TITLE: Botulinum Toxin A for Migraine Headache: A Review of the Clinical Effectiveness

DATE: 29 October 2008

CONTEXT AND POLICY ISSUES:

Botulinum toxin is a potent neurotoxin that causes muscle paralysis by blocking the release of acetylcholine at neuromuscular junctions. Botulinum toxin occurs in several subtypes, with type A and B being used in clinical practice since 1989. Botulinum toxin A was marketed in two distinct formulations, Botox® and Dysport®. Minute amounts of botulinum toxin A have been used to decrease muscle spasm and pain in various pain syndromes. The use of botulinum toxin A for migraine headache, an off-label indication through pericranial superficial intramuscular injections, requires a review of its clinical effectiveness.

RESEARCH QUESTION:

What is the clinical effectiveness of botulinum toxin A for reduction in pain and improvement of functioning in patients with migraine headache?

METHODS:

A limited literature search was conducted on key health technology assessment resources, including PubMed, OVID’s Embase, the Cochrane Library (Issue 3, 2008), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international HTA agencies, and a focused Internet search. Results include articles published between 2003 and September 2008, and are limited to English language publications only. Filters were applied to limit the retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, other controlled clinical trials, and observational studies. Internet links are provided, where available.

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SUMMARY OF FINDINGS:

Our literature search identified one systematic review\textsuperscript{11} and six recent randomized controlled trials (RCTs)\textsuperscript{12-17} on the efficacy of botulinum toxin A in the treatment of migraine headache. The qualitative systematic review, with literature search ending 2004, and covering 5 randomized and 3 non-randomized trials including 470 patients, concluded that botulinum toxin A injection does not reduce frequency and severity of migraine headache.

The six recent trials that are not included in the above systematic review are all randomized placebo-controlled trials.\textsuperscript{12-17} Over 200 patients were included in four of these trials, whereas two trials were small, with 32 patients. All six trials used Botox\textsuperscript{®} as the formulation of botulinum toxin A. Five out of six trials showed there was no statistically difference between the effect of botulinum toxin A injection and placebo on migraine frequency and severity.\textsuperscript{12-16} One small-size trial showed a statistically significant decrease in migraine headache frequency with botulinum toxin A compared to placebo.\textsuperscript{17} Results from the trials are summarized in table 1.

Table 1: Results from the RCTs on the Use of Botulinum Toxin A for Migraine Headache

<table>
<thead>
<tr>
<th>Studies</th>
<th>Number of patients/Follow-up time</th>
<th>Outcomes</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saper et al\textsuperscript{12} (2007)</td>
<td>232 patients/3 months</td>
<td>Migraine frequency and severity</td>
<td>No statistically significant differences</td>
</tr>
<tr>
<td>Vo et al\textsuperscript{13} (2007)</td>
<td>32 patients/3 months</td>
<td>Migraine frequency and severity</td>
<td>No statistically significant differences</td>
</tr>
<tr>
<td>Relja et al\textsuperscript{14} (2007)</td>
<td>495 patients/9 months</td>
<td>Migraine frequency</td>
<td>No statistically significant differences</td>
</tr>
<tr>
<td>Aurora et al\textsuperscript{15} (2007)</td>
<td>369 patients/11 months</td>
<td>Migraine frequency</td>
<td>No statistically significant differences</td>
</tr>
<tr>
<td>Elkind et al\textsuperscript{16} (2006)</td>
<td>418 patients/4 months</td>
<td>Migraine frequency</td>
<td>No statistically significant differences</td>
</tr>
<tr>
<td>Anand et al\textsuperscript{17} (2006)</td>
<td>32 patients/3 months</td>
<td>Migraine frequency</td>
<td>Statistically significant decrease</td>
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CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:

Data from the systematic review and five out of six randomized controlled trials do not support the use of botulinum toxin A for the treatment of migraine headache. Despite the fact that new theories were suggested for the pathophysiology of migraine headache,\textsuperscript{18,19} the inability of superficially-injected botulinum toxin A to significantly affect central neuronal processes may explain its lack of efficacy. The use of botulinum toxin A for the treatment of migraine headache needs to be cautioned in light of the current evidence.

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REFERENCES:

