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The Effectiveness of Adjunctive Therapies Following Botulinum Toxin Type A Injections in Children with Cerebral Palsy

Narantsetseg Tsegmid[1,2], Delgerjargal Dorjbal[3], Nasantogtokh Erdenebileg[4], Batchimeg Shirmen[1,2], Gerelmaa Zagd[5], Baljinnyam Avirmed[1,2]

[1]Department of Rehabilitation Medicine, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia; [2]Mongolia-Japan hospital, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia; [3]Department of Rehabilitation Medicine, Fujita Health University, Toyoake, Japan; [4]National Center for Maternal and Child Health, Ulaanbaatar, Mongolia; [5]Department of Pediatric Medicine, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia

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Corresponding Author
Narantsetseg Tsegmid (MD, MSc)
Department of Rehabilitation Medicine, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar 14210, Mongolia
Phone: +976-9975-5523
E-mail: narantsetseg.ts@mnums.edu.mn
ORCID: https://orcid.org/0000-0002-8132-0254

Objectives: To investigate the effectiveness of intermittent vs. continuous adjunctive therapies following BoNT-A injections for children with cerebral palsy (CP).

Methods: A quasi-experimental study was conducted with 80 participants with CP who received adjunctive therapies including physiotherapy and functional electrical stimulation after BoNT-A injections. The participants were randomly divided into two groups. In group A, half of the participants received intermittently adjunctive therapies. In group B, adjunctive therapies were organized continuously for another half. We measured changes in spasticity and dynamic spasticity used by the Modified Ashworth Scale and the Modified Tardieu Scale, and gross motor function used the Gross Motor Function Measure-88. Measurement of spasticity was carried out pre-injections and then 1- and 3-months post-injections. Measurement of gross motor function was organized pre- and post-injections.

Results: The effectiveness of BoNT-A injections presented significant improvement in spasticity and gross motor function when it was combined with adjunctive therapies. The continuous adjunctive therapies had a greater reduction of spasticity. Both intermittent and continuous adjunctive therapies had a significant improvement in gross motor function.

Conclusions: Our findings add to the evidence of the effectiveness of using different intervals of short-term adjunctive therapies for children with CP after BoNT-A injections.

Keywords: Neurotoxin A, Rehabilitation, Electrical stimulation, Physiotherapy, Spasticit

Introduction

Botulinum toxin type A (BoNT-A) is a first-line and standardized treatment for reducing spasticity in children with Cerebral Palsy (CP) [1,2]. In particular, Koman et al. in 1993 [3] and Graham et al. in 1994 [4] first reported evidence on the effectiveness and safety of BoNT-A injections in managing dynamic spasticity for children with CP. Spastic CP is the most common cause of motor disability in childhood [5,6]. The disability of a child, classified by the Gross Motor Function Classification

