Botulinum toxin in the management of spasticity in adults

Lynne Turner-Stokes and Anthony Ward

Lynne Turner-Stokes DM FRCP, Herbert Dunhill Chair of Rehabilitation, King's College London
Director, Regional Rehabilitation Unit, Northwick Park Hospital, Middlesex

Anthony Ward FRCP FRCP Edin, Director, North Staffordshire Rehabilitation Centre, North Staffordshire Hospital, Stoke-on-Trent

Clin Med JRCPL 2002;**2**:128–30

ABSTRACT – Botulinum toxin (BTX) is a powerful neurotoxin which blocks cholinergic transmission at the neuromuscular junction. Judiciously applied, it can reduce local muscle overactivity while maintaining the strength in other muscles. To date BTX has not been licensed for use in spasticity in the UK and the literature pertaining to clinical practice is still relatively scant. However, controlled trials have provided evidence of the effectiveness of BTX both in reducing spasticity itself and in achieving functional gain. The guidance given here to clinicians involved in the management of spasticity covers the types of patient suitable for treatment using BTX, the appropriate dosage, and the necessary follow-up procedures and documentation.

Background

What is spasticity and why does it matter?

Spasticity is overactivity in the muscles which follows damage to the brain or spinal cord, eg after stroke, trauma or hypoxic insult. It may take the form of sustained high tone spasms, intermittent spasms, or a mixture of the two. Uncontrolled spasticity leads to permanent shortening (contracture) in the muscles and soft tissues.

Spasticity matters because it causes pain and deformity which:

- increase disability (reduced mobility, self-care, ease of maintaining hygiene etc)
- increase complications, eg pressure sores
- feed into a vicious cycle of poor posture which in turn exacerbates the spasticity.

However, spasticity is not always harmful. Patients with upper motor neurone weakness may rely on the increased tone to maintain their ability to stand and walk.

How is spasticity treated?

The mainstay of treatment is physical and involves:

- active treatment of exacerbating factors such as infection, pain, constipation and other nociceptive influences
- careful positioning throughout 24 hours to maintain muscle length and reduce deformity
- a regular physiotherapy programme which may include stretching and splinting.

In addition, medical and surgical intervention may be required:

- Antispasmodic drugs (eg baclofen, tizanidine, diazepam or dantrolene) may be used to reduce spasticity. However, they also produce generalised weakness, so tone reduction may be at the expense of lost function.
- Where there is already contracture, surgical release may correct deformity and facilitate better postures (eg standing) to prevent further spasticity.

What can Botulinum toxin do?

Botulinum toxin (BTX) is a powerful neurotoxin which blocks cholinergic transmission at the neuromuscular junction. Injected into spastic muscles it produces localised paralysis of the selected muscle(s). Judiciously applied, it can reduce local muscle overactivity, while maintaining the strength in other muscles. Deformity can be corrected without generalised weakness, and function is maintained.

The direct effect of BTX itself is relatively short-lived (about 3–4 months). However, if the muscle can be stretched or active function regained during this window, continued physical management may then be sufficient to manage spasticity, so the benefits can be long lasting.

In post acute stroke or brain injury, spasticity may mask the return of voluntary muscle movement. If permanent contracture develops, this function may be lost for ever. There is a window of opportunity, therefore, when active spasticity management can improve muscle control and may reduce long-term disability. Timing and the clinical expertise to recognise the underlying potential for motor recovery become critical.

Management of spasticity therefore requires the coordinated input of a highly specialist team of therapists, nurses and doctors to provide the best results.

Why are guidelines needed for the use of BTX in spasticity management?

In the light of emerging evidence for its effectiveness in the management of spasticity, a UK licence application is underway for the use of BTX in the management of spasticity. Currently three different preparations of Botulinum toxin are available: two of type A and one of type B. They have different potencies and the doses are not interchangeable.

BTX is potentially extremely useful in the management of spasticity, but is relatively expensive and may be dangerous in the doses that may be required. Moreover, repeated administration can result in the development of neutralising antibodies so that further injection has no effect. It is therefore important that its use is confined to practice which ensures the maximal effect.

What is the evidence that BTX works?

