The Effects of an Early Physical Therapy Intervention for Very Preterm, Very Low Birth Weight Infants: A Randomized Controlled Clinical Trial

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Purpose: A randomized controlled clinical trial was used to investigate effects of physical therapy (PT) intervention on motor outcome of infants born very preterm with very low birth weight (VLBW). Methods: Seventy-two infants born very preterm with VLBW were randomly assigned to a nontreatment (NT) (n = 38) or treatment (T) (n = 34) group. The T group received developmental PT from birth until four months corrected age (CA) weekdays during the infant’s neonatal stay and on a needs- and problem-orientated basis thereafter. The NT group received no intervention. Both groups were assessed at four months CA using the Alberta Infant Motor Scale (AIMS) as was a control group of 14 infants born full term. Parental compliance was measured using a parent questionnaire. Results: PT intervention had no significant effect on the T group’s motor performance. However, no T group subjects had abnormal motor development at four months CA when compared to the NT group (16%) and the control group (14%) (p = 0.09). The T group subjects with high levels of parental compliance had better scores on the AIMS than those with lower parental compliance (p = 0.05). Conclusion: PT intervention does not significantly affect motor performance of infants born very preterm with VLBW at four months CA. Parental compliance and intervention frequency may have influenced the outcome. Preliminary evidence suggests that neonatal and early PT may reduce the incidence of motor delay among infants born very preterm with VLBW. Follow-up of this group is recommended to ascertain the long-term benefits of this type of early PT. (Pediatr Phys Ther 2005;17:107–119) Key words: clinical trial, randomized controlled trial, child development, infant/newborn, infant/premature/physiology, infant/very low birth weight/physiology, motor activity/physiology, motor skills disorders/diagnosis, physical therapy (specialty)/methods

INTRODUCTION

The increase in the survival rate of infants born very preterm (<32 weeks)¹ with very low birth weight (VLBW) (<1500 g) over the past two decades has resulted in a growing concern over the quality of life of these surviving infants.²⁻⁵ Follow-up studies have shown that the infant born very preterm with VLBW is at high risk of cerebral palsy (CP) and other developmental deficits.⁶⁻⁸ One motor phenomenon that has been identified as occurring among approximately one third of the preterm population in early infancy is transient dystonia,⁹,¹⁰ more recently referred to as a faulty muscle power regulation.¹¹ Although the etiology of this condition is unknown, there are suggestions that this disorder is nonneurological, with a predominance of hyperextension of the trunk and extensor tone of the
Transient dystonia has been linked to motor difficulties in early infancy, namely, in relation to rotational skills, gross motor skill acquisition, and quality of fine motor skill performance.\(^3\)\(^,\)\(^12\)\(^-\)\(^14\) Additionally, a relationship has been documented between the presence of this disorder in infancy and motor performance at school age.\(^1\)\(^6\)\(^,\)\(^17\)

Experts who have examined this disorder suggest that it may be prevented and treated by early developmental physical therapy (PT) to facilitate the flexor development of infants born preterm.\(^1\)\(^2\)\(^,\)\(^14\)\(^,\)\(^17\)\(^,\)\(^18\) In addition, early PT intervention is advocated to enhance the motor development of the infant with CP by promoting variable movement and sensorimotor experiences and by preventing musculoskeletal complications.\(^19\)\(^-\)\(^21\)

**Problem-Orientated Developmental Approach**

Several approaches have been adopted by therapists working to optimize the development of the infant born preterm; these include supplemental stimulations\(^22\) and environmental modifications such as those used in the neonatal individualized developmental care and assessment program.\(^23\) One other method is a problem-orientated developmental intervention that employs therapeutic handling and postural support.\(^24\)\(^-\)\(^27\)

This clinical approach appears to be based predominantly on the neurodevelopmental approach.\(^25\)\(^-\)\(^29\) However, these approaches are not completely distinct from each other, and so when using any stimulating intervention with the infant at high risk, the importance of adapting that intervention to the infant’s behavioral needs at that time has been highlighted in the literature.\(^26\)\(^,\)\(^27\)\(^,\)\(^30\)\(^,\)\(^31\) Any direct intervention must also be structured around the infant, with the optimal time for stimulation being when the infant is awake, alert, and content.\(^32\)

The intervention under study is based on the problem-orientated developmental approach to the management of the preterm infant, in which consideration is given to the infant’s responses.

**Effectiveness of Early PT Interventions**

Despite the growth of neonatal developmental PT and follow-up programs for the infant born very preterm, these have been supplemented by add-on interventions based on these results as to how infants born preterm who are more vulnerable would respond to the PT program, i.e., those born at <32 weeks gestation and weighing <1500 g.

