

Research Article

Evaluation of botulinum toxin injection therapeutic effect in patients with spasticity of different etiologies: Experience in Minia University Hospital



Muhammad Mumdouh Ismail¹, Wael Talaat Soliman¹, Rasha Nady Saleh¹, Rehab G. Taha¹, and Mohamed Abdelkader¹

¹Neuropsychiatry Department, Faculty of Medicine, Minia University, Minia, Egypt

DOI: 10.21608/mjmr.2023.211600.1398

Abstract

Background: Different techniques for management of spasticity have been proposed, including positioning, splinting and casting, cryotherapy and electrical stimulation, most of them have little evidence to support their application. This study aims at studying the therapeutic effect of botulinum toxin injection in patients with spasticity of different etiologies, recruited from the Neurology outpatient clinic of Minia University Hospital, using different evaluation tools. **Methods:** Thirty four patients (15 males, 19 females) were included in the period between October, 2022 and January, 2023. Their age ranged from 6 to 62 years, suffering from different upper motor neuron syndromes. Patients were subjected to history taking and neurological examination. Patients were evaluated by Modified Ashworth Scale, Barthel Index and Cochin Scale just before injection, 6 and 12 weeks after injection. **Results:** According to the three used evaluation tools, patients showed highly significant improvement when examined in the 2nd visit (6 weeks after injection) in comparison with the 1st visit (just before injection). Improvement continued significantly also when patients examined in the 3rd visit (12 weeks after injection) in comparison with the 1st visit. But the difference in improvement between the 3rd and 2nd visits was not statistically significant. **Conclusion:** Botulinum toxin is recommended in treatment of spasticity. It was simple, effective and safe.

Keywords: Botulinum toxin; injection; spasticity

Introduction

Different techniques for management of spasticity have been proposed, including positioning, splinting and casting, cryotherapy and electrical stimulation, most of them have little evidence to support their application ⁽¹⁾. The main aim in treatment of spastic muscles is to maintain their length to allow adequate positioning of limbs and prevent soft tissue shortening ⁽²⁾. Botulinum toxin blocks the release of acetylcholine from nerve ending to muscle, therefore the muscle relaxes ⁽³⁾. Improvement of spasticity after botulinum toxin injection starts within 3-7 days and can persist for 2-6 months. Repeated injections are usually needed ⁽⁴⁾. This study aims at studying the therapeutic effect of

botulinum toxin injection in patients with spasticity of different etiologies, recruited from the Neurology outpatient clinic of Minia University Hospital, using different evaluation tools.

Patients and methods

Thirty four patients (15 males, 19 females) were included in the period between October, 2022 and January, 2023. Their age ranged from 6 to 62 years, suffering from upper motor neuron syndromes based on clinical and radiological data. Patients' diagnoses included (stroke, cerebral palsy "CP", hereditary spastic paraparesis "HPS" and others e.g. multiple sclerosis "MS" and post encephalitic). They were recruited from the

Neurology outpatient clinic in Minia University Hospital. Patients with rapidly progressive disorders and patients with associated extrapyramidal movements were excluded. All patients were subjected to full history taking, general examination and meticulous neurological examination. All patients were evaluated by Modified Ashworth Scale for the degree of muscle spasticity⁽⁵⁾, and Barthel Index for activities of daily living⁽⁶⁾. Fourteen patients with hand spasticity were evaluated also by Cochin Scale of hand function⁽⁷⁾. Evaluation has been done just before injection, 6 and 12 weeks after injection. The used preparation of botulinum toxin was botulinum toxin type A (BTX-A) "BOTOX®". BOTOX was administered in doses ranging from 50-300 units according to each patient's individual pattern of spasticity.

Statistical Analysis:

Data were statistically described in terms of mean \pm standard deviation (\pm SD). Comparison of numerical variables within group was done using Wilcoxon signed rank test for paired (matched) samples. P values less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 20 for Microsoft Windows.

Ethical Approval

The research was conducted after the approval of the Ethical Review Committee of Faculty of Medicine, Minia University (Approval No. 653/2023). All patients (or

their 1st degree relatives) signed an informed consent before the intervention clarifying advantages, disadvantages, and possible complications.

Results

Thirty four patients (15 males and 19 females) ranging in age between 6 to 62 years old, with a Mean \pm SD of (18.69 \pm 15.35), were included. The duration of illness ranged from 6 months to 28 years. Our 34 patients were of different diagnoses (CP 15 patients, HSP 10 patients, stroke 6 patients, 2 patients with MS and one patient post encephalitic). The overall injected muscles were counted 132 muscles, distributed into (Flexor digitorum superficialis 13, flexor digitorum profundus 8, pronator teres 9, pronator quadratus 5, flexor pollicis longus 7, flexor pollicis brevis 5, flexor carpi ulnaris 6, flexor carpi radialis 5, biceps 2, gastrocnemius 37, soleus 29 and quadriceps 6). The number of muscles injected in each patient ranged from one muscle to nine muscles, with Mean \pm SD of (3.88 \pm 1.93). The procedure was simple and no side effects have been reported.

