Spasticity in children and young people with non-progressive brain disorders: management of spasticity, co-existing motor disorders and their early musculoskeletal complications

Botulinum toxin

Study details	Participants	Interventions	Methods	Outcomes	Comments
Authors Ackman,J.D., Russman,B.S., Thomas,S.S., Buckon,C.E., Sussman,M.D., Masso,P., Sanders,J., D'Astous,J., Aiona,M.D., Shriners Hospitals,B.T.X. **Year of publication** 2005 **Country** USA **Ref ID** 64332 **Design** Randomised controlled study **Aim of study** A multicentre randomised placebo controlled trial to investigate the single and cumulative effectiveness (three repeated treatments) of BoNT, casting and the combination of BoNT and casting to reduce dynamic equinus during gait in children with spastic CP.	**Inclusion Criteria** Diagnosis of spastic hemiplegia or diplegia, aged between 3 and 10 years, independent ambulators without assistive devices, ambulate in functional equinus (toe-toe or toe-heel pattern), neutral ankle position with full knee extension **Exclusion Criteria** Previous orthopaedic surgery to tendo-achilles or subtalar joint, no BoNT injections in previous 6 months, hip or knee flexion contractures greater than 10°. **Baseline Characteristics** 39 children with cerebral palsy were included (Results for 12 children receiving BoNT alone not reported here) Number of participants Placebo + cast = 14 BoNT + cast = 13	**BoNT treatment** BoNT A type : Not specified Dilution : 100U/cm^3 Maximum total dose : Not stated Dosage and Muscle Selection : 4U/body weight for each gastrocnemius muscle. Injections were performed by the physician-investigator at each hospital and made into the medial and lateral gastrocnemius muscles using a 23-27 guage needle Sedation and pain management : choices were at the discretion of the physician Placebo injections : No details provided but given with similar methods to BoNT Injections were given following evaluation at baseline, 3 months and 6 months (ie three treatments) **Therapy treatment** At each treatment visit children received a cast which remained on for 3weeks. Casts were applied by the same physical	Appropriate randomisation method : Yes Allocation concealment adequate : Yes Groups comparable at baseline : Yes Participants blinded to treatment allocation : Yes Caregivers blinded to treatment allocation : Yes Length of follow up similar for each group : Yes No of participants not completing treatment (by group) : Casting alone = 1, BoNT + casting = 1 Outcome assessment methods valid : Yes Investigators blinded to treatment allocation : Yes Limitations : Serious, no analysis or results across groups provided, results estimated from graphs	Primary outcome measures included: Gait analysis (velocity, stride length and ankle kinematics of ankle dorsiflexion at initial contact (DFIC) and peak dorsiflexion in swing (PDFSw)) using a Vicon motion system Secondary outcome measures included : triceps surae spasticity (Ashworth and Tardieu), passive and active dorsiflexion, ankle dorsiflexion and plantarflexion strength and ankle power generation Outcomes were measured at baseline, 3months, 6 months, 7.5 months, and 12 months <u>Ashworth score at ankle – mean change 3 months (read from graph)</u> Placebo + cast = -0.5 p ≤0.02 (reported)(estimated final score 2.1±0.8) BoNT + cast = -0.2 p = no SD (reported)(estimated final score 2.4±0.5) <u>Ashworth score at ankle – mean change 6 months (read from graph)</u> Placebo + cast = 0.4 p ≤0.02 (reported)(estimated final score 2.2±0.7) BoNT + cast = 0.4 p = no SD (reported)(estimated final score 2.2±0.6)	Unrestricted educational grant from Allergan Inc Consent: All parents signed an informed consent form approved by each Institutional Review Board Ethical approval : Research Integrity Office at Oregon Health and Sciences University

	Mean age (months) Placebo + cast = 68 BoNT + cast = 72 Mean age of all 39 participants =70 months Age range of all 39 participants = 3 to 9 years Age range (months) Placebo + cast = 36-108 BoNT + cast = 41-99 Number with hemiplegia Placebo + cast = 10 BoNT + cast = 8 Number with diplegia Placebo + cast = 4 BoNT + cast = 5 Males Placebo + cast = 6 BoNT + cast = 6 GMFCS level I Placebo + cast = 14 BoNT + cast = 12 GMFCS level II Placebo + cast = 0 BoNT + cast = 1 Ashworth score at ankle (read from graph) Placebo + cast = 2.6±1.0 BoNT + cast = 2.6±0.9 Active dorsiflexion at	therapist, physician or casting technician during each visit. The child was positioned prone with the knee flexed to 90° . The foot was placed in a subtalar neutral with the ankle in 0 to 5 of dorsiflexion. The bottom of the cast was flattened and a cast shoe was provided to allow walking during the 3 weekd of cast wear. After cast removal children were instructed to wear their AFOs (solid ankle, posterior leaf spring or articulated) during the day and night with removal of the AFO for 2-4 hrs during the evening. New casts were applied following evaluation at baseline, 3 months and 6 months (ie three treatments) **Comparisons** Placebo injection and casting vs BoNT injection and casting	Imprecision : Insufficient recruitment of participants reduced power of study to identify statistically significant differences between treatment groups Other considerations : Study terminated early due to recruitment difficulties. Approximately 90 children met the inclusion criteria, although only 39 children agreed to participate. A higher than 50% refusal rate by parents with children who could be included, primarily because parents did not want their children to receive a placebo when they could receive BoNT, at no cost and without a rigorous follow up schedule. Power analysis Initial : 25 children/group would give a 90% probability of detecting at least a 5° change in ankle kinematics, 0.15m/s change in velocity and a 0.10m change in stride	<u>Active dorsiflexion at ankle – mean change at 3 months (read from graph)</u> - Placebo + cast = 1° p = no SD (reported)(estimated final score -11°±20) BoNT + cast = 3° p = no SD (reported)(estimated final score -15°±20) <u>Active dorsiflexion at ankle – mean change at 6 months (read from graph)</u> - Placebo + cast = 4° p = no SD (reported)(estimated final score -8°±13) BoNT + cast = 7° p = no SD (reported)(estimated final score -11°±14) <u>Velocity (m/s) mean change 3 months (read from graph)</u> - Placebo + cast = -0.05, p = no SD (reported) (estimated final score 0.8±0.2) BoNT + cast = 0.15 p = no SD (reported) (estimated final score 1.05±0.15) <u>Velocity mean change 6 months (as reported, read from graph)</u> - Placebo + cast = 0.05 p = no SD (reported) (estimated final score 0.9±0.25) BoNT + cast = 0.1 p = no SD (reported) (estimated final score 1.0±0.15) <u>Adverse Effects</u> - Placebo + cast = none reported BoNT + cast = one child fell more often immediately after treatment, although	

	ankle – (as reported, read from graph) Placebo + cast = -12°±14 BoNT + cast = -18°±16 Velocity (read from graph) Placebo + cast = 0.85±0.25 BoNT + cast = 0.9±0.25		length Post-hoc : With 13 children/ group, the power to detect a 5° change in ankle kinematics was reduced to 66%, whereas the power to detect a change in velocity of 0.15m/s and stride length of 0.10m was reduced to 55% Block design randomisation for every three children enrolled at each centre, randomly allocating one child to each treatment group. Children were also randomised by diagnostic group to ensure even distribution of children with hemiplegia and diplegia within each treatment group.	this resolved within 1 to 2 weeks. There were no pressure sores or injuries associated with the casts or their removal in either group and no casts were removed early.	

Study details	Participants	Interventions	Methods	Outcomes	Comments
Authors Hoare BJ, Wallen MA, Imms C, Villanueva E, Rawicki HB, Carey L. Botulinum toxin A as an adjunct to treatment in the management of the upper limb in children with spastic cerebral palsy (UPDATE). Cochrane Database of Systematic Reviews 2010, Issue 1. Art. No.: CD003469. DOI: 10.1002/14651858.CD003469.pub4. **Year of publication** 2010 **Country** Australia **Ref ID** **Design** Cochrane Review **Aim of study** To assess the effectiveness of injections of BoNT-A or BoNT-A and occupational therapy in the treatment of the upper limb in children with CP.	**Inclusion Criteria** All randomised controlled trials (RCTs) comparing BoNT-A injection or BoNT-A injection and occupational therapy in the upper limb(s) with other types of treatment (including no treatment or placebo) in children with CP. **Exclusion Criteria** Within the seven individual RCTs relevant here, the most common reasons for exclusion were if children had received BoNT treatment to the upper limb in the previous 6 -12 months, if they had had previous surgery on the affected limb, if they had fixed contractures or if parents were unwilling to give up other upper limb interventions during treatment eg splints or casts. **Baseline Characteristics** Ten RCTs were included in the entire systematic review - Boyd 2004, Corry 1997, Fehlings 2000, Greaves 2004, Karamura 2007, Koman 2007, Lowe	**BoNT treatment** All RCTs used Botox administered in multilevel injections in one session. The majority of RCTs used a standard dilution of 100U Botox /1.0ml saline. However, Speth 2005, used low concentration of 50U Botox /1.0ml saline and Lowe 2006 used a high concentration of 200U Botox /1ml saline. Maximum doses ranged from 220U to 410U. Doses were also expressed in U/kg for the different muscles that were injected. Six RCTs used electrical stimulation to locate the muscle (two additionally used EMG - Greaves 2004, Lowe 2006) and one used anatomical knowledge and palpation (Fehlings 2000). Four trials used general anaesthesia during the procedure (Boyd 2004, Fehlings 2000, Russo 2007, Speth 2005), one used general anaesthesia or sedation (Greaves 2004), one used sedation and analgesia (Lowe 2006) and one used sedation and local anaesthesia (Wallen 2007). **Therapy treatment** Boyd 2004 An upper limb training program was provided for one hour once a	Two reviewers independently reviewed titles and abstracts of articles retrieved using the aforementioned search strategy. Trials that clearly failed tomeet the inclusion criteria were not reviewed further. Those that could not be excluded were retrieved and reviewed in full-text by the two reviewers. In all instances, differences of opinion were resolved by discussion. Those thatmet criteria were retrieved and reviewed in detail. Quality of trials: Two reviewers independently assessed the methodological quality of the included trials using the PEDro scale with discrepancies resolved by discussion. A point is given for each of the following (maximum score = 10): random allocation; allocation concealment; prognostic similarity at baseline;	Optimisation of movement Modified Ashworth scale - shoulder adductors One RCT included Greaves 2004 4 Months Greaves 2004: log(Odds Ratio) : -1.609, SE :0.894, Odds Ratio : 0.20 [0.03, 1.15] Modified Ashworth scale - elbow flexors Two RCTs included Russo 2007, Wallen 2007 3 Months Russo 2007 : log(Odds Ratio) : -2.62 SE :0.722 Odds Ratio : 0.07 [0.02, 0.30] Wallen 2007 : log(Odds Ratio) : -1.102 SE :0.686 Odds Ratio : 0.33 [0.09, 1.27] Meta analysis : Odds Ratio (Fixed, 95% CI) 0.16 [0.06, 0.43] 6 Months Russo 2007 : log(Odds Ratio) : -2.296 SE :0.694 Odds Ratio : 0.10 [0.03, 0.39] Wallen 2007 : log(Odds Ratio) :0.06 SE :0.69 Odds Ratio : 1.06 [0.27, 4.11] Meta analysis : Odds Ratio (Fixed, 95% CI) 0.33 [0.13, 0.86] Modified Tardieu scale - elbow flexors (change from baseline R2-R1) One RCT included Greaves 2004 4 Months Greaves 2004 : BoNT and OT group n= 9, Mean : -24.44 SD : 33.95 OT group n= 9, Mean : -3.89 SD : 41.23 Mean difference :-20.55 [-55.44, 14.34] Elbow extension PROM (change from	Details of funding for the review are not stated

