A Comparison of Outcome of Surgical Treatment of Migraine Headaches Using a Constellation of Symptoms versus Botulinum Toxin Type A to Identify the Trigger Sites

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Background: This study was designed to assess whether preoperative trigger-site confirmation using botulinum toxin type A injections significantly improved migraine surgery outcomes.

Methods: The medical charts of 335 migraine surgery patients were reviewed. Patients who received stepwise diagnostic botulinum toxin type A injections were placed in the botulinum toxin type A group (n = 245). Patients who did not receive botulinum toxin type A or received only therapeutic botulinum toxin type A were placed in the control group (n = 90). The preoperative and 12-month postoperative migraine headache frequency, duration, and intensity were compared to determine the success of the operations.

Results: Seventy-two of 90 control patients (80 percent) experienced a significant improvement (a decrease of at least 50 percent in migraine headache frequency, duration, or intensity) at 12 months after surgery, with 29 (32 percent) reporting complete elimination. Of the 245 botulinum toxin type A patients, 207 (84 percent) experienced a significant improvement, with 89 (36 percent) experiencing complete elimination. The surgical success rate of the botulinum toxin type A group was not significantly higher than that of the control group (p = 0.33).

Conclusions: Confirmation of trigger sites using botulinum toxin type A does not significantly improve the outcome of migraine surgery. Although botulinum toxin type A can be a useful diagnostic tool, this study demonstrates that there is no statistically significant difference between the injection of botulinum toxin type A and the use of a constellation of symptoms to identify trigger sites. (*Plast. Reconstr. Surg.* 129: 413, 2012.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, III.

Migraine headaches affect over 35 million Americans, or approximately 17 percent of women and 6 percent of men in the United States.[1–4] Approximately one-fourth of all households has one member who suffer from migraine headaches.[1] The symptoms commonly interfere with daily function and include unilateral or bilateral throbbing pain, nausea, vomiting, photophobia, and phonophobia.[5] Most migraine headache sufferers manage their symptoms with a combination of nonpharmacologic treatment (e.g., avoiding environmental triggers) and pharmacologic interventions (e.g., acute abortive, acute analgesic, and prophylactic medications).[2,3] It is estimated that the annual cost for these medications alone is $1.5 billion and the overall cost of treatment of migraine headaches is $13 billion.[6]

Although there is no widely accepted cure at this time, the senior author (B.G.) has developed surgical interventions for long-term amelioration and elimination of migraine headaches by deactivating migraine trigger sites.[7] These operations were shown to be significantly more successful

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at reducing migraine headaches than sham operations,[8] and results have been replicated by other research teams.[9,10]

Migraine surgery can be performed at four common trigger sites: trigger site I, frontal triggers, where glabellar muscles or vessels accompanying the nerves may irritate the supratrochlear and supraorbital nerves to cause frontal headaches; trigger site II, temporal triggers, where the temporalis muscle or the vessels adjacent to the nerve may cause inflammation of the zygomaticotemporal branch of the trigeminal nerve to induce temporal headaches; trigger site III, rhinogenic triggers, where intranasal abnormality (e.g., deviated septum, spurs, contact between the turbinates and the septum, concha bullosa, septa bullosa) may irritate the trigeminal end branches to cause paranasal and retrobulbar headaches; and trigger site IV, occipital triggers, where the semispinalis capitis muscle or the occipital artery can irritate the occipital nerve to cause occipital headaches.

Localized botulinum toxin type A injections have been used to detect and confirm suspected trigger sites I, II, and IV in migraine headache patients before surgery. Botulinum toxin type A is a 1295–amino acid neurotoxin derived from the bacterium *Clostridium botulinum*, and acts to interrupt neuromuscular transmission by blocking the presynaptic release of acetylcholine.[11] The onset of action of botulinum toxin type A begins after 3 to 4 days, and the neuromuscular junction typically regains its full function 3 to 4 months after initial injection. Injections are targeted directly into muscle, where nerve terminals reside, to weaken the musculature. Aside from diagnostic purposes, botulinum toxin type A injections have also been approved by the U.S. Food and Drug Administration for temporary reduction of migraine headaches.[12]

Therapeutic botulinum toxin type A injections are administered in multiple sites per visit in the head and neck to induce maximal effect on migraine headaches.[12] In contrast, preoperative diagnostic botulinum toxin type A injections are administered at one trigger site per visit, starting with the most common and severe trigger site based on the patient's constellation of symptoms. If necessary, subsequent trigger-site injections are given 1 month apart, up to a maximum of three sites, until all trigger sites are confirmed.[13] A potential benefit of testing with botulinum toxin type A is that it may complement and/or confirm suspected trigger sites. The shortcoming of testing with botulinum toxin type A is the lengthy diagnostic period, which may significantly delay surgical intervention. Diagnostic trigger-site injection may take up to 3 months, as only one trigger site is injected per month. In addition, surgery cannot be performed within 3 months of injections into the corrugator site, as these muscles atrophy significantly after injection, making resection extremely difficult. Furthermore, this method of detection of the trigger sites is not convenient for out-of-town or out-of-country patients, who will have to travel several times to the site where the treating team resides.

