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Effectiveness of Serial Casting Alone and in Combination with Botulinum Neurotoxin in Pediatric Spastic Cerebral Palsy Patients

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Abstract

Purpose: This study evaluated the changes in gait of pediatric cerebral palsy patients after serial casting alone and serial casting in conjunction with botulinum neurotoxin treatments.

Methods: Retrospective data of 31 children were investigated. Sixteen children were treated with serial casting combined with BoNT injection and 15 children were treated only with serial casting treatment. GAITRite was used to collect velocity, cadence, swing %, stance %, step length, stride length, and step time parameters to compare the outcomes of the treatments.

Results: Combined treatment group unaffected side swing % showed a statistically significant difference at completion ($M = 35.16 \pm 1.21$; $M = 32.46 \pm 1.38$; $t(15) = 2.12$, $p = 0.049$). Unaffected side stance % at pre-intervention was statistically different for serial casting only and the combined treatment groups ($M = 61.69 \pm 0.73$; $M = 64.88 \pm 1.20$; $t(14) = -2.273$, $p = 0.039$). Pre- and post-intervention hemiplegic side swing % comparison was statistically significant for the serial casting only group ($M = 40.87 \pm 0.57$; $M = 42.39 \pm 0.79$, $t(14) = -0.151$, $p = 0.032$). The baseline velocity of the combined treatment group was slower than the serial casting-only group (88 ± 11.2 vs. 107 ± 14.4 (cm/s), $p=0.007$).

Conclusions: This investigation suggests that for patients, who have poor ambulation quality, abnormal spatiotemporal gait parameters, and significant spasticity at pre-intervention, BoNT in conjunction with serial casting is more effective for improving ambulation quality. Serial casting can be used in conjunction with botulinum neurotoxin, which is efficient in muscle morphology and function regulation by reducing spasticity.

Keywords: Botulinum Neurotoxin, Cerebral Palsy, Gross Motor Functional Classification, Serial Casting, Spasticity

1. Introduction

The main cause of motor impairments in children is cerebral palsy (CP). There are 3.6 incidences of cerebral palsy for every 1000 children worldwide, affecting over 18 million people of all ages. In ambulatory children with CP, dynamic ankle equinus changes the location of the ankle during locomotion and results in abnormal gait patterns that shorten the posterior muscle group and produce plantar flexion contracture [12]. Surgery can be performed, but as children who are still growing do not benefit from it, non-operative treatments are utilized to postpone surgery until skeletal maturity [19]. When surgery is not advised, botulinum neurotoxin (BoNT) injections, serial casting, or a mix of pharmacological and biomechanical therapies are frequently used. To reestablish the proper balance between the agonist and antagonist muscles, BoNT lowers the tone of hyperactive muscles. The primary goal of using BoNT is to enhance gait by inducing graduated levels of muscular weakness by adjusting the toxin injection dose [2], [7], [17], [18], [23], [29]. Chemodenervation with BoNT is reversible, repeatable, and has been shown to benefit people with cerebral palsy [4], [9], [13], [15]. For ambulatory children with GMFCS I–III, the main advantages of the treatment include increased range of motion (ROM) and decreased muscle stiffness. BoNT specifically inhibits Acetylcholine release presynaptically at the peripheral neuromuscular connections of the targeted muscles, which has neurotoxic and paralytic consequences [5].

Serial casting, which involves applying a series of casts with increasingly different angles to gradually modify the joint position, has previously been used to minimize the development of ankle contractures and equinus [8]. A rise in the passive muscular stretch was observed after therapy in individuals who had only serial casting, according to recent investigations [21]. Increased ankle ROM and decreased resistance to stretching have been seen in children with CP and idiopathic toe walking but changes in gait characteristics like velocity and stride length have not been seen [8].

