

Effect of botulinum toxin A & task-specific training on upper limb function in post-stroke focal dystonia

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Abstract

Objective: To determine the effect of botulinum toxin A and task-specific training on upper limb function in post-stroke focal dystonia patients.

Methods: A randomised control trial was conducted at hospitals in Rawalpindi and Islamabad, Pakistan, from October 2015 to September 2016. The subjects were recruited using non-probability purposive sampling and were divided equally into control and experimental groups by sealed envelope method. The experimental group received botulinum toxin A followed by task-specific training, while the control group received only task-specific training for 8 weeks. Data was collected at baseline, after 4 weeks and 8 weeks by using upper extremity items of Motor Assessment Scale and Fugl-Meyer Assessment scale of upper limb.

Results: There were 43 subjects divided into two equal groups of 23(50%) each. In the experimental group, mean age of patients was 43.57 ± 10.94 years while in the control group it was 48.75 ± 10.75 years ($p=0.135$). There were 15(71.4%) male and 6(28.6%) female patients in the experimental group and 9(45%) were male and 11(55%) were female in the control group. Both groups showed significant improvements on the Motor Assessment Scale and Fugl-Meyer Assessment scale ($p<0.01$), but no significant differences were observed between the groups at baseline, after 4 and 8 weeks of intervention ($p>0.05$).

Conclusion: Eight weeks of task-specific training improved upper limb function in post-stroke focal dystonia patients.

Keywords: Task-specific training, Upper limb function, Post-stroke dystonia. (JPMA 68: 526; 2018)

Introduction

Stroke is a major disabling disease affecting around 15 million people all over the world. In Pakistan almost 350,000 people get affected by it every year.¹ The complications associated with it are very challenging and have a long-lasting impact; movement disorders are one of them. Movement disorders have a wide spectrum, including spasticity, chorea, tics, athetosis, myoclonus, asterix, hemiballismus, dystonia and many more. Some of these disorders present in the acute stage; like chorea and hemiballismus, others develop in later stages of stroke; among them the most common is the dystonia.² As established clinically and also in literature that the distal parts like hand and feet are the last to recover after stroke, so late-developing dystonia is also common in these areas. When dystonia occurs in individual body part, it is labelled as focal dystonia. It severely limits the function of hand and foot making the person disabled and dependent on others for their activities of daily living.³ The frequency of post-stroke dystonia was reported as 17% in Lausanne stroke registry and 29% in Ecuador stroke registry.⁴ So far

many hypotheses have been given to explain the development of this complication, but what is the actual cause, is still debatable. Some studies have shown it to develop after injury to specific areas of brain like basal ganglia, thalamus and hypothalamus;⁵⁻⁷ while others claim it to develop as a result of additional complication of spasticity after stroke.⁸ Although exact mechanism is still not understood, all theories have consensus that there is maladaptive plasticity that occurs in the brain resulting in development of focal dystonia.⁹

In the past not much attention has been given to treat this disabling motor complication of stroke. Various treatment strategies have been used lately for the treatment of focal dystonia including both pharmacological and non-pharmacological treatment. Botulinum toxin type A (BoNT-A), deep brain stimulation, transcranial direct current stimulation, kinesio taping, splinting, shock-wave therapy, and constraint induced movement therapy have provided promising results for the treatment of focal dystonia.¹⁰⁻¹⁴ To date, none of these interventions in combination have been adopted for the treatment of post-stroke focal dystonia. The current study was planned to determine the effects of botulinum toxin type A combined with task-specific therapy, for the treatment of post-stroke focal dystonia of upper limb. This study will

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help to design a specific protocol for improving upper limb function after post-stroke focal dystonia.

