Intensive Intermittent Physical Therapy in Infants with Cerebral Palsy: A Randomized Controlled Pilot Study

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ABSTRACT: **Background:** The effectiveness of intensive versus standard physical therapy for motor progress in children with cerebral palsy is controversial. Sitting acquisition is considered an important developmental milestone.

Objectives: To assess the acquisition of sitting and gross motor progress in infants with cerebral palsy treated with intermittent intensive physical therapy as compared to a matched group treated with a standard physical therapy regimen.

Methods: We conducted a randomized controlled crossover study in 10 infants aged 12–22 months with cerebral palsy; 5 were assigned to the intensive intermittent therapy group and 5 to the control group. After 4 weeks of baseline intervention, the intervention program was administered to the experimental group for 8 weeks and the regularly scheduled weekly program to the comparison group, targeting sitting as the treatment goal. Thereafter the comparison group crossed over. The Gross Motor Function Measure 66 and 88 (GMFM 66 and 88) were used at 4 week intervals.

Results: The intermittent intensive regimen yielded a mean improvement of 7.8% as compared to 1.2% with the standard treatment. However, these results were attributed to infants with a low functional level only ($P < 0.01$).

Conclusions: Goal-directed intensive intermittent regimen could possibly be beneficial in infants with a low functional level.

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KEY WORDS: cerebral palsy (CP), physical therapy, sitting, randomized trial

To date there is no compelling evidence on the type and length of therapy for children with cerebral palsy. It was found that a high-frequency physical therapy regimen, regardless of the type of intervention, enhances treatment results [1,2]. The few studies that investigated the effectiveness of long-term intensive physical therapy treatment in children with CP did not find a significant benefit [3]. Investigating an intensive regimen for a 6 month period, Bower et al. [3] noted a relatively low participation rate due to the difficulties inherent in this regimen [3]. Trahan and Malouin in their uncontrolled study in five children found a significant improvement in motor scores after an intensive intermittent intervention [4]. In most studies examining the effectiveness of treating children with CP the age range of the subjects was 2–12 years [5].

Because of the great variation in age and the level of CP severity, it is difficult to draw clear conclusions regarding the appropriate therapy intensity required for the acquisition of motor skills in infants with CP. Determining the intensity of therapy in children younger than 2 years old is crucial since this developmental period is characterized by increased neurological plasticity, a condition in which it might be possible to change the functional level before faulty motor patterns and habits are formed [6]. The excess of synapses for future selection, rising to approximately twice that in the adult brain by age 2 years, has also been demonstrated [7]. Evidence for brain plasticity and specifically motor systems was derived from studies in cerebral palsy that used constraint-induced movement therapy and functional imaging methodology [8].

Bower and colleagues [3] found that defining one central treatment goal increases the effectiveness of treatment. Sitting acquisition in young infants with CP usually occurs between the age of 12 and 24 months [9]. Achieving functional ability in sitting is important for children with CP since they spend a significant amount of time sitting even if they have not acquired any other form of mobility [10-12]. The ability to sit is an indication of the functional level of the child with CP. A child with a low functional level is unable to sit independently [13,14]; therefore, sitting constitutes a suitable treatment goal for infants with CP [11,15].

The purpose of this study was to examine the effect of intensive intermittent physical therapy on the acquisition of independent sitting. Based on the expected early-age brain plasticity enhanced by intensely administered exercises on one hand and the importance attributed to sitting acquisition for later development on the other, we hypothesized that there would be a greater improvement in sitting acquisition in a group treated with the intensive intermittent regimen as compared to a matched group of children treated with a standard regimen.

CP = cerebral palsy

PATIENTS AND METHODS

The parents agreed to participate in the study following newspaper advertisements as well as announcements at the various treatment centers throughout the country. The study group comprised 10 infants with CP (2 of whom were twin boys and 2 were twin girls) [Table 1] aged 12 to 24 months. The inclusion criteria were infants under age 24 months who had not yet acquired independent sitting. Exclusion criteria were: a) infants with medical problems (other than cerebral palsy), b) infants awaiting hospitalization or surgery or who experienced either of these within 6 months prior to the study, c) infants with a seizure disorder or a severe sensory deficit, and d) infants who required orthotic devices in their first year of life. Matching was based on gestational age, type of cerebral palsy, developmental functional level, the scores obtained by the subjects in the GMFM (Gross Motor Function Measure 66 and 88 in dimension B), and the classification of the subjects according to the GMFCS (Gross Motor Function Classification System). The study participants were randomly allocated to an experimental (E) or matched comparison group (C) immediately after the first 4 weeks of regular treatment using a card draw by an independent staff member.