With the growing emphasis on evidence-based practice, PT has come under criticism for not evaluating and providing evidence to support practice.\(^37\)

The lack of conclusive evidence of PT interventions with the preterm population may contribute to inconsistent provision of neonatal PT, with only 47% of regional neonatal intensive care units in the UK offering neonatal developmental interventions to infants at high risk.\(^38\) This study was designed to investigate the motor performance of infants born very preterm with VLBW randomly assigned to a treatment and nontreatment group and compared to a comparison full-term control group. The treatment (T) group received a developmental PT intervention designed to facilitate motor development, provided on a basis of (weekdays) from birth to discharge and on a needs-orientated basis from discharge to four months CA. The nontreatment (NT) group received no developmental PT intervention. The Alberta Infant Motor Scale (AIMS) was chosen to assess the motor development of the infants at four months because it
can be used to detect change brought about by a PT intervention.39

METHODS

A randomized controlled clinical trial was conducted at Aberdeen Maternity Hospital from April 1, 1998, to March 31, 2001. Ethical approval was obtained from the Grampian Ethics Committee before participants were recruited to the study.

Subjects

Infants with a GA of <32 weeks and a birth weight (BW) of <1500 g, meeting the following inclusion and exclusion criteria were eligible for the study.

Inclusion Criteria

To be included in the study, infants had to be more than 24 weeks of estimated GA at birth, inborn or transferred to Aberdeen Maternity Hospital Maternity Unit within 48 hours of birth, residing in Grampian, at least one family member with some English language comprehension, and parental consent obtained within 21 days from admission or prior to transfer from an incubator to an open cot, which ever came first.

Exclusion Criteria

Infants were excluded from the study if they had cortical blindness or retinopathy of prematurity causing blindness, had musculoskeletal/congenital abnormalities, were oxygen dependent at four months CA, had severe hydrocephalus requiring a ventriculoperitoneal shunt, demonstrated signs of drug withdrawal, or had a family with a history of social problems (known to the social services department).

A full-term (FT) control group was recruited for assessment at four months chronological age. The recruitment of this geographic sample was considered necessary in order to provide data directly comparable to the preterm sample that was also recruited within a restricted geographic region. The FT control group consisted of infants who were healthy and normally developing. These infants were identified by health visitors in Aberdeen City. The infants had a GA of between 38 and 42 weeks and were white singletons with no antenatal, perinatal, or postnatal complications or any congenital or musculoskeletal abnormalities.

Sample Size

Prior to the commencement of the main study, the principal researcher carried out a pilot study to permit a sample size calculation. Twenty infants born preterm and who met inclusion and exclusion criteria were recruited prior to their discharge from the Neonatal Unit at Aberdeen Maternity Hospital during the period October 1997 to December 1997. The infants were assessed at four months CA by the principal researcher using the AIMS. None of the infants had received PT intervention prior to their assessment. Six (29%) infants in the sample scored ≤10th percentile on the AIMS at the four-month assessment. Based on published statistics regarding the incidence of CP in this population (7.1% to 7.7%),40,41 it was estimated that with PT intervention the percentage of infants scoring ≤10th percentile on the AIMS could be reduced by 67%. From this estimation, it was calculated that a two-group, continuity-corrected chi-square test with a 0.05 two-sided level of significance would have 80% power to detect the difference between a group 1 proportion of 0.30 and a group 2 proportion of 0.10 when the sample size in each group was 49.

Subject Recruitment

During the study period, a cohort of 72 infants born very preterm with VLBW fulfilling the inclusion and exclusion criteria were recruited to the study; 38 infants were randomized to the NT group and 34 to the T group. Randomization was carried out by coin toss, with impartiality ensured by an individual carrying out the procedure who was independent and blinded to the trial. Five infants died before 40 weeks conceptional age, two from the T group and three from the NT group. Two infants from the T group were withdrawn, one by the parents and one because the infant remained oxygen dependent at four months CA; with one infant withdrawn from the NT group by the parents (Fig. 1). Six percent (6%) of the infants did not attend their assessment at four months CA, four from the T group and two from the NT group. Data for 28 infants from the T group, 32 infants from the NT group (Table 1), and 14 infants from the FT control group were available for analysis at the four-month assessment. A summary of infants recruited, the mortality and attrition rates, and those infants whose parents refused consent is provided in Figure 1.

Neonatal Developmental Program

The neonatal developmental program was provided by one of three pediatric physical therapists, the principal researcher predominantly and two other experienced pediatric physical therapists when the principal researcher was unavailable. These pediatric physiotherapists were trained by the principal researcher. This training consisted of the use of the neonatal assessment, the Longitudinal Assessment of the Preterm Infant (LAPI),42,43 neonatal problem-orientated developmental interventions including handling and positioning techniques, and training in behavioral states and adverse signs. The neonatal developmental program was designed to promote symmetry, muscle balance, and movement using postural support and facilitation techniques (see Appendix A). The neonatal developmental intervention was based on literature that has investigated or described neonatal interventions.26,27,29 The researcher also attended a neonatal course prior to the start of the study to consult colleagues and update the researcher’s skills in neonatal interventions, assessment, and follow-up.44

The program began when parental consent had been obtained and the infant had been randomly assigned to the T group. Parents were actively involved in the program,
with meetings scheduled on a weekly basis. At these meetings, the physical therapist educated the parents on postural support, behavioral states, and adverse signs\textsuperscript{23,45} and demonstrated developmental activities to carry out with their infant.

Postural support was started immediately, but interventions involving handling were not begun until the infant tolerated position changes. The physiological response to individual postures was assessed before carrying out any interventions in that posture. Once started, the neonatal developmental program was provided on a daily basis, on weekdays, if physiological and behavioral responses allowed. The length of treatment was dependent on the infant’s medical stability and behavioral state, with a maximum treatment duration of 10 minutes provided the infant’s color remained unchanged and oxygen saturations and heart rate were maintained within normal parameters.\textsuperscript{46} Interventions took place as much as possible midway between feeds with the infant in behavioral state 3 or 4.\textsuperscript{45} That is, when the infant had his or her eyes open and was either moving or not moving.\textsuperscript{45} If the infant displayed any adverse behaviors (eg, an increase in tone, grimacing, hiccupping, fluctuating behavioral state), the intervention was stopped.\textsuperscript{23} Not all activities were performed every treatment session. The choice of treatment activities was dependent on the infant’s responses and the infant’s motor progress.

In addition to the neonatal developmental program, the infants in the T group were assessed on a weekly basis throughout the neonatal period with one or both of the parents present. The assessment used was the LAPI.\textsuperscript{42} This assessment was chosen as it is designed specifically for the infant born preterm and is widely used by physiotherapists in neonatology in the United Kingdom to guide PT treatment during the neonatal period and to identify infants who require PT follow-up after discharge.\textsuperscript{52,44} The LAPI consists of items such as observation of posture, and active responses such as head lag and head control in sitting. These items have demonstrated a longitudinal progression.\textsuperscript{47,48} Assessment of infantile reflexes, spontaneous movement, and atypical features and tone is also included.\textsuperscript{43}
Based on weekly assessments using the LAPI and documentation of the presence of atypical features, the infant is classified as “usual,” “unusual,” or “suspect.” The atypical features assessed are the asymmetrical tonic neck reflex dominance, stereotyped limb movements, spinal hyperextension, hypertonia, hypotonia, and coarse jitters. The LAPI classification system of usual, unusual, or suspect has demonstrated predictive validity to six years of age and was used to allocate the appropriate developmental follow-up following discharge (Table 2).

On discharge, the parents were advised on home play and equipment use for their infants. Prone play was promoted; baby walkers and baby bouncers or jumpers were discouraged. This advice was based on research that has found that the use of baby walkers can have a detrimental effect on motor development. In addition, prone play is suggested in the research to promote motor development. The parents were educated on how to play with their infants in supine and supported sitting positions, thus promoting symmetry and muscle balance. Additional advice was provided if the infant demonstrated any individual deviations in motor development or tone.

Follow-up Developmental Program

The follow-up developmental program was provided by the principal researcher if the infant resided in Aberdeen City; otherwise, the therapy was provided by the appropriate community pediatric physical therapist. All the physical therapists involved in providing the follow-up developmental program received education regarding preterm development and detailed information about the research program.

Between discharge and the four-month assessment, advice on play activities was given to the parent by the therapist; this advice was based on the infant’s progress and developmental needs. The PT intervention during this period was based on a knowledge of infant development, along with literature that has described early interventions and activities. The PT intervention was also formulated in anticipation of the motor disorders that