	2006, Russo 2007, Speth 2005, Wallen 2007. Seven RCTs were included in the one comparison that was relevant to this guideline - Boyd 2004, Fehlings 2000, Greaves 2004, Lowe 2006, Russo 2007, Speth 2005, Wallen 2007. 259 children aged between 1y 11m and 16 were included in total. 6/7 of these RCTs included children with hemiplegia, although 39% of the children included in one study had quadriplegia and 15% had triplegia (Wallen 2007). Five studies included children with upper limb spasticity of Ashworth greater than or equal to level 2 (Fehlings 2000, Greaves 2004, Lowe 2006, Russo 2007, Wallen 2007), one study included children with upper limb spasticity of Ashworth of level 1 (Boyd 2004) and it is unclear for Speth 2005. .	week for 6 weeks by an occupational therapist blinded to group allocation. The program utilised principles of motor skills learning, occupational performance and goal attainment. Children were also encouraged to undertake 30minutes of daily training at home for at least six days per week for 12 weeks. No casts or splints were used. Fehlings 2000 Community based occupational therapy at a minimum frequency of one session every two weeks. An occupational therapy manual with guidelines was developed for the study and sent to participating occupational therapists. The guidelines incorporated activities for upper extremity strengthening and the development of skills for daily living. Greaves 2004 Individualised occupational therapy twice weekly, one hour sessions for 6 weeks (Total number of sessions: Treatment Group = 11.8 (0.4), Control Group = 11.5 (0.5). Therapy provided by non-blinded study occupational therapist and community occupational therapists.	subject blinding; therapist blinding; assessor blinding; greater than 85% follow up of one key outcome; intention to treat analysis; between group statistical comparison of at least one key outcome, and reporting of point estimates and measures of variability of at least one key outcome. PEDro quality ratings ranged from 6/10 to 10/10. The Cochrane team sought data from the authors of the seven trials included in their review. The data sought was the mean change from baseline values (and standard deviations) for the experimental and controls groups for entry into RevMan. This is the best although time consuming method to solve missing data issues. The authors classified the measures using the ICF (WHO 2001) according to the	baseline) Two RCTs included Fehlings 2000, Wallen 2007 3 Months Fehlings 2000 : BoNT and OT group n= 14, Mean : 5.46 SD : 11.74 OT group n= 15 Mean : 3 SD : 12.83 Mean difference : 2.46 [-6.48, 11.40] Wallen 2007 : BoNT and OT group n= 20 Mean : 1.3 SD : 6.3 OT group n= 16, Mean : 1.5 SD : 3.6 Mean difference : -0.20 [-3.48, 3.08] Meta analysis : Mean Difference (IV, Random, 95% CI) 0.11 [-2.96, 3.19] 6 Months Fehlings 2000 : BoNT and OT group n= 14, Mean : 2.84 SD : 6.69 OT group n= 15, Mean : 0.79 SD : 9.32 Mean difference : 2.05 [-3.83, 7.93] Wallen 2007 : BoNT and OT group n= 20, Mean : -0.5 SD : 5.8 OT group n= 17, Mean : 0.6 SD : 6.1 Mean difference : -0.20 [-3.48, 3.08] Meta analysis : Mean Difference (IV, Random, 95% CI) -0.15 [-3.38, 3.07] Modified Ashworth scale - pronators Two RCTs included Greaves 2004, Wallen 2007 3 Months Wallen 2007 : log(Odds Ratio) : 0.459 SE :0.637 Odds Ratio : 1.58 [0.45, 5.52] 4 Months Greaves 2004 : log(Odds Ratio) : -2.003 SE : 1.005 Odds Ratio : 0.13 [0.02, 0.97] 6 Months Wallen 2007 : log(Odds Ratio) : 0.404 SE : 0.977 Odds Ratio : 1.50 [0.22, 10.16]	

		Intervention used goal setting, general training, goal directed training and a home program. Dynamic and static splinting were used. Treatment group received 1.4 (SD 2.3) extra sessions of occupational therapy compared with 0.5 (SD1.1) in the control group between the end of intervention and six week follow-up. Lowe 2006 Occupational therapy from the same occupational therapist. Frequency and intensity not reported. Treatment, driven by the family, included a suite of intervention offered by the therapist including functional training, strengthening, splinting, casting and motor learning. Individualised family goals with mutually agreed levels of attainment were used to guide treatment. Individualised home programmes were developed with the family to implement in goal-relevant contexts of home or school/pre-school. Russo 2007 Weekly occupational therapy sessions for 4weeks.The focus of each therapy sessionwas on upper extremity weightbearing, balls skills, fine	domains they assessed (acknowledging that some of the measures include items that assess change across multiple domains of the ICF (for example the COPM). Relevant outcomes for this guideline are: Body functions and body structures (changes in physiological systems or in anatomical structures). Difficulties in this domain are referred to as impairments. • Spasticity (Tardieu scale or modified Tardieu scale (MTS)) • Muscle tone (Ashworth scale, modified Ashworth scale (MAS)) • Active range of motion (AROM) • Passive range of motion (PROM) Activity (execution of a task or action by an individual). Difficulties in these areas are referred to as activity limitations. • Individual goal identification, rating	Supination AROM (change from baseline) One RCT included Speth 2005 3 Months Speth 2005 : BoNT and OT group n= 10, Mean : 9.3 SD : 15.11 OT group n= 10, Mean : 25.6 SD : 22.32 Mean difference : -16.30 [-33.01, 0.41] 6 months Speth 2005 : BoNT and OT group n= 10, Mean : 13.3 SD : 28.91 OT group n= 10, Mean : 21.7 SD : 35.43 Mean difference : - -8.40 [-36.74, 19.94] Forearm supination PROM (change from baseline) Two RCTs included Fehlings 2000, Wallen 2007 3 Months Fehlings 2000: BoNT and OT group n= 14, Mean : 5.15 SD : 8.1 OT group n= 15, Mean : 1.67 SD : 6.28 Mean difference : 3.48 [-1.82, 8.78] Wallen 2007: BoNT and OT group n= 20, Mean : 2.5 SD : 9.5 OT group n= 16, Mean : -1.6 SD : 16.1 Mean difference : - 4.10 [-4.82, 13.02] Meta analysis : Mean Difference (IV, Random, 95% CI) 3.64 [-0.92, 8.20] 6 Months Fehlings 2000 : BoNT and OT group n= 14, Mean : 3 SD : 12.08 OT group n= 15, Mean : 0.64 SD : 6.62 Mean difference : 2.36 [-4.80, 9.52] Wallen 2007 : BoNT and OT group n= 20, Mean : -0.3 SD : 15.5 OT group n= 17, Mean : 0.6 SD : 10 Mean difference : -0.90 [-9.19, 7.39] Meta analysis : Mean Difference (IV, Random, 95% CI) 0.97 [-4.45, 6.39]	

		motor strengthening (through the use of resistive putty-based activities) and bilateral functional activities (which included activities assisting finger agility and dexterity). Speth 2005 30 minutes physiotherapy and 30 minutes occupational therapy three times a week for 6 months. A treatment protocol including strength and coordination and task specific training was made for each level of hand function impairment (Zancolli grade). This was tailored to the individual child based on individual goal setting and clinical reasoning. All children wore a night splint. During the day children with Zancolli IIB wore a cock-up splint almost all day. Children with less impairment used a wrist cockup splint or web-space splint only during specific activities Wallen 2007 One week after baseline assessment children received 1 hour a week of occupational therapy for 12 weeks. Therapy was provided by the children's usual occupational therapist or at the The Children's Hospital at	and scaling (Canadian Occupational Performance Measure (COPM), Goal Attainment Scaling (GAS)). • Activities of Daily Living Skills (Pediatric Evaluation ofDisability Inventory (PEDI). Participation (involvement in a life situation). Difficulties in these areas are referred to as participation restrictions. • None identified in the studies reviewed. Outcomes independent of ICF domains Health related quality of life and self perceived competence • Child Health Questionnaire (CHQ). • Pediatric Quality of Life (PedsQL).	Modified Ashworth scale - wrist flexors Three RCTs included Greaves 2004, Russo 2007, Wallen 2007 3 Months Russo 2004 : log(Odds Ratio) : -4.781 SE : 1.057 Odds Ratio : 0.01 [0.00, 0.07] Wallen 2007 : log(Odds Ratio) : -1.35 SE : 0.67 Odds Ratio : 0.26 [0.07, 0.96] Meta analysis : Odds Ratio (Fixed, 95% CI) 0.10 [0.03, 0.29] 4 Months Greaves 2004 : log(Odds Ratio) : -1.026 SE : 0.842 Odds Ratio : 0.36 [0.07, 1.87] 6 Months Russo 2007 : log(Odds Ratio) : -3.095 SE : 0.747 Odds Ratio : 0.05 [0.01, 0.20] Wallen 2007 : log(Odds Ratio) : -0.57 SE : 0.62 Odds Ratio : 0.57 [0.17, 1.91] Meta analysis : Odds Ratio (Fixed, 95% CI) 0.20 [0.08, 0.51] Modified Tardieu scale - wrist flexors (change from baseline R2-R1) Two RCTs included Greaves 2004, Wallen 2007 3 Months Wallen 2007: BoNT and OT group n= 20 Mean : -27.75 SD : 17.43 OT group n= 16 Mean : -5.94 SD : 18.46 Mean difference : -21.81 [-33.65, -9.97] 4 Months Greaves 2004: BoNT and OT group n= 10 Mean : -12.78 SD : 28.73 OT group n= 10 Mean : -2.22 SD : 15.63 Mean difference : -10.56 [-30.83, 9.71] 6 Months Wallen 2007: BoNT and OT group n= 20 Mean : -10.25 SD : 30.02	

