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Combined effect of botulinum toxin and splinting on motor components and function of people suffering a stroke

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Abstract

Background: Spasticity is one of the problems after a stroke. Due to this increase in muscle tone, patients are confronted with problems in motor control and difficulties in activities of daily living and complications such as shortness and contracture. The aim of this study was to examine the effects of the simultaneous use of both splint and botulinum toxin-A (BTX-A) injection on spasticity, range of motion and upper extremity function in a 3-month period.

Methods: In this study a comparison was done between three groups of interventions, conducted in rehabilitation clinics in Tehran. Sixty people with chronic stroke were recruited. Based on the inclusion criteria, a total of 39 stroke patients after completing the consent forms were entered to intervention groups; splint or botulinum toxin injection or combined splint/botulinum toxin injection. They were followed up about three months and the evaluations were done monthly. Goniometry was the method to measure the range of motion, and Modified Ashworth Scale was used to examine the spasticity and the upper extremity function was scored based on Fugl-Meyer Assessment. Statistical analysis was done using SPSS 17. And ANOVAs was used for comparison between groups and times. Significance was set at 0.05.

Results: All outcome measures were improved within each group but the differences between splint group and BTX-A group and the BTX-A-splint group was not significant in most outcomes during the 3 periods (first evaluation until end of the first month, the end of first month until the end of second month, the end of second month until the end of the third month) ($p>0.05$). The results also showed that the changes in elbow`s spasticity ($p=0.05$) and wrist`s spasticity ($p=0.007$) and upper extremity function ($p=0.04$) were obvious between the three groups over the 3-months and the difference in the group of combined use of botulinum toxin, and the splint was more than other groups.

Conclusion: In this study, the effects of botulinum toxin injection and Volar-Dorsal Wrist/Hand Immobilization splint and the combined use of botulinum injection and splint were obvious in all groups but was not significantly different between the interventions in a 3-month follow-up.

Keywords: Splinting, Botulinum toxin, Stroke, Hand function.

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Introduction

Annually, 15 million people worldwide suffer a stroke. Of these, 5 million dies and another 5 million are left permanently disabled, placing a burden on family and community (1). The epidemiology of stroke and its subtypes in the Middle East is unclear. A study provided evidence that the incidence of stroke in Iran is considerably greater than in most Western countries, with stroke occurring at younger ages around 45 years old. Ischemic stroke incidence was also considerably greater than reported in other regions (2). Stroke is a common cause of disability. One of the complications after a cerebrovascular acci-

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dent is spasticity or muscle hyper-tonicity that is determined with an increase in speed-dependent resistance against passive tension and the intensive stretch reflexes. After a stroke, due to the rise of muscle tone, increased reflex activity and reduced inhibitory control, patients are confronted with problems in motor control and this problem also lead to difficulties in activities of daily living and complications such as shortness and contracture (3). The most recovery of neuromuscular system may occur within the six months after the accident. Long-term recovery period of these systems may be associated with problems such as spasticity, rigidity, and defects in motor functions such as synkinesis (involuntary movements in other parts, while moving another extremity). Neurolysis, denervation with chemicals and casting techniques are considered as treatment methods to resolve these complications (3,4). Alongside current spasticity preventions such as stretch, exercise, and positioning, treatment options include oral anti-spasm drugs, blocking by phenol, baclofen and botulinum toxin local injections (5). Oral antispasmodic medications often have limited and short-term effects and result in complications such as weakness, dizziness and dry mouth (6,7). Neurolysis by injecting phenol or alcohol effectively reduces spasticity (8,9), but is followed by severe pain, And the invasive method of intrathecal baclofen injection besides good results leads to severe reactions such as nausea, vomiting and headache(10,11). Botulinum Toxin as a degenerative chemical drug with reversible clinical effects is another way to reduce muscle spasticity in stroke patients. Botulinum Toxin causes a neuromuscular block in acetylcholine release, thereby preventing neuromuscular transmission and muscle contraction and many studies have reported the effects of this drug on spasticity (12-16). And various papers have reported different results. Hesse, Bhakta and their colleagues studied the impact of botulinum toxin on spasticity and concluded that the injection of botulinum toxin is a safe and effective method for reducing disability in spastic patients (17,18). Also, splints are therapeutic devices discussed to prevent contracture and spasm progression; it has been reported any bad application of splint can cause deformity and may worsen the spasm (19,20). Therefore, the proper use and wearing of splint by the patients should be checked by a therapist (19). Two groups of orthoses for the treatment of spasticity are: 1 - progressive orthoses: that is applied to improve the range of motion in affected joints by increasing the amount of slow stretch created in the joint. This orthosis can be used to modify or prevent spasm, particularly if the spasm remains after injection of botulinum toxin. 2 - Serial orthoses: work as progressive orthoses but the difference is, they are prescribed as a brace, which gradually increase the range of motion (19). In this study, we used a type called volar-dorsal static (immobilization) splint that works through the application of serial static force (19). Because of the specific structure of this splint, the patient is able to touch objects on the palm, and this is considered as an advantage over other splints. Since the use of splint and injections of botulinum toxin have their particular costs for many families, thus efficiency and comparison of these interventions are important to resolve patient`s problems. Hill in 1994, in an article, explained that the method of extremity casting was more effective than conventional methods such as passive range of motion exercises, static stretching and splinting (21). But another study by Cusick, Novak, and Lannin in 2007, has been reported different results such as weakness due to immobilization condition in the casting method (22). And finally, most of the studies didn't show accurate effects of splints in reducing spasticity because of methodological limitations such as lack of inappropriate assessment and lack of control groups. Lai and colleagues in 2009 studied the effects of botulinum toxin Injection accompanied by Occupational Therapy, and also examined the use of a dynamic splint along with those