System (GMFCS) [7], provides a common language to describe the functional performance and to allow a more accurate subject stratification for research and clinical practice [7-10]. Besides, the international consensus [11,12] recommends the appropriate use of BoNT-A injections including treatment algorithms, doses, injection techniques, target muscles, and their safety and efficacy in the pediatric population. In light of this consensus [11,12], several reliable measurement tools [10,13-16] are widely applied for children with CP. Specifically, the Gross Motor Function Measure (GMFM-88) [13] is a clinical observational tool to measure changes in the gross motor function [10,17]. For target muscle selection, the Modified Ashworth Scale (MAS)[15] and the Modified Tardieu Scale (MTS) [14] are two clinical rating scales to quantify spasticity [11,14-16]. Regarding the injection techniques, many researchers [18-21] revealed that the use of ultrasound for children with CP is crucial helpful to find targeted muscles for BoNT-A injections, such as avoiding the wrong target muscles, reducing tone, relieving pain or not requiring sedation [22-24]. As discussed in the latest consensus statement on the use of BoNT-A injections for pediatric patients [11] and other empirical studies [23-28] that suggest a combination of adjunctive therapies, especially physiotherapy, enhances the effect of ultrasound-guided BoNT-A injections [25,26,28]. Since BoNT-A injections are together with physiotherapy, they play a key role in effecting changes in lived health (i.e., activities and participation) [2,25,28,29] in line with the International Classification and Functioning (ICF) [30,31]. Physiotherapy following BoNT-A injections can consist of physical exercises that aim to reduce lower limb spasticity, improve muscle strength and gross motor function, and also to prevent secondary complications [2,25,32-34]. Besides, some studies [35-38] found that functional electrical stimulation (FES) has been used as an adjunct to physiotherapy to support the effectiveness of BoNT-A injections and the strength of antagonistic muscles. However, depending on the application concerning intervals (e.g., timing and frequency), the effectiveness of adjunctive therapies may change [26,39,40]. Although adjunctive therapies can enhance the effectiveness of BoNT-A injections [27,35,37], there is currently no consensus on the content and interval [11,26,40-42]. To the best of our knowledge, existing research [11,24,28,36-38,40,42] shows that the combination of spasticity management that comprises BoNT-A injections and physiotherapy together with FES can result in the maximized effectiveness for children with complex health conditions such as CP. Further clinical studies are needed, particularly to examine adjunctive therapies used in the combination with BoNT-A injections [1,26,39-41]. In Mongolia, except for some studies [43,44] on the outcomes of rehabilitation of adults with stroke, there is a lack of studies on the outcomes of rehabilitation of children, including cerebral palsy. Hence, this study contributes to the knowledge base on post-injection spasticity management of evidence-based interventions to improve the gross motor function of children with CP. Specifically, the aim of our study was to investigate the effectiveness of different intervals including intermittent vs. continuous adjunctive therapies following BoNT-A injections for children with CP.

Material and Methods

Study design

We used a quasi-experimental study design to compare the results of 2 methods of rehabilitation after BoNT-A injection. In group A, half of the participants received intermittently adjunctive therapies. In group B, adjunctive therapies were organized continuously for another half. We followed two group participants who received adjunctive therapies after BoNT-A injections forward through time and to collect data. We evaluated the outcome of adjunctive therapies before BoNT-A injection and during adjunctive therapies at 1 and 3 months and compared the two groups. A quasi-experimental study is an intervention study and differs from a clinical trial in that it differs in randomization and blinding. The interventional design can evaluate our study aims concerning both therapeutic agents (e.g., treatments) and prevention (e.g., management), and also is more likely to be free from biases [45,46].

Sampling and participants

A total of 315 children with CP who had visited the outpatient rehabilitation clinic at the Mongolia-Japan Hospital of the Mongolian National University of Medical Sciences, from November 2018 to January 2022, were registered and screened. We conducted a clinical examination of all these children and reviewed their medical records. Our clinical examination included the measurement of spasticity using the MAS [15] and MTS [14], and also the assessment of gross motor function using the GMFCS [7]. Spasticity is quantified with the MAS and MTS [16].

The GMFCS is a five-level classification that distinguishes abilities and limitations in gross motor function based on a child's current self-initiated movements [7]. The medical records presented age, gender, diagnosis, and history of treatment or intervention. Based on the medical records and the clinical examination, the following inclusion criteria were applied: (a) children aged between 24-144 months, (b) who had been diagnosed with spastic hemiplegic or diplegic CP, (c) were able to walk and stand with or without assistance (GMFCS level II-III), (d) had spasticity interfering with the functioning including only toe walking, scissoring, and crouch gait, (e) had no fixed contractures, and (f) were able to understand and follow commands. We excluded children who received chemo denervation treatments within the last six months, had previously undergone a selective rhizotomy or an orthopedic surgery, and had been diagnosed with epilepsy. Besides, children with allergies to the toxin were excluded. Finally, 80 children met the inclusion criteria and were invited to participate in our study.

Intervention

According to the recent international consensus on the use of BoNT-A injections [11], all 80 participants had once ultrasound-guided injections of BoNT-A (Neuronox®, Medytox Inc., Seoul, Korea) to the targeted spasticity muscle. A total dose ranged between 50 and 380 units (U) of BoNT-A (0.8 to 3.6 U/kg), using 4 ml of normal saline to provide a solution containing 50 U/ml. Furthermore, injected muscles of every participant were different as a result of the spasticity measurement. Particularly, injected muscles were the medial and lateral heads of the gastrocnemius, the medial hamstrings, and the hip adductors. In each muscle, two site injections were performed (1.5 to 3.6 U/kg). Moreover, other injected muscles included the tibialis posterior, which was injected at one site (0.8 to 1.5 U/kg).

Within 30 minutes after the ultrasound-guided injections of BoNT-A, all participants received the same adjunctive therapy (i.e., physiotherapy and FES). Afterward, the participants were randomly divided into group A (n=40) and group B (n=40). In both groups, the interval of conducting the adjunctive therapy was diverse. Participants in group A received the adjunctive therapy intermittently (i.e., 5 times per week in the first month, no therapy in the second month, and 2 times per week in the last month). Group B participants received the adjunctive therapy continuously (i.e., 2 times per week throughout 3 months). Physiotherapy techniques covered various exercises to encourage muscle strengthening and stretching. These exercises lasted between 20 and 30 minutes for each participant. FES was applied to the injected muscles with the aim of boosting BoNT-A injections 1-week post-injection. From the second week, FES was applied to the antagonistic muscles to improve their strengthening. FES lasted 30 minutes for each participant.

Outcome measures

We performed the measurement of changes in (1) spasticity and (2) gross motor function in both groups A and B. For the study participants, pre- and post-injection measurements are essential to review changes in spasticity and gross motor function [22,24].

(1) Measurement of changes in spasticity

Lower limb spasticity was measured using the MAS [15], and dynamic spasticity was measured using the MTS [14]. The measured muscles were bilateral or unilateral hip adductor, knee flexor, and plantar flexor. Muscle tone was measured using the MAS [15], a 6-point rating scale with a range of 0 to 4. To analyze statistically, a MAS grade of 1+ was altered to 2. The MAS grades of 2, 3, and 4 were also altered to 3, 4, and 5. For the MTS [14], two levels of lower limb joint angle were measured after slow and fast stretching of the joint, concerning R2 and R1 angles. For the period of a rapid stretch of the spastic lower limb muscle, R1 was identified as the point in the ROM at which a first catch was felt. R2 was identified as the total passive ROM. Dynamic spasticity was characterized by R2-R1. We used manual goniometry to measure the joint angles for R1 and R2. Spasticity and dynamic spasticity were assessed pre-injections and then 1- and 3-months post-injections.

(2) Measurement of changes in gross motor function

We measured changes in the gross motor function of the participants using the GMFM-88 [13]. The GMFM-88 is a main observational measure that was validated to assess the gross motor function of a child with CP. The 88 items of the GMFM are grouped into the following five dimensions: (A) lying and rolling, (B) sitting, (C) crawling and kneeling, (D) standing, and (E) walking, running, and jumping. Besides, the items are scored on 4-point ordinal scales (0=cannot initiate, 1=initiates, 2=partially completes item, and 3=completes item independently). Each participant was screened to allow a maximum of three trials for each item [13]. Furthermore, changes in the gross motor function of the participants were assessed through observation by giving

verbal instructions in the physiotherapy room and using some necessary equipment (e.g., mats, stairs, and balls). We organized this measurement pre-injections and then 3 months post-injections.

Testing protocol and reliability

To ensure the reliability of measurements on the spasticity [14-16] and gross motor function [13], four health professionals independently performed. These health professionals had assessed spasticity and gross motor function for 5-10 years of experience and also attended several trainings prior to the start of this study. Two of them were rehabilitation doctors, who measured spasticity. The MAS [15] was used to measure each participant and then the MTS [14] was used 30 minutes afterward. With a 30-min rest period between measurements, inter-rater reliability was examined [16]. The other two were physiotherapists, who assessed gross motor function. The GMFM-88 [13] lasted approximately 1 hour. All results were recorded separately for each rater and blinded for the assessment. A third rehabilitation doctor compiled and analyzed the data of these four raters. The measurements were conducted while the participants were emotionally stable (e.g., with no fear). Re-test reliability for each spasticity measurement [16] (i.e., pre-injections, 1- and 3-months post-injections) and the GMFM-88 [13] (i.e., pre-injections and 3 months post-injections) was repeated at the next day after.