		Westmead. Therapy programs were individualised and included techniques to improve impairment (e.g. stretching, casting, splinting) and enhancing activities (e.g. motor training, environmental modification and practice of specific goal activities). **Comparisons** Comparisons reviewed were : 1) BoNT-A vs placebo or no treatment 2) BoNT-A and therapy vs therapy only 3) BoNT-A and therapy vs BoNT only 4) BoNT-A and therapy vs placebo or no treatment 5) BoNT-A only vs therapy only 6) High dose BoNT-A vs Low dose BoNT-A Comparison 2 was the only comparison prioritised by the GDG		OT group n= 17 Mean : -12.06 SD : 28.29 Mean difference : 1.81 [-17.00, 20.62] <u>Wrist extension AROM (change from baseline)</u> One RCT included Speth 2005 Three months <u>Speth 2005</u> : BoNT and OT group n=10, Mean : 35.4, SD : 30.48 OT group n=10 Mean : 20.7 SD : 20.08 Mean difference : 14.70 [-7.92, 37.32] Six months <u>Speth 2005</u> : BoNT and OT group n=10, Mean : 34.2, SD : 30.19 OT group n=10, Mean :18.6, SD : 18.54 Mean difference : 15.60 [-6.36, 37.56] <u>Wrist extension PROM (change from baseline)</u> One RCT included Fehlings 2000 Three months <u>Fehlings 2000</u> : BoNT and OT group n=14, Mean : 4.58, SD : 11.92 OT group n=15 Mean : 1.27 SD : 9.91 Mean difference : 3.31 [-4.70, 11.32] Six months <u>Fehlings 2000</u> : BoNT and OT group n=14, Mean : 2, SD : 15.02 OT group n=15, Mean :2.07, SD : 11.49 Mean difference : -0.07 [-9.85, 9.71] <u>Palmar thumb abduction PROM (change from baseline)</u> One RCT included Fehlings 2000 Three months <u>Fehlings 2000</u> :BoNT and OT group n=14, Mean : 1.46, SD : 8.52	

				OT group n=15 Mean : -0.6 SD : 10.01 Mean difference : 2.06 [-4.69, 8.81] Six months Fehlings 2000 : BoNT and OT group n=14, Mean : 2.77, SD : 8.12 OT group n=15, Mean : 1.21, SD : 6.96 Mean difference : 1.56 [-3.96, 7.08] Optimisation of Function - Goal Attainment Scaling (change from baseline) – Parent Five RCTs included Boyd 2004, Greaves 2004, Lowe 2006, Russo 2007, Wallen 2007 Three months Boyd 2004 : BoNT and OT group n=15, Mean : 15.4 SD : 7.61 OT group n=15, Mean : 13.34 SD : 13.68 Mean difference : 2.06 [-5.86, 9.98] Lowe 2006 : BoNT and OT group n=21, Mean : 19.55 SD : 11.06 OT group n=2, Mean : 10.21 SD : 7.95 Mean difference : 9.34 [3.51, 15.17] Russo 2007 : BoNT and OT group n=21, Mean : 21.93 SD : 13.95 OT group n=22, Mean : 8.91 SD : 10.1 Mean difference : 13.02 [5.71, 20.33] Wallen 2007: BoNT and OT group n=20, Mean : 30.8 SD : 12.33 OT group n=17, Mean : 22.18 SD : 10.62 Mean difference : 8.62 [1.22, 16.02] Meta analysis : Mean Difference (IV, Random, 95% CI) 8.52 [4.42, 12.62] Four months :	

				Greaves 2004 : BoNT and OT group n=10, Mean : 35.95 SD : 9.31 OT group n=10, Mean : 26.74 SD :9.29 Mean Difference (IV, Random, 95% CI) 9.21 [1.06, 17.36] Six months Lowe 2006 : BoNT and OT group n=21 Mean : 24.28 SD : 10.32 OT group n=21 Mean : 15.13 SD : 8.04 Mean difference : 9.15 [3.55, 14.75] Russo 2007 : BoNT and OT group n=21 Mean : 20.4 SD : 17.81 OT group n=22 Mean : 16.58 SD : 15.26 Mean difference : 3.82 [-6.11, 13.75] Wallen 2007 : BoNT and OT group n=20, Mean : 31.5 SD :13.35 OT group n=17, Mean : 31.35 SD : 11.09 Mean difference : 0.15 [-7.73, 8.03] Meta analysis : Mean Difference (IV, Random, 95% CI) 5.04 [-0.75, 10.83] COPM Performance (change from baseline) Four RCTs included Boyd 2004, Greaves 2004, Lowe 2006, Wallen 2007 Three months Boyd 2004 : BoNT and OT group n=15, Mean : 4.44 SD : 1.42 OT group n=15, Mean : 4.09 SD : 2.45 Mean difference : 0.35 [-1.08, 1.78] Lowe 2006 : BoNT and OT group n=21, Mean : 1.99 SD : 1.12 OT group n=21, Mean : 1.14 SD :	

				1.13 Mean difference : 0.85 [0.17, 1.53] Wallen 2007 : BoNT and OT group n=20, Mean : 2.9 SD : 1.8 OT group n=17, Mean : 2.1 SD :1.7 Mean difference : 0.80 [-0.33, 1.93] Meta analysis : Mean Difference (IV, Random, 95% CI) 0.77 [0.23, 1.31] Four months Greaves 2004 : BoNT and OT group n= 10, Mean : 2.32 SD : 1.19 OT group n=10, Mean : 1.72 SD : 1.68 Mean Difference (IV, Random, 95% CI) 0.60 [-0.68, 1.88] Six months Lowe 2006 BoNT and OT group n=21, Mean : 2.56 SD :1.16 OT group n=21, Mean : 2.31 SD : 1.6 Mean difference : 0.25 [-0.60, 1.10] Wallen 2007 : BoNT and OT group n=20, Mean : 3.4 SD : 2.0 OT group n=17, Mean : 2.7 SD : 1.8 Mean difference : 0.70 [-0.52, 1.92] Meta analysis : Mean Difference (IV, Random, 95% CI) 0.40 [-0.30, 1.09] PEDI scaled score – Functional Skills (change from baseline) Three RCTs included Boyd 2004, Fehlings 2000, Wallen 2007 Three months Boyd 2004 : BoNT and OT group	

				n=15, Mean : 6.14 SD : 9.7 OT group n=15, Mean : 8.43 SD : 17.31 Mean difference : -2.29 [-12.33, 7.75] Fehlings 2000 : BoNT and OT group n=14, Mean : 2.78 SD : 3.72 OT group n=15, Mean : 1.09 SD : 4.07 Mean difference : 1.69 [-1.15, 4.53] Wallen 2007 : BoNT and OT group n=20, Mean : 3.0 SD : 3.9 OT group n= 17, Mean : 3.4 SD : 5.3 Mean difference : -0.40 [-3.44, 2.64] Meta analysis : Mean Difference (IV, Random, 95% CI) 0.60 [-1.44, 2.63] Six months Fehlings 2000 : BoNT and OT group n=14, Mean : 5.5 SD : 4.54 OT group n=15, Mean : 3.3 SD : 6.05 Mean difference : 2.20 [-1.68, 6.08] Wallen 2007 : BoNT and OT group n=20, Mean : 3.9 SD : 3.3 OT group n= 17, Mean : 4.0 SD :7.9 Mean difference : -0.10 [-4.12, 3.92] Meta analysis : Mean Difference (IV, Random, 95% CI) 1.09 [-1.70, 3.88] PEDI scaled score – Caregiver assistance (change from baseline) One RCT included Wallen 2007	

				Three months Wallen 2007 : BoNT and OT group n=20, Mean : 2.1 SD : 11.2 OT group n=17, Mean : 8.4 SD :14.3 Mean difference : -6.30 [-14.68, 2.08] Six months Wallen 2007 : BoNT and OT group n=20, Mean : 2.1 SD : 11.2 OT group n=17, Mean : 8.4 SD :14.3 Mean difference : -6.30 [-14.68, 2.08] Quality of life Three RCTs included Boyd 2004, Fehlings 2000, Wallen 2007 CHQ –physical functioning 3 months Boyd 2004 : BoNT and OT group n=15, Mean : 1.86 SD : 23.71 OT group n=15, Mean : -6.24 SD : not reported Mean difference : not estimable Wallen 2007 : BoNT and OT group n=20, Mean : 2.12 SD : OT group n=17, Mean : SD : Mean difference (95% CI): Russo 2007 : BoNT and OT group n=21, Mean : 2.12 SD : 21.04 OT group n=22, Mean : 5.56 SD : 23.76 Mean difference (95% CI): -3.44 (-16.84 to 9.96) 6 months Wallen 2007 : BoNT and OT	

				group n=20, Mean : SD : OT group n=17, Mean : SD : Mean difference (95% CI): Russo 2007 : BoNT and OT group n=21, Mean : 3.70 SD : 28.30 OT group n=22, Mean : 1.26 SD : 24.66 Mean difference (95% CI): 2.44 (-13.46 to 18.34) CHQ – role emotional 3 months Boyd 2004 : BoNT and OT group n=15, Mean : 9.6 SD : 23.121 OT group n=15, Mean : 0.74 SD : 39.41 Mean difference (95% CI): 8.86 (-14 to 31.98) Wallen 2007 : BoNT and OT group n=20, Mean : SD : OT group n=17, Mean : SD : Mean difference (95% CI): Russo 2007 : BoNT and OT group n=21, Mean : 1.06 SD : 36.34 OT group n=22, Mean : 3.16 SD : 27.92 Mean difference (95% CI): -2.12 (-21.90 to 17.66) 6 months Wallen 2007 : BoNT and OT group n=20, Mean : SD : OT group n=17, Mean : SD : Mean difference (95% CI): Russo 2007 : BoNT and OT group n=21, Mean :3.18 SD : 36.54	

