CME

Randomized Controlled Trial on Effectiveness of Intermittent Serial Casting on Spastic Equinus Foot in Children with Cerebral Palsy After Botulinum Toxin-A Treatment

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Objective: Physical therapy (PT) and botulinum toxin-A (BTX-A) injections are widely used in the treatment of spastic equinus foot due to cerebral palsy. The aim of this study was to show effects of intermittent serial casting (SC) in addition to standard treatment on spasticity, passive range of motion (PROM), and gait.

Design: Fifty-one ambulatory patients, treated by BTX-A to plantar flexor muscles, were randomly assigned to casting or control groups in a 2:1 ratio. Both groups received PT for 3 weeks. Casting group additionally received intermittent SC during 3 consecutive weekends. Assessments included Modified Ashworth Scale (MAS), Tardieu Scale, Observational Gait Scale (OGS), and Physician Global Assessment at baseline and posttreatment weeks 4 and 12.

Results: Significant improvements in PROM, MAS, Tardieu Scale, and OGS were recorded in both groups ($P < 0.001$ for all). Average changes in MAS, PROM, angle of catch, spasticity angle, and OGS of the casting group were significantly higher than those of the controls at week 4 ($P = 0.006$, $P = 0.002$, $P < 0.001$, $P = 0.005$, $P = 0.011$), and 12 ($P = 0.013$, $P < 0.001$, $P < 0.001$, $P = 0.011$, $P < 0.001$). Follow-up Physician Global Assessment also favored casting group ($P < 0.001$ for both).

Conclusions: Combining intermittent SC with BTX-A injections and PT might provide additional benefits for spastic equinus foot.

Key Words: Cerebral palsy, Equinus deformity, Plaster casts, Botulinum toxin A, Contracture, Muscle spasticity

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CME Objectives: Upon completion of this article, the reader should be able to: (1) identify treatment options for spastic equinus goot in children with cerebral palsy; (2) explain different approaches of serial casting with an additional model of intermittent casting; and (3) describe the potential benefits of combined treatment modalities, including intermittent serial casting, for spastic equinus foot in children with cerebral palsy.

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Spasticity is not only the most common motor disorder but also the main cause of slowly developing secondary problems like contractures and bony deformities in children with cerebral palsy (CP). Spastic equinus foot is a very common problem in children with CP and can be primarily due to spasticity of the plantar muscle complex, sometimes being exacerbated by the weakness of the antagonist dorsiflexor muscles, and can involve soft tissue and joint contractures. According to definition, when muscle activity caused by velocity-dependent pathological stretch reflex activation is responsible for the increased resistance to passive motion, then it is termed as spasticity. However, non-neural mechanical properties of soft tissue and joint structures such as stiffness and viscosity can also contribute to increased resistance to passive stretch. In most children with CP who have spastic equinus foot, both neural and non-neural components exist.[1] In a recent systemic review aiming to describe the best available evidence for interventions in children with CP, botulinum toxin-A (BTX-A) injections and casting were strongly recommended for spasticity and contracture management, respectively.[2] Although there is evidence in the literature suggesting that combined treatment of casting and BTX-A injections might have additional benefits in short- and long-term outcomes to either treatment alone and might provide a better patient compliance in patients with

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CP,[3–6] the optimal strategy for this combined treatment is still not known. Newman et al.[7] reported less painful episodes and better spasticity measurements at 3- and 6-month follow-ups with a combined treatment of delayed casting than immediate serial casting with BTX-A injections. In their prospective randomized study to define the optimal strategy for the combined treatment of BTX-A with casting in children with CP, Desloovere et al.[8] reported slightly more pronounced benefits mainly in the proximal joints, better compliance to casting, and less time needed to achieve their defined treatment goal, which was dorsiflexion of 10 degrees at ankle joint in children who were casted after injections compared to those who were casted before injections.

Skin irritation or breakdown, painful episodes, cast breakdown, edema, tendonitis, weakness, and stiffness are some of the adverse effects reported after serial casting.[9–11] Moreover, casting, especially when prolonged, might complicate activities of daily living by increasing the risk of falls or causing problems in bathing.[12,13] Recent evidence from literature favors early goal-oriented, activity-based, intensive, and repetitive motor trainings in enriched environments to optimize neuroplasticity in children with CP.[14] Prolonged serial casting might also interfere with these activity-based intensive rehabilitation options.