Statistical analysis

We recorded the following information on our study form and then exported it into Excel: age; gender; weight; CP type; GMFCS level; target muscle group; dose of BoNT-A injections; pre-injection and 1- and 3-months post-injection assessment using the MAS and MTS [16]; and pre- and post-injection assessment using the GMFM-88 [13]. Two independent researchers checked all exported data for bias. Afterward, data were analyzed using STATA 16 software.

Descriptive statistics were presented as mean and standard deviation (SD) for continuous variables. Categorical variables were expressed as numbers and percentages. The distribution of continuous variables was calculated by the Kolmogorov-Smirnov test. Pearson's chi-square test was used to determine differences between categorical variables (i.e., gender, CP type, and GMFCS level) in both groups. Furthermore, we used Student's t-test to describe the difference in the mean of continuous variables between the two groups. Repeated measure analysis of variance (repeated measure ANOVA) was used to assess changes over three months for each group. In addition, a mixed effect model in repeated measure ANOVA was used to assess whether the therapy method had an effect on the results 3 months post-injection. The least significant difference (LSD) test is a multiple-comparison correction used when several dependent or independent statistical tests are being performed simultaneously. The least significant difference (LSD) test is used in the context of the analysis of variance when the F-ratio suggests rejection of the null hypothesis H 0, that is, when the difference between the population means is significant. Moreover, statistical differences in the GMFM-88 [13] pre- and post-injection were calculated using the Paired sample t-test. If the p-value of the hypothesis test was less than 0.05, the alternative hypothesis is considered statistically significant.

Ethics

This study received ethics approval from the Mongolian National University of Medical Sciences in Ulaanbaatar, Mongolia (2018/3-16). A parent of each participant confirmed their interest and signed an informed consent form before our prospective interventional study.

Results

1. Participant characteristics

A total of 80 participants were invited to attend and completed the present study. Table 1 shows the characteristics of the participants. Age of the participants ranged from 24 to 128 months with a mean age of 66.7±24.5 months. In both groups, there was no significant difference in general characteristics and the dose of BoNT-A injections (Table 1).

Table 1. Characteristics of the study participants in both groups.

Demographics, baseline clinical characteristics, and BoNT-A injection doses	Group A mean±SD or n (%) (n=40)	Group B mean±SD or n (%) (n=40)	p value
Age (months)	64.3 (25.4)	69.1 (23.5)	0.262
Gender (male)	27 (67.5%)	21 (52.5%)	0.171
Weight (kg)	16.6 (3.7)	19.8 (7.5)	0.029
CP type (diplegia)	33 (82.5%)	36 (90.0%)	0.301
GMFCS level (II)	15 (37.5%)	18 (45.0%)	0.275
BoNT-A injection dose			
GCM	3.6±0.4	3.0±0.5	0.051
TP	1.0±0.3	1.1±0.3	0.241
MH	1.5±0.1	2.7±0.4	0.118
HA	3.0±0.5	2.7±0.5	0.085

Group A -Intermittently adjunctive therapies. Group B -Continuously adjunctive therapies. GMFCS-gross motor function classification system. BoNT-A- botulinum toxin-A.

2. Changes in spasticity

Table 2 presents changes in spasticity of the participants in both groups. The tone of the lower extremity was measured by the MAS and MTS to show statistically significant changes. Post-hoc analysis demonstrated a significant reduction in spasticity and dynamic spasticity at both 1- and 3-months post-injection compared to pre-injection in each group (p=0.000). Compared between the two groups, B group showed a significantly greater reduction in spasticity and dynamic spasticity of the ankle plantar flexors with knee flexion and extension as well as the hip adductor with knee flexion and extension 3 months post-injection (Table 2, 3).

