# Otolaryngology-Head and Neck Surgery

**Official Journal of the AMERICAN ACADEMY OF OTOLARYNGOLOGY-HEAD AND NECK SURGERY FOUNDATION, INC. and the AMERICAN ACADEMY OF OTOLARYNGIC ALLERGY**

**DECEMBER 2000**

**VOLUME 123**

**NUMBER 6**

## ORIGINAL ARTICLES

- Botulinum toxin type A (BOTOX) for treatment of migraine headaches  
  W.J. Binder et al  
  669
- Apoptosis in the developing human aortic arch cartilage  
  L. Mankarious and J. Anstey  
  677
- A meta-analysis of oxacillinase use with tonsillectomy  
  A.C. Goldman et al  
  682
- Chronic rhinosinusitis: Allergy and sinus computed tomography relationships  
  I.A. Ennouvel and S.B. Shah  
  687
- Management of nasopharyngeal stenosis after uvulopalatopharyngoplasty  
  Y.P. Kreipl and A. Kacker  
  692
- Value of flow cytometry with fine needle aspiration biopsy in patients with head and neck lymphoma  
  C. R. Cannon and D. Fehring  
  696
- Ultrasound-guided fine-needle aspiration and thyroid disease  
  K.A. Nevidlo et al  
  700
- Lymphatic malformation: Predictive factors for recurrence  
  L.J. Fiegelman et al  
  704
- Cutaneous mastocytosis of the oral cavity  
  S. H. Weksler et al  
  711
- Bone-screw mandible fixation: An intraoperative alternative to arch bars  
  A.J. Varinian and A. Avi  
  718

For additional Original Articles, see Table of Contents, p. 5A.

## CASE REPORTS

- Endobronchial placement of a safety pin during intubation  
  M. K. Way  
  742
- Cavernous sinus thrombosis complicating odontogenic parapharyngeal space neck abscess: A case report and discussion  
  D. Feldman et al  
  744
- Unusual presentation of a rare naso-tumor  
  D. Crow et al  
  746
- Primary melanoma of the sphenoid sinus  
  N. Y. Busaba  
  748

## DRUG/DEVICE CAPSULE

- Nasal septal clamp  
  R. Raman and M. B. Dhonn  
  750

## INTERNATIONAL ORIGINAL ARTICLES

- Otogenic brain abscess: Review of 41 cases  
  L. Sennoaglou and B. Szeri  
  751
- The Nijmegen cochlear implant questionnaire  
  J. T. Hindrik et al  
  756
- Increased retinal image velocity after vestibular lesion  
  T. R. Hinoven et al  
  766

For additional International Original Articles, see Table of Contents, p. 7A.

## CLINICAL PHOTOGRAPHS

- Head and neck manifestations of B-cell chronic lymphocytic leukemia  
  R. Cohen-Kerem  
  784

LETTERS TO THE EDITOR

- ANNUAL MEETING  
  Denver, Colorado  
  September 9-12, 2001

INDEX TO VOLUME 123  

Mosby
Botulinum toxin type A (BOTOX) for treatment of migraine headaches: An open-label study

WILLIAM J. BINDER, MD, FACS, MITCHELL F. BRAIN, MD, ANDREW BUSTER, MD, FACS, LARRY D. SCHEIDENROCK, MD, FACS, and JANICE M. POGODA, PhD, Los Angeles and San Francisco, California, and New York, New York.

OBJECTIVE: The object of this clinical experience was to evaluate the correlation between percutaneous botulinum toxin type A (BOTOX, Allergan Corp, Irvine, CA) administration and alleviation of migraine headache symptoms.

