# Spasticity Management Research Review™

Making Education Easy

Issue 4 – 2013


## In this issue:



**Abbreviations used in this issue:**

**BoNT** = botulinum toxin
**ESWT** = extracorporeal shock wave therapy
**ITB** = intrathecal baclofen
**MS** = multiple sclerosis

## Welcome to issue four of Spasticity Management Research Review.

This issue includes two papers that examine the effects of extracorporeal shock wave therapy in the management of post-stroke spasticity and chronic hemiplegia, respectively, while a third paper describes outcomes with segmental muscle vibration in multiple sclerosis spasticity. Although the authors of these studies perceive various benefits with these therapeutic modalities, the evidence remains unconvincing for now.

In another paper, US researchers summarise injection patterns of onabotulinumtoxinA in adult patients treated for upper- or lower-limb spasticity. They report quite extensive variation in dosing practices and they note that practitioners need to be aware of local regulatory approvals and regulations.

We hope you find this edition of interest to your clinical practice and we welcome your comments and feedback.

Kind Regards,


**Associate Professor Barry Rawicki**

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## OnabotulinumtoxinA muscle injection patterns in adult spasticity: a systematic literature review

**Authors:** Nalysnyk L et al.


**Summary:** These researchers systematically reviewed the published evidence on injection patterns (i.e., muscle distribution, dosing) of onabotulinumtoxinA in adult patients treated for any cause of spasticity. The review included 70 clinical trials and observational studies (28 randomised, 5 nonrandomised, and 37 single-arm studies) published between 1990 and 2011 reporting data on muscles injected with onabotulinumtoxinA involving a total of 2163 adult patients. The most frequently injected upper-limb muscles were the flexor carpi radialis (64.0% of patients), flexor carpi ulnaris (59.1%), flexor digitorum superficialis (57.2%), flexor digitorum profundus (52.5%), and biceps brachii (38.8%). The most frequently injected lower-limb muscles were the gastrocnemius (66.1% of patients), soleus (54.7%), and tibialis posterior (50.5%). The overall dose range reported was 5–200 U for upper-limb muscles and 10–400 U for lower-limb muscles.


**Comment:** There are a number of articles considering the use of botulinum toxin in spasticity management. The first of these is this review of muscle selection for injection of onabotulinumtoxinA (Botox, Allergan) in the upper and lower limb, reviewing 70 articles published between 1990 and 2011. Not surprisingly, wrist and finger flexors are the most frequently muscles in the upper limb and gastrocnemius, soleus and tibialis posterior in the lower limb. The article is descriptive and non-judgemental. I found it very interesting. Of particular interest to me was that the flexor carpi radialis is the most commonly injected upper limb muscle whereas anatomically by nature of its course the flexor carpi ulnaris is a much stronger muscle and in my experience more frequently a problem than the flexor carpi radialis. Equally, the flexor digitorum superficialis in my clinical practice is much more likely to have symptomatic spasticity than the flexor digitorum profundus. I was also a little surprised that the biceps, the main supinator of the arm, was the most frequently injected elbow flexor.

***Reference: BMC Neurol 2013;13(1):118***
http://www.biomedcentral.com/1471-2377/13/118



Spasticity Management Research Review™

**Independent commentary by Associate Professor Barry Rawicki**, who is a physician in rehabilitation medicine, having obtained his medical degree at the University of Melbourne in 1978, and his specialist qualifications in rehabilitation medicine in 1985. He was appointed Associate Professor in the Department of Medicine, Monash University in 1999. He is the Medical Director of Paediatric Rehabilitation for the Victorian Paediatric Rehabilitation Service at Monash Children's Hospital. He is medical head of the Southern Health Clinical Gait Analysis Laboratory at Kingston Centre. Barry is head of rehabilitation for Epworth Rehabilitation Brighton. His main clinical and research interests are in spasticity management and gait analysis. He was involved in much of the pioneering work in Australia in the use of both botulinum toxin and intrathecal baclofen in spasticity management. His other clinical, research and procedural interests are in chronic neurology and pain management. He has published a number of papers and two book chapters in these areas.