| TABLE 1 | Comparison of neonatal and maternal risk factors between the preterm groups |
|---------------------------------|---------------------------------|------------------|-----------------|
| Neonatal and Maternal Risk Factors | NT Group (N = 32) | T Group (N = 28) | p Value* |
| Mean BW (g) (SD) | 1159.1 (372.7) | 1321.4 (400.2) | 0.109† |
| Mean GA (wk) (SD) | 28.7 (2.4) | 29.6 (2.0) | 0.122† |
| Gender | | | |
| Male, no. (%) | 20 (62) | 16 (57) | 0.79 |
| Female, no. (%) | 12 (38) | 12 (43) | |
| APGAR score <5 @ 1 min, no. (%) | 10 (32) | 4 (14) | 0.33 |
| APGAR score <5 @ 5 min, no. (%) | 3 (10) | 2 (9) | 1.00 |
| Small for GA, no. (%) (BW <10th percentile) | 6 (19) | 6 (21) | 1.00 |
| IVH/PVL, no. (%) | | | |
| Normal | 17 (53) | 10 (36) | 0.35 |
| Grade I/II | 12 (38) | 13 (46) | 0.35 |
| Grade III/IV/PVL | 3 (9) | 5 (18) | 1.00 |
| Received surfactant, no. (%) | 18 (60) | 16 (57) | |
| Diagnosis of chronic lung disease, no. (%) | 10 (31) | 7 (25) | 0.78 |
| Received betamethasone, no. (%) | 22 (73) | 18 (64) | 0.57 |
| Cesarean delivery, no. (%) | 23 (72) | 13 (46) | 0.065 |
| Multiple births, no. (%) | 8 (25) | 9 (32) | 0.58 |

* Significance level (two-tailed), chi-square test.
† Significance level (two-tailed), independent samples t test.

NT = nontreatment; T = treatment; BW = birth weight; GA = gestational age; IVH/PVL = intraventricular hemorrhage (Papile) and periventricular leukomalacia.

**TABLE 2**

Follow-up arrangements based on the classification of the infant at its final assessment using the Longitudinal Assessment of the Preterm Infant

<table>
<thead>
<tr>
<th>Classification</th>
<th>Follow-up Arrangements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual</td>
<td>Follow-up appointment and physiotherapy assessment at one month CA. If the infant displays normal tone, movement, and infant development, further follow-up is not required.</td>
</tr>
<tr>
<td>Unusual</td>
<td>Follow-up appointment and physiotherapy appointment one month CA. If the infant displays normal tone, movement, and infant development, further follow-up is not required. If there is an abnormality of movement, tone, or posture or a delay in development at one month CA, the infant is seen every two weeks until four months CA.</td>
</tr>
<tr>
<td>Suspect</td>
<td>Follow-up at two-week intervals until four months CA.</td>
</tr>
</tbody>
</table>

CA = corrected age.
have been described in the introduction as being evident among infants born preterm, such as overextension, poor rotation development, asymmetry, muscle imbalance, and motor delay.

The frequency of this intervention was based on the classification of the infant at discharge according to the LAPI (Table 2). The PT for infants classified as suspect was carried out either at the infant’s home or at the Physical Therapy Department, Royal Aberdeen Children’s Hospital, whichever the family preferred. All the PT assessments carried out at one month CA were conducted at the Physical Therapy Department, Royal Aberdeen Children’s Hospital, by the principal researcher. The PT sessions were 60 minutes in length; 40 minutes were allocated by the physiotherapist for the assessment and treatment of the infant and 20 minutes for parental instruction. Individualized advice and treatment, aside from that included in Appendix 2, were provided by the physical therapist if developmental problems were identified that required additional advice or treatment.

Four-Month Assessment

At the four-month assessment, the AIMS was used to measure the motor development of the infants born preterm and FT. Assessments were conducted by an independent examiner (J.R.), blind to the group assignment of the infants. The AIMS is a reliable norm-referenced observational tool that has been validated for use from term to 18 months of age with infants born preterm and FT. The AIMS measures qualitative aspects of movement and is sensitive to changes in an infant’s motor performance. The AIMS can also be used to identify infants who are delayed in their gross motor development. An AIMS raw score is based on the number of gross motor positions and movements that the infant has shown during the assessment while prone, supine, sitting, and standing. The raw score is translated into a percentile ranking that can be compared to the percentile ranks of the normative age-matched sample of infants. As a guideline, a cutoff point of the 10th percentile is recommended to identify infants with abnormal motor development.

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To ensure that administration and scoring of the AIMS by the independent examiner were consistent with the AIMS manual, intrarater and interrater reliability was assessed using videotapes of the four-month assessments of the FT control group. An experienced pediatric physical therapist analyzed and scored the video recordings in addition to J.R. to provide the data to evaluate interrater reliability. The intraclass correlation coefficient for interrater and intratester reliability was 0.97.

