

Joint lavage has also been suggested as a treatment option. Some studies have reported this to improve function, reduce clicking, and reduce joint pain,[4] while others have reported no significant improvement.[5] Arthroscopic disc repositioning has also been reported as a treatment option and has proved to be more cosmetically acceptable than open surgery, but requires higher skills and extensive training.[6] It has been proposed that uncoordinated function between the muscle bundles of the upper head and the superior part of the lower head of the lateral pterygoid (LP) muscle could lead to abnormal movements of the disc therefore causing a click. Further investigation on the relationship between disc displacement and attachment of the LP directly

0901-5027/060759 + 06 $36.00/0

into the disc has been carried out,[7,8] and a close relationship has been claimed between anterior disc displacement with reduction (ADDR) and the activities of the LP; this was also concluded after two electromyographic studies.[2,9]

Botulinum toxins (BTX) were first recognized by Christian Andreas in 1817, when he found that food-borne botulism was due to a toxin that paralyzed skeletal muscles and parasympathetic function. He further suggested that these toxins could be used to treat involuntary muscular spasms and movements.[10] The therapeutic value of BTX is due to its ability to cause chemodenervation and to produce local paralysis when injected into a muscle.[10] Several serotypes of BTX have been discovered, of which BTX-A is the one approved for human application, with the best results and least complications. The therapeutic use of BTX-A includes cases of blepharospasm, oromandibular dystonia, laryngeal dystonia, hemifacial spasm, cervical dystonia, tremors, and tics.[10,11] BTX-A has been shown to be effective in the treatment of many TMDs.[1,2,12,13] Its success in treating cases of ADDR was reported in a study conducted on two patients.[2] The aim of the present study was to further investigate the effect of BTX-A injection in the LP on TMJ clicking based on the theory suggesting that the hyperactivity of the muscle is an etiologic factor of the click.

Patients and methods

The study enrolled six patients (one male, five females) with a total of 11 joints; patients were aged a mean 26.55 ± 5.66 years. All patients were selected from the outpatient clinic, complaining of a painless TMJ click with no muscle tenderness, associated with ADDR confirmed by magnetic resonance imaging (MRI). A thorough clinical examination and medical history were taken, and candidates with neuromuscular disorders (e.g. myasthenia gravis) and musculoskeletal disorders were excluded. All patients were informed and consented on the procedures to be followed throughout the study. MRI was ordered for all the affected joints to confirm the clinical diagnosis (ADDR) and to document the disc position before injection (parasagittal T2 slices). The images were made on a 1.5 T machine with the following parameters: TR, 3190; TE, 66; slice thickness, 3 mm; interslice gap, 0.3 mm. The TMJ disorders fulfilled stage I or II of Wilke's staging of internal derangement.[14] The preoperative maximal inter-incisal opening (MIO), the opening at which the click occurred, and the range of lateral movement were measured using a Vernier calliper, recorded in millimetres (mm) and stored for later statistical analysis.

A BTX-A vial was reconstituted with 2 ml of 0.9% normal saline to obtain a 5 U/0.1 ml solution (BOTOX 100 U powder for solution for injection; *Clostridium botulinum* type A neurotoxin complex, Allergan, Westport Co., Mayo, Ireland); 0.7 ml of this solution containing 35 U BTX-A were then prepared for injection in a 1-ml insulin syringe. This was injected into the ipsilateral LP muscle with the guidance of an electromyogram (EMG) device (Signal Amplifier for BTX-A; Barrett Engineering, Fortuna, CA, USA). With the patient sitting in an upright position on the dental chair, the LP muscle was approached intraorally from the contralateral side with the mouth opened wide. The injection needle was directed towards the neck of the condyle where the LP inserts (Fig. 1). The patient was then instructed to remain in an upright position for 4 h (to reduce diffusion into pharyngeal muscles which may cause nasal regurgitation).