## The effect of extracorporeal shock wave therapy on lower limb spasticity in subacute stroke patients

**Authors:** Moon SW et al.

**Summary:** The effect of extracorporeal shock wave therapy (ESWT) was evaluated on lower limb spasticity in 30 hemiplegic subacute stroke patients with ankle plantar flexor spasticity. ESWT was applied for 1 session/week, with a total of 3 sessions at the musculotendinous junction of medial and lateral gastrocnemius muscles. Patients underwent clinical and biomechanical evaluations at baseline, after sham stimulation, immediately after ESWT, then at 1 week and 4 weeks post-ESWT. Clinical assessments consisted of the Modified Ashworth Scale (MAS), clonus score, passive range of motion of ankle, and Fugl-Myer assessment of the lower limb. An isokinetic dynamometer tested spasticity. Peak eccentric torque (PET) and torque threshold angle (TTA) were analysed at the velocities of 60°/sec, 180°/sec, and 240°/sec. No changes from baseline occurred after sham stimulation. Significant improvements from baseline in MAS scores and PET (180°/sec and 240°/sec) were observed immediately after ESWT and persisted 1 week later, but were no longer significant at 4 weeks after ESWT. PET (60°/sec) and TTA (60°/sec, 180°/sec, and 240°/sec) were significantly improved immediately following ESWT, but were not significant at 1 week and 4 weeks after ESWT.

**Comment:** See adjacent.

***Reference: Ann Rehabil Med 2013;37(4):461-70***
http://tinyurl.com/kqluqds


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## Extracorporeal Shock Wave Therapy reduces upper limb spasticity and improves motricity in patients with chronic hemiplegia: a case series

**Authors:** Troncati F et al.

**Summary:** Twelve patients with chronic hemiplegia underwent two sessions of ESWT and were assessed at baseline, after the treatment, then again at 3 and 6 months. All assessments included evaluations of muscle tone of shoulder adductors, elbow, wrist and finger flexors as determined by the MAS, while motricity, passive range of motion (PROM) and pain subscores of the upper extremity part of the Fugl-Meyer scale were used to assess motor recovery. MAS and Fugl-Meyer scores were significantly improved from baseline immediately after treatment. Effects persisted at 3 and 6 months for MAS, and for motricity and PROM subscores of the Fugl-Meyer scale. Clinical improvement did not correlate with patients' perceived benefit, as determined by scores on a visual analogue scale.

**Comment:** This month, two articles look further at the growing literature on extracorporeal shock wave therapy (ESWT) and another article looks at segmental muscle vibration as physical therapies aimed at managing post stroke (ESWT) or MS spasticity. At this stage, the evidence for long-term benefits from this form of treatment remains unconvincing. In the first of the articles on ESWT (Moon et al.), clinical and biomechanical assessments of spasticity found that three sessions of ESWT produced a very short-lasting reduction in spasticity of the calf. The article concludes, as do many articles on ESWT, that further testing is needed.

The second article on this topic this month (Troncati et al.) looks at upper limb spasticity in chronic hemiplegia in a small number (12) of patients given two treatments of ESWT using only clinical measures. They conclude that "*Two sessions of ESWT seem to have long-term effects in reducing muscle tone ……*". There are of course many problems with this article. Besides the small number of patients leaving the study very underpowered, the assessment leaves much to be desired. The Modified Ashworth Scale (MAS) has been validated for lower limb assessment. Whilst it is frequently used for upper limb assessment, validation does not exist and there is a significant literature showing lack of inter-rater and intra-rater reliability for upper limb and especially for small joints (wrist and fingers). Probably the most telling statement in this study is where the authors note, rather sadly I thought, "*Clinical* [?meaning measured] *improvement was not correlated to the patients' perceived benefit*". To my mind at this stage the numerous studies on ESWT have failed to show that this is likely to be a useful line of treatment.

***Reference: NeuroRehabilitation 2013 Aug 12. [Epub ahead of print]***
http://tinyurl.com/mba2kzh

## Does giving segmental muscle vibration alter the response to botulinum toxin injections in the treatment of spasticity in people with multiple sclerosis?

**Authors:** Paoloni M et al.

**Summary:** This study randomised 42 patients with the secondary progressive form of MS to 1 of 3 groups: Group A, 30 minutes of 120 Hz segmental muscle vibration over the rectus femoris and gastrocnemius medial and lateral, 3 times per week, for a 4-week period; Group B, botulinum toxin A (BoNT-A) injection in the rectus femoris, gastrocnemius medial and lateral and soleus, in combination with segmental muscle vibration; or Group C, BoNT-A alone. All measurements were performed at baseline (T0), then at 10 weeks (T1) and 22 weeks (T2) post-randomisation. In all groups, MAS scores at the knee and ankle decreased significantly over time ($p<0.001$). In Group C, knee and ankle spasticity was significantly increased at T2 compared with T1 ($p<0.05$). Fatigue Severity Scale scores in groups A and C were significantly reduced from T0 (A: 53.6; C: 48.5) at T1 (A: 48.6; $p=0.03$; C: 43.5; $p=0.03$) and T2 (A: 46.7; $p=0.02$; 42.5; $p=0.02$), while no significant differences were observed in group B (T0: 43.4; T1: 37.3; T2: 39.7).