two interventions and reported contracture reduction and range of motion improvement (23). We didn't find any study about the effect of the Volar-Dorsal splint on hand function and the comparison of the effect of splint and BTX-A. So, In this study, through monthly clinical evaluations, the efficacy of BTX-A drug, splinting and BTX-A with splinting were examined to result possibly in the use of these findings in clinics and subsequent research studies.

Methods

Participants

This study has been done in three groups as pretest-posttest design in rehabilitation clinics in Tehran. Sixty patients with chronic stroke were selected by a non-randomized simple method. According to the inclusion criteria, a total of 39 stroke patients after completing the consent forms entered to the study into three groups including putting the splint, BTX-A injection and combined splinting and BTX-A injection groups. Of these, 29 patients completed the study. Thirty patients participated till the end of the second month, and nine patients were missed due to discordance and absence in the assessment sessions. Also one patient died from a second stroke just before the final assessment.

Procedure

Inclusion criteria for the study were: at least a year passed since the last stroke, age between 20 to 64 yrs, score above 22 on the cognitive test of Mini-Mental Status Exam (MMSE), no other neurological diseases, having a maximum spasticity score of 3 on the Modified Ashworth scale (MAS), the ability to sit at least 10 minutes independently on the edge of the bed, and not receiving botulinum toxin or similar splints while entering the study. If any of the patients had the following situations, he/she would be excluded from the research: occurrence of orthopedic lesions in the upper extremity, occurrence of any other neurological disease, absence in posttest evaluation. To make this kind of splint, initially, positive patterns were made in two sizes of men and women for the left or right hand. Then, all splints were fabricated based on the patterns. Splints immobilized the wrist in 10 degrees of extension, thumb in hyper-abduction and fingers in zero, so the angles of splint were the same for all patients. The complete initial data were gathered and recorded. Afterward, the patients received BTX-A injections, splints or splint-BTX-A for three months. In this work, Volar-Dorsal Wrist/Hand Immobilization splint and BTX-A was surveyed. Dosage for each muscle was 50-150 IV based on the bulk of muscles (FCR, FCU, Pronator Teres, FDP, FDS, FPL, and Palmaris Longus). Patients in the splint and splint-BTX-A group were clarified to wear these splints 2 hours a day and all the night (6 to 8 hours) about 3 months. Re-evaluation for three groups was performed at the end of each month. At the end of the first month 31 patients (11; splint – 11; botulinum toxin 9; splint-BTX-A) and finally at the end of the third month, 29 patients (9; splint – 11; botulinum toxin and 9 splint-BTX-A) were present for the assessment. In this 3-month period patients were called and reminded to use the splint. It should be noted that all patients were also participating in a routine Occupational Therapy program three times a week during the study.

Outcome Measure

Before the initiation of the interventions (splinting, botulinum toxin injection or splint-botulinum toxin.) active and passive range of motion of elbow, wrist and metacarpophalangeal joints were assessed. Other outcome measures were elbow and wrist spasticity and upper extremity function. Goniometry was the method to measure the range of motion, and Modified Ashworth Scale was used to examine the spasticity, and the upper extremity function was scored based on Fugl-Meyer Assessment.