STUDY DESIGN AND SETTING: A nonrandomized, open-label study was performed at 4 different test sites. The subjects consisted of 106 patients, predominantly female, who either (1) initially sought BOTOX treatment for hyperfunctional facial lines or other dystonias with concomitant headache disorders, or (2) were candidates for BOTOX treatment specifically for headaches. Headaches were classified as true migraines, possible migraines, or nonmigraines, based on baseline headache characteristics and International Headache Society criteria. BOTOX was injected into the glabellar, temporal, frontal, and/or occipital regions of the head and neck. Main outcome measures were determined by severity and duration of response. The degrees of response were classified as: (1) complete symptom elimination, (2) partial (<50% reduction in headache frequency or severity), and (3) no response (neither 1 nor 2). Duration of response was measured in months for the prophylactic group.

RESULTS: Among 77 true migraine subjects treated prophylactically, 81% (95% confidence interval, 39% to 62%) reported complete response with a mean (SD) response duration of 4.1 (2.6) months; 38% reported partial response with a mean (SD) response duration of 2.7 (1.2) months. Overall improvement was independent of baseline headache characteristics. Seventy percent (95% confidence interval, 35% to 93%) of 10 true migraine patients treated acutely reported complete response with improvement 1 to 2 hours after treatment. No adverse effects were reported.

CONCLUSIONS: BOTOX was found to be a safe and effective therapy for both acute and prophylactic treatment of migraine headaches. Further research is needed to explore and develop the complete potential for the neuroinhibitory effects of botulinum toxin. (Otolaryngol Head Neck Surg 2000;123:669-76.)

Migraine is an episodic neurologic disorder that affects roughly 17% of women and 6% of men. Disability from migraine is profound and affects functioning in the workplace with comorbidity including overlap with other major affective disorders. As such, migraine is a major stressor of the health care providing system. Numerous current therapies have limited benefit and are often accompanied with significant adverse side effects.
Table 1. International Headache Society Criteria for Migraine

<table>
<thead>
<tr>
<th>Diagnostic criteria for migraine without aura</th>
</tr>
</thead>
</table>
| A. Headache attacks lasting 4 to 72 hours (terminated or ame-
  nized with treatment). |
| B. Headache has at least 2 of the following characteristics: |
  - Unilateral location |
  - Pulsating quality |
  - Moderate or severe intensity (interferes with ordinary daily activity and activities). |
  - Aggravation by walking or other regular physical activity. |
  - Duration of at least 4 hours and not due to another nervous system disorder. |
| C. During headache, at least one of the following: |
  - Nausea and vomiting |
  - Photo- and/or phonophobia |

Diagnostic criteria for migraine with aura

<table>
<thead>
<tr>
<th>A. At least 2 attacks fulfilling at least 3 of the following 4 characteristics:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. or more fully reversible aura symptoms including focal cerebral cortical and/or hemispheric dysfunction.</td>
</tr>
<tr>
<td>B. At least 1 aura symptom develops gradually over more than 4 minutes or 2 or more symptoms occur in succession.</td>
</tr>
<tr>
<td>C. No aura symptoms last more than 60 minutes. If more than 1 aura symptom is present, accepted duration is proportionally increased.</td>
</tr>
<tr>
<td>D. Headache follows aura with a delay interval of less than 60 minutes, it may also begin before or simultaneously with the aura.</td>
</tr>
</tbody>
</table>

Fig 1. Injection sites for open-label study of BOTOX efficacy for treatment of migraine headache symptoms. Average number of injection sites given per area: glabellar 3-6; temporal 2-4; forehead 3-6, injections were also administered to the suboccipital area in 2 patients.

Given the known limitations of existing therapies, both acute and long-acting prophylactic therapy that is both effective and well-tolerated is needed.

Botulinum toxin type A (BOTOX) is a paralytic neurotoxin that is approved therapy for blepharospasm, strabismus, and hemifacial spasm and has been safely used for dystonia, spasticity, tremor and other neuromuscular disorders of inappropriate muscular contraction. It is commonplace for use in the treatment of wrinkles and hyperfunctional lines of the face. The inhibition of the vesicular release of the primary neurotransmitter, acetylcholine (Ach), at the neuromuscular junction is thought to be responsible for the chemodenervating action of botulinum toxin and the therapeutic effect causing muscle paresis or paralysis. However, botulinum toxins are known to have a blocking action on the parasympathetic nervous system that may also inhibit the release of a number of neurotransmitters and neuropeptides other than Ach or produce a blocking role in the transmission of different neural impulses.