Patients and Methods

This randomised control trial was conducted at Rawalpindi Medical College and Allied hospitals, Chambeli Rehabilitation Centre, Rawalpindi, and the Neurocounsel Islamabad, Pakistan, from October 2015 to September 2016. After taking approval from institutional ethical review committee, patients having ischaemic or haemorrhagic unilateral stroke were included. The sample size was calculated using World Health Organisation (WHO) sample-size calculator with level of significance as 5% and power of test as 95% for both the motor assessment scale (MAS) and the Fugl-Meyer assessment (FMA) scale. For MAS, the population variance was calculated as 1.93 and test value of the population mean was kept 0 with anticipated population mean as 3.48. For FMA scale, the population variance was calculated as 51.98 and test value of the population mean was kept 0 with anticipated population mean as 8.6.^{15,16} The initial screening of the patients was done using non-probability purposive sampling. The selected patients were randomly allocated equally to control and experimental groups by using sealed envelope method. A computer-generated list was generated for the patients mentioning the numbers and groups as either experimental or control which was sealed in an envelope by a third person other than the therapist. Each sequential patient who gave written informed consent for enrolment in the study was presented with all envelopes in a box, from which after shuffling they picked an envelope of their choice and handed it over to the neurologist. The neurologist then allocated the patients according to the randomly selected envelope, either to experimental or control group. The patients remained blinded throughout the study regarding group allocation. Patients presenting with at least 6 months post-stroke history and having post-stroke focal dystonia or spastic dystonia of upper limb causing limitations in daily activities were incorporated in the study, while patients having acute stroke, idiopathic dystonia or dystonia due to degenerative conditions were excluded. Also excluded were patients having polyneuropathies, previous exposure or allergy to BoNT-A, fixed contracture or deformities in upper limb.

All patients in the experimental group received a BoNT-A injection. The injected total dose for individual patient in the experimental group was 100 units which is equivalent to approximately 300-500 Units of Dysport (the other type of BoNT-A available). The Botox was injected by the neuro-physician intramuscularly using insulin U100 syringe and determination of muscles for injection was

assessed clinically. The following muscles were targeted for injection; Flexor digitorum superficialis, Flexor digitorum profundus, Flexor carpi ulnaris, Flexor carpi radialis, Brachialis, Biceps brachii, Triceps brachii, Extensor pollicis longus and Flexor pollicis Longus muscle, depending upon the type of focal dystonia. The intrinsic muscles were not injected as injecting them might cause a complete paralysis and the study was focussed more on the large muscle groups instead of small ones. Without Electromyography (EMG) the dose adjustment and isolation of these small muscles was difficult and EMG was not available for the current study. After one week of administration of the injections, a tailored task-specific training protocol was started. The task-specific training programme was provided for the duration of one hour, at a frequency of three times a week for a total of 8 weeks by trained physical therapist. In the control group, patients received only task-specific training for one hour, three times a week for total of 8 weeks. Tasks were divided into three sets (each set with a repetition of 20) (Table-1).

Data was collected at baseline, after 4 weeks and then after 8 weeks by using upper extremity items of MAS and FMA scale of upper limb (FMA-UL). MAS is a valid tool for use in chronic stroke population with reliability of 0.9417 and FMA-UL has excellent reliability (Intraclass correlation coefficient (ICC) = 0.95) and validity (0.74) in stroke population.¹⁸ Data analysis was performed using SPSS 21 and both descriptive and inferential statistics were performed. After checking normality of data by Shapiro Wilk test, repeated measures analysis of variance (ANOVA) with Bonferroni Post-Hoc was applied to check the changes in 3 different readings over period of time and independent samples t-test was used to compare the differences of means between the groups with 0.05 value of alpha level of significance.

Results

Of the 61 patients assessed for eligibility, 46 patients were enrolled and divided into two equal groups of 23(50%) each. Subsequently, 3(13%) patients dropped out from the control group and 2(8.7%) from the experimental group (Figure-1).

Mean age of patients was 43.57 ± 10.94 years in experimental group and 48.75 ± 10.75 years in control group ($p=0.135$). According to gender distribution, 15(71.4%) patients were male and 6(28.6%) were female in experimental group, while 9(45%) were male and 11(55%) were female in the control group. Patients whose right side was affected were 17(81%) in experimental group and 12(60%) in control group, and those who had their left side affected were 4(19%) in experimental group

Table-1: Task-specific exercises administered for patients.