Over the past 5 years, the senior author has gradually reduced the diagnostic use of botulinum toxin type A in his migraine surgery patients because the majority of his patients were from outside the greater Cleveland, Ohio, area. It is suspected that the analysis of the patient's constellation of symptoms and the physical examination can be as effective at predicting migraine trigger sites as preoperative testing with botulinum toxin type A. The constellations of symptoms for each trigger site are listed in Tables 1 through 4. The purpose of this study is to evaluate whether preoperative trigger-site detection with botulinum toxin type A significantly increases migraine surgery success.

PATIENTS AND METHODS

Patient Selection

Institutional review board approval was obtained for this retrospective chart review study. The subjects consisted of patients who had undergone migraine surgery performed by a single surgeon (B.G.) between January 1, 2001, and March 31, 2010, had been followed for at least 1 year, and had completed a 12-month follow-up survey. There were 335 patients who fit these in-

Table 1. Constellation of Symptoms Related to the Frontal Migraine Headache

The pain starts above the eyebrows
The pain usually starts in the afternoon
There is strong corrugator muscle activity causing deep frown lines on animation and repose
The points of emergence of the supraorbital and supratrochlear nerves from the corrugator muscle or the foramen are tender to the touch
Patients commonly have eyelid ptosis on the affected side at the time of active pain
Pressure on these sites may abort the MH during the initial stages
Application of cold or warm compresses on these sites often reduces or stops the pain
The pain is usually imploding in nature
Stress often can result in triggering MH

MH, migraine headache.

Table 2. Constellation of Symptoms Related to the Temporal Migraine Headache

The pain starts in the temple area approximately 17 mm lateral and 6 mm cephalad to the lateral canthus
Patients usually wake up in the morning with pain after clenching or grinding their teeth all night
Often, the pain is associated with tenderness of the temporalis or masseteric muscle
One may see wearing of the dental facets
Rubbing or pressing the exit point of the zygomaticotemporal branch of the trigeminal nerve from the deep temporal fascia can stop or reduce the pain in the beginning
Application of cold or warm compresses to this point may reduce or stop the pain
The pain is characterized as imploding
Stress can trigger MH in this site

MH, migraine headache.

Table 3. Constellation of Symptoms Related to the Rhinogenic Migraine Headache

The pain starts behind the eye
Patient commonly wakes up with the pain in the morning or at night
Commonly, the MH is triggered by weather changes
Rhinorrhea can accompany the pain on the affected side
This type of MH can be related to the nasal allergy episodes
Menstrual cycles can trigger MH
The pain is usually described as exploding
Concha bullosa, septal deviation with contact between the turbinates and the septum, septa bullosa, and Haller's cell can be seen on the CT scan

MH, migraine headache; CT, computed tomographic.

Table 4. Constellation of Symptoms Related to the Occipital Migraine Headache

The pain starts at the point of exit of the greater occipital nerve from the semispinalis capitis muscle (3.5 cm caudal to the occipital tuberosity and 1.5 cm off the midline)
There is no specific starting time for the pain
The patients may have a history of neck splash
The neck muscles are usually tight
Heavy exercise can trigger MH
Compression of this site can stop the pain in the early stage, whereas at the later stage, this point is tender
Application of cold or heat at this site may result in some improvement in the pain
Stress can be a trigger for occipital MH

MH, migraine headache.

clusion criteria. All patients completed a baseline Migraine Headache Questionnaire before surgery and at 12 months after surgery. These self-reported questionnaires assess the frequency (migraines per month), duration (in days), and intensity (based on a visual analogue scale from 1 to 10, with 10 being the most severe) of migraine headaches experienced by each patient before and after surgery.