While performing initial clinical trials of BOTOX treatment for hyperfunctional lines of the face, the senior author (WJ.B.) discovered a correlation between pericranial BOTOX and the alleviation of migraine headache symptoms. The use of BOTOX to reduce migraine pain was not immediately obvious because there is no clear cut mechanism of action that could explain its clinical effect. Consequently, the 3 other authors (M.F.B., A.R., L.D.S.) were contacted and asked to retrospectively review their patients who had received BOTOX for wrinkles or other dystonias. Patients with concurrent headache disorders as well as other patients requiring treatment only for headaches were then prospectively treated to determine whether the relationship between BOTOX treatment and the alleviation of migraine symptoms was meaningful and could be replicated by other physicians. We hereby report the results from our combined, multicenter, open-label study on the efficacy of BOTOX in both the acute and prophylactic management of migraine.

METHODS

Subjects considered for participation were authors’ patients who (1) had received BOTOX injections for the treatment of hyperfunctional facial lines or dystonias who had concomitant headache disorders, or (2) were candidates for treatment specifically for headache dis-

orders. Patients received treatment at cosmetic surgery, otorhinolaryngology, and movement disorder/dystonia clin-
ic. All patients included in the open-label study signed informed consent (based on the standard guidelines of dosing and administration of BOTOX for blepharospasm and hyperfunctional lines). and were permitted to continue chronic and rescue medications (other than
Table 2. Type of treatment administered and migraine classification of patients treated with BOTOX (n = 106)

<table>
<thead>
<tr>
<th>Migraine classification</th>
<th>Prophylactic</th>
<th>Acute</th>
<th>Both prophylactic and acute</th>
</tr>
</thead>
<tbody>
<tr>
<td>True</td>
<td>69</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Partial</td>
<td>15</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>NOS</td>
<td>9</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Based on self-reported baseline headache frequency and International Headache Society criteria for migraines with or without aura.

BOTOX as needed. On the basis of self-reported baseline history of headache episodes, subjects were classified into 1 of 3 groups: true migraine, possible migraine, and nonmigraine. "True migraine" subjects satisfied 4 of the International Headache Society (IHS) criteria for migraine with or without aura. "Possible migraine" subjects satisfied 2 or 3 of the IHS criteria; all others fulfilling less than 2 IHS criteria were defined as "nonmigraine" subjects (Table 3).8

Prospective treatments were administered both prophylactically and for acute migraine episodes. Some subjects received both prophylactic and acute treatments; however, no subsequent treatments were administered until follow-up data had been collected for the preceding session. BOTOX was injected into glabellar, temporal, frontal, and, in 2 patients, the suboccipital regions of the head and neck (Fig. 1). Sites of injection, numbers of injections, and doses per injection were given according to the standard already determined for the treatment of hyperfunctional facial lines and facial dystonias.3 All of the physicians were experienced injectors of BOTOX. Subjects injected specifically for headaches tended to receive larger doses as the study progressed. Length of follow-up varied by patient (corresponding with office visits or based on phone contact), ranging from 1 to 6 months (3 patients were evaluated at 3 weeks).

For each subject, treating physicians documented dose per injected site, total dose injected, area injected, and, at follow-up, self-reported treatment benefit and adverse effects. Subjects were asked to report both qualitative (degree of response) and quantitative (duration of response) assessments of treatment benefit. Degrees of response were categorized as: (1) complete response (elimination of headache symptoms), (2) partial response (at least 50% reduction in frequency or severity of headaches), and (3) no response (less than 50% reduction in frequency or severity of headaches). Subjects lost to follow-up were classified as nonresponders for analysis purposes. Standard forms were used by all treating physicians for collection of baseline and outcome data.

