TITLE: Botulinum Toxin A for Muscle Spasm of Various Anatomic Origins: A Review of the Clinical Effectiveness

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CONTEXT AND POLICY ISSUES:

Botulinum toxin is a potent neurotoxin that causes muscle paralysis by blocking the release of acetylcholine at neuromuscular junctions.\(^1\) Botulinum toxin occurs in several subtypes, with type A and B being used in clinical practice since 1989.\(^2\) Botulinum toxin A was marketed in two distinct formulations, Botox\(^®\) and Dysport\(^®\).\(^3\) Minute amounts of botulinum toxin A have been used to decrease muscle spasm and pain in various pain syndromes.\(^4,5\) While the use of botulinum toxin A on various muscle spasm conditions such as hemifascial spasm,\(^6\) blepharospasm,\(^7\) and cervical dystonia,\(^8,9,10\) is well documented and approved, its use for different off label-muscle spasm conditions is increasing,\(^12,13\) and 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 muscle spasm of various anatomic origins?

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.
SUMMARY OF FINDINGS:

Our literature search identified one Cochrane systematic review and one retrospective study on the use of botulinum toxin for the treatment of spasmodic dysphonia,15,16 one retrospective study for the treatment of pharyngeal constrictor muscle spasm,17 one randomized controlled trial (RCT) for pelvic floor muscle spasm,18 and one prospective study for the treatment of spastic toe clawing.19

The Cochrane review15 identified only one old RCT (1991) that reported significant beneficial effects of botulinum toxin A on physiological functioning and listener perception among 13 participants as compared to placebo. The four trials on different muscle spasm conditions, all using Botox®, showed botulinum toxin A can reduce spasm severity. Results from the trials are summarized in table 1.

Table 1: Results from the Trials on the Use of Botulinum Toxin A for Various Muscle Spasm Conditions

<table>
<thead>
<tr>
<th>Studies</th>
<th>Design, number of patients</th>
<th>Indication</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Holden et al16</td>
<td>Retrospective study, 13 patients</td>
<td>Adductor spasmodic dysphonia</td>
<td>97% (145/150 treatments) had spasm reduction</td>
</tr>
<tr>
<td>Hamaker et al17</td>
<td>Retrospective study, 62 patients</td>
<td>Pharyngeal constrictor muscle spasm</td>
<td>79% (49/62 patients) had spasm and pain reduction</td>
</tr>
<tr>
<td>Abbott et al18</td>
<td>Randomized controlled trial, 60 patients</td>
<td>Pelvic floor spasm</td>
<td>Statistically significant reduction of muscle spasm</td>
</tr>
<tr>
<td>Lim et al19</td>
<td>Prospective study, 7 patients</td>
<td>Spastic toe clawing</td>
<td>86% (6/7 patients) had pain reduction</td>
</tr>
</tbody>
</table>

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:

Limited data showed the beneficial effect of botulinum toxin A in various off-label muscle spasm conditions. This may be an indication that the well-known mechanism of action of the toxin, through reduction of synaptic outflow of acetylcholine at the neuromuscular junctions,1,3,20 exerts its effect, not only in approved conditions, but also in other muscle spasm conditions. Two of the studies were small (13 and 7 patients)16,19 and only one was a randomized controlled trial,18 whereas the other three trials were observational studies which can be subject to selection bias. Larger randomized controlled trials are needed to reconfirm the beneficial effect of botulinum toxin A in these off-label indications.

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