Week I & II	Week III & IV	Week V & VI	Week VII & VIII
<ul style="list-style-type: none"> ◆ Reaching for glass on table ◆ Pushing bottle aside ◆ Rolling a tin under hand ◆ Impact on thera putty 	<ul style="list-style-type: none"> ◆ Elbow locked and hit the bottle with wrist ◆ Glass to mouth ◆ Bimanual tasks pouring and transferring water 	<ul style="list-style-type: none"> ◆ Finger Tap ◆ Fold Towel ◆ Card Pick ◆ Drawing dots and lines on paper ◆ Block lifting of different colours ◆ Switch On and off 	<ul style="list-style-type: none"> ◆ Turning pages of newspaper ◆ Coin swipe ◆ Picking Ludo bullets ◆ Catching & throwing Ball ◆ Threading macronis

Table-2: Repeated Measures ANOVA showing variation in Mean±SD along with F and P values at baseline, after 4 weeks and after 8 weeks of intervention.

Variable		Baseline (Mean ±SD)	Week 4 (Mean±SD)	Week 8 (Mean±SD)	F Value	P Value
MAS	Control	5.35±2.62	6.25±2.78	7.80±2.58	40.78	<0.001***
	Experimental	5.19±2.80	6.95±3.02	9.43±3.58	43.85	<0.001***
FMA-UL	Control	33.45±6.01	34.90±6.28	37.05±7.14	9.09	0.002**
	Experimental	33.67±7.74	36.24±7.46	40.19±8.69	26.84	<0.001***

ANOVA: Analysis of variance. SD: Standard variation

MAS: Motor Assessment scale

FMA-UL= Fugl- Meyer Assessment- Upper limb.

Table-3: Independent Samples T test showing comparison between the groups at baseline, after 4 weeks and after 8 weeks.

Variable		Control Mean±SD	Experimental Mean±SD	P value
MAS	Baseline	5.35±2.62	5.19±2.80	0.85
	At 4 weeks	6.25±2.78	6.95±3.02	0.44
	At 8 weeks	7.80±2.58	9.43±3.58	0.10
FMA-UL	Baseline	33.45±6.01	33.67±7.74	0.92
	At 4 weeks	34.90±6.28	36.24±7.46	0.54
	At 8 weeks	37.05±7.14	40.19±8.69	0.21

SD: Standard variation. MAS: Motor Assessment scale

FMA-UL= Fugl- Meyer Assessment- Upper limb.

Table-4: Post Hoc Test showing week wise comparison from baseline to week 8.

Variable		Mean±SD	Mean±SD	Mean Difference	P value
Baseline-week 4					
MAS	Experimental	5.19±2.80	6.95±3.02	1.76	<0.001***
	Control	5.35±2.62	6.25±2.78	0.90	<0.001***
FMA-UL	Experimental	33.67±7.74	36.24±7.46	2.57	0.038*
	Control	33.45±6.01	34.90±6.28	1.45	0.015*
Week 4-Week 8					
MAS	Experimental	6.95±3.02	9.43±3.58	2.48	<0.001***
	Control	6.25±2.78	7.80±2.58	1.55	<0.001***
FMA-UL	Experimental	36.24±7.46	40.19±8.69	3.95	<0.001***
	Control	34.90±6.28	37.05±7.14	2.15	0.004**
Baseline-Week 8					
MAS	Experimental	5.19±2.80	9.43±3.58	4.24	<0.001***
	Control	5.35±2.62	7.80±2.58	2.45	<0.001***
FMA-UL	Experimental	33.67±7.74	40.19±8.69	6.52	<0.001***
	Control	33.45±6.01	37.05±7.14	3.60	0.001**

SD: Standard variation. MAS: Motor Assessment scale.

FMA-UL= Fugl- Meyer Assessment- Upper limb.