				OT group n=22, 1. Mean : -1.06 SD : 33.68 Mean difference (95% CI): 4.24 (-16.79 to 25.27) CHQ – role physical 3 months Boyd 2004 : BoNT and OT group n=15, Mean : 3.1 SD : 30.63 OT group n=15, Mean : -11.6SD : 52.14 Mean difference (95% CI): 14.70 (-15.90 to 45.30) Wallen 2007 : BoNT and OT group n=20, Mean : SD : OT group n=17, Mean : SD : Mean difference (95% CI): Russo 2007 : BoNT and OT group n=21, Mean : 5.00 SD : 14.41 OT group n=22, Mean : 3.18 SD : 31.89 Mean difference (95% CI): 1.82 (-12.86 to 16.50) 6 months Wallen 2007 : BoNT and OT group n=20, Mean : SD : OT group n=17, Mean : SD : Mean difference (95% CI): Russo 2007 : BoNT and OT group n=21, Mean : 5.00 SD : 37.89 OT group n=22, Mean : 4.76 SD : 35.80 Mean difference (95% CI): 0.24 (-21.78 to 22.26) Adverse Effects	

				Boyd 2004 : No major adverse events reported. Three children were noted to have decreased extension of the index finger that impaired the pinch grip tasks at 3 week follow-up (n=2 BoNT-A group and n=1 control group). These were resolved by 6 weeks. Fehlings 2000 : Weak grasp (n=1 Tx group) lasting 2 weeks. Greaves 2005 : No adverse events Lowe 2006 : There were 31 adverse events reported by 15 participants and no between-group difference. No events were considered related to BoNT-A by the South Eastern Sydney Area Health Service review panel. Russo 2007 : There were 29 adverse events reported by 20 participants over six months. Control group - 5 reported serious adverse events (2 hospital admissions for seizures in 1 child with epilepsy, 3 hospital admissions for medical reasons in another) . Intervention group - One significant adverse event reported in a child with epilepsy (admission to hospital after a seizure). Other minor adverse events	

				included; feeling unwell after the anaesthetic (n=4); excessive weakness in the injected limb (n=5) which was prolonged in 2 children; headache (n=2); flu like symptom (n=1) for one day; fainting episodes (n=1) on a hot day; anxiety (n=1) and depression (n=1) in an adolescents with past histories; alopecia (n=1) and fatigue (n=1). Speth 2005 : No adverse events Wallen 2007 : Adverse events for each group were as follows; BoNT-A/OT group - (Frequency n = 5) including nausea and vomiting 3 days post-injection, unsettled a few days after injection, vomiting post nitrous oxide, flu symptoms 2 weeks post-injection, sick and coughing 2-3 weeks postinjection) OT group - (Frequency n = 4) including illness at 1 week, illness at 2 weeks post baseline, ill at 2 week appointment, sick with rash at 2-4 weeks post baseline)	

Study details	Participants	Interventions	Methods	Outcomes	Comments
Authors Kanovsky,P., Bares,M., Severa,S., Richardson,A., Dysport Paediatric Limb Spasticity Study Group. **Year of publication** 2009 **Country** European multicentre study **Ref ID** 64662 **Design** Randomised controlled study **Aim of study** To compare the long term efficacy and tolerability of two dosage regimens of BoNT-A (repeat treatments once every 4 months vs once yearly) in children with CP and lower limb spasticity.	**Inclusion Criteria** Children aged 1 to 8 years with a clinical diagnosis of diplegic cerebral palsy were recruited by 18 European centres. Participants had to be able to walk with or without a walking aid or orthosis, have the potential to benefit from injections of BoNT-A to the gastrocnemius (judged by investigator) and be able to achieve 10° passive dorasl dorsiflexion. **Exclusion Criteria** Children were excluded if: 1) the investigator perceived a clinical need for surgery to the affected limbs within 2 years 2) they were judged to need multilevel injections of BoNT-A 3) they had a significant foot deformity (the inability to obtain calcaneum neutral position during measurement of maximum passive ankle dorsiflexion for which the muscle was stretched passively to give maximum dorsiflexion with the knee in full extension)	**BoNT treatment** BoNT type : Dysport Dilution : not detailed Maximum total dose : For children > 33kg 1000U/treatment cycle Dosage and Muscle Selection : 30 LD_{50}U/kg of body weight BoNT-A was divided equally between both limbs. The gastrocnemius muscle was injected in two locations : the junction of the proximal quarter and the distal three-quarters of the gastrocnemius. Ijection volume at each site = 0.5mL (total injection volume = 2.0mL) Location of injection site : Palpation of the femoral and calcaneal insertions Sedation and pain management : Midazolam and topical anaesthetic cream given <u>Four monthly group</u> Children had 7 sessions (at baseline and then 4monthly up to years) <u>Yearly group</u> Children had 3 sessions (at baseline , 1 year and two years) **Therapy treatment** Physiotherapy, n(%) 4 monthly group = Continued during study 80 (73), Stopped before study 23 (21) Yearly group = Continued during study 67 (64), Stopped before	Appropriate randomisation method : Yes Allocation concealment adequate : Yes Groups comparable at baseline : Yes Participants blinded to treatment allocation : No Caregivers blinded to treatment allocation : Yes Length of follow up similar for each group : 28 months, yes No of participants not completing treatment (by group) : Four monthly group = 19, yearly group= 18 Outcome assessment methods valid : Yes Investigators blinded to treatment allocation : Yes	<u>GMFM Overall score -</u> Median change from baseline at month 28 Four monthly group = 8.6 Yearly group = 5.9 p=NS <u>GMFM Goal total score -</u> Median change from baseline at month 28 Four monthly group = 12.3 Yearly group = 9 p=NS <u>Adverse events</u> <u>All adverse events</u> Four monthly group = 89/110 (81%) Yearly group = 88/104 (85%) p=NS <u>Pain</u> Four monthly group = 19/110 (17%) Yearly group = 22/104 (21%) p=NS <u>Infection</u> Four monthly group = 17/110 (15%) Yearly group = 18/104 (17%) p=NS <u>Weakness</u> Four monthly group = 15/110 (14%) Yearly group = 15/104 (14%) p=NS <u>Cough increased</u> Four monthly group = 15/110 (14%) Yearly group = 11/104 (11%) p=NS	No details given. First 3 authors stated a conflict of interest as they were in receipt of research funds from Ipsen Ltd UK (manufactures Dysport). The fourth named author was an employee of Ipsen Ltd UK Ethical Approval : Local ethics committee or institutional review boards at different centres Consent : Parents/guardians gave written consent before the study

	4) they had had previous surgery on the affected muscle 5)they had any known sensitivity to BoNT-A 6) they had a generalise disorder of muscle activity 7) aminoglycoside antibiotics or spectinomycin were being used 8) they were unwilling or unable to comply with the protocol 9) they had received BoNT-A treatment during the 9 months previous to study entry except for participants of two previous studies who could enter provided any treatment benefit had disappeared completely and any adverse events considered possibly or probably related to study medication had resolved **Baseline Characteristics** 214 children were included (Czech Republic =69, France =1, Italy =3, Poland =98, Slovak Republic = 17, Spain =24 and UK = 2). 4 monthly group = 110 yearly group = 104 Overall 83% of children	study 36 (35) **Comparisons** Four monthly BoNT-A treatment vs Yearly BoNT-A treatment		<u>Surgical intervention</u> Four monthly group = 12/110 (11%) Yearly group = 13/104 (13%) p=NS <u>Fever</u> Four monthly group = 13/110 (12%) Yearly group = 9/104 (9%) p=NS <u>Convulsions</u> Four monthly group = 6/110 (5%) Yearly group = 14/104 (13%) p=0.044 <u>Development of fixed contractures</u> Four monthly group = 10/110 (9%) Yearly group = 7/104 (7%) <u>Time to develop fixed contractures</u> Hazard Ratio = 0.734 95%CI [0.28 to 1.94] p=0.533 <u>Referral for surgery to correct fixed contractures</u> Four monthly group = 8/110 (7%) Yearly group = 4/104 (4%) <u>Time to referral for surgery</u> Hazard Ratio = 0.381 95%CI [0.10 to 1.45] p=0.381 <u>Neutralising antibodies</u> One patient in each group had antibodies at baseline. 5 patients (2%) in total developed neautralising antibodies over the 2 year study period.	

	completed the study. Key demographics described as "well balanced". Any significant differences are not reported Age Mean (SD) 4 monthly group = 3years 8 months (1y 6m) yearly group = 4 years 4 months (1y 6m) Age Range 4 monthly group = 1-8 years yearly group = 2-8 years Sex (female) n 4 monthly group = 71 yearly group = 57 Race White(%) 4 monthly group = 110 (100) yearly group = 104 (100) Maximum Passive Ankle Dorsiflexion, median (range) 4 monthly group = Better leg 15.00° (10.00 - 33.00), Worse leg 11.67° (9.67 - 24.00) yearly group = Better leg 15.33° (10.00 - 32.67), Worse leg 11.67° (10.00 - 22.33)			Four monthly group = 4 patients developed Yearly group = 1 patient developed In four patients the levels of antibodies were low or low-intermediate In one patient the levels of antibodies were high	