There is a growing body of evidence that BTX is effective in the management of spasticity. Most of the research has been conducted in stroke. Double-blinded placebo-controlled trials have shown it to be safe and effective in the management of spasticity in both the upper limb[1,2] and the lower limb[3,4]. Studies in multiple sclerosis[5,6] have demonstrated functional benefits in the management of hip adductor spasticity. As yet there are no definitive studies of the use of BTX in dynamic function (eg improving gait) in adults. However, several studies of the management of cerebral palsy in children demonstrate improvement of dynamic function with BTX injection[7–10].

Several studies on the effects of different doses[6] have demonstrated that large doses are often needed to achieve measurable functional gain, but as yet there is little clear evidence to inform precise management strategy or selection of appropriate cases. There is some evidence for the use of splinting/casting to enhance the effects of BTX[11,12] and also for the use of electrical stimulation[13]. For the present, specific recommendations for management must rely on clinical opinion rather than research evidence.

Guidelines for the use of BTX

The patients to whom guidelines apply

The guidelines apply to adults with spasticity resulting from damage to the central nervous system including:

- stroke
- brain injury resulting from trauma, hypoxia, inflammation or poisoning
- spinal cord injury
- progressive neurological conditions, eg multiple sclerosis
- cerebral palsy.

The application of these guidelines

These guidelines apply to all clinicians who may be involved in the administration of BTX, including doctors, therapists and nurses. They are also relevant to managers who may be involved in the provision of services for management of spasticity in adults, whether in the hospital or the community. The specialties and services concerned are:

- neurology
- services for management of acute and chronic strokes
- care of the elderly
- rehabilitation
- services to support people with chronic disability.

Principles of coordinated spasticity management using BTX

- Management of spasticity should be undertaken by a coordinated multidisciplinary team (MDT), rather than by clinicians in isolation.
- Before using BTX, the team must ensure that appropriate physical management is in place and available post injection, and that remediable provocative factors have been excluded.
- BTX must be injected only by clinicians with sufficient knowledge of functional anatomy, experience in diagnosis and management of spasticity and knowledge of appropriate clinical dosing regimens.
- BTX injection must be part of a rehabilitation programme involving post-injection exercise, muscle stretch and/or splinting, to achieve an optimal beneficial clinical effect.

BTX injection

- Patients should be selected for BTX on the basis of:
  - focal spasticity
  - dynamic spastic component
  - clearly identified goals for treatment and anticipated functional gains.
- Patients and their families/carers should be given appropriate information prior to treatment and should agree goals before treatment is given.
- Informed consent should be obtained from patients prior to injection. If the patient does not have the mental capacity to consent, current trust policies for obtaining consent should be followed.
- The maximum dose used in a single treatment should not exceed 1,500 u Dysport® (Ipsen) or 400 u Botox® (Allergan) or 10,000 u Neurobloc® (Elan Pharma).

Follow-up and documentation

- Injections should be accompanied by a formal assessment of outcome. Appropriate measures should be identified as part of the goal-setting process.
- All injections should be followed by:
  - therapy review in 1–14 days for assessment and, if necessary, splinting

  - medical/MDT review at 4–6 weeks to assess effect, patient status and functional gains
  - review at 3–4 months to plan future management.
- Documentation for all injections should include:
  - a clear statement of treatment goals
  - baseline outcome measures appropriate to those goals
  - BTX agent, dose, dilution and muscles injected
  - follow-up treatment plan
  - evaluation of outcome and repeat measures
  - plans for future management.

Services

- Services administering BTX should have access to staff with the relevant expertise and adequate space, facilities and equipment for splinting/orthotics.
- Clinicians should have access to facilities to aid in assessment, selection and treatment planning, eg electromyography (EMG).
- Ideally clinicians should familiarise themselves with a single agent to avoid confusion over dose.

Training

Training programmes should be in place to ensure that clinicians in all the relevant disciplines have the required knowledge and skill to use BTX. Training can be provided through formal courses or on-the-job learning through observing experienced clinicians. Formal evaluation methods should be established to ensure the necessary knowledge, experience and skills to perform the technique and provide the service.