Statistical Analysis

We calculated the descriptive and analytic statistics using SPSS 17. To investigate whether one of the groups changed more than the other group at the end of 1st, 2nd and 3rd month, we calculated the change of scores (changes in the scores of each variable in each month) for each group. We compared them using One Way ANOVA, and Tukey method was used as post-Hoc multiple comparisons. We also used analyzes of variance (ANOVAs) with repeated measures with a between-subject factor at three levels (3 groups) and a within-subject factor at four levels (time: baseline, 1st month, 2st month, 3rd month). The interaction of group and time served to determine the efficacy of the each therapy on the outcome measures. Significance was set at 0.05.

Results

The mean age of the patients was 49.90 yrs in drug injection group, 52.55 yrs in the splint group and 54.32 yrs in Botox-splint group .The average time passed since a stroke in the botulinum toxin injection group was 28.81 months, 29.22 months in the splint group and 26.22 months in Botox-splint group. Mean cognitive scores (MMSE) was 25.81 in the injection group, 27.44 in the splint group and 27.22 in Botox-splint group (Table 1).

According to Table 2, results of the active range of elbow in the second month was significant (0.02) and Tukey test showed that this difference was due to the difference between BTX-A and splint group. And the changes in scores of other variables were not significant between groups (Table 2).

Table 3 presents the motor recovery, spasticity and range of motion of patients at baseline, end of first, and two and the end of the third month. According to the results contained in Table 3, all variables in both groups have been improved to some extent, but just the difference between three groups was significant in Fugl-Meyer Assessment (FMA), Elbow MAS And Wrist MAS outcome. And differences between three groups in other variables was not significant (Table 3).

Discussion

Results of this study showed that after 3 months of Volar-Dorsal Wrist/Hand Immobilization splint, Botulinum toxin injection, and simultaneous use of these two interventions, all variables have improved but the difference between three groups in a 3 period (time sequence) (first evaluation until end of the first month, the end of the first month until the end of the second month, the end of the second month until the end of the third month) was not significant in most outcomes. Reason for this lack of meaningfulness can be the low sample size. To get better results, more samples may be needed in the hope that future studies will pursue this issue. Changes in severity of spasticity in these three periods (first evaluation until the end of the first month, the end of the first month until the end of the second month, the end of the second month until the end of the third month) were not significant between groups. This may be due to low reliability and low sensitivity of MAS (24). Perhaps because MAS evaluates thixotropy and fixed muscle contracture in addition to spasticity, this test is incompetence. It seems electrophysiological assessments like Hmax/Mmax tests are good criterion for measuring spasticity. A study in 2005 by Pizzi and colleagues have shown that

Table1. The characteristics of three study groups

Variable	Botox (n=11)	Splint (n=9)	Botox-splint (n=9)
Age (y)	49.9±10.84	52.5±10.41	54.3±8.97
Sex (women/men)	7/4	4/5	4/5
Time since stroke (m)	28.8±22.97	29.2±13.90	26.2±23.53
Mean MMSE	25.8±3.60	27.4±2.69	27.2±2.94
Side (right/left)	6/5	5/4	2./7

Table 2. Between-group differences in change scores for spasticity, active/passive range of motion and function

	Baseline to1 st Month				1 st to 2 nd Month				2 nd to 3rd Month			
Parameter	Botox group	Splint group	Botox-splint group	p	Botox group	Splint group	Botox-splint group	p	Botox group	Splint group	Botox-splint group	p
Elbow MAS*	0.27	0.33	0.55	0.81	0.18	0	-0.11	0.73	0.09	1	0.33	0.20
Wrist MAS	1.09	0.22	1	0.06	-0.18	0	0.11	0.70	-0.45	0	0	0.30
Elbow AROM*	5.63	-5	-13.88	0.40	-17	20	9.33	0.02	-5.63	-8.75	-5.66	0.98
Elbow PROM*	-.90	-1.66	-5	0.60	-1.81	0	7.22	0.16	1.81	0	-0.55	0.30
Wrist AROM	-1.90	-3.66	-5.44	0.90	3.63	-1.75	-14.77	0.47	-9.27	1.25	-2.55	0.60
Wrist PROM	-7.27	-10	-9.44	0.90	-10	7.5	-4.44	0.40	-1.36	-3.75	-3.33	0.90
MP* AROM	۳,۹۰	-4.77	-23.88	0.15	-5.27	-3.75	-1.11	0.55	-2	4.5	0.33	0.30
MP PROM	-1.36	-2.22	8.88	0.20	-2.72	2.5	1.11	0.20	2.72	-5	-0.55	0.07
FMA*	-2.09	-2.11	-9.88	0.42	-2.18	1.25	-2.44	0.20	-4.72	-3.25	-2.33	0.70