Patients were grouped into either the botulinum toxin type A group or the control group. The patient's medical records indicated whether the patient had received preoperative diagnostic botulinum toxin type A injections performed at suspected trigger sites. Although many migraine patients received multiple head and neck botulinum toxin type A injections for therapeutic purposes, these generalized injections were not site-specific and did not contribute to the localization of trigger sites. Only the patients who received diagnostic, stepwise, single-site botulinum toxin type A injections strictly for trigger-site determination were grouped into the botulinum toxin type A group. The control patients either never received botulinum toxin type A or had received multiple-site botulinum toxin type A injections purely for therapeutic purposes.

Surgical Procedures

Surgery was performed on one or any combination of trigger sites in the same setting: trigger site I (frontal trigger site), removal of the glabellar muscle group (corrugator supercilii, depressor supercilii, and the lateral portion of procerus muscles) to decompress the supraorbital and supratrochlear nerves; trigger site II (temporal trigger site), avulsion of the zygomaticotemporal branch of the trigeminal nerve; trigger site III (rhinogenic trigger site), septoplasty and turbinectomy; and trigger site IV (occipital trigger site), removal of a small segment of the semispinalis capitis muscle to decompress the greater occipital nerve or remove the occipital artery. Surgery was performed in the same way for both the botulinum toxin type A and control groups. A more in-depth description of the above procedures can be found in our previously published reports.[13–20]

Statistical Analysis

The migraine headache index was calculated by multiplying the frequency, duration, and intensity of migraine headaches. A 50 percent or greater reduction in migraine headache index at 12 months indicated a successful operation. Two-tailed, two-sample homoscedastic *t* tests were used to compare 12-month success rates of the botulinum toxin type A and control groups. The mean migraine index, frequency, duration, and intensity at 12 months after surgery and baseline were also compared within and between the botulinum toxin type A and control groups. The surgical success at specific trigger sites was also analyzed. A

value of $p < 0.05$ was considered significant. Furthermore, a comparison of success rates by year was determined to elucidate whether an improvement in surgical technique over time had contributed to the success rates obtained. All statistical analyses were completed using Microsoft Excel 2007 Data Analysis Tool (Microsoft, Inc., Redmond, Wash.), and JMP8 (SAS Institute, Inc., Cary, N.C.).

RESULTS

Overall Surgery Outcome: Botulinum Toxin Type A versus Control

Of the 335 patients included in this study, 245 received diagnostic stepwise injections of botulinum toxin type A (botulinum toxin type A group) and the remaining 90 patients either never received botulinum toxin type A or previously received nondiagnostic multiple-site botulinum toxin type A injections for therapeutic purposes only (control group). Of the 245 botulinum toxin type A patients, 207 (84 percent) experienced a greater than or equal to 50 percent reduction in migraine index, with 89 (36 percent) experiencing complete elimination of migraine headaches. Of the 90 patients in the control group, 72 (80 percent) experienced a greater than or equal to 50 percent reduction in migraine index, with 29 (32 percent) reporting elimination. The surgery success rates (percentage of patients who experienced ≥50 percent reduction in migraine index) of the botulinum toxin type A group (84 percent) and control group (80 percent) were not significantly different ($p = 0.33$). The percentage of migraine elimination in the botulinum toxin type A group (36 percent) and the control group (32 percent) were also not significantly different ($p = 0.49$). The mean reduction in migraine index was 72.9 ± 57.1 percent in the botulinum toxin type A group compared with 68.4 ± 51.2 percent in the control group ($p = 0.51$).

Surgery Outcome by Migraine Variable

In the control group, all measured variables improved significantly at 12 months (Table 5). The mean migraine frequency was 17.3 ± 9.5 at baseline compared with 7.3 ± 9.1 at 12 months ($p < 0.0001$). The mean migraine duration was 1.0 ± 1.1 days at baseline compared with 0.6 ± 1.2 days at 12 months ($p < 0.002$). The mean migraine intensity at baseline was 8.5 ± 2.3 compared with 4.7 ± 3.6 at 12 months ($p < 0.0001$). The mean migraine index at baseline was 91.2 ± 94.5 compared with 7.1 ± 13.2 at 12 months ($p < 0.0001$).

In the botulinum toxin type A group, all measured variables also improved significantly at 12 months (Table 5). The mean migraine frequency was 11.7 ± 8.2 at baseline compared with 3.8 ± 5.4 at 12 months ($p < 0.0001$). The mean migraine duration was 1.1 ± 1.8 days at baseline compared with 0.4 ± 0.9 day at 12 months ($p < 0.0001$). The mean migraine intensity at baseline was 7.7 ± 1.9 compared with 4.0 ± 3.5 at 12 months ($p < 0.0001$). The mean migraine index at baseline was 96.2 ± 132.4 compared with 23.7 ± 45.9 at 12 months ($p < 0.0001$).