The study was approved by the Helsinki Committee of the medical center. Both parents of all infants signed an informed consent prior to participating in the study and agreed to publication of the results.

Table 1. Characteristics of CP infants and control

Subject	Gender	Age (mos)	GMFC	Tonus	Type of CP	GMFM-66 BL	GMFM-88 Sitting
Experimental group							
2	F	12	V	Mixed	Quadriplegia	20.5	8.3
4	F	24	V	Mixed	Quadriplegia	22.6	10
6	F	12	V	Spastic	Quadriplegia	26.6	18.3
8	M	14	V	Mixed	Diplegia	27.3	20
10	F	12	III	Spastic	Diplegia	39.4	31.6
Mean		14.8				27.3	17.6
Comparison group							
1	F	15	V	Mixed	Quadriplegia	19.7	15
3	F	22	V	Spastic	Quadriplegia	17.1	11.7
5	M	22	V	Mixed	Quadriplegia	21.2	13.3
7	M	14	IV	Mixed	Diplegia	34.3	33.3
9	F	21	III	Spastic	Diplegia	38.9	23.3
Mean		18.8				26.2	19

F = female, M = male, GMFCS = Gross Motor Function Classification System, GMFM = Gross Motor Function Measure (66 = total score, 88 = sitting domain), CP = cerebral palsy, BL = baseline, Quadriplegia = all four limbs equally involved, Diplegia = lower limbs involved more than upper limbs

Following the child's assignment to the group each subject's baseline function (gross motor achievements) was remeasured with GMFM 66 [16], GMFM 88 [17] and GMFCS [18]. These assessments were conducted prior to the start of the intervention and every 4 weeks thereafter. Young infants with cerebral palsy classified as GMFCS levels IV-V are unable to maintain a sitting position without a caregiver's support. Those at GMFCS level III have a partial ability to maintain independent sitting and have difficulty reaching out of and resuming the support base, e.g., when reaching for an object [13,14].

- **Baseline Phase (A):** a 90 minute treatment was administered to each infant once a week for 4 weeks by the same physical therapist.
- **Intervention Phase (B):** group E received one therapy session for 4 consecutive days in one week with a treatment regimen identical to that applied during the baseline phase followed by a 3 week respite during which no intervention was administered. The same schedule was repeated during the second 4 week period (B2). At the end of each month an assessment using GMFM 66, 88 (Dimension B) and GMFCS was conducted. During this period (B,B2), the comparison group C was treated for 8 weeks once a week (A1,A2) and evaluated with the same measurement tools applied in group E. Following the first 8 week phase, the subjects of group C crossed over to be treated with the experimental intensive treatment regimen for 8 additional weeks (C1,C2) followed by the same assessments as in the previous phase.

To assess the maintenance of the achievements, 4 weeks after the intervention – while the infants resumed their regular treatment at the child development center – the children from the experimental group were evaluated using the same measurements.

The intervention was provided at the children's homes or daycare center with the attendance of a parent. Each intervention session combined three components, as proposed by Bower [3]:

- the manual treatment component, which used sensory techniques guiding the infant's movement by means of graded stimulation, as practiced with the Neuro Developmental Treatment approach [19]
- the training exercise component, which focused on helping the subjects perform staged development-related functions – rolling over, sitting and standing, with an emphasis of sitting
- the management component, which consisted of guidance for the parent or assistant with handling and positioning within the scope of daily activities at home (playing, eating, locomotion) [19]. Parents in both groups were encouraged to continue the program at home.

GMFM = Gross Motor Function Measure
GMFCS = Gross Motor Function Classification System

MEASUREMENTS

The following standardized and validated scales [17] were used:

- GMFM 88 [17], which includes 88 gross motor items organized into five dimensions. Each item is scored on a four-point ordinal scale. Only scores obtained for the sitting, dimension B, were applied in the present study [20]
- GMFM 66 [21,22], with a scale score ranging from 0 (expressing least ability) to 100 (expressing highly developed motor skills).

STATISTICAL ANALYSIS

Analysis was conducted on dimension B (sitting) scores from the GMFM 88 and the scores obtained from the GMFM 66. The following items were analyzed: changes in the mean achievement in the various research phases, changes in the sitting score, and an examination of the change trend over time. Analysis of variance and the Tukey test were employed.

The hypothesis whereby the improvement score of the experimental group for sitting was higher than the comparison group's score following the period before crossing over was tested with the formula: (B2E-AE)-(AE-BLE) => (A2C-AC)-(AC-BLC), where B2E = after 8 weeks intervention in group E, AE = after 4 weeks of baseline in group E, BLE = baseline in the experimental group E, A2C = after 8 weeks standard routine treatment in group C, AC = after 4 weeks of baseline in group C, and BLC = baseline in group C.