*MAS: Modified Ashworth Scale, AROM: Active Range of Motion, PROM: Passive Range of Motion, MP:MetacarpoPhalengeal, FMA: Fugl-Meyer Assessment

Table 3. Motor Recovery, Spasticity, and Passive/Active Range Of Motion Scores of Patients at Baseline, 1st Month, 2st Month and 3rd Month

	Group	pretreatment	1st Month	2nd Month	3st Month	Δ(95٪)	p*
Elbow MAS	Botox	2	1.7	1.5	1.4	0.54(0.08 , 1.007)	0.05
	Splint	1.5	1.2	1.7	0.77	0.77(0.43 , 1.11)	
	Botox-splint	2.3	1.7	1.8	1.55	0.77(0.03 , 1.52)	
Wrist MAS	Botox	2.9	1.8	2	2.4	0.45(-0.24 , 1.15)	0.01
	Splint	2.7	2.5	3.2	2.3	0.44(-0.23 , 1.12)	
	Botox-splint	3.5	2.5	2.44	1.4	1.14(0.39 , 1.82)	
Elbow AROM	Botox	59.7	54.9	71.8	77.45	-17.72(-55.51 , 20.06)	0.50
	Splint	84.4	89.44	68.75	81.66	2.7(-25.14 , 30.69)	
	Botox-splint	59.4	73.33	64	69.66	-10.22(-37.94 ,7.77)	
Elbow PROM	Botox	1.34	1.35	1.36	1.35	-0.9(-3.43 , 1.61)	0.50
	Splint	1.33	1.35	1.35	1.35	-1.6(-5.96 , 2.63)	
	Botox-splint	1.29	1.34	1.27	1.27	1.6(-17.64 , 20.97)	
Wrist AROM	Botox	16.54	18.45	14.81	24.09	-7.54(-17.51 , 2.42)	0.30
	Splint	7.22	10.88	13.75	13.22	-6(-16.13 , 4.13)	
	Botox-splint	19.44	24.88	39.66	42.22	-22.77(-62.25, 16.7)	
Wrist PROM	Botox	1.54	1.61	1.71	1.72	-18.63(-36.91 , -0.35)	0.40
	Splint	1.37	1.47	1.45	1.55	-17.22(-37.29 , 2.85)	
	Botox-splint	1.27	1.36	1.41	1.44	-17.22(-78.32 , 43.88)	
MP AROM	Botox	11.36	7.45	12.72	14.27	-3.36(-8.96 , 2.23)	0.18
	Splint	2.44	7.22	10	9.66	-7.22(-12.54 , -1.89)	
	Botox-splint	6.11	30	31.11	30.77	-24.66(-66.78 , 17.45)	
MP PROM	Botox	94.09	95.45	98.18	94.45	-1.36(-4 , 1.27)	0.47
	Splint	91.66	93.88	88.75	95	-3.33(-11.48 , 4.81)	
	Botox-splint	90	81.11	80	80	9.44(-12.33 , 31.22)	
FMA	Botox	21.27	23.36	25.54	30.27	-9(-15.87 , -2.21)	0.04
	Splint	23.22	25.33	19	27.88	-4.66(-9.95 , 0.61)	
	Botox-splint	18.22	28.11	30.55	32.88	-14.66(-33.08 , 3.75)	

* Δ, mean change at 3rd Month from baseline. ANOVA for repeated measures.