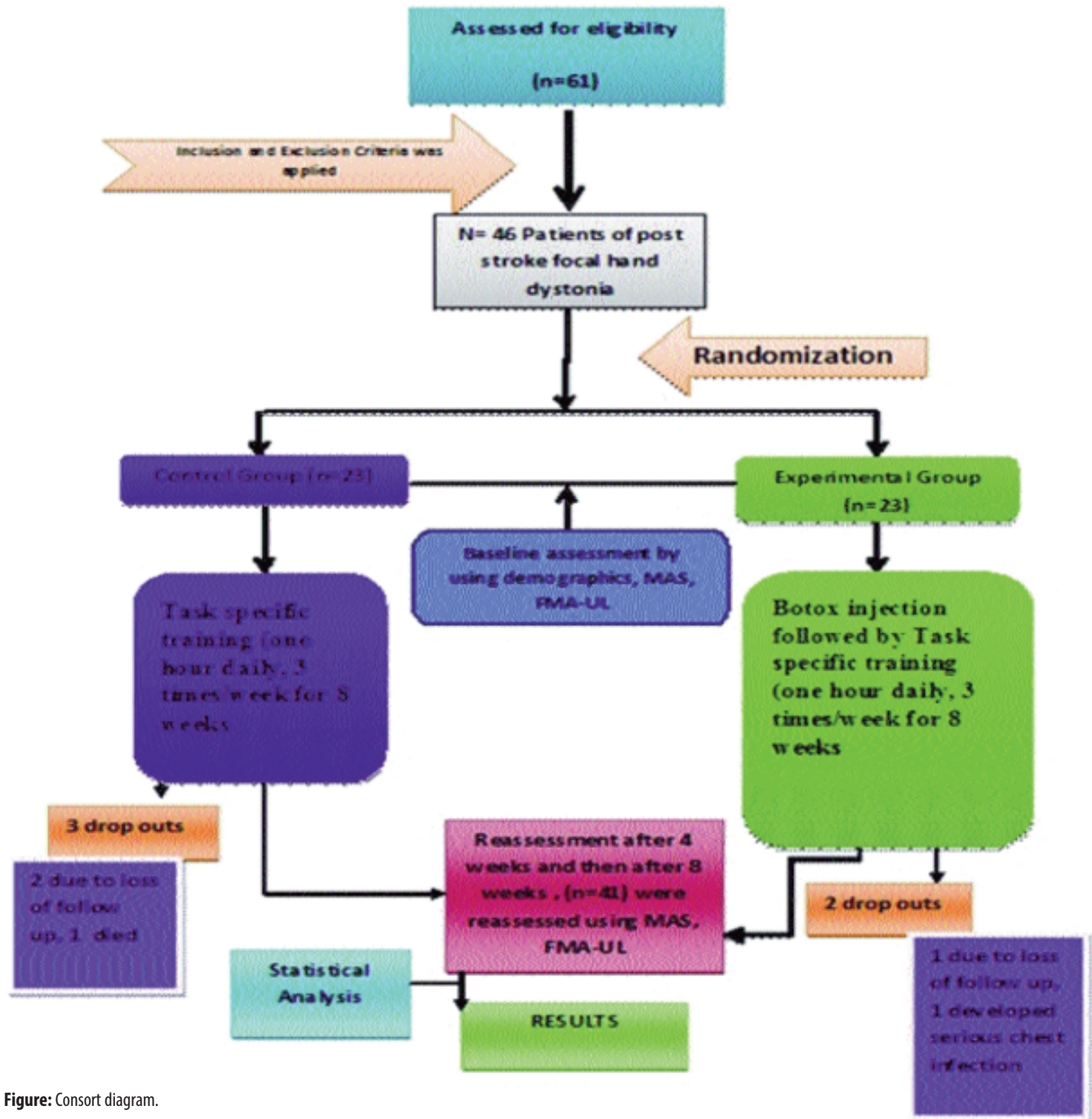


Figure: Consort diagram.

and 8(40%) in control group, respectively. In experimental group, 13(61.9%) patients suffered from ischaemic stroke, while in control group the figure was 16(80%). Likewise, in experimental group, 8(38.1%) suffered from haemorrhagic stroke and in control group the figure was 4(20%).

