Botulinum toxin A for myofascial trigger point injection: A qualitative systematic review

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Abstract

Botulinum toxin injection is used to treat various pain conditions including muscle spasticity, dystonia, headache and myofascial pain. Results are conflicting regarding the use of Botulinum toxin for trigger point injection in terms of improvement in pain. The aim of this study was to carry out a systematic review to assess the evidence for efficacy of Botulinum toxin A (BTA) compared with placebo for myofascial trigger point injection.

Electronic databases on Medline, Cochrane Library, Scopus, CINAHL were queried using key words such as “botulinum toxin”, “myofascial pain”, “trigger point”, “chronic pain” and “musculoskeletal pain”. Relevant published randomized controlled trials that described the use of BTA as injection therapy for trigger points were considered for inclusion. The five-item 0–16 point Oxford Pain Validity Scale (OPVS) was used as a selection criteria for suitable clinical trials. Trials were also assessed based on quality using the Oxford Rating Scale. Data extracted from qualified trials included outcome measures such as pain intensity and pain pressure threshold. All studies were ranked according to the OPVS and the authors’ conclusions were compared.

Five clinical trials met the inclusion criteria. One trial concluded that BTA was effective, and four concluded that it was not effective for reducing pain arising from trigger points. OPVS scores ranged from 8 to 14 with the negative studies corresponding with higher validity scores. The current evidence does not support the use of BTA injection in trigger points for myofascial pain. The data is limited and clinically heterogeneous.

Keywords: Botulinum toxin; Myofascial pain; Trigger point; Chronic pain; Trial validity; Systematic review

1. Introduction

1.1. Botulinum toxin for trigger point injection

Botulinum toxin is a potent neurotoxin produced by the bacterium Clostridium botulinum. It causes flaccid muscle paralysis by blocking acetylcholine (ACh) release at the neuromuscular junction. Botulinum toxin occurs in several subtypes, with Type A and B being used in clinical practice after Food and Drug Administration (FDA) approval in 1989 and 2000, respectively. Botulinum toxin A (BTA) has been used in a variety of pain conditions including focal dystonia, spasticity, myofascial pain syndrome and headaches (Lang, 2003; Raj, 2003).

Myofascial pain syndrome (MPS) is a regional condition of muscle pain and stiffness characterized by the presence of myofascial trigger points (TPs). Clinically, these TPs are focal hypersensitive taut bands that produce a local twitch response and typical referred pain pattern on palpation (Simons et al., 1999; Borg-Stein and
Simons, 2002). MPS is considered a distinct disorder with major and minor diagnostic criteria whereas the term myofascial pain is used more broadly and refers to soft tissue pain of unclear etiology (Cohen et al., 2004).

Pain arising from a TP is believed to result from an excessive release of ACh from the neuromuscular junction after chronic muscle contraction. Such an “integrated trigger point hypothesis” involves local myofascial tissues, the central nervous system and biomechanical factors (McPartland, 2004). Dysfunctional motor endplates have been implicated as the underlying etiology of TPs (Simons et al., 1999). BTA binds to the motor endplate presynaptic membrane and is internalized by receptor-mediated endocytosis. ACh release at the neuromuscular junction is then inhibited as BTA causes cleavage of the plasma membrane bound peptide, SNAP-25, preventing vesicle-dependent neurotransmitter release (Montecucco and Schiavo, 1995; Raj, 2003). This leads to chemodenervation in the affected muscle and reduces muscle tension and pain. The onset of action varies from a few days to two weeks. The duration of action of BTA corresponds to the period of functional denervation, which is between three to four months. Measurement of isometric forces in dogs indicated a ten-week duration of effect of BTA (Childers et al., 1998). Recovery of muscle function occurs with neural regeneration as evident histologically by neuronal sprouting, reinnervation, enlargement of existing endplates as well as formation of new endplates (Raj, 2003).

BTA injection has been compared with other modalities of treatment such as local anesthetic, corticosteroid and normal saline injection as well as dry needling. Although there are numerous published reports on the use of BTA injection for TPs, the current evidence is not sufficient for a general recommendation on the use of BTA in this condition (Reilich et al., 2004). There are very few randomized, controlled trials (RCTs) comparing BTA with an active control or with placebo for treating myofascial pain and the conclusions have been conflicting.