	GMFM median (range) 4 monthly group = 75.9 (16.8 - 98.6) yearly group = 77.9 (10.0 - 100.0) Use of aids and orthoses n(%) 4 monthly group = 48 (44) yearly group = 44 (42) Other medications for CP n(%) 4 monthly group = Continued during study 16(15), Stopped before study 13(12) yearly group = Continued during study 13(13), Stopped before study 22(21) Age at diagnosis mean (SD) 4 monthly group = 13.2 months (10.4) yearly group = 15.4 months (12.8) Neutralising antibodies 2 of all patients had antibodies at baseline Epilepsy, epileptic syndrome, partial epilepsy or febrile convulsions at baseline				

	4 monthly group = 4 patients yearly group = 10 patients				

Study details	Participants	Interventions	Methods	Outcomes	Comments
Authors Kay,R.M., Rethlefsen,S.A., Fern-Buneo,A., Wren,T.A.L., Skaggs,D.L. **Year of publication** 2004 **Country** USA **Ref ID** 64668 **Design** Randomised controlled study **Aim of study** The main objective was to determine whether better outcomes are achieved when BoNT-A is added to the casting regimen in the management of children with cerebral palsy who have plantar flexion or equinus contractures as well as dynamic spasticity.	**Inclusion Criteria** Inclusion criteria were : 1) a diagnosis of cerebral palsy with associated spastic diplegia, hemiplegia or quadriplegia 2) an age of four years or more 3) a plantar flexion or equinus contracture associated with a decreased range of passive dorsiflexion of ≤0º with the knee extended 4) an ability to walk independently with or without assistive devices 5) no history of orthopaedic surgery or selective doral rhizotomy in the preceding twelve months. **Exclusion Criteria** Children with a "mixed cerebral palsy", ataxia or athetosis were excluded from the study **Baseline Characteristics** Number of participants Casting only : 12 (20 limbs) Casting +BoNT : 11 (16 limbs) Age Casting only : 7.3 ± 3.3 Casting +BoNT : 6.9 ± 2.8 p=0.9020	**BoNT treatment** BoNT type : Botox Dilution : Not stated Maximum total dose : 400U per subject Dosage and Muscle Selection : 8U/body weight into the affected gastrocnemius muscle or muscles. Injections were performed by the physician-investigator and were also made bilaterally into the soleus in one subject and into the medial hamstrings of two others. Location of injection site : Not stated Sedation and pain management : Details not provided **Therapy treatment** Serial casting for equinus contracture was performed on all children by the same experienced physiotherapist and aide. Short leg fibreglass walking casts were applied and changed every 2 weeks until ≥5° of dorsiflexion was reached with the knee extended. Csts were applied with the ankle in neutral supination-pronation and in maximum passive dorsiflexion. Csts were lined with stockinette and Websril and polycushion was applied over osseous prominences. Support for the longitudinal arch was incorporated into the cast, and an extension was added for	Appropriate randomisation method : Yes, random number generator Allocation concealment adequate : Yes Groups comparable at baseline : Yes Participants blinded to treatment allocation : Unclear Caregivers blinded to treatment allocation : Unclear Length of follow up similar for each group : Yes No of participants not completing treatment (by group) : Casting alone =2, BoNT + casting = 1 Outcome assessment methods valid : Yes Investigators blinded to treatment allocation : No Limitations : serious, unclear or lack of blinding Other considerations : none	The outcome measures included : - duration of casting required for contracture resolution - differences in passive dorsiflexion, spasticity and peak dorsiflexion during the stance and swing phases for each limb. - Plantar flexor spasticity - Gross Motor Function Measure scores (dimensions C, D and E) Outcomes were assessed at baseline, 3, 6, 9 and 12 months (6, 9 and 12 months results reported in graphs) <u>Plantar flexor spasticity, modified Ashworth grade at 3 months, change from baseline</u> Casting alone : -1.1 ± 1.2 Casting and BoNT : -0.9 ± 1.0 Mean difference =0.20 [-0.52 to 0.92] p = 0.59 <u>Plantar flexor spasticity, modified Ashworth grade at 6 months, change from baseline (read from graph)</u> Casting alone : -1.2 ± 1.3 Casting and BoNT : -0.26 ± 1.14 Mean difference = 1.46 [0.66 to 2.26] p = 0.0003 <u>GMFM (C, D and E) % score at 3 months, change from baseline</u> Casting alone : -1.3 ± 5.1 Casting and BoNT : 2.5 ± 7.5 Mean difference = 3.80 [-0.50 to 8.10] p = 0.08 <u>GMFM (C, D and E) % score at 6 months, change from baseline (read from graph)</u>	Funding: One or more of the authors received grants or outside funding from Allergan Incorporated in support of their research or preparation of this manuscript. Consent: Informed consent was obtained from the parents or guardians of children enrolled in this study Ethical Approval: The institutional review board

	Female Casting only : 6 Casting +BoNT :5 p=1.0 Walking ability Casting only : Aided = 3, Independent = 9 Casting +BoNT : Aided = 2, Independent = 9 p=1.0 Type of cerebral palsy Casting only : Hemiplegia = 4, Diplegia = 7, Quadriplegia = 1 Casting +BoNT : Hemiplegia = 5, Diplegia = 6, Quadriplegia = 0 p=0.6802 Physical therapy (number of days/year) Casting only : 22.1 ± 27.6 Casting +BoNT : 28.4 ± 36.6 p=0.7742 Physical therapy (total number of hours) Casting only : 16.7 ± 21.3 Casting +BoNT : 19.5 ± 28.6 p = 0.914 Previous multilevel orthopaedic surgery Casting only : 2 children Casting +BoNT : 1 child	support under the hindfoot(when the ankle was plantar flexed) or the forefoot (when the ankle was dosrilexed) to allow the patient to walk without hyperextension or excessive flexion of the knee. Cst shoes were used during walking. Hemiplegic children were cast on the affected side only. Dipleig and quadriplegic children were managed with bilateral casting (except one child with asymptomatic diplegia who was manged with unilateral csting for a unilateral contracture). After casting, the children were given new bivalved fibreglass splints, positioned in maximum passive dorsiflexion for nightime use. The children were provided with AFOs (type decided by treating physian and physical therapist, all orthoses from same certified orthotist) for daytime wear upon completion of serial casting. Other therapy Subjects who received physical therapy continued their regular regiment throughout the course of the study. The treating physical therapists completed a treatment log for each subject. Parent-reported compliance with brace wear was also recorded for each child.		Casting alone : 1.83 ± 3.17 Casting and BoNT : 2.84 ± 3.33 Mean difference = 1.01 [-1.13 to 3.15] p = 0.36	
	Each child's surgery had been performed over four years previously	**Comparisons** Serial casting alone vs BoNT and serial casting			

Study details	Participants	Interventions	Methods	Outcomes	Comments
Authors Kwon,J.Y., Hwang,J.H., Kim,J.S. **Year of publication** 2010 **Country** South Korea **Ref ID** 64711 **Design** Randomised controlled study **Aim of study** To compare the clinical outcomes of two different injection techniques, one guided by electrical stimulation and the other by ultrasound, for botulinum toxin A injection into calf muscles for the treatment of spastic equinus in children with cerebal palsy	**Inclusion Criteria** 1) diagnosis of cerebral palsy 2) ambulation with or without devices or assistance 3) spastic equinus gait 4) Gross Motor Function Classification System level up to level III **Exclusion Criteria** 1) age >7 years~ 2) previous serial casting or botulinum toxin A treatment within 6 months before enrollment 3) previous lower limb surgery 4) failure to attend for follow-up assessment at 3 months **Baseline Characteristics** The Final cohort comprised of 30 children Number of patients Ultrasound group = 14 Electrical stimulation group = 16 Age (mean ± SD, months) Ultrasound group = 49.3 ± 19.4 Electrical stimulation group = 45.9 ± 18.3 Gender (Male:Female	**BoNT treatment** Every participant received 4 U/kg of Botox (Allergan, Irvine, CA) per gastrocnemius Dilution used was 100 units per 5 ml of 0.9% saline Botox was injected into the gastrocnemius at 4-6 points in total, with 2-3 points each on the medial and lateral heads **Therapy treatment** <u>Ultrasound-guided group</u> Ultrasonography carried out using the Sonoace ultrasound system (Medison Co., Ltd.) using a 7.5 MHz linear transducer <u>Electrical stimulation-guided group</u> Electrical stimulation was performed by the nerve stimulation of an EMG machine (Viking IV, Nicolet, Germany) Stimulating current: 5-10mA Duration: 0.1 msec **Comparisons** Ultrasound-guided Botox injection compared to electrical stimulation-guided injection	Study was a pseudo-randmised, prospective controlled trial Following informed consent, all children with cerebral palsy who met the inclusion criteria at an out-patient clinic of St. Vincent's Hospital, Suwon, South Korea, between March 2007 and June 2008, were recruited Participants were enrolled in separate categories according to their level under the Gross Motor Function Classification System and then alternately assigned to one of the two groups, as the parents/guardians had no particular preference All children were sedated by oral chloral hydrate and/or intravenous midazolam and lidocaine cream was applied at injection site 1 hour before procedure Standard injection sites	Modified Ashworth scale [median (interquartile range)] <u>With knee extended</u> Ultrasound group: - Baseline = 3(3–3) - at 3 months = 3(2–3); P < 0.05 Electrical stimulation group: - Baseline = 3(3–3) - at 3 months = 3(2–3); P > 0.05 <u>With knee flexed</u> Ultrasound group: - Baseline = 2(2–3) - at 3 months = 2(2–2); P < 0.05 Electrical stimulation group: - Baseline = 2(2–3) - at 3 months = 1(2–2); P > 0.05 Modified Tardieu scale (mean ± SD) <u>R1 with knee extended</u> Ultrasound group: - Baseline = −17.1 ± 10.7 - at 3 months = −6.7 ± 14.3; P < 0.05 Electrical stimulation group: - Baseline = −16.8 ± 12.2 - at 3 months = −11.4 ± 11.9; P > 0.05 <u>R2 with knee extended</u> Ultrasound group: - Baseline = 6.7 ± 17.0 - at 3 months = 14.6 ± 13.4; P < 0.05 Electrical stimulation group: - Baseline = 11.6 ± 12.9; - at 3 months = 13.4 ± 15.5; P > 0.05	None reported