Significant difference was found in MAS and FMA-UL over the period of time, in both groups ($p < 0.01$) (Table-2).

However, no significant difference was observed between the groups at baseline, after 4 and 8 weeks of intervention ($p > 0.05$) on both MAS and FMA-UL scales (Table-3). For further analysis, post-hoc test was applied to evaluate the variations in different weeks (Table-4)

Discussion

To the best of our knowledge, there was no study conducted in Pakistan till date focussing on the

treatment of focal hand dystonia after stroke. The current study showed marked improvements in upper extremity function in both groups after 8 weeks of intervention. The beneficial effects of BoNT-A in treating focal dystonia has been described in many international studies and is considered as a treatment of choice in dealing with patients of focal dystonia.¹⁹ Siniscalchi reported that post-stroke dystonia can be managed effectively by means of botulinum toxin. He reported that mechanism of post-stroke spasticity and post-stroke dystonia are different as post-stroke spasticity has associated muscular weakness and it gets aggravated by impulses that tend to inhibit it, while post-stroke dystonia has over activity that developed as a result of decreased inhibition. Botulinum toxin is effective in treating post-stroke dystonia as it blocks the release of acetylcholine.⁵ Jung et al narrated in their case report that dystonia developed after stroke, showed improvement with botulinum toxin and helped in improving the functions of lower limb. In the current study both groups showed significant results.¹² Yoshimura et al. did a study for investigating the effects of botulinum toxin type A in different types of limb dystonia including post-stroke dystonia and reported significant improvements in the dystonic patients.¹¹ The results of current study showed marked improvements in post-stroke focal hand dystonia after BoNT-A injection given in combination with task-specific training and as well as task-specific training alone. Literature has also supported the use of BoNT-A for improvement in functions in post-stroke patients by reducing hypertonia and modulating neural plasticity even at cortical level.^{11,20,21} Other than botulinum toxin, few other treatment options were found which provided good results regarding treatment of post-stroke dystonia, they included deep brain stimulation and shock wave therapy. Meythaler found that continuously infused intrathecal baclofen also have beneficial effects in post-stroke dystonia.²² In another study it was found that secondary dystonia shows improvement after receiving extra dural motor stimulation; they reported it as a first series on this treatment regime.²³

Lesion in different areas of brain produces different types of dystonias like; spontaneous dystonia, action dystonia, fixed dystonia or sometimes a combination.²⁴ All types of dystonia significantly impairs the function of hand affecting the functional independence of the patient. Batool et al. compared constraint induced movement therapy (CIMT) with motor relearning programme and evaluated the effects on upper limb function in post-stroke patients after three weeks of intervention. The study reported significant improvements on upper limb items of motor assessment scale in CIMT group in which

unaffected arm was constrained and task-specific activities were practiced with affected arm only, while in motor relearning programme only task-specific activities were used without restraining unaffected arm and showed no significant improvement on motor assessment scale.¹⁶ However, in current study, significant improvements were reported on motor assessment scale with task-specific training. This contradiction might have occurred as in the current study intervention was provided for 8 weeks while in the reported study the intervention was for three weeks only. A review on task-specific activity of hand has also shown its effectiveness with significant improvements in FMA scale for upper limb in stroke population as shown by the results of the current study.²⁵

The limitation of the current study was a short follow-up period. Larger studies with appropriate sample size should be conducted which may look for the effects in the long term, especially when the effects of botulinum toxin resolves. There is limited literature available regarding treatment of post-stroke focal hand dystonia. The current study has focussed more on one type of physiotherapy treatment; different physiotherapy treatments should also be evaluated for the management of this disabling post-stroke complication.

Conclusion

Task-specific training improved function of upper limb in patients suffering from post-stroke focal dystonia either given in combination with BoNT-A or alone. BoNT-A and task-specific training in combination were as effective as task-specific training alone for the treatment of post-stroke focal dystonia.

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Conflict of Interest: None.

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