RESULTS

The characteristics and GMFM scores of the two groups are depicted in Table 1. The magnitude of improvement observed in group E using the GMFM 88 following phase B as compared to phase A ranged between 0.7 (7%) and 8.9 (28.33%) (average improvement of 13.9, 17%) [Table 2]. The improvement in the GMFM 88 for group C at the end of phase A2 relative to phase A ranged between 0.4 (3.33%) and 12.7 (38.34%) in three subjects, while no change in one subject and regression in another were observed (average improvement of 3.4, 12%) [Table 2]. These findings were not statistically significant. Using the formula to identify intervention effect suggests an increased benefit from the experimental intervention in group E, 1.3 (SD 1.1) (7.8%) as compared to the comparison intervention in group C, 0.2 (SD 1.7) (1.2%). This result was not statistically significant.

ANOVA demonstrated a statistically significant difference in the extent of the change at the end of phase B as compared to phase A between the various function levels [$F(2,4) = 28.58$, < 0.01]. The Tukey test to assess the origin of the difference revealed that infants at level V improve significantly more than those at levels III and IV. No statistically significant difference was found between the scores of level III infants and those of level IV infants.

Table 2. Maximal achievement percentage attained at sitting

Experimental group					
Subject	**BL**	**A**	**A-BL**	**B**	**B-A**
2	8.3	10	1.6	20	10
4	18.3	20	1.7	26.6	6.6
6	10	10	0	0	-10
8	20	43.3	23.3	66.6	23.3
10	31.6	51.6	20	80	28
Mean	17.6	27	9.3	44	17
Comparison group					
Subject	**BL**	**A**	**A-BL**	**A2**	**A2-A**
1	15	18.3	3.3	18.3	0
3	11.7	18.3	6.5	16.6	-1.7
5	13.3	15	1.6	18.3	3.3
7	33.3	58.3	25	96.6	38.3
9	23.3	58.3	30	78.6	20.3
Mean	19	33.6	13.3	45.7	12.1

BL = baseline, A = one treatment weekly for 4 weeks, A2 = second period of one treatment weekly for 4 weeks, B = intensive intermittent phase

A significant interaction effect was found between group and function level [$F(2,4) = 6.403$, $P = 0.05$]. Infants at the lowest function level who were treated with an intensive intermittent schedule gained the most as compared to infants treated with the routine schedule.

As indicated in Table 3, the five subjects in group E acquired maximal sitting position in the intensive phase and only one during the regular treatment phase. Of all the infants, five infants at GMFCS V progressed primarily in the intensive phase and only one in the regular phase, whereas at the higher function level only one progressed in the intensive phase.

DISCUSSION

This pilot study suggests that the benefit of an intermittent intensive goal-directed intervention is in doubt. However, this schedule might be adequate for children with more severe involvement. (GMFCS V). This study, to our knowledge, is the first to evaluate an intermittent intensive program with regard to sitting acquisition using a randomized design and blinded assessment of the results.

A comparison of the findings relating to groups of varying functional levels (regardless of the distribution of the research groups) showed that an improvement in achievements in the group of subjects with a low function level during either one of the intensive B phases [Table 3] was significantly higher: five of them acquired the highest improvement percentage during an intensive phase versus one that improved most during the regular phase. This finding conforms to the

Table 3. Summary of the findings related to sitting, the phase during which the highest achievements were attained and the percentage of the contribution