A t test was used to test differences in continuous variables (dose, age, duration of benefit) between baseline groups (frequent/severe migraines vs infrequent/mild migraines); approximate z tests were used when homogeneity of variance was violated.2 Fisher's exact test was used to test differences in categorical variables (injection site, gender, treatment response) between baseline groups and to test differences in baseline characteristics (gender, age, headache frequency, and severity) among migraine classification groups; for the latter, age and headache frequency were categorized with approximate quartiles as cutpoints based on distributions among all subjects. Analysis of variance was used to test for differences in response by dose, injection site, age, and gender; analysis of covariance was used when adjustment for baseline characteristics was necessary. Ninety-five percent confidence intervals (CI) were calculated for proportions of responders by assuming a binomial distribution. All tests were 2-sided with a 0.05 significance level.

**RESULTS**

Treatment response data were obtained on 106 subjects: 93 received prophylactic treatment, 4 received
treatment for an acute migraine episode, and 9 additional patients treated acutely were also followed prophylactically and included in both categories for analysis (Table 2). Seventy-nine (75%) subjects were classified as having true migraine, 18 (17%) as having possible migraine, and 9 (9%) as having nonmigraine headaches. Most subjects were female (90%), 36 to 60 years old (66%), and reported severe symptoms (51%) 2 to 3 times per month (34%) (Table 5). Headache severity but not frequency differed by migraine classification (P = 0.03); migraine subjects were more likely than possible or true migraine subjects to report less severe headaches. Gender and age were similar among migraine classification groups.

Prophylactic Treatments

The mean (SD) dose of BOTOX administered among 102 subjects treated prophylactically was 31.0 (17.5) units (range, 5 to 110). True migraine subjects with self-reported high baseline frequency (at least 3 times/month) received higher total doses than those with low baseline frequency (mean [SD] dose = 35.5 [20.7] vs 27.7 [11.3]; P = 0.06) and were more likely to receive temporal injections (P = 0.01); however, neither dose nor injection site depended on self-reported baseline migraine severity. Both age and gender were unrelated to baseline frequency and severity.

Among 57 true migraine subjects treated prophylactically, 51% (95% CI, 39% to 62%) reported complete
Fig 3. Self-reported duration of treatment response among 77 true migraine subjects treated prophylactically.

Fig 4. Proportion (95% CI) of self-reported complete responders among 77 true migraine subjects treated prophylactically by injection site.

response with mean (SD) duration of benefit of 4.1 (2.4) months. Subjects with low baseline frequency were more likely to report complete response than subjects with high baseline frequency (P = 0.00; similarly, subjects with low baseline headache severity (less than severe) were more likely to report complete response than subjects with high baseline severity (P = 0.07). However, the proportion of subjects reporting improvement (complete or partial response) did not depend on baseline frequency or severity (Fig 2). Overall response levels, mean (SD) self-reported duration of response was 3.2 (2.3) months (Fig 3). Response duration did not differ by baseline frequency, either overall (mean [SD], 3.2 [2.8] and 3.0 [1.4] months for low and high baseline frequency, respectively) or among complete responders (mean [SD], 4.2 [3.3] and 4.0 [1.0] months for low and high baseline frequency, respectively). Complete responders with severe baseline headaches had somewhat longer response durations (mean [SD], 4.6 [3.1] months) than those with less severe baseline headaches (mean [SD], 3.7 [2.3] months).

After adjustment for baseline frequency, there was no evidence of dose-response; however, injection site was a significant predictor of complete response. Cephalic injections were more likely to produce complete responders than any other site or combination of sites (P = 0.00; Fig 4). Complete responders were significantly older (mean [SD] age, 48 [12] years) than
partially responders (mean SD = 43 [9] years) and non-
responders (mean SD, 41 [13] years) (P = 0.02). 
Response did not depend on gender.

An additional 38% of true migraine subjects report-
ed partial response (95% CI or complete or partial 
response, 79% to 95%) with a mean (SD) duration of 
benefit of 2.7 (1.2) months. Mean (SD) duration of ben-
efit among nonresponders was 1.3 (1.5) months.