At baseline, the mean migraine frequency was significantly higher in the control group than in the botulinum toxin type A group ($p < 0.0001$). The mean baseline migraine intensity was also significantly higher in the control group than in the botulinum toxin type A group ($p < 0.001$). There was no significant difference between the mean migraine duration in the control and botulinum toxin type A groups at baseline ($p = 0.73$).

Surgery Outcome by Trigger Site: Botulinum Toxin Type A versus Control

The success rates for all operations that included trigger site I were not significantly different in the botulinum toxin type A (87 percent) and control (90 percent) groups ($p = 0.53$). The success rates for all operations that included trigger site II were also not significantly different between

Table 5. Surgery Outcome at 12 Months

	BTA			Control		
Variable	**Baseline**	**12 Mo**	***p****	**Baseline**	**12 Mo**	***p****
Frequency (MH/month)	11.7 ± 8.2	3.8 ± 5.4	<0.0001	17.3 ± 9.5	7.3 ± 9.1	<0.0001
Duration (days)	1.1 ± 1.8	0.4 ± 0.9	<0.0001	1.0 ± 1.1	0.6 ± 1.2	0.0015
Intensity (analogue scale, 0–10)	7.7 ± 1.9	4.0 ± 3.5	<0.0001	8.5 ± 2.3	4.7 ± 3.6	<0.0001
Migraine index (frequency × duration × intensity)	96.2 ± 132.4	23.7 ± 45.9	<0.0001	91.2 ± 94.5	7.1 ± 13.2	<0.0001

BTA, botulinum toxin type A; MH, migraine headaches.
*p values obtained from two-sample homoscedastic t tests.

botulinum toxin type A (87 percent) and control (86 percent) groups ($p = 0.83$). Furthermore, the success rates for trigger site III operations were not statistically different between botulinum toxin type A (85 percent) and control (81 percent) groups ($p = 0.50$). Finally, the success rates for trigger site IV operations were not statistically different between botulinum toxin type A (90 percent) and control (81 percent) groups ($p = 0.14$). These results are summarized in Table 6.

Surgery Outcome by Year

The practice of using botulinum toxin type A testing as a diagnostic tool for trigger-site confirmation decreased steadily each year starting in 2006 (Table 7). By 2010, botulinum toxin type A testing was used on 17 percent of migraine surgery patients, compared with 86 percent in 2001 ($p < 0.0001$). However, the surgical success in 2010 (67 percent) was not significantly lower than in 2001 (81 percent) ($p = 0.37$). The most significant decrease in botulinum toxin type A testing began in 2009. Botulinum toxin type A testing was used in only 20 percent of patients in 2009 and 2010, compared with 81 percent from 2001 to 2008 ($p < 0.0001$). The surgery success rate of all patients in 2009 and 2010 was 73 percent compared with 85 percent from 2001 to 2008 ($p = 0.06$). The surgery success rate of control patients in 2009 and 2010 was 72 percent compared with 85 percent from 2001 to 2008 ($p = 0.14$). The surgery success rate of botulinum toxin type A patients in 2009 and 2010 was 78 percent compared with 85 percent from 2003 to 2008 ($p = 0.57$).

Table 6. Surgery Outcomes at Specific Trigger Sites

	BTA		Control		
Trigger Site*	No.	Success Rate (%)	No.	Success Rate (%)	p†
I	186	87	67	90	0.53
II	164	87	70	86	0.83
III	124	85	68	81	0.50
IV	86	90	57	81	0.14

BTA, botulinum toxin type A.
*Trigger site indicates all operations that included the indicated trigger site (e.g., trigger site I includes surgery at site I only and surgery at site I with any combination of other trigger sites).
†*p* values were obtained from two-sample homoscedastic *t* tests comparing success rates between botulinum toxin type A and control.