Patients were recalled weekly during the first month, then monthly for three more months. The same preoperative measurements were taken at each of the follow-up sessions. MRI was ordered at the end of the follow-up period with the same parameters as used preoperatively. The pre- and postoperative MR images were compared for a change in disc position antero-posteriorly. The most centralized image in the closed mouth position in the pre- and postoperative MR images was chosen and an *x*–*y* graph drawn according to the set of anatomic points adapted from Arayasantiparb and Tsuchimochi.[15] The *x*-axis extended from the lowest point of the articular eminence to the highest point of the external auditory meatus. The *y*-axis was drawn automatically by the Plot Digitizer computer program (Plot Digitizer Program 2.5.0, Joseph A. Huwaldt) perpendicular to the *x*-axis extending from the lowest point of the articular eminence. The anterior-most and posterior-most points of the articular disc were chosen and the program calculated their (*x*, *y*) coordinates, which were saved for the pre- and post-injection images of the same joint. Distances between the disc points and the head of the condyle were calculated using the formula:

$$\sqrt{(x_2 - x_1) + (y_2 - y_1)^2}$$

The anatomic assessment points were as follows: point T: lowest point of the articular eminence – and will mark the (0,0) point of the (*x*,*y*) graph to be drawn; point DA: anterior-most convexity of the articular disc; point DP: posterior-most convexity of the articular disc; point C: uppermost point of the mandibular condyle; point GP: lowermost point of the posterior glenoid tubercle – and will mark the (10,0) point on the graph to be drawn; and point A: the uppermost point of the external auditory meatus. The mathematical formula $\sqrt{\ }(a_2 - a_1)2 + (b_2 - b_1)^2$ was used to determine the difference between the two points pre- and postoperatively, i.e. the coordinates of the anterior point of the disc (point A) were compared pre- and postoperatively and the same for the posterior point of the disc

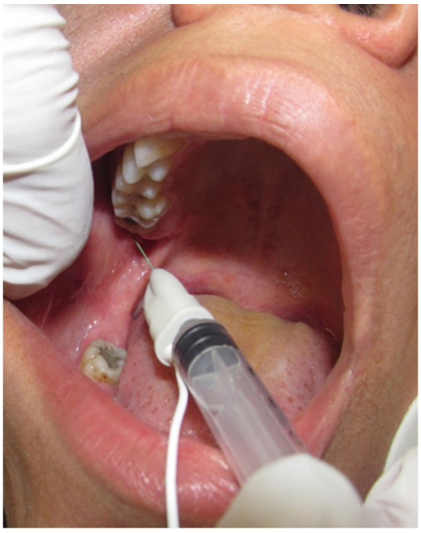

Fig. 1. Botulinum toxin type A (BTX-A) injection in the lateral pterygoid muscle.

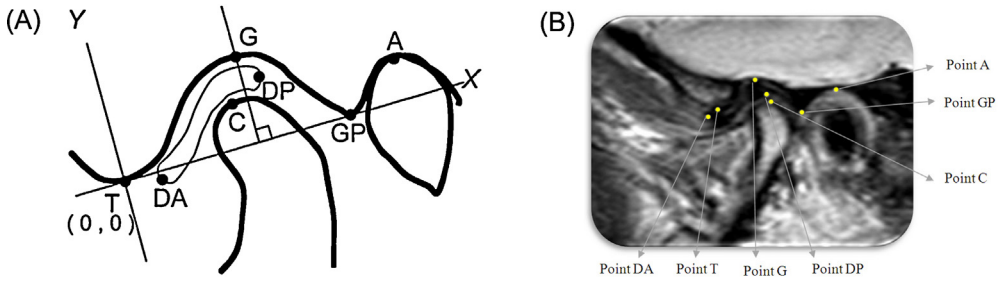

Fig. 2. Diagrammatic illustration (A) and MR application (B) of the anatomical assessment points according to Arayasantiparb and Tsuchimochi.[15]

(point B) (where a_1, a_2 are the x-coordinates of point A pre- and postoperatively, respectively, and similarly for the coordinates of point B) (Fig. 2).