Table 2. Changes in spasticity of the participants in both groups

Variables	Group A Mean (SD)			p value[a]	Group B Mean (SD)			p value[a]	Between groups p value[b]
	Pre-injection	1 month post-injection	3 months post-injection		Pre-injection	1 month post-injection	3 months post-injection		
MAS (scores)									
Ankle PF with knee flexion	2.89 (0.67)	1.75 (0.73)	1.58 (0.6)	0.000	2.61 (0.59)	1.53 (0.6)	1.42 (1.48)	0.000	0.042
Ankle PF with knee extension	3.72 (0.45)	2.67 (0.53)	2.44 (0.61)	0.000	3.55 (0.55)	2.5 (0.6)	1.92 (0.67)	0.000	0.000
Popliteal angle	3.2 (0.8)	2.3 (1.3)	2.3 (1.01)	0.000	3.3 (0.8)	2.2 (1.2)	1.8 (1.2)	0.000	0.762
Hip Add with knee flexion	2.83 (0.65)	1.67 (0.71)	1.6 (0.67)	0.000	2.63 (0.69)	1.59 (0.64)	1.41 (0.64)	0.000	0.421
Hip Add with knee extension	3.73 (0.45)	2.73 (0.45)	2.62 (0.56)	0.000	3.44 (0.51)	2.48 (0.58)	2.04 (0.71)	0.000	0.001
MTS – R1 (degrees)									
Ankle PF with knee flexion	-7.78 (9.74)	7.78 (8.32)	7.64 (7.41)	0.000	-2.24 (10.82)	10.92 (7.61)	15 (6.26)	0.000	0.031
Ankle PF with knee extension	-14.21 (11.54)	-4.58 (7.69)	-2.08 (8.05)	0.000	-14.21 (11.54)	0.79 (8.66)	6.84 (8.09)	0.000	0.021
Popliteal angle	50.6 (16.4)	35.0 (16.3)	27.4 (15.6)	0.000	55.8 (16.3)	33.3 (17.5)	28.3 (15.7)	0.000	0.612

Hip Add with knee flexion	28.17 (8.15)	39.67 (9.19)	38.33 (8.84)	0.000	32.04 (9.73)	43.15 (9.32)	44.26 (9.48)	0.000	0.036
Hip Add with knee extension	15.5 (6.61)	29.33 (8.17)	27.83 (8.48)	0.000	16.48 (7.82)	27.78 (8.13)	32.04 (9.93)	0.000	0.044
MTS - R2 (degrees)									
Ankle PF with knee flexion	15 (7.93)	25.56 (7.35)	23.47 (6.74)	0.000	20 (6.04)	27.76 (6.01)	28.95 (5.22)	0.000	0.043
Ankle PF with knee extension	0.97 (8.6)	12.22 (7.31)	11.67 (6.44)	0.000	7.24 (8.44)	16.58 (7.36)	19.47 (6.34)	0.000	0.013
Popliteal angle	25.0 (16.7)	15.0 (10.0)	11.8 (9.7)	0.000	24.2 (16.6)	15.0 (11.0)	11.7 (9.8)	0.000	0.511
Hip Add with knee flexion	49.33 (10.81)	59.0 (9.04)	56.33 (8.5)	0.000	51.85 (10.57)	60.37 (8.98)	60.56 (8.81)	0.000	0.046
Hip Add with knee extension	31.17 (10.31)	43.33 (9.32)	40.83 (10.4)	0.000	31.11 (9.84)	43.15 (10.3)	46.11 (9.23)	0.000	0.053

MAS-modified Ashworth scale, MTS-modified Tardei scale. Ankle PF: ankle plantar flexors; Hip Add: hip adductors, Group A - Intermittently adjunctive therapies. Group B - Continuously adjunctive therapies, a-Repeated ANOVA test, b- Mixed effect model

Table 3. Adjustment for multiple comparisons: The least significant difference (LSD) test after repeated measure ANOVA