Ankle dorsiflexion and gross motor function improved more in the combined treatment group than in the BoNT injections alone when the kinematic characteristics of the two treatments were examined [11]. Compared to BoNT treatment, combined treatment has been shown to increase walking speed [6]. In a different research, combination therapy dramatically increased ankle ROM and increased ankle joint angular velocity [25]. Contrarily, the combined therapy group returned to spasticity, contracture, and ankle equinus more quickly than serial casting, according to the findings of a prospective randomized experiment [1]. Two studies that evaluated all three treatments—BoNT, serial casting, and BoNT combined with serial casting—found that both groups who underwent serial casting improved their ankle ROM more than the BoNT-only group. Contrarily, no overall change in velocity or stride length was obtained in any of the groups, even though the patients in the combination group had more severe contractures and lower ROM at the start of the research [30]. Pediatric CP patients with dynamic equinus have benefited from serial casting and BoNT treatments, either individually or in combination [10], [14], [16], [20], [22], [26], [27], [28]. However, serial casting and the combined treatment's effectiveness on gait quality and spatiotemporal parameters have not been studied. This retrospective study evaluated the changes in gait after serial casting combined with BoNT compared to serial casting-only treatments for children diagnosed with hemiplegia and spasticity secondary to CP.

2. Materials and Methods

2.1. Participants

This study reviewed the health records of 31 children (15 female, 16 male) between the ages of 4 and 16 (mean= 7.4 ± 3.6 years) diagnosed with CP [24] receiving serial casting treatment for dynamic equinus and gait-related spasticity impairments. This retrospective cohort study was conducted at Children's Specialized Hospital, New Jersey, USA. Participants were diagnosed with unilateral hemiparesis, had a Gross Motor Functional Classification System

(GMFCS) level of I-III, and had a Modified Ashworth Scale (MAS) score of 3 or below. Determination of the sample size was done with G-Power (GPower - Universität Düsseldorf) version 3.2.1. Fifteen children were included in the "serial casting only" group (independent samples t-test, 0.68 effect size, 5% standard deviation, and 95% accuracy rate (z=1.96)). Sixteen children were included in the "combined treatment" group (independent samples t-test, 0.66 effect size, 5% standard deviation, and 95% accuracy rate (z=1.96)). Overall, with 31 patients, the sample size requirements were statistically satisfied (independent samples t-test satisfies 0.95 actual power and 0.52 effect size (5% standard deviation, 95% accuracy rate (z=1.96)). The included participants had CP diagnosis with dynamic ankle equinus and they were between 4 and 16 years old of age. Inclusion criteria included patients, who had normal joint range of motion required for ambulation, had appropriate cognitive status and ability to communicate, and had no previous history of surgical intervention for spasticity. Participants were ambulatory with or without assistive devices, such as loft strand crutches or walkers (GMFCS I-III,) and had the ability to follow simple instructions, non-ambulatory children were excluded from the study (Table 1). Patients, who had a previous diagnosis that may cause exercise intolerance (uncontrolled hypertension, coronary artery disease, cardiac arrhythmia or congestive heart failure, etc.), received treatment for heart attack, heart surgery, or acute heart failure within 3 months before the date of enrollment in the study, had severe cognitive or psychiatric problems and received or received medical treatment with a diagnosis of epilepsy, were not included in the study.

Table 1: General Characteristics of Participants (Distribution of age, weight, height, sex and GMFCS level)

Age (years)	Weight (N)	Height (cm)	Boys n (%)	Girls n (%)	Total n (%)
1-3	0	0	0 (0)	0 (0)	0 (0)
4-6	195	113	7 (47)	4 (25)	11 (36)
7-9	270	130	5 (33)	7 (45)	12 (39)
10-12	345	145	0 (0)	2 (12)	2 (6)
13-15	412	156	3 (20)	3 (18)	6 (19)

GMFCS Level	Boys n (%)	Girls n (%)	Total n (%)
I	9 (53)	9 (65)	18 (59)
II	7 (41)	4 (28)	11 (35)
III	1 (6)	0 (0)	1 (3)
IV	0 (0)	1 (7)	1 (3)
V	0 (0)	0 (0)	0 (0)

(Number of children, n (%), in relation to age, sex, and GMFCS level (GMFCS = Gross Motor Function Classification System.))

Sixteen children were treated with serial casting combined with BoNT injection (on the hemiplegic side) and 15 children were treated only with serial casting treatment. Group assignments were done according to the clinical recommendations of the same treating physician at the same outpatient pediatric rehabilitation hospital. All physical therapy sessions were performed by the same licensed physical therapist. Ethics committee approval was obtained from the Institutional Review Board of Children's Specialized Hospital, Mountainside, New Jersey, USA with issue number: E-736-12, March 1st, 2018. Consent was obtained from the patients and their parent(s) prior to the investigation.