DISCUSSION

An increase in the number of patients traveling long distances along with development of the constellation of the symptoms that were associated with specific trigger sites compelled the senior author to rely on the symptoms along with computed tomographic scan findings (only for the rhinogenic migraine headaches) in detecting the trigger sites. The absence of a statistical difference between surgical success rates in botulinum toxin type A and control groups in this study suggests that testing with botulinum toxin type A is not always necessary for the localization of migraine trigger sites. Although both groups had success rates greater than 80 percent, there was still a small contingent of patients whose symptoms were not significantly alleviated by surgery. It is the senior author's belief that the failure to detect and deactivate the trigger sites contributed substantially to this suboptimal success rate. One has to consider that in our previous studies, approximately 10 percent of the patients were excluded based on the lack of response to the injection of botulinum toxin type A. It is difficult to ascertain whether this contributed to a slight but statistically nonsignificant reduction in the success rate. Furthermore, 11 percent of patients who underwent surgery at all four trigger sites did not respond positively, suggesting the presence of additional trigger sites. Less common trigger sites have been discovered over the past 11 years, including the auriculotemporal branch of the trigeminal nerve and the lesser

Table 7. Botulinum Toxin Type A Testing and Surgery Outcome by Year

Year	Total Operations	Successful Operations	Total Success (%)	% in BTA Group	BTA Success (%)	% in Control Group	Control Success (%)
2001	21	17	81	86	78	14	100
2002	90	80	89	97	89	3	100
2003	46	40	87	72	88	28	85
2004	40	34	85	82	82	18	100
2005	42	36	86	83	83	17	100
2006	18	12	67	72	62	28	80
2007	16	12	75	56	100	44	43
2008	17	16	94	47	100	53	89
2009	33	25	76	21	71	79	77
2010	12	8	67	17	100	83	60

BTA, botulinum toxin type A.

occipital nerves. The surgical intervention for these additional trigger sites has been discussed in previous publications.[7,21]

The data also indicate that the mean baseline frequency and severity of migraine headaches experienced by patients in the control group were higher than in the botulinum toxin type A group. This trend correlates with the increase in the complexity of cases in recent years. As knowledge of the pathophysiology of migraine headaches and of anatomical variations has grown, so has the complexity of patient cases—patients who would have been rejected for surgery several years ago are now accepted. Many of these complex control cases included patients who were unresponsive to botulinum toxin type A injections. Despite the higher baseline migraine frequency and intensity in control patients, they experienced essentially the same average reduction in migraine index as the botulinum toxin type A patients, indicating that a higher baseline migraine index does not hinder the success of the operations.

Testing with botulinum toxin type A has been a part of the diagnostic protocol for migraine surgery since 2000, when the senior author first used surgical techniques for migraine management. However, stepwise testing with botulinum toxin type A requires multiple visits at 1-month intervals and is not feasible for out-of-state or out-of-country patients, who must travel long distances for single-site botulinum toxin type A injections in multiple, consecutive months. Furthermore, botulinum toxin type A may also be ineffective in some individuals who develop blocking antibodies to the toxin, leading to false-negative results for trigger-site identification.[22–24] Although the prevalence of botulinum toxin type A resistance is less than 5 percent,[25] testing with botulinum toxin type A in these patients may actually hinder the correct diagnosis of trigger sites. In addition, botulinum toxin type A injection adds to the cost of migraine care that may not be reimbursed by a third party.

If the patient's constellation of symptoms does not clearly indicate a specific trigger site, single-site phased injection of botulinum toxin type A or a nerve block can abet the confirmation. Unlike botulinum toxin type A, local anesthetics such as lidocaine have a fast onset of less than 90 seconds and a short half-life of less than 2 hours,[26] allowing almost immediate relief from migraine headache symptoms if injected into the correct trigger site(s). However, a nerve block is only helpful when applied in patients who present with migraine headaches at the time of the office visit.

We believe the trigger site can be reliably identified by analyzing each patient's symptoms, physical examination, and computed tomographic scan without the necessary use of preoperative botulinum toxin type A injections. The most reliable of these symptoms is the precise location of the pain at the beginning of migraine headaches. However, botulinum toxin type A injection was extremely helpful in the development of Tables 1 through 4. Thus, we recommend injection of botulinum toxin type A or nerve blocks to confirm the trigger sites for those surgeons who are in their early stages of serving these patients, until they develop the necessary level of comfort and expertise.

CONCLUSIONS

This study confirms that the use of stepwise botulinum toxin type A injections at potential trigger sites before migraine surgery does not significantly improve surgical outcome. Trigger sites can be successfully determined using the patient's constellation of symptoms alone.