Statistical analysis

The statistical analysis was performed using SPSS version 15 (Statistical Package for the Social Sciences; Echosoft Corp., USA). Data were presented as the mean ± standard deviation. One-way analysis of variance (ANOVA) was used to compare variables within the studied group of patients. A post hoc test was done to identify the different group if the ANOVA test was positive. A one-sample Student's *t*-test was used to compare one studied variable to a test constant value. In all tests, results were considered statistically significant if the *P*-value was equal to or less than 0.05.

Results

The study included six patients with a total of 11 joints; all of the patients complained of a painless audible click, either unilaterally or bilaterally. Four joints had a reciprocal click, while the other seven joints had a single opening click. The click had been heard and felt by the patients within a period of time ranging from 6 months to 2 years, with a progressive increase in magnitude. The immediate postoperative period was uneventful for all except one patient; this patient had a preoperative bilateral click and showed signs of dysphagia, nasal tone of voice, and regurgitation 5 days after the injection, which disappeared 9 days later.

On the first week postoperatively, the clicking sound disappeared for all joints except one joint that had persistent click; this then disappeared after the first week. At the third and fourth months, the clicking sound had returned in only one joint, while the remaining joints showed no click (Fig. 3). The mean MIO preoperatively was 41.55 mm, it then dropped at the first week postoperatively to 22.64 mm. At the end of the fourth month there was a statistically insignificant decrease in the MIO with the mean being 38.55 mm (as seen in Fig. 4). The mean lateral movement preoperatively was 15.82 mm; at the end of the second week postoperatively it dropped to 11.00 mm, then there was a gradual increase in the mean lateral movement throughout the follow-up period until it reached 17.27 mm at the end of the fourth month. The difference between the preoperative lateral movement and that postoperatively was found to be statistically insignificant. Figure 5 shows pre- and postoperative MRI of the disc for one of the cases; using a Photoshop program the preoperative disc was coloured in yellow and the postoperative disc was coloured in blue. These two MR images were overlapped and the transparency of the postoperative image was adjusted to visualize the change of disc position pre- and postoperatively, as seen in Fig. 6.

A one-sample Student's *t*-test was used to compare the mean values of both point A and point B to a preoperative hypothetical value of 0. The mean differences between the coordinates of each of point A and point B pre- and postoperatively were 0.62 and 0.83, respectively, which were found to be statistically significant with *P*-values of 0.001 (Table 1).

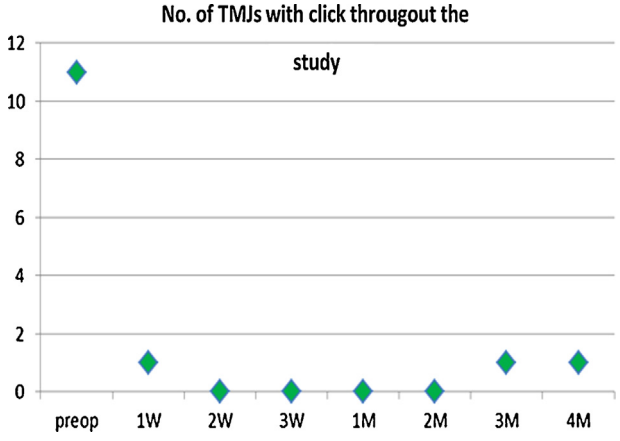

Fig. 3. Scatter chart showing presence of click throughout the study period.

Discussion

As generally agreed, conservative treatment should always be the first line of treatment for TMDs. Most published studies have focused mainly on treating pain and functional limitation. Few studies[16,17] addressing the problem of painless click have been reported in the literature even though it is a common complaint. The present study was designed following the promising preliminary results of Bakke et al.[2] on the successful use of BTX-A injection for TMJ clicking.