This study was carried out to systematically evaluate the existing literature concerning the use of BTA injection for myofascial pain in TPs. Our primary aim was to critically examine the relevant RCTs qualitatively and assess the evidence for the efficacy of BTA injection for TPs.

2. Methods

2.1. Searches

We performed searches without language restriction on Medline (1966–2006), The Cochrane Central Register of Controlled Trials (2006), Scopus and CINAHL. The last electronic search was performed in June 2006. Key words used for the search included the following: “botulinum toxin”, “myofascial pain”, “trigger point”, “chronic pain”, “musculoskeletal pain”, “injections”, and “blocks”. The search also included bibliographies of review articles and all retrieved reports. Authors of original publications were not contacted.

2.2. Selection criteria

All published RCTs comparing BTA injection of TPs with either an active or inactive control in the treatment of myofascial pain and group size ≥ 10 were included in the review. The criterion for group size was based on the Oxford Pain Validity Scale (OPVS) inclusion criteria (Smith et al., 2000). Inadequate group sizes may result in a wrong estimate of the treatment effect (Moore et al., 1998). Only double-blind and single-blind trials were included. Studies that are not blinded are prone to bias and may overestimate treatment effects (Schulz et al., 1995). Open-label clinical trials, case series, case reports, review articles, expert opinions and abstracts were excluded. We intentionally excluded studies that merely investigated BTA injection for muscle spasm and pain with no documentation of TPs.

2.3. Data extraction, quality and validity assessment

One author (K.Y.H.) screened the abstracts of all retrieved reports and excluded those that did not meet the inclusion criteria. Both authors then independently read all included reports. Data were extracted and summarized into a table based on study design, number of patients, patient characteristics, dosing regimen, site(s) of injection, analgesic outcome measures and authors’ conclusion. The quality of the studies was graded using the Oxford Rating Scale (Jadad et al., 1996b) and validity of the studies was assessed using the OPVS (Smith et al., 2000). Discrepancies in scores were resolved by discussion.

3. Results

Twenty-one relevant titles were identified from our literature search (Fig. 1). Five open-label trials (Lang, 2000; De Andres et al., 2003; Lang, 2004; Vasan et al., 2004; Ney et al., 2006), one retrospective cohort study (Wheeler and Goolkasian, 1998), one duplicate publication (Freund and Schwartz, 2000a) and two case reports (Acquadro and Borodic, 1994; Diaz and Gould, 1999) were excluded. There were 12 RCTs. Three studies evaluated BTA injection into the piriformis muscle (Porta, 2000; Childers et al., 2002; Fishman et al., 2002). While piriformis syndrome is considered myofascial pain with similar pathophysiology, these studies were excluded because the diagnosis of TP based on the criteria mentioned above was not established. Three other studies
were excluded because group size was less than 10 (Cheshire et al., 1994; Graboski et al., 2005; Kamanli et al., 2005). One study investigated the effectiveness of BTA injection in patients with low back pain but it was excluded from the review because only three of the 31 patients (<10%) had TPs on examination (Foster et al., 2001). Table 1 shows the excluded trials. Of the remaining five studies that met our inclusion criteria, BTA was compared with normal saline injection into TPs. A summary of these studies is presented in Table 2. These five trials generated a total of 173 BTA injections versus 99 saline injections in 272 patients.

The designs of these trials were diverse in many areas including inclusion criteria, location of myofascial TPs, number and site of injection, study duration, BTA dosing regimen and outcome measures. In addition, there was little or no information about concurrent oral analgesic therapy, rescue medication or physical therapy in many of these studies. Therefore, we did not pool the data for meta-analysis. Instead, a qualitative systematic review was performed and studies were ranked according to the OPVS scores (Smith et al., 2000) (Table 3). Included studies were also ranked according to quality scores using the Oxford Rating Scale (Jadad et al., 1996b) (Table 4).

### 3.1. Trial evaluation

Ojala et al. (2006) compared small injectate volumes (0.15–0.35 ml) of BTA with saline in a double-blind, crossover trial. They did not show any difference in pain scores and pain pressure threshold (PPT) at the TP between the two groups. No attempt was made to standardize or calculate the total amount of paracetamol allowed as rescue medication during the study period. OPVS score was 12/16. Quality score was 4/5.