In this clinical trial aiming to overcome the issues with patient compliance, adverse effects and combined treatment options, an intermittent serial casting model was developed. The aim of this prospective, randomized, controlled trial (RCT) was to show the effectiveness of intermittent serial casting when combined with physical therapy after BTX-A injections on spasticity, passive range of motion (PROM), and gait of children with CP.

MATERIALS AND METHODS

This randomized controlled study was performed in a connected setting of the department of physical medicine and rehabilitation (PMR), outpatient rehabilitation center, and occupational therapy school of a university hospital. Written informed consent was taken from all the patients and their families, and the study was approved by the ethics committee of Kocaeli University School of Medicine KOU/KAEK 20/11-268.

Eighty-two patients with a diagnosis of CP were screened for the study. Inclusion criteria for the study were as follows: having a diagnosis of CP according to Rosenbaum criteria,[15] having diplegic or hemiplegic type of involvement, having a Gross Motor Functional Classification System level of I, II, or III, being 3 to 17 years old, having a unilateral or bilateral spastic equinus foot deformity with shortening of plantar flexor muscles that did not allow the ankle with extended knee to dorsiflex more than 80 degrees (or −10 to neutral), having a Modified Ashworth Scale (MAS) score of 3 in the plantar flexor muscle complex, and being scheduled for Abobotulinumtoxin-A (Dysport) treatment to plantar flexor muscle group with a minimum of 10 U/kg or 300 U. Patients with cognitive dysfunction, presenting pain in the lower extremities, with a history of orthopedic surgery within the last 12 months, with dystonia, infection or skin breakdown, vascular disease, fracture or dislocation in the lower extremities were excluded.

Fifty-four eligible patients were randomly assigned to casting group or control group in a ratio of 2:1 (Fig. 1). A computer-assisted randomization list was created using casting twice and control once as treatment groups and 3 and 6 as block sizes. Botulinum toxin-A injections were applied under moderate to deep sedation to all patients except 2 older patients in the casting group and 1 patient in the control group. Muscle selection, doses, and dilution for each patient were individualized based on body weight (BW), severity of spasticity, clinical examination, and gait pattern. Botulinum toxin-A (Dysport, Ipsen-Gen Ilac, 112-92) was injected into target muscles under the guidance of electrical stimulation. All patients received injections to plantar flexor muscle group; 23 patients in the casting group and 10 in controls received multilevel injections. Muscles other than plantar flexors injected were medial hamstrings, adductors, and/or iliopsoas. Total dose did not exceed 40 U/kg BW or 1000 U in any patient. Both groups received a physical therapy program of 1 hour per session, 5 sessions per week (during weekdays) for 3 weeks. Physical therapy mainly consisted of stretching and strengthening exercises,

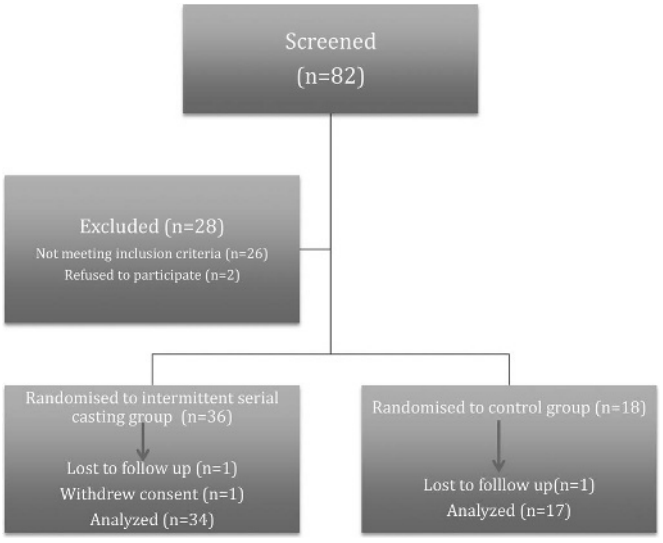

FIGURE 1. Patients' disposition.