using a volar splint about three months reduced spasticity and this improvement was only seen with neurophysiological tests, and the MAS results were not significant (25). The data in Table 3 shows that either at the end of the first month or the end of second and the third months, the impact on wrist spasticity was significantly different between groups and the changes in a group of combined use of Botulinum toxin injection and splint were more than other groups, respectively. Also according to the results contained in Table 2 and 3, the level of spasticity in each group has decreased. Spasticity Reduction in the Botox splint group has been more than two other groups. It is presented that trend of spasticity reduction in the splint group has been constant during three months of study. But botulinum toxin injection trend has been a different process so that at first there was a period of a great reduction in the severity of

spasticity and after the first month this outcome gradually increased again. This could indicate that effect of botulinum toxin injection on spasticity is temporary. This issue approves the pharmacodynamics properties of botulinum toxin, which neurotransmission restores by neural sprouting process, almost after 3months (26). So, according to the ascending trend of spasticity improvement in the combined treatments group and the splint group and the unstable trend of spasticity improvement in the group of botulinum toxin injection, it can be said that perhaps the time (3 months) was not enough to get more definite results for comparing the interventions impacts. We hope that future research will pursue this issue. Kirazli and colleagues in 1998 concluded that injecting botulinum toxin into spastic soleus muscles has a significant reduction in the muscle's spasticity in the second and fourth weeks, but this decrease was not seen at the end of weeks 8 and 12 (27). But in another study by Eduardo, the results were different from our study and spasticity continued to diminish even up to 32 weeks after injection of the botulinum toxin and these changes were significant (28). The results depicted in Table 2 show that during the second month the impact on the range of motion of the elbow between three interventions is significantly different. These differences were calculated using the Tukey test. This level of significance is because of the large difference between the mean changes in splint and BTX-A group. Changes of active and passive wrist range of motion showed improvement in all three groups and in the Botox - Splint group were more than other groups. But these changes between groups were not significantly different in these times (the first assessment, the first end, the end of the second month, and the end of the third month), these results would be as a result of low sample sizes too. In Wallen`s study among 4 groups of cerebral palsy children (botulinum toxin injection, botulinum toxin injection along with occupational therapy, occupational therapy, and control) similar effects on upper extremity were reported (29). In contrast to our work, Eduardo reported that range of motion may improve up to 32 weeks after injection of the botulinum toxin. The advantages of that research seem to be an evaluation of isolated muscles and adjusting injection doses based on the need of each muscle (28). MP joint`s active range of motion changes in all three groups had a little change, and the difference was not evident between the three groups. Although the change process in patients who used the splint was a gradual and continuous improvement, injection of botulinum toxin clearly decreased the active range of motion in the first month that can be caused by temporary poisoning and weakening effect of this drug on muscles. This active ROM reduction was modulated at the third month, perhaps because of the time passed and a decrease in drug`s effect. Changes in passive range of motion of MP joints were not evident either within or between groups, and these results were predictable due to a complete passive range of motion in most patients at the baseline. Upper extremity function, as well as other variables, didn't show a significant difference between interventions at the end of treatment, but the trend of changes in all groups showed significant improvement and the trend of combined group was better than two other groups. Obviously, the function of upper limb is associated with range of motion and muscle tone, therefore in this study lack of significant results of the tone and range of motion in time periods (the first assessment to the end of the first month, first month until the end of the second month, second month until the end of the third month), insignificant results of upper limb`s function can be normal. Due to significant changes in spasticity at different times (the first assessment, the end of the first month, the end of the second month, and the end of the third month), it was predictable that the results of upper extremity functions might change significantly between the three groups at

different times (the first assessment, the end of the first month end second month, third month and the end) (Table 3). Research in 2000 by Gracise and colleagues has shown that upper limb function will improve in certain tasks. Gracise explained this improvement with regard to the better perception of the senses and reduced spasticity and increased the range of motion in some joints of the affected hemiplegic side as an outcome of using of a Garment (19). Katz and colleagues in a study showed a strong correlation between spasticity and hand function (30). Although the scales such as the MAS give little clinical information with low validity and sensitivity to changes, they are still being used in many types of research (24). In a case report by Shun-fen sun, it was concluded that botulinum toxin injection accompanied with any other treatment such as CIMT, improves spasticity of upper limb (31). Our results could confirm the studies of researchers who have reported that functional effects of botulinum toxin would be more beneficial when accompanied by the muscle retraining and splinting (32).

Conclusion

In this study, the effects of botulinum toxin injection and Volar-Dorsal Wrist/Hand Immobilization splint and the combined use of botulinum injection and splint were not significantly different between the interventions in a 3-month follow-up.

Limitation

Using the splint by the participants at the correct time and the low number of strokes people with our inclusion criteria were the limitations of this study.

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