**Table 1**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Reason for exclusion</th>
<th>Authors' conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ney et al. (2006)</td>
<td>Open-label trial</td>
<td>BTA efficacious</td>
</tr>
<tr>
<td>Vasan et al. (2004)</td>
<td>Open-label trial</td>
<td>BTA efficacious</td>
</tr>
<tr>
<td>De Andres et al. (2003)</td>
<td>Open-label trial</td>
<td>BTA efficacious</td>
</tr>
<tr>
<td>Lang (2000)</td>
<td>Open-label trial</td>
<td>BTA efficacious</td>
</tr>
<tr>
<td>Wheeler and Goolkasian (1998)</td>
<td>Retrospective cohort study</td>
<td>BTA efficacious</td>
</tr>
<tr>
<td>Freund and Schwartz (2000a)</td>
<td>Duplicate report</td>
<td>BTA efficacious</td>
</tr>
<tr>
<td>Diaz and Gould (1999)</td>
<td>Case report</td>
<td>BTA efficacious</td>
</tr>
<tr>
<td>Acquadro and Borodic (1994)</td>
<td>Case report</td>
<td>BTA efficacious</td>
</tr>
<tr>
<td>Childers et al. (2002)</td>
<td>BTA injection for piriformis syndrome</td>
<td>BTA efficacious</td>
</tr>
<tr>
<td>Fishman et al. (2002)</td>
<td>BTA injection for piriformis syndrome</td>
<td>BTA efficacious</td>
</tr>
<tr>
<td>Porta (2000)</td>
<td>BTA injection into piriformis, scalenus anterior and iliopsoas</td>
<td>BTA efficacious</td>
</tr>
<tr>
<td>Graboski et al. (2005)</td>
<td>&lt;10 patients enrolled</td>
<td>BTA comparable to bupivacaine</td>
</tr>
<tr>
<td>Kamanli et al. (2005)</td>
<td>&lt;10 patients enrolled</td>
<td>BTA comparable to lidocaine</td>
</tr>
<tr>
<td>Cheshire et al. (1994)</td>
<td>&lt;10 patients enrolled</td>
<td>BTA efficacious</td>
</tr>
<tr>
<td>Foster et al. (2001)</td>
<td>&lt;10% of patients had TPs</td>
<td>BTA efficacious</td>
</tr>
</tbody>
</table>

BTA, Botulinum toxin A; TP, trigger point.
Table 2
Randomized controlled trials of Botulinum toxin A injection for myofascial pain

<table>
<thead>
<tr>
<th>Author</th>
<th>Study design</th>
<th>Location of pain</th>
<th>Duration of pain</th>
<th>Dose regimen (BTA/control)</th>
<th>No. of patients</th>
<th>Age (mean ± SD)</th>
<th>Concurrent therapy</th>
<th>Study duration</th>
<th>Outcome Measures</th>
<th>Results</th>
<th>Author’s conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ojala et al. (2006)</td>
<td>Double-blind, randomized, crossover</td>
<td>Neck and shoulder</td>
<td>10.0 ± 8.6 months</td>
<td>(i) 28 ± 6 U BTA (15–35 U); 5 U per TP (ii) Saline</td>
<td>(i) 15 (ii) 16</td>
<td>44.4 ± 7.7</td>
<td>Paracetamol</td>
<td>4 Weeks</td>
<td>VAS pain score at 4 weeks; VRS (efficacy); PPT</td>
<td>No difference in VAS, PPT and VRS (efficacy) (P &gt; 0.05)</td>
<td>Negative</td>
</tr>
<tr>
<td>Ferrante et al. (2005)</td>
<td>Double-blind, randomized</td>
<td>Neck and shoulder</td>
<td>&gt;6 months</td>
<td>(i) 10 U BTA (ii) 25 U BTA (iii) 50 U BTA in each TP (Max. 5 TP per patient) (iv) Saline</td>
<td>(i) 32 (ii) 34 (iii) 31 (iv) 35</td>
<td>45.3 ± 10.9</td>
<td>Standardized regimen of amitriptyline, ibuprofen and propoxyphene-acetaminophen</td>
<td>12 Weeks</td>
<td>VAS pain score at 24 h and 1, 2, 4, 6, 8 and 12 weeks; rescue medication use; PPT; SF-36</td>
<td>No difference in VAS, PPT and rescue dosing (P &gt; 0.05); lower score in BTA group for SF-36 emotional subscale (P &lt; 0.05)</td>
<td>Negative</td>
</tr>
<tr>
<td>Wheeler et al. (2001)</td>
<td>Double-blind, randomized</td>
<td>Cervico-thoracic</td>
<td>8.6 ± 9.6 years</td>
<td>(i) 231 ± 50.1 U BTA (ii) Saline</td>
<td>(i) 25 (4 dropouts) (ii) 25 (1 dropout) (iii) 14 (ii) 12</td>
<td>43.6 ± 10.7</td>
<td>NR</td>
<td>16 Weeks</td>
<td>NPAD; global assessment of improvement; SF-36</td>
<td>No difference (P &gt; 0.05)</td>
<td>Negative</td>
</tr>
<tr>
<td>Freund and Schwartz (2000b)</td>
<td>Double-blind, randomized</td>
<td>Cervical</td>
<td>&gt;6 months</td>
<td>(i) 20 U BTA (ii) saline</td>
<td>(i) 11 (ii) 11</td>
<td>40.7 (ii) 43.4 (iii) 38.1</td>
<td>NR</td>
<td>4 Weeks</td>
<td>No difference in PPT, NPAD and subjective assessment (P &gt; 0.05)</td>
<td>Positive</td>
<td></td>
</tr>
<tr>
<td>Wheeler et al. (1998)</td>
<td>Double-blind, randomized</td>
<td>Cervico-thoracic</td>
<td>(i) 93.02 days (ii) 1038.3 days (iii) 1067.5 days</td>
<td>(i) 50 U BTA (ii) 100 U BTA in each TP (iii) saline</td>
<td>(i) 11 (ii) 11 (iii) 11</td>
<td>NR</td>
<td>NR</td>
<td>4 Months</td>
<td>No difference in PPT, NPAD and subjective assessment (P &gt; 0.05)</td>
<td>Negative</td>
<td></td>
</tr>
</tbody>
</table>