TABLE 1. Demographic parameters of the casting and control groups

Group	Age* (Mean ± SD)	Sex	Type of Involvement	GMFCS (I/II/III)
Casting group	76.9 ± 36	21 M (61.8%) 13 F (38.2%)	25 diplegic (73.5%) 9 hemiplegic (26.5%)	6 (17.6%)/17 (50%)/11 (32.4%)
Control group	75.5 ± 37.5	11 M (64.7%) 6 F (35.3%)	12 diplegic (70.6%) 5 hemiplegic (29.4%)	5 (29.4%)/8 (47.1%)/4 (23.5%)
P	0.757	0.839	0.826	0.339

*Months.

GMFCS, Gross Motor Function Classification System; F, female; M, male.

weight bearing, balance, proprioception, and ambulation training. The casting group additionally received a series of progressive casting, first one at post–BTX-A treatment week 1, each for 72 hours, and during 3 consecutive weekends. Casting was applied by the same senior orthotist using a dual cast, which consists of a standard short leg plaster cast and a circular cast from below the knee to above the knee. The position of the ankle joint was progressively changed according to the improvement in passive dorsiflexion of the patient. With respect to study protocol during cast application, it was not allowed to exceed 100 degrees (or +10 degrees from neutral) of ankle PROM; any patients with ankle PROM beyond this range should be casted at 100 degrees.

All patients were followed for 12 weeks regarding muscle tone, PROM, gait function, and adverse events. Muscle tone and spasticity were measured by MAS[16] and Tardieu scales.[17] Within the Tardieu Scale, angle of arrest of the ankle joint at slow speed, angle of catch at fast speed (XV3), spasticity grade (Y), and spasticity angle (X) were recorded. Angles of arrest and catch were measured by a goniometer and angle of arrest of the ankle joint at slow speed was recorded as PROM. Patients were videotaped at each visit for the evaluation of gait function by Observational Gait Scale (OGS).[18] Modified Ashworth Scale, Tardieu, and OGS assessments were done by a physician who was blind to their treatment protocol. Overall response to treatment was also assessed by a 9-point scale of Physician Global Assessment (PGA) from −4 (markedly worse) to 4 (markedly improved). Assessments by MAS, Tardieu scale, OGS of the more affected side and PGA were done at baseline, week 4, and week 12.

Statistical Analysis

Modified Ashworth Scale and PROM were primary outcome measures, whereas Tardieu, OGS, and PGA were secondary. Sample size was estimated with respect to similar superiority trials.[2,4,8] Demographic results were expressed as percentage or as mean ± standard deviation. Comparison of the baseline, week 4, and week 12 within-group evaluations of spasticity measurements PROM, OGS, and PGA were performed using Friedman test. Modified Ashworth Scale scores of 0, 1, +1, 2, 3, and 4 were first converted to 0, 1, 2, 3, 4, and 5, respectively, before statistical analysis was performed. All comparisons between independent group medians were applied by the Mann-Whitney *U* test. All analyses used a confidence interval of 95% and a significance level of <0.05.

RESULTS

The study started recruiting patients in September 2014 and was completed in November 2015. Two patients in the casting group and 1 patient in the control group discontinued their treatment, as 2 were lost to follow-up and 1 withdrew consent (Fig. 1). Demographic parameters of the remaining 51 patients are shown in Table 1. No statistically significant differences were found between the casting and control groups regarding age, sex, type of involvement, and Gross Motor Functional Classification System levels ($P > 0.05$ for all parameters).

The spasticity measurements by MAS and Tardieu scale of casting and control groups are given in Table 2. No significant differences were noted between casting and control groups regarding baseline spasticity data ($P > 0.05$ for all parameters). Statistically significant improvements in MAS, PROM, XV3, and X were recorded in both of the groups ($P < 0.001$ for all parameters of each group). A significant decrease in Y was also noted in the casting group ($P < 0.001$). Post hoc analysis of this data revealed that statistical significance was reached at week 4 and sustained at week 12 for all parameters ($P < 0.05$ for all).