2.2. Methods

GAITRite (Franklin, NJ, USA) is an instrumented walkway system used for collecting spatiotemporal parameters during walking on a 10-meter walkway at self-selected walking speed. The reliability and validity of the system have previously been shown in children with and without disabilities [3]. The average values of three consecutive strides were used for analysis. Data were collected at the beginning and at the end of the 8th week of the treatment.

Serial casting was administered to the affected sides of each patient and replaced weekly. The first data collection was done at the first visit before the earliest cast was administered. The final set of data was collected at the end of the eighth week when the last cast was removed.

Muscle selection, doses, and dilution rates were individualized for each patient based on body weight and severity of spasticity. BoNT was injected into the target muscle(s) of the affected sides under the guidance of electrical stimulation and ultrasound at the first visit to the hospital before the first cast was administered. Both groups received a physical therapy program of 2 hours per week before the new cast administration. Physical therapy included stretching weight bearing, balance, proprioception, and ambulation exercises. Step time (s), step length (cm), swing %, stance %, stride length (cm), cadence (steps/min) and velocity (cm/s) parameters were collected and compared for two groups.

2.3. Statistical Methods

Each patient performed the normal walking activity 5 times on the instrumented walkway. The averages of the five trials were analyzed and reported. All continuous variables were presented as mean ± SD and were subjected to statistical analysis. The Kolmogorov-Smirnov normality test was conducted to examine the distribution of the continuous variables. A paired samples t-test and independent samples t-test were used in the research. A paired-sample t-test was established to compare the mean differences between the pre and post-outcome measures of the two treatment groups. An independent samples t-test was used to evaluate the pre- and post-outcome measures of both groups. The statistical analysis was performed using SPSS (version 12, Chicago, IL). All analyses used a confidence interval of 95% and a significance level of <0.05.

3. Results

The health records of thirty-one participants were analyzed. No significant differences were found between age, gender, or the GMCFS level of the combined treatment group or serial

casting group. Improvements in cadence, step time, cycle time, and step length were not statistically significant. Looking at the GMFCS levels, the numbers of participants at levels I and II are similar, but the numbers of participants at levels III and IV were lower.

The baseline velocity of the combined treatment group was slower than the serial casting-only group (88±11.2 vs. 107±14.4 (cm/s), p=0.007), but the difference between the groups at completion was not significant (91±15.2 vs. 106±21.0 (cm/s), p=0.035). The swing phase percentage of the unaffected side for the combined treatment group has increased and showed a statistically significant difference between pre-treatment and post-treatment measures (M = 35.16 ±1.21; M = 32.46 ± 1.38; t (15) = 2.12, p = 0.049). Swing phase percentages of the affected side and stance phase percentage of the unaffected side of the serial casting-only group have increased and showed statistically significant differences between pre and post-treatment measures (M = 40.87± 0.57; M = 42.39±0.79, t (14) = -0.151, p = 0.032 respectively) and (M = 61.69± 0.73, M = 64.12± 0.76; t (14) = -5.261, p=0.001 respectively). The stance percentage of the unaffected side of the combined treatment group pre-intervention outcomes showed statistically significant differences compared to serial casting only group pre-intervention outcomes (M = 61.69± 0.73; M = 64.88±1.20; t (14) = -2.273, p = 0.039 respectively) (Figure 1).

The stride length of the unaffected and affected sides of the combined treatment group at pre-intervention did not show a statistically significant difference compared to post-intervention outcomes (M = 83.38±5.16 cm; M = 72.87±8.45 cm; p = 0.141 respectively). (Table 2)

Table 2: Means, SD of Spatiotemporal Measures for Combined Treatment (BoNT and Serial Casting) and Serial Casting Alone Groups

	Serial Casting Alone Group (n=15)													
	Step Time (s)		**Step Length (cm)**		**Swing %**		**Stance %**		**Stride Length (cm)**		**Cadence (steps/min)**		**Velocity (cm/s)**	
	pre	**post**	**pre**	**post**	**pre**	**post**	**pre**	**post**	**pre**	**post**	**pre**	**Post**	**pre**	**post**
Hemiparetic Side	0.47± 0.02	0.54± 0.04	49.82 ±2.05	50.39 ±3.05	40.87 ±0.57	42.39 ±0.79	59.17 ±0.57	58.03 ±0.84	98.40 ±3.54	100.56 ±5.47	135.33 ±4.67	127.68 ±6.11	107.59 ±14.4	106 ±21.66