BDI, Beck Depression Inventory; BTA, Botulinum toxin A; NPAD, Neck Pain and Disability Scale; NR, not reported; PPT, pain pressure threshold; SF-36, 36-item short-form health survey; TP, trigger point; VAS, Visual Analogue Scale; VRS, verbal reporting score.
Ferrante et al. compared the efficacy of three different doses of BTA (10, 25 and 50U) with saline for TP injection (Ferrante et al., 2005). This was the only RCT that prescribed a standardized regimen of amitriptyline, ibuprofen and propoxyphene–acetaminophen as well as myofascial release physical therapy to all patients during the 12-week study period. No significant difference was found between the BTA groups and placebo group for VAS pain scores, pressure algometry and rescue medication. The authors did not specify the number of patients recruited or the number of dropouts, if any, in their study. OPVS score was 14/16. Quality score was 4/5.

Wheeler et al. compared the therapeutic efficacy of BTA injection of neck muscle TPs with normal saline (Wheeler et al., 2001). There was no statistically significant difference between treatment and control groups. However, we disagreed with the authors’ choice of using $2 \times 5$ unweighted means analysis for statistical testing. Repeated measures designs are more accurate because subjects are observed on 5 separate occasions during the study period. OPVS score was 8/16. Quality score was 4/5.

In an earlier study by the same authors, 33 participants were divided randomly to receive either 50 or 100 U of BTA or normal saline (Wheeler et al., 1998). Similarly, no differences were found between the groups. OPVS score was 12/16. Quality score was 2/5.

Freund and Schwartz investigated BTA injection of cervical TPs in patients with whiplash-associated disorder (Freund and Schwartz, 2000b). Five TPs were injected with a total of 100 U BTA or with saline. The treatment group showed a trend toward improvement in range of motion of the neck and reduction in pain at two weeks postinjection. At four weeks, there was a statistically significant improvement in subjective pain scores in the BTA group. OPVS score was 8/16. Quality score was 4/5.

### 3.2. OPVS and quality scores

Table 3 shows the itemized OPVS scores for the included trials. The trials had validity scores that ranged from 8 to 14. A breakdown of scoring based on quality (Jadad et al., 1996b) is presented in Table 4. Quality scores ranged from 2 to 4. Four of the five included studies concluded that BTA injection was not better than saline injection for improving myofascial TP pain. The only study with a positive conclusion had a low OPVS score of 8 (Freund and Schwartz, 2000b). Therefore, the evidence for analgesic efficacy of BTA injection for TPs in the treatment of myofascial pain is not convincing.