The mean MAS and PROM of the casting group were significantly better than those of the control group both at week 4 ($P = 0.006$, $P = 0.013$) and 12 ($P = 0.015$, $P = 0.013$); XV3 and

TABLE 2. Modified Ashworth Scale and Tardieu Scale results of casting and control groups (mean ± SD)

	Baseline	Week 4	Week 12	*P*
MAS				
Casting group	4 ± 0	1.8 ± 0.8	2.4 ± 0.8	<0.001
Control group	4 ± 0	2.6 ± 0.9	3.1 ± 0.9	<0.001
P	1	0.006	0.013	
XV1 (PROM)				
Casting group	79.8 ± 9.2	99.5 ± 13.1	93.0 ± 11.5	<0.001
Control group	79.4 ± 9.0	89.4 ± 13.8	83.5 ± 12.7	<0.001
P	0.752	0.015	0.013	
XV3				
Casting group	51.7 ± 10.2	87.6 ± 14.2	77.8 ± 13.8	<0.001
Control group	52.6 ± 11.2	71.1 ± 15.1	63.0 ± 15.6	<0.001
P	0.838	0.677	0.002	
Y				
Casting group	2.2 ± 0.4	2.0 ± 0.3	2.0 ± 0.3	0.001
Control group	2.1 ± 0.4	2.0 ± 0.000	2.1 ± 0.3	0.097
P	0.634	0.006	0.419	
X				
Casting group	28.1 ± 7.1	12.1 ± 6.9	15.3 ± 7.8	<0.001
Control group	27.1 ± 6.4	17.9 ± 6.4	20.0 ± 5.6	<0.001
P	0.616	0.09	0.038	

XV1, angle of arrest at slow speed.

X at week 12 ($P = 0.002$, $P = 0.038$); and Y at week 4 ($P = 0.006$). The average changes in MAS, PROM, XV3, and X of the casting group were significantly higher than those of the control group both at week 4 ($P = 0.006$, $P = 0.002$, $P < 0.001$, $P = 0.005$), and at week 12 ($P = 0.013$, $P < 0.001$, $P < 0.001$, $P = 0.011$).

An 83.8% and 46.4% post hoc power was calculated for primary end point mean of decrease in MAS, and 82.1% and 71.8% post hoc power was calculated for primary end point mean of increase in PROM at week 4 and 12, respectively.

The mean OGS total sores and PGA results of the casting and control groups are shown in Table 3. Statistically significant improvements in OGS were recorded in both groups ($P < 0.001$ in both groups). Although no significant differences were noted between the groups at baseline and at weeks 4 and 12 ($P > 0.05$ for all), the average amount of change in the casting group was significantly higher than that of the control group both at weeks 4 and 12 ($P = 0.011$, $P < 0.001$). Physician Global Assessment scores of the casting group at week 4 and 12 were significantly higher than those of the control group ($P < 0.001$ for both).

No adverse effects were recorded in the control group, whereas short leg cast breakdown occurred in one of the patients in the casting group in the first session requiring replacement with a new one. No other adverse event was reported in either of the 2 groups.

DISCUSSION

The results of this prospective, randomized, controlled clinical study showed that a well-defined population of children who have spastic equinus foot due to CP might have additional benefits when BTX-A injections and physical therapy were combined with a treatment of intermittent serial casting. These intermittent serial casting periods might provide additional benefits on reduction of spasticity, improvement in PROM, and improvement in gait function of these children.