The initial diagnosis of ADDR was obtained by clinical examination. The definitive diagnosis was confirmed after studying the MR images of the candidates and clearly identifying an anteriorly displaced articular disc in the closed mouth position and disc reduction in the open mouth position. Imaging of the TMJ using MRI remains the most accurate method for diagnosing ADD.[18] T2 parasagittal slices in both the open and closed mouth positions were used to locate the disc position, as has been implemented in several studies due to the easier identification of the disc in this sequence.[2,19]

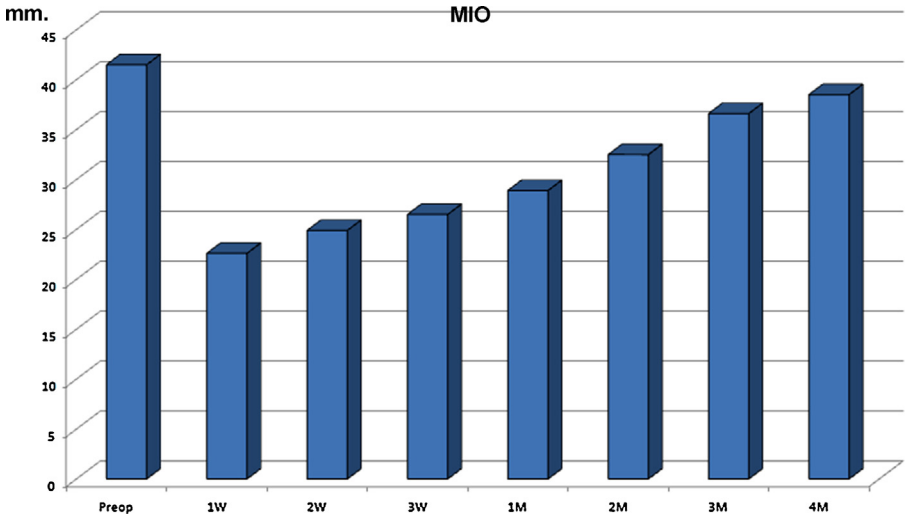

Fig. 4. Bar chart showing the mean maximal inter-incisal opening (MIO) in millimetres throughout the study period.

In the present study a single BTX-A injection was used; this was determined on the basis of the preliminary results of the study of Bakke et al.[2] In the stated study a second dose was injected 4 months after the first to augment the effect of the first injection. In the current study, a second injection was only used in cases of a recurring click, which was the case in only one joint. However, follow-up of that case is beyond the scope of the current study. The amount of BTX injected into a muscle depends on its size and location. For other masticatory muscles (temporalis and masseter) the recommended amount of BTX for each muscle ranges from 40 to 60 U each at several injection points.[20] Since the LP is a small muscle and located deeply and adjacent to several structures that may be affected by seepage, it requires a lower amount and the injection is made at a single point. In the present study the LPs of the selected candidates were injected with 35 U of BTX-A as used in earlier studies showing positive results with a 30–35-U dose.[2] Other researchers have used 50 U in the LP for complaints other than painless clicks, but this was accompanied by a higher percentage of side effects such as dysphagia.[21] In the current study the muscle was approached intraorally as was reported by Bakke et al.[2] The extraoral approach implemented in other studies[22,23] was avoided as it carries a higher risk of haemorrhage and intravascular injection due to the proximity to the maxillary artery and the pterygoid venous plexus. Intravascular injection of large amounts of BTX may mimic the symptoms of botulism and it was found to be quite annoying to the patients and required skin preparation.

The last follow-up was set at 4 months postoperatively. Several studies have emphasized that the effect of a single injection of BTX fades within a period of around 4 months,[2,20] which is in agreement with the manufacturer's information. At the end of the 4-month follow-up period of the present study, all patients had regained their normal range of function (MIO or range of lateral movement), in accordance with the results of Bakke et al.[2] In the literature, other masticatory muscles regained their bite force after BTX injection within a period of 3–4 months.[24] The results of the current study showed that the peak drop in both clinical parameters (MIO and lateral movement) occurred within the first 2 weeks post-injection and a gradual recovery started from the third week. This is in agreement with the results of earlier studies.[20,24] The disappearance of the click in all joints during the period from 2 weeks to 2 months supports the theory of the LP's pull and its effect on the disc position. Moreover, disappearance of the click after injection of the muscle at the insertion of the lower head of the LP supports the conclusion drawn by earlier studies that both heads function as a 'single motor unit'.[25,26]

The results of the present study showed a statistically insignificant decrease in