### 4. Discussion

#### 4.1. Quality versus validity

Meta-analyses pool data from RCTs and assign different weighting based on trial size and effect size (quantitative systematic reviews). A trial is graded based on adequacy of blinding, randomization, concealment of allocation and description of withdrawals and dropouts to determine the quality of the study (Jadad et al., 1996a). On the other hand, qualitative systematic reviews summarize and present findings from clinical trials and form a general conclusion based on the number of positive versus negative outcomes of a particular intervention. Vote-counting based on the number of positive versus negative trials is based on each trial’s...
own estimate of positive or negative, and takes no account of how valid this estimate might be (Smith et al., 2000). In contrast to meta-analyses, trial and effect sizes are ignored since data are not pooled.

Quality of a study has to be differentiated from validity. A trial with a good quality score (adequately randomized and blinded) may have low validity score if there are shortcomings in the study design. Deficiencies in blinding, sample size, outcome measurement or data analysis will reduce the validity of a trial (Smith et al., 2000). Clinical trials included in qualitative systematic reviews are usually screened for quality. Only high quality trials are pooled in meta-analysis to provide an overall estimate of treatment efficacy using various measures such as weighted mean difference, odds ratio or number-needed-to-treat. This approach cannot be used for qualitative systematic reviews because trial methodologies are commonly too disparate. The presence of a greater number of positive trials with low validity will skew the results and may lead to inaccurate conclusions. By taking into account all aspects of the study design, including trial size, blinding and statistical interpretation, Smith et al. (2000) constructed a tool, the Oxford Pain Validity Scale (OPVS), to assess the validity of trials in interventions in pain (Appendix 1). This tool contains items empirically known to affect the validity of trial findings.

4.2. Efficacy of BTA injection

We performed a qualitative systematic review of RCTs comparing BTA with saline injection in treating pain in myofascial TPs. Five RCTs were included in our systematic review. Four of the five trials found no difference between BTA injection and placebo injection. Only one study showed that BTA was more efficacious than normal saline. Quantitative analysis was not performed due to considerable dissimilarities in the methodology of the clinical trials. The diagnosis of MPS is empirical and a proposed criteria (Tunks and Crook, 1999) include: (1) a regional pain complaint; (2) pain or paresthesia in the typical distribution of the TP; (3) a taut band in the muscle; (4) exquisite tenderness in the taut band; and (5) restricted range of movement in the affected muscle. Criteria 1–4 have to be met in all patients. The patients should also have one of these three minor criteria: (1) reproduction of pain complaint by pressure on the TP; (2) local twitch response in the taut band; and (3) alleviation of the TP by stretch. Besides the study conducted by Ojala et al. (2006), the other trials did not utilize this definition as part of their inclusion criteria. Different injectate volumes were also described, ranging from 0.05 to 6 ml. BTA concentration ranged between 5 and 150 U. The smaller volumes and BTA concentrations were used in the study by Ojala et al. (2006) and the largest volume and BTA concentration were used by Wheeler et al. (2001). In one study, patients who had more than five active TPs were excluded from the study (Ferrante et al., 2005) while the other clinical trials did not limit the number of TPs a patient could have. Patients’ concurrent analgesic medications during the study period were notstandardized in four of the five RCTs. Ferrante et al. ensured that all enrolled patients were maintained on a common analgesic regimen and also measured the amount of rescue medication used as an outcome (Ferrante et al., 2005). Porta emphasized that adjunctive physical therapy is a critical part of treating myofascial pain after BTA injection as stretching exercises interrupt the vicious cycle of muscle spasm and pain (Porta, 2000). However, physical therapy during the study period was only reported in two of the included studies (Porta, 2000; Ferrante et al., 2005). Other than VAS pain intensity, other outcome measures among the clinical trials were too disparate to allow pooling of data. Therefore, proceeding with a meta-analysis injudiciously may lead to misleading conclusions.

In order to give more weight to better conducted clinical trials and strengthen the conclusion of our systematic review, we adopted the OPVS described by Smith et al. (2000). OPVS scoring ranks clinical trials based on validity using criteria that includes blinding, group size, outcome measures, internal sensitivity and data analysis. We found that the RCTs with higher OPVS scores were more likely to have negative conclusions.