In children with CP, spasticity can alter muscle structure and hinder everyday activities such as gait. Children with CP develop mature gait later than normal children do, and there is general agreement that surgery to improve gait function should be avoided until gait has matured.[19,20] Early surgical interventions have a higher risk of failure and relapse. Besides, repeated muscle and tendon surgeries should be avoided to prevent weakness. To improve the overall condition, reach optimal motor functioning, and prevent the development of secondary problems like soft tissue contractures and skeletal deformities, an early, comprehensive, and combined treatment approach including both pharmacological and rehabilitative interventions are needed in these children. Molenaers et al.[21] showed that repeated BTX-A treatments with an integrated approach can help to prevent the development of contractures and bony deformities and therefore may lessen the complexity of surgery and may help to delay the surgery. The general indication for BTX-A injection was the presence of dynamic contracture, in the absence of a fixed myostatic contracture. However, in many cases, both dynamic and myostatic components exist together. Accurate management in these cases requires a careful evaluation, combined intervention plan including casting and/or orthoses, and a close follow-up. Casting has been recommended as a treatment option in the management of spastic equinus in children with CP for several decades. Although most of the studies reported additional benefits with combined treatment of BTX-A and serial casting[3–6] for the treatment of spastic equinus foot in children with CP, there are some studies favoring serial casting only.[13,22] In their prospective randomized trial, Kay et al.[22] reported that additional use of BTX-A to a serial casting regimen led to earlier recurrence of spasticity, contracture, and equinus during gait, and suggested that serial casting alone is preferable for the treatment of fixed equinus contractures in children with CP. Arriving at a general conclusion from the current literature is limited because of varied protocol designs on type of casting (serial/inhibitive or short leg/long leg), clinical characteristics of the patients (amount of dynamic and static properties, spasticity grading), and contents of the interventions (target muscle selection, applied dosage, and injection technique for BTX-A). In this clinical trial, the intention-to-treat population was selected to have a MAS score of 3 in the plantar flexor muscle complex and limited ankle dorsiflexion range of at least −10 degrees from neutral to have a group that would need and benefit from this intervention plan according to our experience. A short leg plaster cast was combined by an above-the-knee cast to provide an efficient stretching not only to soleus but also to gastrocnemius muscle. A minimum dosage of 10 U/kg was determined for BTX-A intervention because of its dose-dependent efficacy. Botulinum toxin-A is an important treatment in children with CP because it is safe in young children and allows combined treatment. The reduction in muscle tone by this selective treatment provides an opportunity to allow and optimize the effects of other treatments including physical therapy, orthoses, or casting. Decreased muscle tone and/or reduced pain might improve the tolerance to stretching exercises, might enhance an underlying masked voluntary control of the antagonist muscles, and further provide more benefits from strengthening exercises and improve motor functioning, might allow or ease shoe wear, orthotic wear, or casting, and optimize their effectiveness by lengthening the period of orthotic wear or providing a better range for casting. Altered effectiveness of each intervention by the combined treatment approach in this clinical trial might even be more complex by the hybrid model of BTX-A injection followed by physical therapy and intermittent serial casting.

This is the first clinical study about a combined treatment approach with intermittent serial casting. Although assessments were done by a blind assessor to treatment program, blinding could be overshadowed by the presence of the patients with their casts in the clinic after application and for removal. This could be considered as a limitation and the strict inclusion

TABLE 3. Observational Gait Scale and PGA results of casting and control groups (mean ± SD)

	Baseline	Week 4	Week 12	*P*
OGS				
Casting group	7.5 ± 2.9	11.9 ± 2.7	10.5 ± 3.1	<0.001
Control group	8.5 ± 2.7	11.5 ± 2.8	9.5 ± 3.0	<0.001
P	0.344	0.481	0.171	
PGA				
Casting group	N/A	2.6 ± 0.6	2.3 ± 0.9	N/A
Control group	N/A	1.6 ± 0.7	1.3 ± 0.7	N/A
P	N/A	<0.001	<0.001	

criteria regarding baseline spasticity score and PROM of the ankle joint as the main strength of the study. In this study, MAS and PROM were the primary outcome measurements and results favored the intermittent serial casting group. Significant improvements in spasticity were also recorded by Tardieu scale. Another positive aspect of the study was the transfer of these gains to functional level as shown by PGA and OGS.

CONCLUSION

The results of this randomized controlled study showed that a well-defined population of children who have spastic equinus foot due to CP might have additional benefits not only in spasticity and PROM but also in gait function when BTX-A injections and physical therapy were combined with a treatment of intermittent serial casting.

SUPPLEMENTARY CHECKLIST

CONSORT Checklist: http://links.lww.com/PHM/A336

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