According to Modified Ashworth Scale, Barthel Index and Cochin Scale, patients showed highly significant improvement when examined in the 2nd visit (6 weeks after injection) in comparison with the 1st visit (just before injection). Improvement continued significantly also when patients examined in the 3rd visit (12 weeks after injection) in comparison with the 1st visit. But the difference in improvement between the 3rd and 2nd visits was not statistically significant. (Tables 1, 2 and 3) (Figures 1, 2 and 3)

Table 1: Modified Ashworth Scale

MAS 1 N = 132	MAS 2 N = 132	MAS 3 N = 132	P 1	P 2	P 3
Mean \pm SD	Mean \pm SD	Mean \pm SD			
2.98 \pm 0.96	1.31 \pm 1.16	1.22 \pm 1.09	<0.0001**	0.736	<0.0001**

MAS: Modified Ashworth scale, MAS 1 = pre-injection evaluation, MAS 2 = 6 weeks after injection evaluation, MAS 3 = 12 weeks after injection evaluation, P 1= P value between MAS 1 & MAS 2, P 2 = P value between MAS 2 & MAS 3, P 3 = P value between MAS 1 & MAS 3

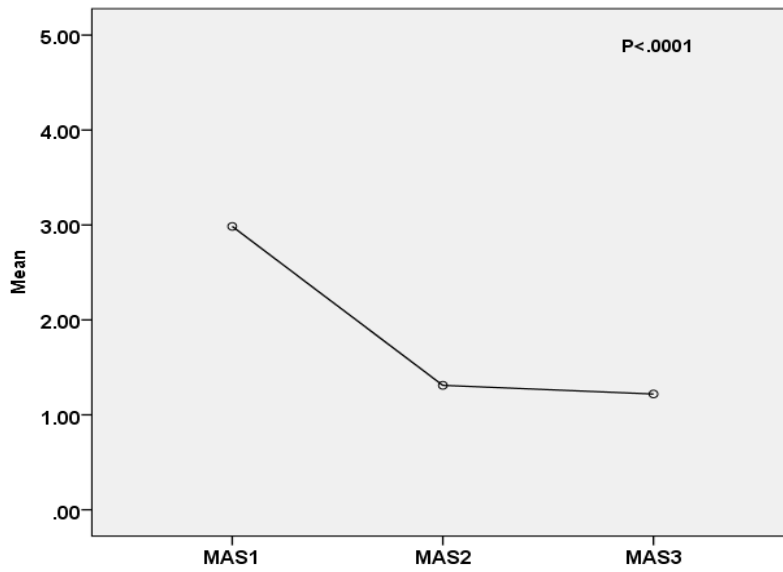


Figure (1): Modified Ashworth Scale

Table (2): Barthel index

Barthel 1 N = 34	Barthel 2 N = 34	Barthel 3 N = 34	P 1	P 2	P 3
Mean ± SD	Mean ± SD	Mean ± SD			
89.56 ± 14.89	91.91 ± 11.87	92.65 ± 11.43	0.013*	0.507	0.008**

Barthel1 = pre-injection evaluation, Barthel 2 = 6 weeks after injection evaluation, Barthel 3 = 12 weeks after injection evaluation, P 1 = P value between Barthel 1 & Barthel 2, P 2 = P value between Barthel2 & Barthel 3, P 3 = P value between Barthel 1 & Barthel 3



Figure (2): Barthel Index

Table (3): Cochin Scale

Cochin 1 N = 14	Cochin 2 N = 14	Cochin 3 N = 14	P 1	P 2	P 3
Mean ± SD	Mean ± SD	Mean ± SD			
55.57 ± 11.46	36.86 ± 11.83	34.57 ± 9.15	<0.0001**	0.726	<0.0001**

Cochin 1 = pre-injection evaluation, Cochin2 = 6 weeks after injection evaluation, Cochin 3 = 12 weeks after injection evaluation, P 1= P value betweenCochin 1 &Cochin2, P 2 = P value between Cochin2 &Cochin3, P 3 = P value betweenCochin 1 &Cochin 3