Dry needling, local anesthetic, steroid and saline injection have been used for treating TPs in the past (Frost et al., 1980; Cummings and White, 2001). The injected substance did not appear to be the critical factor as dry needling had similar efficacy (Garvey et al., 1989; Cummings and White, 2001). One recent study demonstrated that dry needling reduced pain scores and PPTs as well as BTA or lidocaine injection (Kamanli et al., 2005). It is therefore not surprising that BTA injection has been shown to be effective in reducing myofascial pain in various prospective, open-label studies (Lang, 2000, 2004; De Andres et al., 2003; Vasan et al., 2004; Ney et al., 2006).

The role of BTA injection in reducing pain associated with TPs was not supported by our review. There are many possible explanations why BTA injection of TPs does not effectively reduce pain. Firstly, successful chemodenervation using BTA depends on delivering an adequate quantity of BTA to the motor endplate zone. However, the optimal quantity of BTA has not been determined and it is reasonable to believe that larger muscles require larger doses of BTA. The decrease in endplate noise prevalence is dependent on the dose of BTA in animal studies (Kuan et al., 2002). Head-to-head comparison between different BTA preparations (Botox®, Allergan Inc., USA; and Dysport®, Ipsen Limited, UK) also suggests that there may be differences in
efficacy, duration of action and adverse effects (Rosales et al., 2006). The type of BTA preparation was not specified in a number of studies.

Secondly, the volume of injectate may be an important consideration. BTA diffuses readily through muscles and across fascial planes to adjacent muscles away from the site of injection. Theoretically, injection of a larger volume of BTA should improve efficacy. However, this was not demonstrated in one study that used a high mean BTA dose of more than 200 U (Wheeler et al., 2001).

Thirdly, distance from the site of injection to the motor endplate zone is important. BTA has been shown to suppress endplate noise at myofascial TPs in animal studies (Kuan et al., 2002). However, localization of TPs clinically is a crude and inaccurate method of determining the endplate zone and electromyography (EMG) may be helpful in bringing the needle closer to the endplate zone (Childers et al., 1998). Targeting motor endplate zones can be difficult without EMG, especially in the presence of contracted muscles within a taut band (Childers et al., 1998).

Lastly, flexors and extensors of the axial musculature are antagonistic and maintain posture. In a patient with existing postural abnormality, weakening one set of muscles with BTA injection without considering the antagonistic muscles can potentially enhance the aberration and increase pain (Ferrante et al., 2005).

The pathophysiology of pain in TPs is not completely understood. If excessive ACh release with resultant post-junctional muscle changes is the only etiology of TP pain, BTA injection should lead to improvement in symptoms. Other postulated mechanisms of pain in TPs include muscle spindle hyperactivity, endplate hyperactivity, focal dystonia and psychosomatic origin (Cohen et al., 2004).

4.3. Limitations

Table 1 shows that all open-label trials demonstrated efficacy of BTA injection in the treatment of myofascial pain in TPs. These trials were not considered in our review because lack of blinding introduces bias in outcome measurements (Schulz et al., 1995). Three other studies were excluded because of the small sample sizes. Small study group sizes may lead to erroneous treatment outcomes (Moore et al., 1998). Of these three studies, only one study showed that TP injection with BTA was better than saline (Cheshire et al., 1994). The other two studies did not demonstrate better pain outcomes when BTA was compared with local anesthetic injection (Graboski et al., 2005; Kamanli et al., 2005).

Therefore, a limitation of our review is the small number of clinical trials included. Although four of the five studies did not show that BTA was efficacious for TP injection, the limited number of trials may not allow us to come to a definite conclusion confidently about the utility of this technique. In addition, the findings of our review cannot be extended to explain the efficacy of BTA for “non-trigger point” injections. Chronic myofascial pain involving deeper muscles such as the piriformis or iliopsoas muscles may demonstrate tenderness on palpation, but are unlikely to fit the diagnosis of “trigger point”. Two studies have shown that BTA injection was effective for treating piriformis syndrome (Childers et al., 2002; Fishman et al., 2002). A third study demonstrated efficacy of BTA injection for myofascial pain in the piriformis, iliopsoas and scalenus anterior muscles (Porta, 2000). These studies were carried out using fluoroscopic, electromyographic or electrophysiologic guidance. Thus, BTA injection for deep muscles – especially when such modalities are used – may have a useful role in treating myofascial pain. We did not evaluate the use of BTA injection for such pain conditions in this review.