Unaffected Side	0.43± 0.02	0.44± 0.03	48.17 ±1.93	51.08 ±2.62	38.32 ±0.73	35.84 ±0.76	61.69 ±0.73	64.12 ±0.76	98.54 ±3.45	101.43 ±5.33				

Combined Treatment (BoNT and Serial Casting) Group (n=16)														
	Step Time (s)		**Step Length (cm)**		**Swing %**		**Stance %**		**Stride Length (cm)**		**Cadence (steps/min)**		**Velocity (cm/s)**	
	pre	**post**	**pre**	**post**	**pre**	**post**	**pre**	**post**	**pre**	**post**	**pre**	**Post**	**pre**	**post**
Hemiparetic Side	0.51± 0.02	0.52± 0.03	43.29 ±2.80	43.53 ±3.65	42.32 ±0.90	44.28 ±1.11	54.44 ±3.29	55.73 ±1.11	82.88 ±5.18	72.16± 8.46	127.30 ±5.83	134.48 ±5.38	88.22± 11.2	91.31± 15.2
Unaffected Side	0.44± 0.02	0.40± 0.02	39.37 ±2.73	43.33 ±3.33	35.16 ±1.21	32.46 ±1.38	64.88 ±1.20	66.32 ±1.71	83.38 ±5.16	72.87± 8.45				
All data are presented as mean ± standard error. The spatiotemporal parameters were normalized to the leg lengths of the participants.														

4. Discussion

Options for improving the ambulation of children with CP and spasticity should be considered adeptly. Early, ideal, and thorough treatment is required for these patients to enhance motor capabilities and prevent bone abnormalities. The findings demonstrated that children with hemiplegic CP benefit further from serial casting in combination with BoNT injection therapy, particularly if the degree of stiffness is significant. To control the spatiotemporal parameters, such as the stance/swing percentages and stride length, combined treatment is more effective than serial casting alone.

It may be inferred from several studies and several decades of clinical use that BoNT and serial casting treatments, when used correctly and on time, enhance the spatiotemporal characteristics of children with CP's afflicted side. BoNT therapy decreases spasticity, results in less muscle strength loss [14], [15], and lowers the possibility of muscles or tendons extending. Similarly, serial casting improves ankle range of motion and lessens stiffness. In the absence of a fixed myostatic contracture, BoNT injection primarily meets expectations regarding spasticity by enabling dynamic contracture. To increase the ROM of the ankle joint, casting has been suggested as a possible treatment.

The findings of this study may be evaluated considering these limitations: (1) this retrospective study did not report the control group results; rather it investigated the

spatiotemporal parameters of children with CP, treated with serial casting with and without BoNT (2) the population size is relatively small, however, it satisfies the statistical power requirements and (3) the group assignments of the participants were not performed randomly, in fact, same clinician recommendation- depending on the severity of spasticity- was considered during group assignments for each participant. A further aim is to investigate the long-term effects of the interventions on a larger population.

5. Conclusions

This investigation suggests that for patients, who have poor ambulation quality, significantly unnatural spatiotemporal gait parameters, and significant spasticity at pre-intervention, BoNT in conjunction with serial casting is more effective for improving ambulation quality. Besides, if improved ankle ROM is the goal of the treatment, then serial casting is essential and should be included in the treatment plan because achieving the desired ankle ROM and therefore improving spatiotemporal parameter symmetry in a shorter period is critical for managing the surgical interventions more efficiently. If these interventions are insufficient, surgical interventions should be considered depending on the patient's medical condition, age, and physical development.

This exploratory study showed the efficacy of two treatments in terms of spatiotemporal parameters. The results do not provide a decisive sign of the effectiveness of serial casting used with or without BoNT, yet it suggests that patients may obtain improved spatiotemporal parameters at the completion of the combined treatment.

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Figure Legends

Figure 1: Bar graph comparing spatiotemporal parameters of Serial Casting and Serial Casting with BoNT Treatments. Solid black bars represent pre-treatment and dashed bars represent the post-treatment outcomes. The statistically different parameters are indicated with *.