Variables	Group A			Group B		
	P-value of measurements differences					
	Pre-injection and 1 month post-injection (p value)	Pre-injection and 3 month post-injection (p value)	1 month and 3 months post-injection (p value)	Pre-injection and1 month post-injection (p value)	Pre-injection and 3 month post-injection (p value)	1 month and 3 months post-injection (p value)
MAS (scores)						
Ankle PF with knee flexion	0.003	0.000	0.046	0.001	0.000	0.001
Ankle PF with knee extension	0.012	0.000	0.056	0.036	0.000	0.003
Popliteal angle	0.006	0.000	0.097	0.001	0.000	0.045
Hip Add with knee flexion	0.031	0.000	0.088	0.001	0.000	0.023
Hip Add with knee extension	0.041	0.000	0.046	0.012	0.000	0.011
MTS – R1 (degrees)						
Ankle PF with knee flexion	0.036	0.000	0.165	0.041	0.000	0.313
Ankle PF with knee extension	0.002	0.000	0.025	0.000	0.000	0.001
Popliteal angle	0.000	0.000	0.017	0.000	0.000	0.001
Hip Add with knee flexion	0.000	0.000	0.000	0.000	0.000	0.000
Hip Add with knee extension	0.000	0.000	0.002	0.000	0.000	0.000
MTS - R2 (degrees)						
Ankle PF with knee flexion	0.000	0.000	0.094	0.000	0.000	0.033
Ankle PF with knee extension	0.000	0.000	0.056	0.000	0.000	0.002
Popliteal angle	0.000	0.000	0.035	0.000	0.000	0.010
Hip Add with knee flexion	0.000	0.000	0.061	0.000	0.000	0.205
Hip Add with knee extension	0.000	0.000	0.134	0.000	0.000	0.503

Group A - Intermittently adjunctive therapies. Group B - Continuously adjunctive therapies. MAS- modified Ashworth scale. MTS- modified Tardei scale. Ankle PF-ankle plantar flexion. Hip add-hip adductor.

3. Changes in gross motor function

Table 3 summarizes changes in gross motor function of the participants in both groups. 3 months post-injection, gross motor function of the participants in each group showed statistically significant improvement. However, only for dimension A (i.e., lying and rolling) there was no statistical difference in each group pre- and post-injection. Between the two groups, changes in the GMFM-88 pre- and post-injection were no significant differences (Table 4).

Table 4. Changes in gross motor function of the participants in both groups.

GMFM-88 dimensions	Group A Mean (SD)		p value	Group B Mean (SD)		p value
	Pre-injection	Post-injection		Pre-injection	Post-injection	
Lying and Rolling (A)	50.5 (3.16)	50.6 (2.53)	0.323	50.98 (0.16)	51.0 (0.1)	0.324
Crawling and kneeling (B)	55.5 (9.97)	56.7 (8.61)	0.011	56.85 (8.82)	58.33 (5.02)	0.026
Sitting (C)	34.65 (10.43)	36.5 (9.67)	0.000	36.33 (8.12)	38.85 (6.55)	0.000
Standing (D)	16.35 (11.61)	18.93 (11.29)	0.000	20.85 (12.69)	25.55 (10.97)	0.000
Walking, running, jumping (E)	16.18 (19.02)	19.05 (20.01)	0.000	19.7 (17.09)	25.53 (19.21)	0.000
Total	173.18 (44.01)	181.78 (42.44)	0.014	184.7 (38.72)	199.25 (35.31)	0.021

Group A - Intermittently adjunctive therapies. Group B - Continuously adjunctive therapies. GMFM – gross motor function measurement.

Discussion

The present study has shown that the comparison of the effectiveness between intervals as intermittent vs. continuous adjunctive therapies following BoNT-A injections led to reductions in spasticity and improvements in gross motor function in children with CP. Our statistical analysis revealed the following important findings. Firstly, the effectiveness of BoNT-A injections presented significant improvement in changes in spasticity and gross motor function after three months when it was combined with adjunctive therapies including physiotherapy and FES. Secondly, while continuous adjunctive therapy had a stronger effect on lower limb spasticity and dynamic spasticity, both intermittent and continuous adjunctive therapies had a significant effect on gross motor function. Overall, our results may add to the current knowledge to optimize spasticity management for pediatric CP rehabilitation. Similar to the findings of previous research [25,29,33,34,47,48], our study confirmed a statistically significant improvement of changes in spasticity and gross motor function as a result of the combined use of adjunctive therapies and BoNT-A injections. Some study results showed significantly greater improvement in GMFM scores when BoNT-A treatment was combined with a physical therapy program than when BoNT-A was used alone. Before BoNT-A injection, mean GMFM values were 58.1 ± 10.9, four weeks after injection they were 61.8 ± 11, and six weeks later they were 65.2 ± 1 in the group in which botulinum toxin A injection was combined with physiotherapy. In our study, the GMFM-88 total score was 184.7±38.72 before injection and 199.25±35.31 at 12 weeks after BoNT-A injection combined with physiotherapy and FES. Moreover, the international consensus statement [11] recommends those adjunctive therapies following BoNT-A injections such as physiotherapy, serial casting and transcutaneous electrical nerve stimulation for limb hypertonicity. Indeed, BoNT-A injections should only be given as part of a comprehensive approach for reducing spasticity [9,27]. Besides, the latest worldwide survey [26] found that the majority of clinicians often used physiotherapy as an adjunct, especially, active exercises and stretching programs within 30 minutes of BoNT-A injections. In addition to the evidence on the combination of physiotherapy [25,28,29], many other studies [35,36,39,40,42] suggested that FES should be applied to the injected muscles rapidly after BoNT-A injections. Because FES may maximize the effectiveness of BoNT-A injections in children with spasticity [36,38]. The systematic analysis [35] also highlighted the duration of FES coincides with the timing of BoNT-A injections, ranging from 30 to 60 minutes. However, the worldwide survey [26] describing the context of developing and developed countries addressed several barriers in the provision of adjunctive therapies (e.g., physiotherapy, casting, and FES).