Acute Treatments

The mean (SD) dose of BOTOX administered among 
13 subjects, all females, treated for acute migraine 
episodes was 31 (15.2) units (range, 16 to 54). Among 
10 true migraine subjects, 70% (95% CI, 35% to 93%) 
reported complete response, and all responders experi-
enced improvement 1 to 2 hours after treatment. The 
most common injection site was the glabella, either 
alone (70%) or combined with injections in the fore-
head (61%). Response did not depend on age.

Adverse Events

There were no reported cases of true ocular signs, 
diplopia, facial nerve or expression problems, keratoauto-
yth, or idiosyncratic or allergic reactions as a result of 
BOTOX treatment. Two subjects reported transient 
brow ptosis; other adverse effects were limited to tran-
sient local pain and ecchymosis at the injection site.

DISCUSSION

The cause of migraine headache continues to be 
speculative with vascular, neuronal, and myofascial 
hypotheses. Recent family studies have shown an asso-
ciation with essential tremor, cerebellar disease, and a 
prominent chameleopathy in the hemiplegic form of the 
disease, suggesting that migraine is a heterogeneous 
and often genetic disorder. The trigeminomeningeal theory of migraine pro-
poses a reflex whereby different trigeminal neurons transmit pain sensation back to the central nervous sys-
tem triggering autonomic pathway activation via the 
facial nerve, involving the pterygopalatine and ocul gan-
via and resulting in inflammation. This mechanism sets up a cycle triggregating pain via trigeminal neurons and the efferent parasympathetic pathway producing feedback vasodilation. Vasodilation is thought to be mediated by the release of potent vasoactive com-
ounds from parasympathetic neurons innervating the 
pericranial vasculature. One of these vasoactive pep-
tides, vasoactive intestinal peptide (VIP), has been his-
tologically identified at nerves associated with large 
arteries and intracranial vessels supplying the tongue, 
sublingual gland, nose, and eyes. In cats, Goadsby and 
Shelley proposed that the neurogenic vasodilator 
response mediated by the trigeminovascular nerves may 
be produced by VIP. Antibodies to VIP have been 
shown to block the neurogenic vasodilatory response 
produced by electrical stimulation of either the locus 
coeruleus or the pterygopalatine ganglion in cats, and 
vasoactive peptide release into the extracranial circula-
tion has been observed after activation of the trigemino-
vascular system and in patients experiencing migraine. Other theories involving vascular, supraspinal, and 
myofascial components that contribute in varying 
degrees have been proposed to try to explain the symp-
tom complex of migraine. However, pharmacologic 
action on neurotransmitters and their sites of action is 
central to most current 5 hydroxytryptamine agonist-
like (sumatriptan) treatment regimens to stop the ongo-
ing migraine cycle. Local injections of botulinum toxin into excessive muscle contraction have been successful in relieving 
symptoms due to numerous medical and cosmetic condi-
tions. Early in the clinical use of botulinum toxin, we 
appreciated that pain relief alone can be a prominent 
component of its therapeutic benefit. The basis for 
pain relief in muscle contraction disorders is not known 
and was assumed to be due to the relief of muscle 
tension. However, in early reports it was also observed 
that after treatment of torticollis by BOTOX therapy, the 
relief of pain exceeded the reduction of inappropriate 
muscle contraction; suggesting that BOTOX may act 
via a different pathophysiologic pathway to alleviate 
or eliminate generalized jaw pain other than that related to muscle dysfunction. At this study, we found that the 
dose-duration curve for migraine did not necessarily 
have a direct correlation with the duration of action 
associated with flaccid paralysis of muscles. We also 
observed that in some patients muscle function had 
returned after 3 months, but the effects of the drug on 
the elimination of the headaches had persisted longer. 
Although there have been recent reports on the use of 
BOTOX providing symptomatic relief in tension 
headache, it has also been shown that tension-type 
headache sufferers do not reliably exhibit either abnor-
mal resting levels of pericranial electromyographic 
activity, or abnormal levels of electromyographic activ-
ity in response to stress. Should migraine be precipi-
ted by cranial muscle contraction, then BOTOX 
would prophylaxis against this inciting factor. However, 
the properties exhibited by BOTOX in its inhibitory 
effect on the acute and chronic relief of migraine pain 
and other somatomyology task as nausea and vomit-
ing, visual disturbances, photophobia, and phonophobia 
argues against this as the only simple explanation and 
infers alternative mechanisms of action. Until this 
report, we have found no other referenced citation doc-
mentioning a localized injection of botulinum toxin to the head and neck reducing systemic visceral symptoms. In the acute cases treated, we found that the time required for the elimination of the acute migraine attack was consistently between 1 and 2 hours, whereas the time required for a complete flaccid paralysis to occur is approximately 3 days. Other anecdotal findings were: (1) in a few cases, a smaller amount of BOTOX was required to eliminate headache than that required to cause paralysis of the muscle; (2) in some patients, periorbital sites were injected subcutaneously and not intramuscularly; (3) during long-term follow-up, several patients described a feeling of "disconnection," whereby they felt as if a migrainous episode was present but did not experience the accompanying pain; (4) in some cases, a temporary reduction in pain was noted in one dolentus; and (5) the average dose per patient in these early findings was approximately 31 units per treatment. Recently, however, we have found that a minimal dose of approximately 50 units distributed over the glabella (5 injection sites), bitemporal (3 injection sites per side), and upper forehead (4 injection sites) at a dilution of 4 cc per 100 units has become the most frequent dose/volume/bit rate used.

