Meeting Date	30 August 2017
Topic	The effectiveness of botulinum toxin type A (botox) injections for myofascial pain

Purpose

This purchasing guidance (considered judgement form) accompanies a systematic review commissioned from the International Centre for Allied Health Evidence (iCAHE), University of South Australia. The purposes are to:

1. Review recent (2011 onwards) evidence on the effectiveness and safety of botulinum toxin type A (botox) injections in the management of myofascial pain.
2. Make updated purchasing recommendations on this interventional pain management (IPM) modality.

Background

Myofascial pain syndrome is a chronic pain condition originating in the myofascial tissue (connective tissue or 'fascia' surrounding the muscles). The symptoms include localised and referred pain, tenderness and muscle spasms. Symptoms are associated with hypersensitive spots in the fascia known as myofascial trigger points. Pain is commonly experienced in the lower back, neck or upper body muscles, although any muscles or fascia can be affected.

The etiology of myofascial pain is not well understood. Repetitive musculoskeletal trauma or microtrauma has been suggested as a possible cause. Treatment tends to be multidimensional and may include physical therapies (e.g. massage, exercise, acupuncture) and pharmacotherapy (non-steroidal anti-inflammatory drugs or NSAIDS, injections of various agents).

Injections of botulinum toxin type A (botox) may be used to treat myofascial pain. Botox induces a reversible weakness of skeletal muscle around the injection site, leading to partial denervation and reduced muscle contractions. The effects last for around 12 weeks. Injections of small quantities of botox may therefore be used to treat pain conditions associated with increased involuntary muscle activity.

According to the Medsafe website[1], three formulations of botulinum toxin type A are currently approved for use in New Zealand: Botox® (Allergan New Zealand Limited), Dysport (Pharmacy Retailing NZ Limited) and Xeomin (New Zealand Medical and Scientific Limited). None are specifically indicated or approved for the treatment of myofascial pain.

ACC's IPM guidance on botox injections for myofascial pain was last updated in 2011 and the following purchasing recommendations were made:

- Do not purchase botox injection for the routine treatment of myofascial pain.
- Purchase may be considered on a case by case basis where conventional treatment options have failed or on the recommendation of a registered medical practitioner.

These recommendations were based on the conflicting evidence available at the time.

[1] http://www.medsafe.govt.nz/index.asp visited 21 August 2017.

1. Effectiveness, Volume of Evidence, Applicability / Generalisability and Consistency / Clinical impact

Comment here on the extent to which the service/product/ procedure achieves the desired outcomes. Specific reference needs to be made to safety. Report number needed to treat and harm where possible, any issues concerning the quantity of evidence and its methodological quality and the extent to which the evidence is directly applicable or generalisable to the New Zealand population, and the degree of consistency demonstrated by the available evidence. Where there are conflicting results, indicate how the group formed a judgement as to the overall direction of the evidence. Comment on the clinical impact e.g. size of population, magnitude of effect, relative benefit over other management options, resource implications, balance of risk and benefit.

Volume & quality of studies:

The iCAHE authors identified 5 systematic reviews (SRs) with or without meta-analysis (MA) plus 8 additional randomised controlled trials (RCTs) on botox injections for myofascial pain.

The quality of the SRs was on the whole high (4 high vs. 1 low quality). The quality of the RCTs was more variable, ranging from high (n=3) through acceptable (n=1) to low (n=4).

Key findings from the higher quality studies, where available, are outlined below.

Evidence on effectiveness from SRs

- Botox injections provided no significant pain relief in patients with myofascial pain syndrome (high quality SR/MA of botox injections for chronic musculoskeletal pain by Zhang et al. 2011).
- In another SR, three of four included RCTs[2] reported that botox injections produced no significant difference in pain outcomes compared to placebo (high quality Cochrane SR of botox injections for myofascial pain syndromes [excluding head and neck] by Soares et al. 2014).
- In a further SR, six of seven included RCTs[3] reported no significantly different effects on pain following botox injections compared to placebo (saline) injections (acceptable quality SR on botox injections for cervico-thoracic myofascial pain syndrome by Desai et al. 2014).
- The effect of botox injections on pain was not significantly different to that of placebo (saline) injections, exercise plus analgesics, exercise plus lidocaine injections or exercise plus dry needling (high quality SR of botox injections for neck pain [including myofascial neck pain] by Langevin et al. 2011).
- Botox injections plus exercise showed no short term difference compared to lidocaine injections plus exercise (Langevin et al. 2011, as outlined above).

Evidence on effectiveness from RCTs

Compared to placebo:

- Two high quality RCTs found no difference in pain reduction between botox injections and placebo (saline) injections (Ernberg et al. 2011 [myofascial temporomandibular disorders] and Kwanchuay et al. 2015 [myofascial trigger point of the upper trapezius muscle]).

Relative effectiveness of different treatment parameters, i.e. dosages and injection techniques:

- There was no difference in pain reduction between high (e.g. 480 units) and low (e.g. 200 units) dosages (acceptable quality RCT by Muller-Schwefe et al. 2011 and low quality RCT by Jerosch et al. 2012).
- There was no difference in pain reduction between fixed point, intra-muscular and trigger point injection methods (high quality RCTs by Ernberg and Kwanchuay as outlined above; also the high quality RCT by Benecke et al. 2011 and the low quality RCT by Nicol et al. 2014).