In addition, we did not explore the possible adverse effects that can occur with BTA injection. Localized pain, soreness or bruising may be associated with injection. More significant adverse effects such as ptosis, dysphagia and even anaphylaxis have also been reported (LeWitt and Trosch, 1997; Li et al., 2005).

4.4. Research agenda

Future clinical studies should be adequately powered to ensure sample sizes are large enough and study designs should be double-blinded and appropriately randomized. There should also be well-defined inclusion criteria for MPS. Patients who have myofascial pain secondary to other painful conditions such as facet arthropathy or radiculopathy may be more difficult to treat than patients with primary MPS. Including only patients who have a positive response to local anesthetic injection may be a useful screening tool (Abram, 2005). Clinical trials should also simultaneously control for concurrent use of maintenance and rescue analgesic medication as well as physical therapy. Treatment failure may be related to unemployment status, coexisting psychological or physical stress, smoking and prolonged duration of pain. These factors should be also be made known and compared between treatment and control groups (Hopwood and Abram, 1994; McPartland, 2004). Future studies should seek to determine the right dose and injection technique, and standardization of BTA dosages and injectate volumes in RCTs cannot be over-emphasized.

5. Conclusion

In conclusion, the current evidence does not support the use of BTA injection in TPs for myofascial pain. The data is limited and clinically heterogeneous. BTA does not have greater efficacy when compared with
other injection therapies with normal saline, local anesthetics or even dry needling for superficial TPs commonly involving the cervicothoracic and low back region. Acquisition cost of BTA is high and further studies need to establish its cost-effectiveness for TP injection.

Appendix 1. Oxford Pain Validity Scale (OPVS) (Smith et al., 2000)

The OPVS should only be used on trials which are randomized and have a start group size \( \geq 10 \) for all groups relevant to the review question.

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Blinding</td>
<td>Trial convincingly double-blind?</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Trial convincingly single-blind or unconvincingly double-blind?</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Trial either not blind or the blinding was unclear?</td>
<td>0</td>
</tr>
<tr>
<td>2. Size of trial groups</td>
<td>Group size ( \geq 40 )</td>
<td>3</td>
</tr>
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<td></td>
<td>Group size 30–39</td>
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<tr>
<td></td>
<td>Group size 20–29</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Group size 10–19</td>
<td>0</td>
</tr>
<tr>
<td>3. Outcomes</td>
<td>Look at pre-hoc list of most desirable outcome relevant to the review question:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Results for at least one pre-hoc desirable outcome included, and the outcome was used appropriately</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>There were no results for any of the pre-hoc desirable outcomes, or, a pre-hoc desirable outcome was used inappropriately</td>
<td>0</td>
</tr>
<tr>
<td>4. Baseline pain and internal sensitivity</td>
<td>Look at the baseline levels for the outcomes relevant to the review question:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>For all treatment groups, baseline levels were sufficient for the trialist to be able to measure a change following the intervention. Alternatively, did the trial demonstrate internal sensitivity?</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>For all treatment groups, baseline levels were insufficient to be able to measure a change following intervention, or baseline levels could not be assessed, or internal sensitivity was not demonstrated.</td>
<td>0</td>
</tr>
</tbody>
</table>

5. Data analysis

(i) Definition of outcomes

- Relevant outcomes defined clearly: 1
- Relevant outcomes not defined clearly: 0

(ii) Data presentation: location and dispersion

- Mean data with standard deviations, or dichotomous outcomes, or median with range presented, or sufficient data presented to enable extraction of any of the above: 1
- None of the above presented: 0

(iii) Statistical testing

- Appropriate statistical test, with correction for multiple tests where relevant: 1
- Inappropriate statistical tests were chosen and/or multiple testing was carried out, but with no correction, or, no statistics were carried out: 0

(iv) Handling of dropouts

- Dropout rate either \(<10\%\), or \(>10\%\) and includes intention-to-treat analysis in which dropouts were included appropriately: 1
- Dropout rate \(>10\%\) and dropouts were not included in the analysis, or, it is not possible to calculate a dropout rate from the data presented: 0

Total score =

Author conclusion: trial positive/negative

Reviewer conclusion: trial positive/negative

References

Abram SE. Does botulinum toxin have a role in the management of myofascial pain? Anesthesiology 2005;103:223–4.