Health benefits, costs and risks of BTX

It is estimated that the cost of a treatment with BTX (including assessment, physical aftercare, splinting and review etc over 3–4 months) is around £1,000. Set against this, however, there are major health benefits, many of which have potential cost gains. These include:

- reduced pain and discomfort for the patient
- shorter physiotherapy time to reverse contractures
- less nursing time to provide basic care/hygiene
- avoidance of pressure sores
- increased independence in self-care
- reduced carer burden, lost opportunity costs and health problems among family carers
- improved quality of life, cosmesis and self-esteem, resulting in reduced depression.

Potential organisational barriers

The two most important barriers to the application of these guidelines are (a) time and (b) separate working practices between therapists and doctors. There is a temptation to provide a 'quick fix' to get the patient out of the clinic, rather than spend time planning the coordinated management of spasticity. On top of this, there is a lack of awareness on the part of many doctors of the principles of physical management of spasticity.

Continuing medical education has an important role to play in improving understanding of the nature and pathophysiology of spasticity and the relevant skills of other health professionals in its management.

Guideline development

These guidelines have been prepared by a group of clinicians including doctors, physiotherapists and occupational therapists. For details on their development and accordance with the AGREE criteria, please refer to www.rcplondon.ac.uk.

References

1 Bhakta BB, Cozens JA, Chamberlain MA, Bamford JM. Impact of botulinum toxin type A on disability and carer burden due to arm spasticity after stroke: a randomised double blind placebo-controlled trial. *J Neurol Neurosurg Psychiatry* 2000;**69**:217–21.

2 Simpson DM, Alexander DN, O'Brien CF, Tagliati M *et al.* Botulinum toxin type A in the treatment of upper extremity spasticity: a randomised, double-blind, placebo-controlled trial. *Neurology* 1996;**46**:1306–10.

3 Burbaud P, Wiart L, Dubos JL, Gaujard E *et al.* A randomised, double-blind, placebo-controlled trial of botulinum toxin in the treatment of spastic foot in hemiparetic patients. *J Neurol Neurosurg Psychiatry* 1996;**61**:265–9.

4 Hesse S, Lucke DM, Malezic M, Bertelt C *et al.* Botulinum toxin treatment for lower limb extensor spasticity in chronic hemiparetic patients. *J Neurol Neurosurg Psychiatry* 1994;**57**:1321–4.

5 Snow BJ, Tsui JKC, Bhatt MH, Varelas M *et al.* Treatment of spasticity with botulinum toxin: a double-blind study. *Ann Neurol* 1990:**28**:512–15.

6 Hyman N, Barnes M, Bhakta B, Cozens A *et al.* Botulinum toxin (Dysport) treatment of hip adductor spasticity in multiple sclerosis: a prospective, randomised, double-blind, placebo-controlled, dose ranging study. *J Neurol Neurosurg Psychiatry* 2000;**68**:707–12.

7 Cosgrove AP, Curry AP, Graham HK. Botulinum toxin in the management of the lower limb in cerebral palsy. *Dev Med Child Neurol* 1994;**36**:386–96.

8 Koman CA, Mooney JF, Smith B *et al.* Management of cerebral palsy with botulinum A toxin: preliminary investigation. *J Pediatr Orthop* 1993;**13**:489–95.

9 Gooch JL, Sandell TV. Botulinum toxin for spasticity and athetosis in children with cerebral palsy. *Arch Phys Med Rehabil* 1996; **77**: 508–11.

10 Wong V. Use of botulinum toxin injection in 17 children with spastic cerebral palsy. *Pediatr Neurol* 1998;**18**:124–31.

11 Reiter F, Danni M, Lagalla G, Ceravolo G, Provinciali L Low-dose botulinum toxin with ankle taping for the treatment of spastic equinovarus foot after stroke. *Arch Phys Med Rehabil* 1998; **79**:532–5.

12 Boyd R, Graham HK. Botulinum toxin A in the management of children with cerebral palsy: indications and outcome. *Eur J Neurol* 1997;**4**:S15–22.

13 Hesse S, Reiter F, Konrad M *et al.* Botulinum toxin type A and short term electrical stimulation in the treatment of upper limb flexor spasticity after stroke: a randomised, double-blind, placebo-controlled trial. *Clin Rehab* 1998;**12**:381–8.