	ratio) Ultrasound group = 8:6 Electrical stimulation group = 6:10 Weight (mean ± SD, kg) Ultrasound group = 16.6 ± 6.3 Electrical stimulation group = 15.7 ± 4.1 Legs injected (n) Ultrasound group = 23 Electrical stimulation group = 24 Orthosis Ultrasound group = 1/13 Electrical stimulation group = 1/15		were identified using anatomic landmarks Details reported in the paper	<u>R1 with knee flexed</u> Ultrasound group: - Baseline = 3.0 ± 10.5 - at 3 months = 9.0 ± 13.8; P > 0.05 Electrical stimulation group: - Baseline = 2.6 ± 10.5 - at 3 months = 6.9 ± 17.0; P > 0.05 <u>R2 with knee flexed</u> Ultrasound group: - Baseline = 26.3 ± 16.0 - at 3 months = 29.6 ± 13.7; P > 0.05 Electrical stimulation group: - Baseline = 27.1 ± 10.9 - at 3 months = 28.6 ± 14.1; P > 0.05 Speed of gait (Physician's Rating sacle) [median (interquartile range)] Ultrasound group: - Baseline = 0(0–1) - at 3 months = 1(0–1); P > 0.05 Electrical stimulation group: - Baseline = 0(0–1) - at 3 months = 0(0–1); P > 0.05	

Study details	Participants	Interventions	Methods	Outcomes	Comments
Authors Olesch,C.A., Greaves,S., Imms,C., Reid,S.M., Graham,H.K. **Year of publication** 2010 **Country** Australia **Ref ID** 64828 **Design** Randomised controlled study **Aim of study** A randomised controlled trial of repeat injections of Botulinum toxin-A in the upper extremity of young children with cerebral palsy. This study evaluated the effectiveness of repeated injections of botulinum toxin A (BoNT-A in the hemiplegic upper limb in children with cerebral palsy combined with occupational therapy (OT) compared to OT alone, regarding goal achievement, occupational performance and quality of movement.	**Inclusion Criteria** Children aged 18m to 5 years who had a diagnosis of congenital CP hemiplegia with spasticity affecting upper arm activity but who did not have fixed contractures. Consecutive recruitment of children attending an outpatient CP clinic at a tertiary referral centre **Exclusion Criteria** 1) Children who had undergone upper limb surgery or had upper limb BoNT A injections within the previous 6 months 2) Those whose caregivers were unwilling to cease other upper-limb interventions (such as splinting and casting) during the trial **Baseline Characteristics** Nineteen boys and 3 girls participated. There was no evidence of differences between the groups in : number of boys (treatment group=9, control group=10), mean age (treatment=3.7 years, control=3.7 years), side of hemiplegia (right side: treatment=6, control=7), baseline Peabody score	**BoNT treatment** BoNT-A Type : Botox Dilution : 10U/0.1mL Maximum total dose : Dependant on child's bodyweight Dosage and Muscle Selection : 0.5U/kg dose for adductor pollicis, flexor pollicis longus and flexor digitorum superficialis. 1U/kg for flexor digitorum profundus, flexor carpi radialis, fexor carpi ulnaris and pronator teres. 2U/kg for the biceps brachii Muscle selection by assessment made by an occupational therapist and a physician. Same muscles were targeted at each injection cycle Muscle Localisation : Muscle stimulation Type of Anaesthesia : Short general anaesthesia (sevoflurane) Intervention occurred in three 16-week cycles and included BTX-A injections followed by twice weekly OT for 6 weeks. **Therapy treatment** A generic protocol for the OT intervention was individualised for each child. Therapy was based upon a goal directed approach –	Randomisation : Analyses of between-group differences were undertaken using independent samples t-tests with alpha set at 0.05 Two children did not complete the trial. Allocation to group was concealed from researchers. Occupational therapists were not blinded to group allocation Outcomes were rated by assessor blind to group allocation. PEDro Quality Assessment Good	Primary outcomes included the Canadian Occupational Performance Measure (COPM), Goal Attainment Scale, (GAS) measured at baseline and 4 monthly intervals to 12 months. Secondary outcomes included the Peabody Developmental Fine Motor Scale (Peabody), Quality of Upper Extremity Skills Test (QUEST) and measures of spasticity. Reduction of Spasticity <u>Modified Tardieu scale - elbow flexors (across group comparison of scores)</u> Four months (cycle 1) BoNT and OT group n= 11 Mean : 43.0 SD : 45.7 OT group n=11 Mean : 77.3 SD : 39.3 Mean difference : -34.30 [-70.67, 2.07] Eight months (cycle 2) BoNT and OT group n= 11 Mean : 54.5 SD : 44.1 OT group n=11 Mean : 90.5 SD : 40.3 Mean difference : -36.00 [-71.30, -0.70] Twelve months (cycle 3) BoNT and OT group n= 11 Mean : 34.5 SD : 48.0 OT group n=11 Mean : 77.3 SD : 56.2 Mean difference : -42.80 [-86.48, 0.88] <u>Modified Tardieu scale - forearm pronators (across group comparison of scores)</u> Four months (cycle 1)	Not reported

	(standardized score: treatment=503.6, control=502.6). All children were in GMFCS levels I or II. Age Twenty-four children aged 18 months to 5 years were recruited (mean age=3.7 years [SD=0.9]).	interview with parent to establish goal, task analysis to identify factors hindering or supporting the child's achievement of this goal. Targeted activities to support goal achievement were practised in therapy, and the home based programme used practicing of tasks related to the child's everyday life to support goal achievement. Amount of practice to be undertaken was individualised and adherence to the home programme was not recorded. All children received a twice weekly OT programme for 6 weeks after BoNT injection (or at a comparable time point for the OT only group). The initial 2 weeks of each programme was delivered the study therapist, then for the remaining 4 weeks by either the child's community therapist or by the study therapist Both groups returned to their usual therapy regimens until each 16 wk cycle was completed. **Comparisons** BoNT + OT vs OT alone		BoNT and OT group n= 11 Mean : 48.5 SD : 37.2 OT group n=11 Mean : 75.5 SD : 31.7 Mean difference : -27.00 [-55.88, 1.88] Eight months (cycle 2) BoNT and OT group n= 11 Mean : 39.5 SD : 40.6 OT group n=11 Mean : 77.3 SD : 22.8 Mean difference : -37.80 [-65.32, -10.28] Twelve months (cycle 3) BoNT and OT group n= 11 Mean : 22.7 SD : 33.2 OT group n=11 Mean : 72.7 SD : 28.7 Mean difference : -50.00 [-75.93, -24.07] <u>Modified Tardieu scale - wrist flexors (across group comparison of scores)</u> Four months (cycle 1) BoNT and OT group n= 11 Mean : 11.0 SD : 17.4 OT group n=11 Mean : 29.5 SD : 27.6 Mean difference : -18.50 [-37.78, 0.78] Eight months (cycle 2) BoNT and OT group n= 11 Mean : 7.3 SD : 9.3 OT group n=11 Mean : 25.0 SD : 30.7 Mean difference : -17.70 [-36.66, 1.26] Twelve months (cycle 3) BoNT and OT group n= 11 Mean : 3.2 SD : 7.2	

				OT group n=11 Mean : 24.1 SD : 28.5 Mean difference : -20.90 [-38.27, -3.53] <u>QUEST scores (across group comparison of scores)</u> Total score Four months (cycle 1) BoNT and OT group n= 11 Mean : 76.3 SD : 13.2 OT group n=11 Mean : 70.8 SD : 12.8 Mean difference : 5.50 [-5.37, 16.37] Eight months (cycle 2) BoNT and OT group n= 11 Mean : 76.9 SD : 10.4 OT group n=11 Mean : 69.3 SD : 13.4 Mean difference : 7.60 [-2.42, 17.62] Twelve months (cycle 3) BoNT and OT group n= 11 Mean : 79.6 SD : 8.0 OT group n=11 Mean : 72.9 SD : 11.5 Mean difference : 6.70 [-1.58, 14.98] <u>COPM Performance (change from baseline)</u> Four months (cycle 1) BoNT and OT group n= 11 Mean : 2.4 SD :1.0 OT group n=11 Mean :1.7 SD : 1.4 Mean difference :0.70 [-0.32, 1.72] Eight months (cycle 2) BoNT and OT group n= 11	

				Mean : 2.7 SD : 0.9 OT group n=11 Mean : 1.8 SD : 1.0 Mean difference :0.90 [0.10, 1.70] Twelve months (cycle 3) BoNT and OT group n= 11 Mean : 3.0 SD : 1.3 OT group n=11 Mean : 1.6 SD : 1.2 Mean difference :1.40 [0.35, 2.45] Over whole year (includes goals for entire year) BoNT and OT group n= 11 Mean : 2.5 SD : 1 OT group n=11 Mean : 1.7 SD : 0.6 Mean difference :0.80 [0.11, 1.49] Author reports -0.80 [-0.15, 0.0] <u>Goal Attainment Scale T score</u> Four months (cycle 1) BoNT and OT group n= 11 Mean : 54.1 SD : 9.8 OT group n=11 Mean :48.1 SD : 10.1 Mean difference :6.00 [-2.32, 14.32] Eight months (cycle 2) BoNT and OT group n=11 Mean : 55.0 SD : 4.3 OT group n=11 Mean : 47.3 SD : 11.6 Mean difference :7.70 [0.39, 15.01] Twelve months (cycle 3) BoNT and OT group n=11 Mean : 54.9 SD : 9.5	

				OT group n=11 Mean : 50.0 SD : 7.1 Mean difference : 4.90 [-2.11, 11.91] Over whole year BoNT and OT group n=11 Mean : Incorrect data SD : 6.6 OT group n=11 Mean : 48.8 SD : 8.6 Mean difference : Not estimable <u>Adverse Events</u> Three self resolving adverse events were reported in BoNT/OT group. One child had a maculopapular rash (immunological test to consider if response to BoNT inconclusive).Child continued with treatment without further adverse events. One child developed weakness in index finger after BoNT administration into adductor pollicis. This spontaneously resolved and the child continued with treatment without further adverse events. One child developed prolonged weakness in the finger flexors and thereafter the child did not receive any further BoNT injections at this site, but completed the study with respect to other muscle groups.	