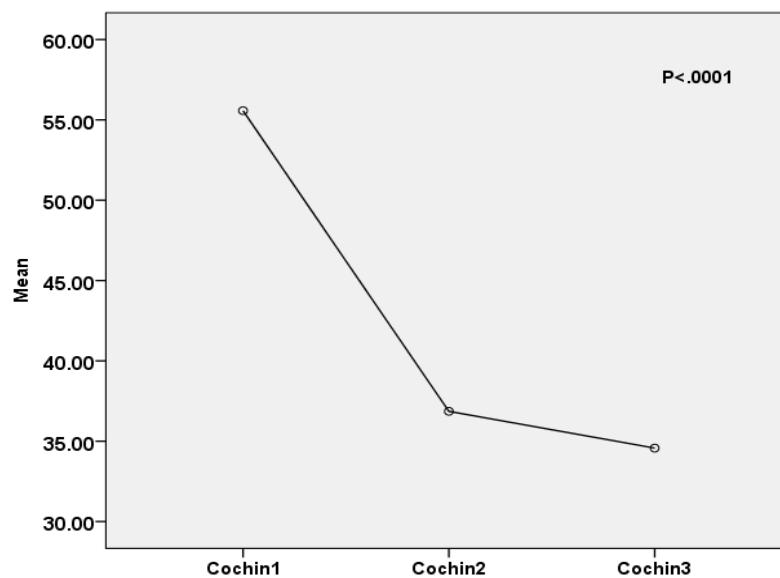


Figure (3): Cochin Scale

Discussion

We conducted this study aiming at evaluating the therapeutic effect of botulinum toxin injection (BOTOX) in patients with spasticity of different etiologies. Improvement was evaluated by Modified Ashworth Scale for the degree of muscle spasticity⁽⁵⁾, Barthel Index for activities of daily living⁽⁶⁾ and Cochin Scale of hand function⁽⁷⁾ just before injection, 6 and 12 weeks after injection. It was important for us to make sure that improvement in patients was significant, not only regarding the degree of muscle spasticity but also in patients’ activities of daily living and their hand function.

Modified Ashworth Scale has been chosen as it was the cornerstone used to assess improvement in the degree of spasticity by

botulinum toxin injection in many previous studies^(8, 9, 10, 11, 12, 13, 14, 15 and 16).

We also used Barthel Index to evaluate improvement in activities of daily living. Barthel Index has been used to assess improvement after botulinum toxin injection by Bakheit et al., (2001); Intiso et al., (2014); Tao et al., (2015)^(8, 12, 14).

We also evaluated improvement in hand function after botulinum toxin injection using Cochin Scale. That was in agreement with Gil et al., (2018) who used Cochin Scale to assess improvement in hand function after botulinum toxin injection⁽¹⁷⁾.

In our study we included patients with spasticity due to upper motor neuron syndromes of different etiologies including

(stroke, CP, HPS, MS and post encephalitic), and significant improvement has been seen in all these patients after botulinum toxin injection. That was in agreement with Bakheit et al., (2001); Woldag and Hummelsheim (2003); Mancini et al., (2005); Fietzek et al., (2014); Tao et al., (2015); Sankaran and Raj (2022) who reported significant improvement in spasticity after botulinum toxin injection in post stroke patients^(8, 9, 10, 11, 14, 16). Moreover, there was an agreement with Simpson et al., (2008); Fietzek et al., (2014); Intiso et al., (2014) who showed improvement in spasticity after botulinum toxin injection in patients with CP and brain injuries^(18, 11, 12).

Thirty four patients ranging in age between 6 to 62 years old, with a Mean \pm SD of (18.69 \pm 15.35), were included. So, patients included children and adults, and significant improvement has been seen both. That was in agreement with the meta-analysis done by Simpson et al., (2008) that evidenced that botulinum toxin should be offered as a treatment option for the treatment of spasticity in both adults and children⁽¹⁸⁾.

The overall injected muscles were counted 132 muscles, distributed in upper and lower limbs, and significant improvement has been seen in both upper and lower limbs. That was in agreement with Bakheit et al., (2001); Woldag and Hummelsheim (2003); Veverka et al., (2019); Sankaran and Raj, (2022) who reported significant improvement in upper limb muscles after botulinum toxin injection in patients with spasticity^(8, 9, 15, 16). In the other hand, Mancini et al., (2005); Fietzek et al., (2014); Tao et al., (2015) showed significant improvement in lower limb muscles^(10, 11, 14). Intiso et al., (2014); Baker and Pereira, (2015) evidenced the improvement in both upper and lower limb muscles^(12, 13).

Conclusion

Botulinum toxin is recommended in treatment of spasticity. It was simple, effective and safe.

References

1. Barnes MP. An overview of the clinical management of spasticity. In: Barnes MP and Johnson GR. (editors). Upper motor neurone syndrome and spasticity. Clinical management and Neurophysiology.