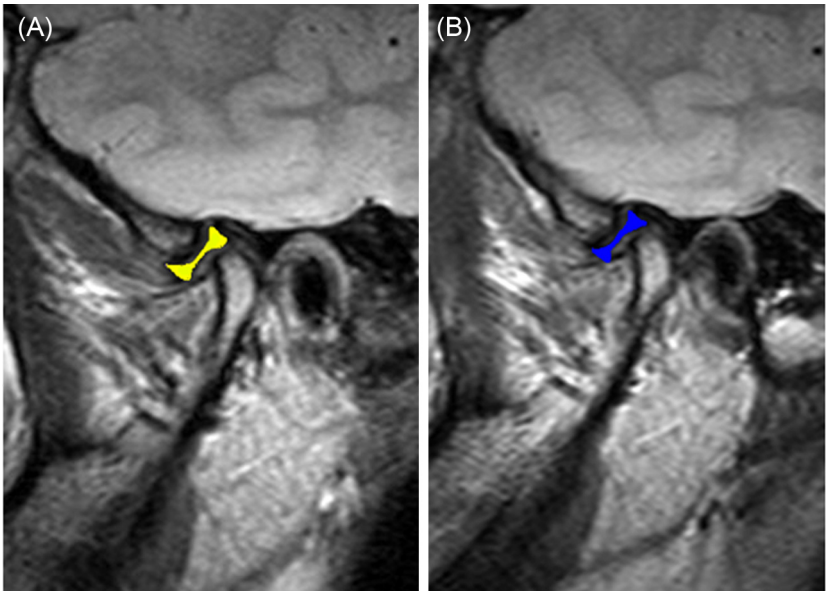

Fig. 5. (A) Preoperative MRI with the articular disc coloured in yellow. (B) Postoperative image of the same joint with the articular disc coloured in blue. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)

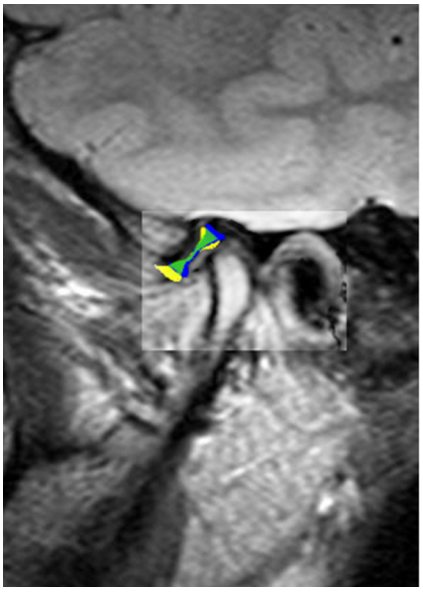

Fig. 6. Postoperative image superimposed on the preoperative image.

Table 1. The minimum, maximum, mean, standard deviation (SD), and *P*-value for the coordinate change for each of the points A and B, respectively.

	Minimum	Maximum	Mean	SD	*P*-value
Point A	0.27	1.07	0.62	0.27	0.001
Point B	0.21	1.74	0.83	0.35	0.001

mean MIO at 4 months post-injection in comparison with the preoperative MIO. Although the specific cause is unknown, this was also noted in the study performed by Kim et al.[24] The insignificant increase in mean lateral range of movement seen in the current study may be attributed to the recovery of a more normal disc–condyle relationship, such that the lateral movement faced less mechanical interference and hence was less click-inducing. No previous studies were found using the range of lateral movement as a clinical parameter. In addition to the clinical measurement, postoperative MR images were also used to quantify any disc position improvement.