[2] The exception was the 2006 RCT by Gobel et al., which reported significant improvements in the botox group.
[3] The exception was again the 2006 RCT by Gobel et al., as outlined above.

Evidence on safety:

- Findings from a single high quality SR suggested that botulinum toxin injections are associated with a greater incidence of adverse events compared to placebo (Soares et al 2014).
- However, a number of high and acceptable quality studies found that adverse events are typically transient and resolve spontaneously (Langevin et al 2011, high quality SR; Desai et al 2014, acceptable quality SR; Ernberg et al 2011 and Kwanchuay et al 2015, high quality RCTs as outlined above).

2. Cost

Where possible and reported in the published research literature any economic analysis of the new treatment is considered. Where possible the following will be considered; total costs of the new intervention and number of claimants likely to be affected are considered, along with comparison with the cost of current treatments or interventions, actuarial assessment of the impact of the intervention on scheme liability (including direct and indirect impact e.g. other services and access), expected "accrued benefit" in terms of quality of life, longer life or speedier return to the workforce, implications of cost to the wider health sector.

The iCAHE review found no evidence on the economic implications of using botox injections to treat myofascial pain.

According to ACC's IPM service schedule, botox injections for myofascial pain cost $807.12 per procedure and are coded IN52. Data on claims and volumes will be presented at the meeting.

3. Equity

The extent to which the intervention reduces disparities in health status - in particular equity of access and health outcome. The extent to which the intervention supports the objectives of the Maori access strategy and will encourage access to assessment, treatment and rehabilitation services for those groups where there is evidence of that access is problematic.

There do not appear to be any equity issues associated with this intervention.

4. Consistency with the intent of the AC Act

Purchasing decisions made by ACC must be consistent with and reflect consideration of factors described in the AC Act [Schedule 1, clause 2 (1 and 2)] and these decisions must be defensible against this statutory requirement in respect of individual claimants.

There do not appear to be any consistency issues associated with this intervention.

5. Possible purchasing options

The options are:

1. Purchase,
2. Do not purchase, or
3. Purchase on a case by case basis on the decision of the Manager Corporate Clinical Advice (or equivalent).

6. Evidence statements

Summarise the advisory group's synthesis of evidence relating to this service, product or procedure, taking the above factors into account, and indicate the evidence level that applies.

Evidence on effectiveness

- The evidence indicates that for general myofascial pain syndrome, botox injections provide no statistically significant pain relief *(level A, based on acceptable to high quality evidence from two SRs)*.
- The evidence indicates that for cervico-thoracic-specific myofascial pain syndrome, there is no statistically significant difference in pain reduction between botox toxin injections and saline solution injections *(level A, based on high quality evidence from two SRs and one RCT)*.
- The evidence indicates that for temporomandibular myofascial pain, there is no statistically significant difference in pain reduction between botox injections and saline solution injections or fascial manipulation *(level B, based on one high and one low quality RCT)*.
- The evidence indicates that there are no significant differences between botox and saline injections in terms of physical or emotional function or global or quality of life scores *(level C, based on high quality evidence from one RCT)*.

Evidence on dosages and techniques

- The evidence indicates that there is no difference in pain reduction when comparing injection dosages of 200 units to 480 units of botox *(level C, based on one acceptable and one low quality RCT)*.
- The evidence indicates that there is no difference in pain reduction when using fixed point, intra-muscular or trigger point injection methods *(level C, based on high quality evidence from three RCTs)*.

Evidence on safety

- The evidence suggests that botox injections may be associated with more adverse events compared to placebo *(level B, based on high quality evidence from one SR)*.
- Adverse events are typically transient and resolve spontaneously *(level A, based on high quality evidence from one SR and two RCTs).*

7. Purchasing recommendations

What recommendation(s) does the advisory group draw from this evidence?

Taking recent evidence into account, it is proposed that the 2010 recommendations be changed as follows:

- **Do not purchase botox injections for the treatment of myofascial pain.**
- **Good practice points:**
  - **Myofascial pain/myofascial pain syndrome is not normally a covered condition.**
  - **Consider differential diagnosis if accepted diagnostic criteria for myofascial pain/myofascial pain syndrome are not met.**
  - **See ACC Pain Glossary (2014)[4] for a description of myofascial pain/myofascial pain syndrome.**

[4] Available to ACC staff on the Sauce at http://thesauce/team-spaces/clinical-resources/pain/pain-glossary/index.htm#MPS

This recommendation was ratified by the Clinical Governance Committee in September 2017.

PGAG discussions

References

ACC (2015). *Service schedule for interventional pain management services*. Wellington, ACC.

For details of other references, please see the iCAHE review:

International Centre for Allied Health Evidence (2017). *Systematic review of the literature: the effectiveness of injection of botulinum neurotoxin for myofascial pain as a form of interventional pain management: technical report*. Adelaide, iCAHE.