Considered Judgement Form

This form is a checklist of issues considered by the PGAG when making purchasing recommendations.

Meeting date: 30 Nov 2010

Intervention: Botox injection for temporomandibular joint pain

Background:
Botox is the name commonly given to botulinum toxin, a neurotoxin produced by the bacterium Clostridium botulinum. When injected, botox works by preventing nerve impulses from reaching a muscle, causing the muscle to relax. It is injected in small quantities to treat neurological disorders characterized by abnormal muscle contractions.

Two formulations of botox are approved by Medsafe: BOTOX® (botulinum toxin type A, Allergan New Zealand Limited) and Dysport® (botulinum toxin type A, New Zealand Medical and Scientific Ltd.). Its use is not approved for temporomandibular joint pain.

IPM 2010 update – summary of findings:
Botox injection for temporomandibular joint (TMJ) pain was not covered by the original IPM guidance released in 2005 because, at that time, no relevant research studies that met our inclusion criteria were identified.

The 2010 IPM update identified only one recent eligible study. This small, but reasonably well-designed, randomised controlled trial failed to consistently demonstrate that botulinum toxin A was superior to placebo saline injections. The intervention may merit further investigation in larger studies:

1. Volume of evidence
Comment here on any issues concerning the quantity of evidence available on this topic and its methodological quality.

Studies reporting on effectiveness
Three studies were identified as potentially eligible (Clark, Stiles et al. 2007; Ihde and Konstantinovic 2007; Kurtoglu, Gur et al. 2008). Upon review, the systematic review carried out by Ihde et al., (2007) did not report on any eligible studies and the review reported by Clarke et al., (2007) was not systematic. Only one study (Kurtoglu, Gur et al. 2008) was considered to be eligible.

Studies considered for safety assessment only
One case report (Volcy, Tepper et al. 2006) and one very small case series (Lee, Chow et al. 2005) were considered for safety outcomes only.
2. **Consistency**  
*Comment here on the degree of consistency demonstrated by the availability of evidence. Where there are conflicting results, indicate how the group formed a judgement as to the overall direction of the evidence.*

Not applicable—one study only.

3. **Applicability**  
*Comment here on the extent to which the evidence is directly applicable in the New Zealand setting. Comment here on how reasonable it is to generalise from the results of the studies used as evidence to the target population for this guideline.*

Moderate-high. The study was carried out at the Clinics of Temporomandibular Disorders of the Cukurova University Dental Faculty, Turkey and designed according to the CONSORT guidelines.

4. **Cost**  
*Comment on any economic costs associated with this service, product or procedure.*

The cost is approximately $750 per procedure and the estimated volume for 2011–2012 is two procedures at a total cost of $1,500.

5. **Clinical Impact**  
*Comment here on the potential clinical impact that the intervention in question might have – e.g. size of patient population; magnitude of effect; relative benefit over other management options; resource implications; balance of risk and benefit.*

**Effectiveness**

Kurtoglu (Kurtoglu, Gur et al. 2008) carried out a small randomised, double blind placebo controlled study of 24 patients aged 15 years and above attending a temporomandibular disorders clinic in Turkey. All of the patients had myofascial pain with or without functional disc displacement. There were 12 patients in each group study group. Twenty of the patients (83.3%) were female, the mean age of patients in the botox group was 29.6 years (range 16 to 53 years, SD ± 12.7 years), and patients in the placebo group had a mean age of 23.4 years (range, 20 to 34 years, SD ± 4.7 years). Three (25%) patients in the botox group and 8 (66.7%) in the placebo group had functional disc displacement and myofascial pain (P = .1).

The primary outcome of the study was not declared, however, it appeared to be change in electromyography (EMG) values. All patients completed a bio-behavioural questionnaire covering pain, disability and psychological status and all of the patients completed the study. No analgesic, anti-inflammatory, or muscle-relaxing agents were allowed during the study.

Both the placebo and botulinum toxin type A (BTX-A) patients improved their pain scores over the study period but in neither case were the changes significant. Neither groups appeared to show improvements in the disability score over the follow-up period. Both groups showed improvement in their psychological state which was significantly different between baseline and day 14 score in the placebo group. There were no evident side effects of treatment.

Patients were selected from 500 clinic patients but sampling criteria for the selection of the 24 study patients were not given. The follow-up period of 28 days may have been too short, particularly given that it has been suggested that “The pain relief from BoNT-A may take several weeks to reach maximal effect” (Song, Schwartz et al. 2007). Given the large number of variables tested, the small number of significant differences detected should be treated with caution (i.e. there is a high possibility of spuriously significant comparisons). Moreover, it would appear that there was a notable placebo effect in the responses for some of the reported variables which also make evaluation of the effectiveness of BTX-A difficult. **Overall, this was a reasonably good quality, well designed study that failed to consistently show that botulinum toxin type-A injections were superior to saline placebo injections. This indication requires further evaluation in larger studies.**

**Serious Adverse events** and complications not previously reported:

Neither of the two studies reviewed for safety outcomes (Lee, Chow et al. 2005; Volcy, Tepper et al. 2006) reported any relevant adverse events.

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6 Generally defined as an event that is fatal, life-threatening, permanently disabling, or requiring admission to hospital.
6. **Other Factors**  
*Indicate here any other factors that you took into account when assessing the evidence base.*

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7. **Evidence Statement**  
*Please summarise the synthesis of the evidence relating to this key question, taking all the above factors into account, and indicate the evidence level which applies.*

<table>
<thead>
<tr>
<th>Weight and consistency of evidence</th>
<th>Evidence Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>One small RCT indicates that this may be a promising approach. No safety issues highlighted in any of the studies examined.</td>
<td>NHMRC evidence level II</td>
</tr>
</tbody>
</table>

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8. **Practice Recommendation (for IPM website)**  
*What clinical practice recommendation(s) can be drawn from this evidence? Please indicate the grade of recommendation(s).*

<table>
<thead>
<tr>
<th>Grade of Recommendation</th>
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<tbody>
<tr>
<td>There was no recommendation for this indication in the 2005 guidance. The 2010 recommendation is:</td>
</tr>
<tr>
<td><em>The routine use of botox injections for the treatment of TMJ pain is not recommended due to insufficient evidence</em></td>
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9. **Purchasing recommendation**  
*What recommendation(s) does the Purchasing Guidance Advisory Group (PGAG) draw from this evidence?*

| Do not purchase botox injection for the treatment of TMJ pain. |
References