- Cambridge: Cambridge University Press. 2001; p. 1-11.
2. Verplancke D, Snape S, Salisbury CF, Jones PW, Ward AB. A randomized controlled trial of botulinum toxin on lower limb spasticity following acute acquired severe brain injury. *Clinical Rehabilitation*. 2005; 19(2): 117-125.
3. Niet M, Nonnekes J, Nijhuis LO, Susanne T, Pasman JW, van de Warrenburg BP, Geurts AC. Start React restores reaction time in HSP: evidence for subcortical release of a motor program. *Journal of Neuroscience*. 2014; 34(1): 275-81.
4. Giovannelli M, Borriello G, Castri P, Prosperini L, Pozzilli C. Early physiotherapy after injection of botulinum toxin increases the beneficial effects on spasticity in patients with multiple sclerosis. *Clinical Rehabilitation*. 2007; 21(4): 331-7.
5. Bohannon RW and Smith MB. Interrater reliability of a modified Ashworth scale of muscle spasticity. *Phys Ther*. 1987; 67(2): 206-7.
6. Collin C, Wade DT, Davies S, Horne V. The Barthel ADL Index: a reliability study. *Int Disabil Stud*. 1988; 10(2): 61-3.
7. Poiraudau S, Chevalier X, Conrozier T, Flippo RM, Lioté F, Noël E, Lefevre-Colau MM, Fermanian J, Revel M, Rhumato R. Reliability, validity, and sensitivity to change of the Cochin hand functional disability scale in hand osteoarthritis. *Osteoarthritis Cartilage*. 2001; 9(6): 570-7.
8. Bakheit M, Pittock S, Moore AP, Wurker M, Otto S, Erbguth F, Coxon L. A randomized, double-blind, placebo-controlled study of the efficacy and safety of botulinum toxin type A in upper limb spasticity in patients with stroke. *Eur J Neurol*. 2001; 8(6): 559-65.
9. Woldag H and Hummelsheim H. Is the reduction of spasticity by botulinum toxin a beneficial for the recovery of motor function of arm and hand in stroke patients? *Eur Neurol*. 2003;50(3): 165-71.
10. Mancini F, Sandrini G, Moglia A, Nappi G, Pacchetti C. A randomised, double-blind, dose-ranging study to evaluate efficacy and safety of three doses of botulinum toxin type A (Botox) for the treatment of spastic foot. *Neurol Sci*. 2005; 26(1): 26-31.

11. Fietzek UM, Kossmehl P, Schelosky L, Ebersbach G, Wissel J. Early botulinum toxin treatment for spastic pes equinovarus--a randomized double-blind placebo-controlled study. *Eur J Neurol.* 2014; 21(8): 1089-95.
12. Intiso D, Simone V, DiRienzo F, Iarossi A, Paziienza L, Santamato A, Maruzzi G, Basciani M. High doses of a new botulinum toxin type A (NT-201) in adult patients with severe spasticity following brain injury and cerebral palsy *NeuroRehabilitation.* 2014;34(3): 515-22.
13. Baker JA and Pereira G. The efficacy of Botulinum Toxin A on improving ease of care in the upper and lower limbs: a systematic review and meta-analysis using the Grades of Recommendation, Assessment, Development and Evaluation approach *Clin Rehabi.* 2015;29(8):731-40.
14. Tao W, Yan D, Li J, Shi Z. Gait improvement by low-dose botulinum toxin A injection treatment of the lower limbs in subacute stroke patients. *J Phys Ther Sci.* 2015; 27(3): 759-62.
15. Veverka T, Hok P, Otruba P, Zapletalová J, Kukolová B, Tüdös Z, Krobot A, Kaňovský P, Hlušík P. Botulinum Toxin Modulates Posterior Parietal Cortex Activation in Post-stroke Spasticity of the Upper Limb. *Front Neurol.* 2019;10: 495.
16. Sankaran R and Raj M. A Comparison of Treatment Options in Focal Post-Stroke Spasticity of the Upper Extremity: A Prospective Longitudinal Cohort Study from Kerala, *India Neurol India.* 2022; 70(3): 913-917.
17. Gil C, Abdoul H, Campagna R, Guerini H, Jeong E, Chagny F, Bedin C, Roren A, Lefèvre-Colau M, Poiraudeau S, Feydy A, Rannou F, Nguyen C. Intra-articular botulinum toxin A for base-of-thumb osteoarthritis: protocol for a randomised trial (RHIBOT). *BMJ Open.* 2018; 8(6): e022337.
18. Simpson DM, Gracies J-M, Graham HK, Miyasaki JM, Naumann M, Russman B, Simpson LL, So Y; Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Assessment: Botulinum neurotoxin for the treatment of spasticity (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology.* 2008; 70(19): 1691-8.