Although Arayasantiparb and Tsuchimochi[15] suggested and used this method to identify cases of disc displacement and the present study used it to quantify disc position changes pre- and postoperatively, both studies agree that the anatomical points are reliable for the detection of disc displacement. The significant differences in positions of points A and B pre- and postoperatively further supports the hypothesis that the LP is responsible for the anterior displacement of the articular disc as concluded by several other studies.[27,28]

Regarding complications/side effects of BTX injection, one patient in the current study suffered from dysphagia, a nasal tone of voice, nasal regurgitation, and flu-like symptoms 5 days after injection, which subsided 9 days later. This is in accordance with the findings of Baizabal-Carvallo et al.[29] The flu-like symptoms are a systemic not a local reaction to injection and have also been reported in cases of non-maxillofacial injection.[30] Local seepage of BTX into pharyngeal/palatal muscles is suggested to be responsible for the nasal regurgitation, specifically due to the temporary paralysis of the velopharyngeal sphincter. In general the procedure is a chair-side procedure, well tolerated by the patient, even without local anaesthesia. The absence of the click even after the end of the paralyzing effect of the BTX suggests that some sort of muscle deprogramming may have occurred within the muscle ensuring that once the effect of the BTX ends, the muscle fibres do not go back to their hyperactive state.

The explanation of the effect of BTX injection in the LP muscle on the painless click requires further investigation. From the results of this study it may be concluded that BTX-A injection in the LP muscle could be considered a successful treatment option for clicking temporomandibular joints. The results also show that the LP appears to be responsible for the temporomandibular joint click. Moreover, both heads of the LP muscle function as a single motor unit. Further research with larger patient samples and longer follow-up periods are advised.

Funding

This research was partially funded by the Faculty of Oral and Dental Medicine, Cairo University.

Competing interests

None declared.

Ethical approval

The Ethics Committee of the Faculty of Oral and Dental Medicine, Cairo University approved the steps of this research.

Acknowledgements. We are grateful to Dr. Amr Maher, Professor of General Anaesthesia, for his unconditional support and efforts in completing the statistical analysis of this research.

References

1. Freund B, Schwartz M, Symington JM. Botulinum toxin: new treatment for temporomandibular disorders. *Br J Oral Maxillofac Surg* 2000;**38**:466–71.
2. Bakke M, Møller E, Werdelin L, Dalager T, Kitai N, Kreiborg S. Treatment of severe temporomandibular joint clicking with botulinum toxin in the lateral pterygoid muscle in two cases of anterior disc displacement. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2005;**100**:693–700.
3. Reston JT, Turkelson CM. Meta-analysis of surgical treatments for temporomandibular articular disorders: a reply to the discussants. *J Oral Maxillofac Surg* 2003;**61**:737–8.
4. Tozoglu S, Al-Belasy FA, Dolwick MF. A review of techniques of lysis and lavage of the TMJ. *Br J Oral Maxillofac Surg* 2010; **49**:302–9.
5. Onder ME, Tuz HH, Koçyiğit D, Kişnişçi RS. Long-term results of arthrocentesis in degenerative temporomandibular disorders. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2009;**107**:e1–5.
6. Goizueta CC, Munoz-Guerra MF. The posterior double pass suture in repositioning of the temporomandibular disc during arthroscopic surgery: a report of 16 cases. *J Craniomaxillofac Surg* 2012;**40**:86–91.
7. Fujita S, Iizuka T, Dauber W. Variation of heads of lateral pterygoid muscle and morphology of articular disc of human temporomandibular joint—anatomical and histological analysis. *J Oral Rehabil* 2001;**28**: 560–71.
8. Wongwatana S, Kronman JH, Clark RE, Kabani S, Mehta N. Anatomic basis for disk displacement in temporomandibular joint (TMJ) dysfunction. *Am J Orthod Dentofacial Orthop* 1994;**105**:257–64.
9. Murray GM, Bhutada M, Peck CC, Phanachet I, Sae-Lee D, Whittle T. The human lateral pterygoid muscle. *Arch Oral Biol* 2007;**52**:377–80.
10. Jankovic J. Botulinum toxin. In: Kompoliti K, Verhagen L, editors. *Encyclopedia of movement disorders*. Oxford: Academic Press; 2010. p. 144–50.
11. Tsui KC. Botulinum toxin as a therapeutic agent. *Pharmacol Ther* 1996;**72**:13–24.
12. Freund B, Schwartz M, Symington JM. The use of botulinum toxin for the treatment of temporomandibular disorders: preliminary findings. *J Oral Maxillofac Surg* 1999;**57**: 916–20.
13. Daelen B, Thorwirth V, Koch A. Treatment of recurrent dislocation of the temporoman-