Research in both migraine and botulinum toxin therapeutics suggests an association between botulinum toxin and the theoretical bases of migraine. The literature on botulinum toxin has, for the most part, focused on its original known mechanism of action that inhibits the release of the neurotransmitter acetylcholine (ACh) in the neuromuscular junction. However, BOTOX also deactivates autonomic nerves; and it has been shown that different neuronal components and systems have different susceptibilities to botulinum toxin.23,28 In addition, botulinum toxin has been shown to have a direct effect on efferent fibers also suggesting that it may block the sensory system as well.29

Shah et al.30 directed the use of botulinum toxin to block parts of the autonomic nervous system for clinically beneficial effects. In these cases, botulinum toxin was used to denervate autonomic nerves either directly or topically, as opposed to its known denervating cholinergic action on skeletal muscle. It was determined that the parasympathetic postganglionic neurons that innervate the canine submandibular glands are susceptible to the anticholinergic effect of botulinum toxin types A and D. Different autonomic systems may have different susceptibilities to the toxin; and BOTOX exerts an anticholinergic effect when applied topically to the nasal mucosa. This provided evidence that the administration of BOTOX either by injection or by diffusion may have an effect on other important sites of action (possibly at the cellular level) in addition to the currently known neuroeffect sites.

Additional research has suggested that botulinum toxins may inhibit the release of a number of neurotransmitters and neuromodulators other than ACh.31 Daily et al.31 proposed that botulinum toxin may have the potential to inhibit the release of any substance that is distributed by a common vesicular release mechanism and thus inhibit the release of different nerve transmitters. Botulinum toxins are metalloproteases that cleave specific proteins involved in vesicular release. This may explain a common target in the release process found in many if not all nerve endings. Through the inhibition of vesicular release, botulinum toxin may inhibit neuropeptides, transmitters, or other neurally released substances that normally modulate neuromuscular, neuroendocrine, or neuroregulatory activity. The selectivity of action of the toxins with respect to which neuretransmitter is inhibited may also be related to the receptor affinity the toxin has on certain nervous terminals. Other clinical applications, such as its action on reducing hyperhydrosis as well as its use on the smooth muscle of the gastrointestinal and urinary tract, are not completely understood.32