**Comment:** This third study, using segmental muscle vibration rather than ESWT is quite well designed, comparing vibration therapy with BoNT and with both. The paper concludes that the combination of BoNT plus vibration reduces spasticity and fatigue. However, on reading the full paper, I found the results did not justify the conclusion with changes on the MAS of only 1 point, certainly within measurement error and not the two-point reduction usually required to denote significant change. Changes in the fatigue scores were similar for all three groups. No group had a change in Barthel.

***Reference: Clin Rehabil 2013;27(9):803-12***
http://cre.sagepub.com/content/27/9/803.abstract

## Clinical experiences with cannabinoids in spasticity management in multiple sclerosis

**Authors:** Lorente Fernández L et al.

**Summary:** Outcomes were examined for 50 patients (median age 47.8 years) with spasticity in multiple sclerosis (MS) treated with inhaled delta-9-tetrahydrocannabinol (THC) in combination with cannabidiol (CBD) between April 2008 and March 2012. Primary progressive MS was diagnosed in 38% of the patients, secondary progressive MS in 44%, and relapsing-remitting MS in 18%. THC/CBD was prescribed for spasticity in 44% of patients, pain in 10%, or for both spasticity and pain in 46%. Of the 16 patients who discontinued treatment, 7 did so because of therapeutic inefficacy, 4 patients withdrew from the study, and 5 patients stopped due to adverse events. The median treatment exposure time was 30 days in patients who discontinued versus 174 days in those who continued treatment throughout the study period. THC/CBD was effective in 80% of patients at a median dose of 5 inhalations/day. Adverse events included dizziness (11 patients), somnolence (6 patients), muscle weakness (7 patients), oral discomfort (2 patients), diarrhoea (3 patients), dry mouth (2 patients), blurred vision (2 patients), agitation (1 patient), nausea (1 patient), and paranoid ideation (1 patient).

**Comment:** This article adds to the rapidly growing literature regarding the use of cannabinoids for spasticity management. As with most (but not all) of the literature this article concerns the spasticity associated with multiple sclerosis. As with most (but not all) of the literature the cannabinoids appear to be effective in modifying spasticity with an acceptable incidence of side effects. It should of course be noted that there are many limitations to this study. It is retrospective, with poorly defined end points; dosing was variable and not controlled; of the initial 56 patients, 22 (40%) either dropped out or discontinued treatment due to side effects, lack of benefit or other undefined reasons.

***Reference: Neurologia 2013 Sep 10. [Epub ahead of print]***
http://www.ncbi.nlm.nih.gov/pubmed/24035293

## Muscle volume alterations in spastic muscles immediately following botulinum toxin type-A treatment in children with cerebral palsy

**Authors:** Williams SA et al.

**Summary:** This paper describes the morphological alterations of muscles in 15 children aged 5–11 years with spastic diplegic cerebral palsy (Gross Motor Function Classification System Levels I [n=9] and II [n=6]) receiving BoNT-A injections for spasticity management. Magnetic resonance imaging and Mimics software assessed muscle volume 2 weeks prior to and 5 weeks after injection. All participants received BoNT-A bilaterally to the gastrocnemius muscle; 5 children also received BoNT-A bilaterally to the medial hamstring muscles. Total muscle group volume of the injected muscle group remained unchanged following BoNT-A, but the injected gastrocnemius muscle volume was reduced by 4.47% from baseline (p=0.01) and soleus muscle volume was decreased by 3.96% (p=0.02). This decrease in muscle volume did not affect function as assessed by the Timed Up and Go test and distance covered in the 6-Minute Walk Test. Muscle strength, as assessed using hand-held dynamometry, was also not statistically different after BoNT-A treatment.

**Comment:** There are two articles that look at muscle atrophy after injection of botulinum toxin. The first of these looks at lower limb muscle volumes, specifically gastrocnemius and medial hamstrings as measured by MRI both before and after injection of Botox BoNT-A. This is a good paper showing that muscle atrophy following BoNT injections is around 5% for the injected muscles, less than that seen in some animal models.

***Reference: Dev Med Child Neurol 2013;55(9):813-20***
http://onlinelibrary.wiley.com/doi/10.1111/dmcn.12200/abstract

## Do skeletal muscle properties recover following repeat onabotulinum toxin A injections?

**Authors:** Fortuna R et al.

**Summary:** This study reports on the extent of muscle recovery after a series of 6 monthly onabotulinum toxin A (BTX-A) 3.5 U/kg injections in skeletally mature New Zealand white rabbits. The animals were divided into 5 groups: Controls (n=5), zero month recovery – BTX-A+0 M (n=5), 1 month recovery – BTX-A+1 M (n=5), 3 months' recovery – BTX-A+3 M (n=5), and 6 months' recovery – BTX-A+6 M (n=7). At each point of recovery, the researchers measured knee extensor strength, muscle mass and percent contractile material in injected and contralateral non-injected muscles. They found that strength and muscle mass were partially and completely recovered in injected and contralateral non-injected muscles in the BTX-A+6 M animals, respectively. The percent of contractile material partially recovered in the injected muscles, but did not recover in the contralateral non-injected muscles.