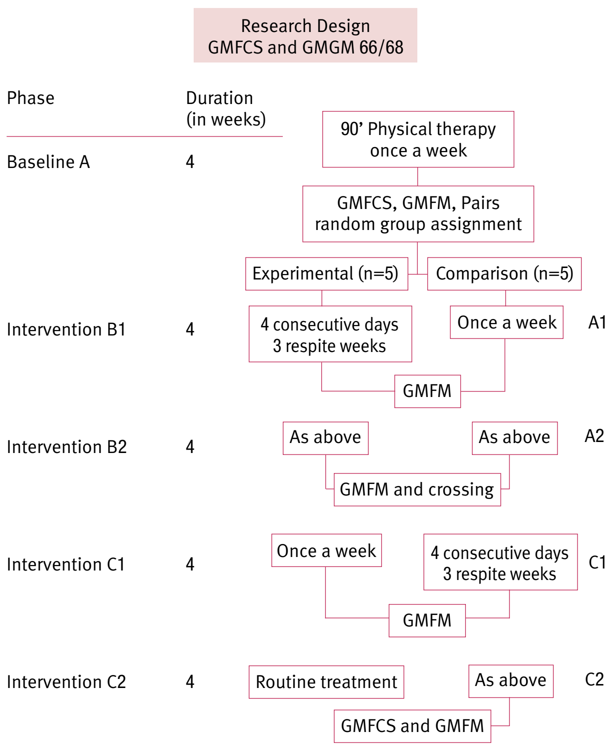
Group	Subject	Achievement change	Maximal change	Contributing phase #	Contribution percentage	Intervention type
Comparison	1	15–20	5	A	30	Regular
Experimental	2	8.3–21.67	13.34	B1	44	Intensive
Comparison	3	11.76–26.67	14.91	C2	28	Intensive
Experimental	4	18.3–28.3	10	B1	65	Intensive
Comparison	5	13.35–25	11.67	C2	45	Intensive
Experimental	6	10–30	20	B1	69	Intensive
Comparison	7	33.33–95	63.34	A	41	Regular
Experimental	8	20–76.67	56.67	A,B1	39+39	Regular = intensive
Comparison	9	23.33–100	76.67	A-A1	45+25	Regular
Experimental	10	31.67–86.67	55	B2	50	Intensive

#See Figure 1 for phases . Achievement change = the score obtained at baseline and the maximal score obtained at the last assessment. Maximal change = the difference between the initial score and the maximal score. Contributing phase = the phase during which maximal score was obtained. Contributing percentage = the proportion of change attributed to the contributing phase

hypothesis that the improvement level is likely to depend on the severity of the subject's impairment, as previously inferred in other studies [3,15]. The scenario where infants with a low function level gained more from intensive intermittent treatment than infants with a high function level conforms to the improvement found by Trahan and Malouin [4] in a similar regimen for five subjects in a low function level group (IV, V). This result is also in line with the findings of Shumway-Cook et al. [23] who found that in subjects with high achievements (scores over 70% in the GMFM) there was a smaller improvement than in subjects with lower achievements. It is not inconceivable that this result is related to the different brain anatomical distribution underlying the motor deficit of the different CP severity grades. The different impact on cortex and basal ganglia was recently reported [24].

The treatment dose consisted of both session length and frequency (simulating pulse treatment). The literature includes studies in which the average treatment is 45 to 60 minutes [4,5]. Odman and Oberg [2] report longer than average treatment sessions, namely 2–4 hours, but not administered individually. The treatment administered by Knox and Evans [25] was the closest in length to that of the present study: a 75 minute treatment three times a week using a similar treatment approach for a period of 6 weeks. However, the exact schedule was not specified. They found an improvement in sitting acquisition during the intensive treatment period as compared to previous studies that investigated the effectiveness of routine treatment using the same approach. Notwithstanding the differential response to the treatment schedule between the groups with an increased response during the experimental intervention in group E and during the standard intervention in group C, the average improvement in all the participants combined was the highest in the first month compared to all the research phases, regardless of the type of intervention. This finding as compared to treatments of shorter duration clearly needs to be investigated further. Timing of habilitative intervention might be an important factor. The age window in the present study (from

Figure 1. Research design and flow



GMFM = gross motor function measure, GMFCS = gross motor function classification scale

12 months on) although still within the period of developing myelination might have been less optimal with an increased plasticity existing at an earlier age. However, previous studies indicate plasticity potential at later stages of the developmental course [7,8].

This study has several limitations: the small number of participants possibly contributes to the lack of statistical significance. It is possible that a larger sample would have increased the statistical power and result in a statistically significant difference. A posteriori power analysis for paired comparisons with an alpha of 0.05 and power of 75% would require the number of participants to be 19. However, the study was meant to examine the feasibility of the design and provide some preliminary observations on the possible benefit of an intervention compared to the schedule commonly employed for children with cerebral palsy. Our preliminary observation of a possible increased gain in children with the more severe involvement should be taken cautiously. While the small sample size does not allow for any definite conclusions, the results of previous studies concurring with ours lend support to their value and should be taken into consideration in future larger studies. It is not inconceivable that longer phases would have resulted in more substantial gains. A longer follow-up monitoring wash-out effect is also needed in such an intervention study. It should be emphasized that while this study pertains to sitting only, future studies addressing other functional and psychological outcomes are warranted.

In conclusion, an intensive intermittent schedule could be of value in enhancing sitting acquisition in children with severe cerebral palsy. However, although it appears as effective as the routinely employed weekly schedule, replication studies employing similar designs are warranted.

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