For instance, lack of time, financial resources, and little evidence [26,27,39,40]. In the scope of the existing studies [25,28], our analysis demonstrated that continuous adjunctive therapies had a robust effect on the reduction in spasticity. But the international consensus [11] as well as clinical studies [28,39,40] summarized that there is a need for further evidence on the exact intervals of adjunctive therapies to boost the effectiveness of BoNT-A injections. Nonetheless, some systematic reviews [25,41] propose that short-term and high-intensity adjunctive therapies have the effectiveness following BoNT-A injections. Though, it is crucial to conduct a clinical assessment using by tools to measure changes in spasticity and gross motor function that are feasible for young children who are too young or unable to be involved in some evaluation processes through the Rehab-Cycle® [13-16]. Like the other clinical studies [2,23,24,32], we used widely applied tools and scales to measure changes in spasticity and gross motor function of children with CP. Another recent systematic review [1] endorsed that the MAS and MTS are still the most widely used in measuring spasticity in clinical settings. Nevertheless, there are limitations of these scales, in terms of validity and reliability issues [16,49]. On the one hand, some studies [16,49] revealed inadequate reliability for the MAS to assess lower limb spasticity between raters. On the other hand, according to various researchers [15,49,50], when the same rater repeats the measurement, there is acceptable reliability for the MAS. Moreover, studies emphasized that these two scales can be used in conjunction to measure lower limb spasticity for optimizing therapy option [14,15,49]. In addition to the measurement of the spasticity [14-16], it is necessary to assess changes in the gross motor function [13]. Many studies [13,17,51,52] and the international consensus statements [11,12] presented that the GMFM-88 is valid and reliable for clinically meaningful changes in gross motor function. In research using BoNT-A injections for samples with CP, the GMFM-88 serves as the primary outcome measurement [13,51], as shown by our results.

Several limitations of this study should be considered. Firstly, in spite of recruiting most of the children with CP who visited our rehabilitation clinic for BoNT-A injections, this study was conducted in a single setting. Secondly, only one type of physiotherapy technique was performed. Thus, the results cannot be generalized to all physiotherapy techniques. Finally, the findings only captured short-term spasticity management. Despite these limitations, a key strength of our study is the use of a standardized clinical measurement tool (i.e., GMFM-88) [13] and rating scales (i.e., MAS and MTS) [16] in the relatively large sample that enabled us to describe changes in spasticity and gross motor function undergoing interventions [2,24]. To consider the limitations of the tools and scales in our study [13,16], we conducted inter-rater and re-test after each measurement with a short follow-up. Also, each measurement was performed by an independent health professional and blinding was done by a third professional.

Future studies may focus on better understanding the origins of changes in spasticity and gross motor function to investigate the long-term or priority efficacy of various adjunctive therapies. It also needs to be investigated whether the effect of combined BoNT-A injection with complementary therapies depends on the age and GMFCS level of the child.

Conclusion

Our findings add to the evidence of the effectiveness of using various intervals of short-term adjunctive therapies, including physiotherapy and FES for children with CP who had BoNT-A injections.

Conflict of Interest

The authors state no conflict of interest.

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