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REFERENCES

1. Lipton RB, Bigal ME, Diamond M, et al. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology* 2007;68:343–349.
2. SynerMed Communications. 21st century prevention and management of migraine headaches. *Clin Courier* 2001;19:1–15.
3. Lipton RB, Stewart WF, Diamond S, Diamond ML, Reed M. Prevalence and burden of migraine in the United States: Data from the American Migraine Study II. *Headache* 2001;41:646–657.
4. Stewart WF, Shechter A, Rasmussen BK. Migraine prevalence: A review of population-based studies. *Neurology* 1994;44(Suppl 4):S17–S23.
5. Moskowitz MA. The neurobiology of vascular head pain. *Ann Neurol.* 1984;16:157–168.
6. Goldberg LD. The cost of migraine and its treatment. *Am J Manag Care* 2005;11(Suppl 2):S62–S67.
7. Guyuron B, Kriegler JS, Davis J, Amini SB. Five-year outcome of surgical treatment of migraine headaches. *Plast Reconstr Surg.* 2010;127:603–608.
8. Guyuron B, Reed D, Kriegler JS, Davis J, Pashmini N, Amini S. A placebo controlled surgical trial for the treatment of migraine headaches. *Plast Reconstr Surg.* 2009;124:461–468.
9. Poggi JT, Grizzell BE, Helmer SD. Confirmation of surgical decompression to relieve migraine headaches. *Plast Reconstr Surg.* 2008;122:115–122; discussion 123–124.
10. Behin F, Behin B, Behin D, Baredes S. Surgical management of contact point headaches. *Headache* 2005;45:204–210.
11. Guyuron B. Botulinum toxin. *Plastic Surgery: Indications, Operations, and Outcomes.* St. Louis: Mosby; 2000.

12. Fenstermacher N, Levin M, Ward T. Pharmacological prevention of migraine. *BMJ.* 2011;342:d583.
13. Guyuron B, Kriegler JS, Davis J, Amini SB. Comprehensive surgical treatment of migraine headaches. *Plast Reconstr Surg.* 2005;115:1–9.
14. Janis JE, Ghavami A, Lemmon JA, Leedy JE, Guyuron B. Anatomy of the corrugator supercilii muscle: Part I. Corrugator topography. *Plast Reconstr Surg.* 2007;120:1647–1653.
15. Dirnberger F, Becker K. Surgical treatment of migraine headaches by corrugator muscle resection. *Plast Reconstr Surg.* 2004;114:652–657; discussion 658–659.
16. Totonchi A, Pashmini N, Guyuron B. The zygomaticotemporal branch of the trigeminal nerve: An anatomical study. *Plast Reconstr Surg.* 2005;115:273–277.
17. Mosser SW, Guyuron B, Janis JE, Rohrich RJ. The anatomy of the greater occipital nerve: Implications for the etiology of migraine headaches. *Plast Reconstr Surg.* 2004;113:693–697; discussion 698–700.
18. Dash K, Janis J, Guyuron B. The lesser and third occipital nerves and migraine headaches. *Plast Reconstr Surg.* 2005; 115:1752–1758; discussion 1759–1760.
19. Guyuron B, Becker DB. Surgical management of migraine headaches. In: Guyuron B, Eriksson E, Persing JA, et al., eds. *Plastic Surgery: Indications and Practice.* New York: Elsevier; 2009.
20. Guyuron B, DiNardo LA. Forehead/brow/soft tissue surgery for migraines. In: Evans G, Persing L, eds. *Soft-Tissue Surgery of the Craniofacial Region.* New York: Informa Healthcare USA; 2007:93–112.
21. Sultaneh A. Migraine: New surgical treatment. Paper presented at: Congress of Neurological Surgeons; September 29-October 4, 2001; San Diego, Calif.
22. Naumann M, Albanese A, Heinen F, Molenaers G, Relja M. Safety and efficacy of botulinum toxin type A following long-term use. *Eur J Neurol.* 2006;13(Suppl 4):35–40.
23. Dressler D, Wohlfahrt K, Meyer-Rogge E, Wiest L, Bigalke H. Antibody-induced failure of botulinum toxin a therapy in cosmetic indications. *Dermatol Surg.* 2010;36(Suppl 4):2182–2187.
24. Jankovic J, Vuong KD, Ahsan J. Comparison of efficacy and immunogenicity of original versus current botulinum toxin in cervical dystonia. *Neurology* 2003;60:1186–1188.
25. Klein AW. Complications and adverse reactions with the use of botulinum toxin. *Dis Mon.* 2002;48:336–356.
26. Schnider TW, Gaeta R, Brose W, Minto CF, Gregg KM, Shafer SL. Derivation and cross-validation of pharmacokinetic parameters for computer-controlled infusion of lidocaine in pain therapy. *Anesthesiology* 1996;84:1043–1050.