In addition to these findings, Suzuki et al.33 in 1990 found a colocalization of other neuropeptides associated with the classical neurotransmitter noradrenaline and acetylcholine to be common in both the central and peripheral nervous systems. Of particular interest to the actions of botulinum toxin is that both VIP and neuropeptide Y were also found to be colocalized with acetylcholine in parasympathetic nerves originating in the sphenopalatine, otic, and lingual carotid ganglia, all of which innervate cerebral arteries. Sala et al.34 used immunohistologic techniques to provide evidence that botulinum toxin may inhibit the release of calcitonin gene-related peptide from motor nerves in rats.34

These observations provide a possible link between the actions of botulinum toxin at cholinergic nerve terminals and its possible antinociceptive effects as well as anti-inflammatory properties. After injection of BOTOX into the muscles of the temple or forehead, it is possible that BOTOX recognizes the cholinergic (parasympathetic) nerves innervating the extracranial vascular structures causing a disruptive effect on the vesicular release of ACh and ACh-like neuropeptides. BOTOX blockade of these neuropeptides may also inhibit neurogenic inflammation, which is thought to play a role in migraine. This sterile inflammation may be due to the release of neuropeptides from sensory (trigeminal) nerves innervating both the intracranial and extracranial vasculature. The parasympathetic nerves that innervate the vessels may be a likely site of action for botulinum toxin.

Otolaryngology- Head and Neck Surgery Volume 123 Number 5

BINDER et al. 675
because of its known cholinergic components and possible colocalization of the other vasodilatory neuropep-
tides. Therefore, botulinum toxin, associated with its
generalized inhibition of vesicular release, may inhibit
the release of a variety of neuroactive substances at the
sensory nerve (V-1) level. These correlations may
explain how botulinum toxin may interrupt the viscous
trigeminal-neurovascular cycle.

CONCLUSION

BOTOX is shown to be a safe and beneficial ther-
apeutic agent in both the acute and prophylactic treatment
of migraine. Double-blind studies have commenced to
determine optimal dosing, patient populations, and the
benefits for patient quality of life. BOTOX effectiveness
might be explained by an inhibitory role on selective
sensory trigeminal nerve endings, the vesicular release
of neurotransmitters, or on the vasculature and extracra-
nial inflammatory process currently thought to con-
tribute to the symptoms during the course of migraine.

We honor the memory of Dr Larry Schoenrock with
the publication of these findings.

REFERENCES

1. Stang PE, Oehlers JT, Celestino DO. Migraine. Patterns of
2. Blitzer A, Bowker WJ, Are J, et al. The management of hyper-
fuctional facial lines with botulinum toxin: a collaborative study of
3. Blitzer W, Blitzer A, Blitzer MA. Treatment of hyperfunctional
lines of the face with botulinum toxin A. Dermatol Surg 1998:24:
1752-1758.
4. Newton LE. The origin, structure, and pharmacological activity of
International Headache Society criteria. Neurology 1994:48:50-
53.
8. Zagami AS. Pathophysiology of migraine and tension-type
9. Blitzer W, Koller WC, Boyett J. Intravenous essential
11. Mortimer MA. The neurology of vascular headache. Ann Neurol
12. Goodfay PJ, Shelley S. High-frequency stimulation of the facial
13. Goodfay PJ, Macdonald GI. Intracranial venous stimulation by
vascular laser: clinical results (VPL). Br J Neurosurg 1985;9:
295-298.
14. Ostrom J, The clinical and pathophysiologial observations in
migraine and tension-type headaches explored by injection of
vascular, sympathetic and myelophylic drugs. Br J Neurosurg 1992:6:
125-132.
recent headache: methodological issues and new empirical
20. Black JD, Dolley JO. Selective location of acceptors for botu-
linum neurotoxin A in the central and peripheral nervous sys-
linum neurotoxic: role of acceptors in targeting to cholinergic
and in the inhibition of the release of several neurotrans-
misses. In: Dowdall MJ, Howseman E, editors. Cellular and molecular
tains two monoclonal neuronal polypeptides and activates in
parasympathetic cerebrovascular nerves originating in the
peptide: possible role in the formation and maintenance of neun-