dibular joint with type A botulinum toxin. *Int J Oral Maxillofac Surg* 1997;**26**:458–60.
14. Wilkes CH. Internal derangements of the temporomandibular joint: pathological variations. *Arch Otolaryngol Head Neck Surg* 1989;**115**:469–77.
15. Arayasantiparb R, Tsuchimochi M. Quantification of disc displacement in internal derangement of the temporomandibular joint using magnetic resonance imaging. *Odontology* 2010;**98**:73–81.
16. Moloney F, Howard JA. Internal derangements of the temporomandibular joint, III. Anterior repositioning splint therapy. *Aust Dent J* 1986;**31**:30–9.
17. Magnusson T, Egermarki I, Carlsson E. A prospective investigation over two decades on signs and symptoms of temporomandibular disorders and associated variables. A final summary. *Acta Odontol Scand* 2005; **63**:99–109.
18. Sommer OJ, Aigner F, Rudisch A, Gruber H, Fritsch H, Millesi W, et al. Cross-sectional and functional imaging of the temporomandibular joint: radiology, pathology, and basic biomechanics of the jaw. *Radiographics* 2003;**23**:e14.
19. Larheim TA. Current trends in temporomandibular joint imaging. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1995; **80**:555–76.
20. Kurtoglu C, Gur O, Kurkcu M, Sertdemir Y, Guler-Uysal F, Uysal H. Effect of botulinum toxin-A in myofascial pain patients with or without functional disc displacement. *J Oral Maxillofac Surg* 2008;**66**:1644–51.
21. Martinez-Perez D, Ruiz-Espiga G. Recurrent temporomandibular joint dislocation treated with botulinum toxin: report of 3 cases. *J Oral Maxillofac Surg* 2004;**62**:244–6.
22. Fu KY, Chen HM, Sun ZP, Zhang ZK, Ma XC. Long-term efficacy of botulinum toxin type A for the treatment of habitual dislocation of the temporomandibular joint. *Br J Oral Maxillofac Surg* 2010;**48**:281–4.
23. Ziegler CM, Haag C, Muhling J. Treatment of recurrent temporomandibular joint dislocation with intramuscular botulinum toxin injection. *Clin Oral Investig* 2003; **7**:52–5.
24. Kim KS, Byun YS, Kim YJ, Kim ST. Muscle weakness after repeated injection of botulinum toxin type A evaluated according to bite force measurement of human masseter muscle. *Dermatol Surg* 2009;**35**:1902–6.
25. Dergin G, Kilic C, Gozneli R, Yildirim D, Garip H, Moroglu S. Evaluating the correlation between the lateral pterygoid muscle attachment type and internal derangement of the temporomandibular joint with an emphasis on MR imaging findings. *J Craniomaxillofac Surg* 2012;**40**:459–63.
26. Ruangsri S, Whittle T, Murray M. Superior head of human lateral pterygoid muscle: single motor unit firing rates during isometric force. *Arch Oral Biol* 2007;**52**:995–1001.
27. Widmalm SE, Williams WJ, Ang BK, McKay DC. Localization of TMJ sounds to side. *J Oral Rehabil* 2002;**29**:911–7.
28. Naidoo LC, Juniper RP. Morphometric analysis of the insertion of the upper head of the lateral pterygoid muscle. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1997;**83**:441–6.
29. Baizabal-Carvallo JF, Jankovic J, Pappert E. Flu-like symptoms following botulinum toxin therapy. *Toxicon* 2011;**58**:1–7.
30. Moore AP, Ade-Hall RA, Smith CT, Rosenbloom L, Walsh HP, Mohamed K, et al. Two-year placebo-controlled trial of botulinum toxin A for leg spasticity in cerebral palsy. *Neurology* 2008;**71**:122–8.

Address:
Aala Shoukry Emara
Oral and Maxillofacial Surgery Department
Faculty of Oral and Dental Medicine
Cairo University
Cairo
Egypt
Tel: +20 1006223948
E-mail: masa2502@gmail.com