**Comment:** This paper looks at the recovery of rabbit muscle following 6 monthly injections of Botox BoNT. The study concludes that full muscle recovery in both the injected muscles and the contralateral muscles does not occur over a further 6 months. The relevance of this intensive treatment protocol in rabbits to human muscle is unclear but it does suggest that human studies should be undertaken.

***Reference: J Biomech 2013;46(14):2426-33***
http://www.jbiomech.com/article/S0021-9290(13)00353-9/abstract

## Intrathecal baclofen therapy in children with severe spasticity: outcome and complications

**Authors:** Walter M et al.

**Summary:** These researchers retrospectively reviewed the medical charts of 15 paediatric patients with congenital brain injuries who underwent intrathecal baclofen (ITB) implantation for treatment of severe spasticity between 2003 and 2009. Preoperative spasticity of the lower limbs was significantly reduced after ITB therapy and there was a corresponding decrease in MAS scores (p<0.05), while baclofen dosage increased (p=0.001). During follow-up, a significant increase in the Cobb angle was observed in the 8 patients with scoliosis prior to ITB therapy (p<0.05). Overall, 10 complications (9 device-related and 1 accidental) occurred in 6 patients, mostly within the first 3 years after implantation.

**Comment:** This article reports a small case series confirming the value of ITB in reducing general lower limb spasticity in a cohort of children with congenital brain injury. Functional outcome measures or changes in nursing requirements are not documented. The worsening of scoliosis in eight patients is noted although there is no comment on whether this is thought to be the natural progression of the scoliosis or related to the ITB. The very high rate of complications (40%) is clearly a cause for concern.

***Reference: Dev Neurorehabil 2013 Aug 26. [Epub ahead of print]***
http://informahealthcare.com/doi/abs/10.3109/17518423.2013.827256

## A randomized controlled trial of selective neurotomy versus botulinum toxin for spastic equinovarus foot after stroke

**Authors:** Bollens B et al.

**Summary:** This study randomised 16 chronic stroke patients presenting with spastic equinovarus of the foot (SEF) into 2 groups: 8 patients underwent a tibial neurotomy and the remaining 8 received BoNT injections. The soleus was treated in all patients, and the tibialis posterior and flexor hallucis longus were treated in about half of all patients. Efficacy evaluations were performed at 2 and 6 months after treatment and were based on the 3 domains of the International Classification of Functioning, Disability and Health. Compared with BoNT, tibial neurotomy resulted in a higher reduction in ankle stiffness (L-path). Both treatments improved ankle kinematics by a comparable extent during gait; neither treatment was associated with muscle weakening. Activity, participation, and quality of life were not significantly altered in either group.

**Comment:** This paper looks at a method of overcoming the relatively short duration of BoNT for the management of spastic equinovarus by performing selective motor neurotomies of nerves to the soleus tibialis posterior and flexor hallucis longus. Although not specifically stated in the paper, it appears branches to the gastrocnemius were preserved. My main issue with this study is the use of a tibial nerve block in the popliteal fossa, where the sensory branches will also be blocked as an assessment tool for the likely success of the surgery. The follow-up time of 6 months is also short for this type of surgery where motor denervation will inevitably lead to atrophy and therefore an uncertain and non-reversible outcome. Even so, I think this study deserves further consideration if the long-term outcomes are considered.

***Reference: Neurorehabil Neural Repair 2013;27(8):695-703***
http://nnr.sagepub.com/content/27/8/695.abstract

## Management of spasticity revisited

**Author:** Graham LA

**Summary:** This review of management strategies for post-stroke spasticity advises that specialist multi-disciplinary goal-centred management programmes are the mainstay of treatment. Pharmacological therapies provide limited benefit; physical and positional management are crucial. Among pharmacological treatments, targeted intramuscular botulinum toxin injection is most often used, while intrathecal therapies are less popular. A team approach and holistic assessment are essential to beneficial outcomes.

**Comment:** This is a simple approach to spasticity, its pathology and its management. It is suitable reading for keen undergraduates or young physicians developing an interest in neurology or rehabilitation medicine wishing to look at the breadth of spasticity without exploring the depths.

***Reference: Age Ageing 2013;42(4):435-41***
http://ageing.oxfordjournals.org/content/42/4/435.abstract





 