Study details	Participants	Interventions	Methods	Outcomes	Comments
Authors Reddihough,D.S., King,J.A., Coleman,G.J., Fosang,A., McCoy,A.T., Thomason,P., Graham,H.K. **Year of publication** 2002 **Country** Australia **Ref ID** 64882 **Design** Randomised controlled study **Aim of study** To compare functional outcome in young children with cerebral palsy when given BoNT treatment with a physiotherapy programme and when given a physiotherapy programme alone in a randomized, cross over trial and to particularly determine what changes might persist at 6 months following injection.	**Inclusion Criteria** Children with spastic diplegia or mild-to-moderate spastic quadriplegia without fixed myostatic contractures, who required active treatment of dynamic contractures in the lower limb that were interfering with function. The following were indication for treatment of spasticity : a) at the hip - children with adductor "scissoring" and difficulties with sitting, standing, toileting and dressing b) at the knee - children with hamstring spasticity causing difficulties in standing or long sitting, loss of knee extension in standing and a walking pattern charaterised by a "crouch gait" c) at the ankle/foot - spasticity of gastrosoleus, the tibialis and peroneal muscles, causing equinus, equinovarus, and equinovalgoid postural problems. These problems manifested as difficulties in achieving a plantigrade position in standing and	**BoNT treatment** BoNT type : Not stated Dilution : Not stated Maximum total dose : max at any one muscle site - 20U, max in any one large muscle group - 120U, max for a first injection - 300U Dosage and Muscle Selection : Dose range was 8-20U/kg body weight, distributed between a minimum of 2 and a maximum of 6 muscle groups. Mean total dose 13.5U/kg body weight. Target muscles were identified by examination and discussion among parents, therapists and an orthopaedic surgeon. The number of injection sites per muscle varied accoring to the number of muscles to be injected and the total dose available according to the child's weight. Location of injection site : Manual methods of muscle identification. Commonly, there were two injection sites per muscle for adductor/hamstrings and four injection sites for the gastrocnemius muscle. The most common injection site was the hamstrings (44 right and 42 left). Calves - 35 right and 36 left. Adductors - 8 children had injections in each adductor muscle Sedation and pain management : Short general anaesthesia **Therapy treatment**	Appropriate randomisation method : Yes Allocation concealment adequate : Unclear Groups comparable at baseline : Yes for GMFCS levels, no other details given Participants blinded to treatment allocation : No Caregivers blinded to treatment allocation : Unclear Length of follow up similar for each group : Yes (6months) although unclear how many assessments made from which children at 3 months or at the mid point of the control treatment period No of participants not completing treatment = 12 : Group 1 = not given , Group 2 = not given Outcome assessment methods valid : Yes Investigators blinded to treatment allocation : Yes Matching of pairs of children according to GMFCS level and age and	Outcomes assessed at baseline, 3 and 6 months for the BoNT treatment period. The protocol stipulated that assessments would only be made at baseline and 6 months during the control period (to improve compliance), however, this was later changed to include an assessment at the mid point of the control period. 19 children had five assessments in total and 30 children had four assessments. Modifed Ashworth scores were taken for right and left calves and hip adductors at 3month/mid-point in control period and 6 months. Only results where a significant difference between treatment periods were reported. MAS Left calf mean change 6 months Therapy alone phase = 0.43± 0.81 (n=35) BoNT and therapy phase = -0.09± 0.78 (n=35) P<0.05 MAS Left adductor mean change 6 months Therapy alone phase = 1± 0.76 (n=8) BoNT and therapy phase = -0.63± 1.06 (n=8) P<0.05 MAS Total score mean change 3 months Therapy alone phase = 1.38 ± 1.30 (n=18) BoNT and therapy phase = -1.13 ± 0.83 (n=18) GMFM Total score mean change 3 months Therapy alone phase = 4.03± 7.05 (n=19)	Support from the Royal Children's Hospital Research Institute, the Murdoch Children's Research Institute (Theme Grant), the Financial MarketsFoundation for Children and the Hugh DT Willinamson Foundation. Ethical approval and parental consent were obtained. No further details given

	walking, frequent falls, orthotic intolerance and footwear problems Children were recruited from CP clinics at the Royal Children's Hospital, Victoria. **Exclusion Criteria** 1) hemiplegia (as more appropriately examined using gait analysis, rather than GMFM) 2) severe spastic quadriplegia 3) had undergone orthopaedic surgery to the lower limb within the 12 months prior to study entry 4) had had either BoNT therapy of inhibitory plasters applied within 6 monthe of the start date of the project 5) were having tone reducing interventions eg ITB for gnerealised spasticity 6) were receiving controversial therapies **Baseline Characteristics** 61 children were recruited. 12 did not continue - 7 required surgery during the study period and 5 were unble to continue with the assessment protocol.	Physiotherapy programme consisted of advice and treatment aimed at improving function and mobility and the provision of appropriate orthotics and walking aids. Approaches included programmes based upon the principles of neurodevelopmental treatment, conductive education, and hydrotherapy. These were delivered in individual or group settings. Children receiving controversial therapies were excluded from the study. Mean number or physiotherapy sessions during the study period Therapy alone phase = 20.9 BoNT and therapy phase = 27.8 **Comparisons** Physiotherapy alone vs BoNT and physiotherapy In the first 6 month treatment period, Group 1 received BoNT injections within 3 weeks of their baseline assessment and physiotherapy programme whilst Group 2 received physiotherapy alone. At the end of the first 6 month treatment period, children in Group 2 received BoNT injections and physiotherapy programme and Group 1 received physiotherapy alone	then randomisation to treatment group Limitations : Other considerations : No wash out period details given (ie presumed that BoNT effects have stopped at 6 months)	BoNT and therapy phase = 2.70±4.62 (n=19) GMFM Total score mean change 6 months Therapy alone phase = 3.44±6.79 (n=49) BoNT and therapy phase = 3.60±7.44 (n=49) GMFM Total score with aids mean change 3 months Therapy alone phase = 2.80±14.40 (n=7) BoNT and therapy phase = 6.52±4.95 (n=7) GMFM Total score with aids mean change 6 months Therapy alone phase = 11.13±11.18 (n=24) BoNT and therapy phase = 3.94±11.60 (n=24) Adverse effects Parents were asked whether their child experienced some form of complication or side effect from the BoNT injection. 4 of 21 parents at 3months and 6 of 23 parents at 6 months agreed that their child had experienced a complication/side effect. Those reported were some level of incontinence, (n=4), short term muscle weakness (n=4) and less specific complaints of the child being “out of sorts” and “a little sick and sore” (n=2). Pain Parents were asked whether their child	

	49 children were in the final cohort Males = 24 Age range = 22 - 80 months Mean age = 4 yrs 1 month Group 1 GMFCS levels (n=22) I = 3, II = 6, III = 9, IV = 4 Group 2 GMFCS levels (n=27) I = 4, II = 5, III = 11, IV = 7			experienced any pain in their legs following injection. 7 of 23 parents at 3months and 4 of 23 parents at 6 months recalled their child having experienced pain Acceptability and tolerability Parental perception was assessed with a short questionnaire which specifically addressed the effects of BoNT treatment at 3 and 6 months after injection. A chi-squared analysis of the results to the question asking whether the parent felt that the BoNT injection had been of benefit to the child demonstrated significantly more positive responses at both 3 and 6 months post-injection ($\chi 2$ = 12.0, $p<0.05$ and $\chi 2$ =7.16, $p<0.05$ respectively). Of those parents who considered BoNT beneficial for their child, 36 of 47 parents at 3months and 35 of 43 parents at 6 months rated the benefit as good, very good or excellent. At 3 months post-injection, of 33 parents who noticed a benefit with BoNT treatment, 26 reported the maximum benefit occurring within 6 weeks of the injection. The remainder (7 parents) reported the maximum benefit occurring 6-12 weeks post-injection. At 6 months post-injection, of 35 parents who noticed a benefit with BoNT treatment, 23 reported the maximum benefit occurring within 1-2months of the injection, 5 reporting maximum	

				benefit at 2 to 3 months and the remainder (7 parents) reporting the maximum benefit occurring 3 to 6 months post-injection.	

Study details	Participants	Interventions	Methods	Outcomes	Comments
Authors Ubhi,T., Bhakta,B.B., Ives,H.L., Allgar,V., Roussounis,S.H. **Year of publication** 2000 **Country** UK **Ref ID** 65031 **Design** Randomised controlled study **Aim of study** To determine whether intramuscular BoNT-A improves walking in children and young people with cerebral palsy	**Inclusion Criteria** Children aged between 2 and 16 years with cerebral palsy and either spastic diplegia or hemiplegia and dynamic equinus with an inability to achieve heel strike because of lower limb spasticity predominantly affecting the calf muscles. Ability to walk with or without walking aids. No previous treatment with BoNT-A. Conventional treatment with physiotherapy and foot orthoses for a minimum of three months prior to treatment. **Exclusion Criteria** Children who had fixed contractures or previous surgery to the lower limb were excluded. **Baseline Characteristics** Forty children were recruited and randomised to treatment groups from 85 consecutive referrals for BoNT-A therapy to the Yorkshire Regional Child Development Centre. The recruitment period was from September 1996 to	**BoNT treatment** BoNT type : Dysport Dilution : 200 U/ml of 0.9% saline Maximum total dose : Not stated Dosage of trial drug : Hemiplegia mean (SD) (U/kg) : BoNT-A group = 16.4 (4.0), Placebo group = 14.4 (1.6) Diplegia mean (SD) (U/kg) : BoNT-A group = 24.8 (3.2), Placebo group = 24.2 (5.4) Muscle Selection : Lateral and medial gastrocnemius muscles were injected with a mean dose of 99 U (BT-A) or 100 U (placebo) each. Soleus was injected with a mean dose of 64 U (BT-A) or 61 U (placebo) Location of injection site : Clinical examination was used for muscle identification. Muscles injected n (%) : Gastrocnemius only : BoNT-A group = 0, Placebo group = 5 (15.1%) Gastrocnemius + soleus : BoNT-A group = 34 (97.1%), Placebo group = 26 (78.8%) Gastrocnemius + hamstrings : BoNT-A group = 1 (2.9%), Placebo group = 0 Gastrocnemius + soleus + hamstrings : BoNT-A group = 0, Placebo group = 2 (6.1%) Sedation and pain management : Topical anaesthesia (EMLA	Appropriate randomisation method : Yes Allocation concealment adequate : Yes Groups comparable at baseline : Yes Participants blinded to treatment allocation : Yes Caregivers blinded to treatment allocation : Yes Length of follow up similar for each group : Yes (12 weeks) No of participants not completing treatment : All children completed treatment although results were not available for all children Outcome assessment methods valid : Yes Investigators blinded to treatment allocation : Yes Other considerations : Numerical details are not presented for all results (publication bias) Post treatment results in initial foot contact from a previous pilot study were used to determine the sample size and power.	Outcomes were assessed at baseline, 2 weeks, 6 weeks and 12 weeks. The primary outcome measure was video gait analysis (VGA). The secondary outcome measures were: gross motor function measure (GMFM), passive ankle dorsiflexion, and physiological cost index (PCI). A change of 6% in the total score or within a dimension of the GMFM was considered to be clinically significant in children with cerebral palsy. Passive ankle dorsiflexion was assessed using a protractor goniometer with the knee in maximum extension. The dorsiflexion summary score was calculated from measurements of the mean of dorsiflexion in each leg in children with diplegia and in the treated leg only for children with hemiplegia. Passive ankle dorsiflexion mean change from baseline BoNT-A group (n=20) = 2.2, 95% CI (−1.4 to 5.9) Placebo group (n=16) = −0.3, 95% CI (−3.3 to 3.8) GMFM GMFM Walking and running at week 12 : Proportion of children who showed greater than 6% change in the GMFM score BoNT-A group = 7/19 - 37% (mean improvement = 9.7%) Placebo group = 1/15 - 7% $\chi^2 = 4.24$, p = 0.04	Funding : Northern & Yorkshire Health Authority and the Special Trustees at St James's University Hospital IPSEN Ltd supplied botulinum toxin (Dysport) and placebo This study was approved by an ethics committee and parents received written and verbal information and gave written consent.

	March 1998. Twenty two children received BT-A and 18 received placebo. One child in the BT-A group was taking oral baclofen regularly. Age at recruitment (years) Median (range) BoNT-A group = 5.5 (2.8–13.9) Placebo group = 6.2 (3.4–16.4) Gender ratio (F:M) BoNT-A group = 12:10 Placebo group = 5:13 Type of cerebral palsy (n) Hemiplegia : BoNT-A group = 9, Placebo group = 3 Diplegia : BoNT-A group = 13, Placebo group = 15 GMFM Lying and rolling Median (IQR) BoNT-A group (n = 21) = 100 (96.1–100) Placebo group (n = 15) = 98.0 (96.1–100) GMFM Sitting Median (IQR) BoNT-A group (n = 21) = 100 (98.3–100) Placebo group (n = 15) =	cream) was applied over injection sites and oral midazolam at a dose of 0.5 mg/kg body weight was offered and accepted by nine children (seven in the BoNT-A group and two in the placebo group). **Therapy treatment** Children received conventional treatment with physiotherapy and foot orthoses for a minimum of three months prior to treatment and this continued unchanged for the duration of the study. **Comparisons** BoNT and usual physiotherapy and orthoses treatment vs Placebo and usual physiotherapy and orthoses treatment All children were offered BoNT-A if clinically indicated at the end of the study.	To give an 80% probability of detecting change at the 5% significance level, fifty six children needed to be recruited into the study. However, only 40 patients were recruited which gave a 70% probability of detecting change at a 5% level.	Six patients failed to complete the GMFM because of a lack of cooperation. Significant differences were not seen in the other dimensions or in the total GMFM score. Adverse events Six children treated with BoNT-A reported adverse events which were self limiting: Two reports of significant post injection calf pain requiring simple analgesia Two reports of increased frequency of falls within the ?rst two weeks after injection One report of wheeziness One report of seizures in a child who was known to be liable to seizures One report of vomiting after injection with placebo The clinical assessors reported no observations of excessive muscle weakness (for example, crouch gait) following trial drug administration.	

	98.3 (96.7–98.3) GMFM Crawling and kneeling Median (IQR) BoNT-A group (n = 21) = 97.6 (90.5–100) Placebo group (n = 15) = 92.9 (78.6–97.6) GMFM Standing Median (IQR) BoNT-A group (n = 21) = 85.9 (60.0–96.8) Placebo group (n = 15) = 71.8 (23.1–79.5) GMFM Walking and running Median (IQR) BoNT-A group (n = 21) = 69.4 (26.4 -86.5) Placebo group (n = 15) = 54.2 (18.1–79.2) GMFM Total Median (IQR) BoNT-A group (n = 21) = 89.0 (74.5–96.3) Placebo group (n = 15) = 84.0 (62.0–90.0)				

Study details	Participants	Interventions	Methods	Outcomes	Comments
Authors Xu,K., Yan,T., Mai,J. **Year of publication** 2009 **Country** China **Ref ID** 65079 **Design** Randomised controlled study **Aim of study** To compare the efficacy of botulinum toxin A injection skills guided by electrical stimulation and that guided by palpation, and to learn whether botulinum toxin A injection improved gait or not, as a means of treating the spasticity of the ankle plantar flexors in ambulant Chinese children with cerebral palsy	**Inclusion Criteria** Children aged 24-120 months with spastic hemiplegic and mild diplegic cerebral palsy; ankle plantar flexors ≥ grade 2 on the modified Ashworth Scale; ability to walk independently; informed consent and compliance with study instructions **Exclusion Criteria** Orthopaedic surgery to the lower limb within 12 months; other lower limb muscles ≥ grade 2 on the modified Ashworth Scale; use of spasticity-reducing interventions e.g. baclofen, dantrium, artane; failure to meet visit schedule **Baseline Characteristics** The Final cohort comprised of 65 children Number of patients Electrical stimulation group = 23 Palpation group = 22 Age (mean ± SD, months) Electrical stimulation group = 55 ± 11.5 Palpation group = 59.4 ± 22.7	**BoNT treatment** Botulinum toxin A diluted in preservative-free, sterile saline to a concentration 100 U/mL The dosages were 3-10 U/kg, limited to no more than 12 U/kg The maximum dose of botulinum toxin A at any one site was 10 U The number of injection sites ranged from 6-8 in the one ankle planatar flexors **Therapy treatment** <u>Physiotherapy</u> Each session lasted 60 to 90 minutes, five days a week for two weeks <u>Electrical stimulation</u> Pulse duration: 0.1 to 0.5 ms Frequencies: 0.66 Hz to 1.00 Hz Amplitude: maximum of 10 mA <u>Palpation</u> Spastic ankle plantar flexors stretched to increase muscle tone, with child in prone position **Comparisons** Botulinum toxin A injection guided by electrical stimulation plus physiotherapy compared to botulinum toxin A injection guided by palpation plus physiotherapy	Ambulant children with cerebral palsy aged 24 to 120 months who met inclusion criteria at Guangzhou Children's Hospital, China, between June 2004 and August 2007, were recruited to the trial Demographic characteristics, spasticity of ankle plantar flexors and functional performance were obtained All participants received physiotherapy three days after botulinum injection In the electrical stimulation group, the motor point in the ankle plantar flexors of the spastic limb were located using a set of electrodes For the palpation group, the spastic ankle flexors were stretched to increase muscle tone and the bulging area of the spastic muscle was located by palpation where the injection was applied	Change of outcome data at three months (i.e. month 3 value − baseline value) (mean ± SD) <u>Electrical stimulation group</u> Passive range of movement, degrees = 20.5 ± 5.2 Modified Ashworth scale = −1.9 ± 0.3 Gross Motor Function measure, D and E dimensions = 18.9 ± 4.0 Walking velocity, m/s = 0.15 ± 0.06 <u>Palpation group</u> Passive range of movement, degrees = 16.2 ± 5.1 Modified Ashworth scale = −1.4 ± 0.5 Gross Motor Function measure, D and E dimensions = 11.3 ± 1.8 Walking velocity, m/s = 0.08 ± 0.04	None reported

	Gender (Male:Female ratio) Electrical stimulation group = 16:7 Palpation group = 15:7 Weight (mean ± SD, kg) Electrical stimulation group = 9.8 ± 1.5 Palpation group = 9.7 ± 1.6 Spastic limb right Electrical stimulation group = 18/23 (56%) Palpation group = 17/22 (55%) Spastic limb left Electrical stimulation group = 14/23 (44%) Palpation group = 14/22 (45%) Passive range of movement (mean ± SD, degrees) Electrical stimulation group = −8.8 ± 6.3 Palpation group = −7.6 ± 6.0 Modified Ashworth Scale (mean ± SD) Electrical stimulation group = 2.8 ± 0.5 Palpation group = 2.7 ± 0.6		Details reported in the paper		

	Gross Motor Function Measure (mean ± SD, D and E dimensions) Electrical stimulation group = 55.8 ± 9.3 Palpation group = 54.5 ± 10.9 Walking velocity (mean ± SD, m/s) Electrical stimulation group = 0.6 ± 0.1 Palpation group = 0.6 ± 0.2 Botulinum toxin A injection sites (mean ± SD) Electrical stimulation group = 7.6 ± 0.7 Palpation group = 7.8 ± 0.8 Botulinum toxin A injection dosage (mean ± SD, U/kg) Electrical stimulation group = 5.7 ± 1.8 Palpation group = 5.8 ± 1.4 Botulinum toxin A injection dosage (mean ± SD, U/site) Electrical stimulation group = 7.0 ± 0.8 Palpation group = 6.9 ± 1.2				