Parental Compliance

A parental questionnaire was designed to examine compliance with the PT program. At the four-month assessment, the parents were asked to document on the questionnaire the nature of the activities given to them at their last PT appointment. A maximum of three activities was given at each appointment. Compliance was rated good if two or more of the activities last given to them by the physiotherapist were recalled, moderate if one activity was remembered, and poor if they did not remember any of the activities prescribed.

Procedure

Following randomization of the infants into the T group or NT group, the nursing and medical staff were informed of the infant’s group allocation by documentation in the nursing records, the medical records, and by a colored sticker placed on each of the infants’ cots. The infant’s parents were also informed of their infant’s group allocation. The use of blinding was considered inappropriate for this particular trial due to the high level of nursing and parental cooperation needed to carry out aspects of the PT intervention. A placebo intervention was not included as it would have involved a handling or stimulation technique, thus potentially affecting the motor outcomes of the infants in the NT group and negating the PT treatment itself.

Infants in the T group received a neonatal developmental program until discharge (Appendix A). At discharge, the infants in the T group received the appropriate advice and were allocated follow-up developmental intervention according to their classification on the LAPI (Table 2 and Appendix B). The follow-up developmental intervention continued to four months CA when infants from the T group and the NT group returned to the Physical Therapy Department, Royal Aberdeen Children’s Hospital, for assessment by an independent examiner (J.R.) using the AIMS. The PT control group attended the Physical Therapy Department, Royal Aberdeen Children’s Hospital, at four months chronological age. These assessments were conducted and videotaped by two final-year physical therapy students. The videos were then analyzed by J.R. using the AIMS. Figure 1 provides a diagrammatic illustration of the procedure.

At 18 months CA, the preterm infants returned to the neonatal follow-up clinic for a routine assessment by a consultant neonatologist with 30 years experience in the follow-up of infants born preterm with VLBW. At this clinic, a diagnosis of CP is made based on a neurological assessment and a developmental examination using the Denver Developmental Screening Test II. The diagnosis of CP was made according to the criteria used by previous authors; that is, the presence of exaggerated deep tendon reflexes, positive Babinski reflexes, increased tone noted on passive movement of the extremities, and abnormal patterns of movement noted on observation, with or without a delay in motor development. Those children who did not have a diagnosis of CP were classified as being neurologically normal.

The severity of CP was categorized according to the infant’s level of mobility at the 18-month assessment. Infants walking independently were categorized as having mild CP; if they were walking with a walking aid or crawling, they were categorized as having moderate CP; and if...
they were not walking and not crawling, they were classified as having severe CP. This classification is taken from Russman and Cage as cited by Ratliffe.61

**Statistical Analysis**

Descriptive statistics were used to explore patient demographics. Descriptive statistics included means and standard deviations if the variables were continuous and normally distributed. Median, interquartile range, and range were provided for continuous variables where the data were not normally distributed (Table 1). To compare the four-month AIMS percentiles among the three groups, the Kruskal-Wallis test was used. For comparison of the number of children with a score of ≤10th percentile on the AIMS in each group, the chi-square test was used. Due to the failure to recruit the required number of infants, it was deemed important to conduct a three-way analysis to reduce the risk of making a type I error. Significant results were further investigated with post hoc comparisons (Bonferroni method). All tests were two-tailed and a p value of <0.05 was regarded as significant. All analyses were performed using SPSS version 10.0.

**RESULTS**

To establish that the randomization process produced two like groups of preterm infants, neonatal and maternal risk factors were compared between the T group and NT group. There were no significant differences on any neonatal or maternal risk factors between the T group and NT group (Table 1). However, there were differences between the two groups of infants born preterm. Twelve (20%) of the preterm sample were diagnosed with CP by or at the 18-month assessment, eight of these infants were from the T group and four were from the NT group.

There were more moderate and severe cases of CP, two cases (24%) and three cases (38%) respectively, among the infants in the T group than in the NT group. In the NT group, there were no moderate cases of CP and only one (25%) severe case (Table 3). Three (38%) of the infants in the T group and three (75%) of the infants in the NT group had mild cases of CP. All the infants in the control group were born FT and were healthy white singletons developing normally.

**Motor Performance on the AIMS**

At the four-month assessment, both preterm groups had greater median percentile ranks on the AIMS than the FT control group (Fig. 2). The NT group had a median percentile rank at the 72.5 percentile (interquartile range (IQR) = 32.5 percentile), the T group had a median percentile rank at the 65th percentile (IQR = 42nd percentile), and the FT control group had a median percentile rank at the 50th percentile (IQR = 50th percentile) (Fig. 2). There were no significant differences between the three group's performance on the AIMS at the four-month assessment (p = 0.191).

Analysis of the motor development of the infants from the T and NT groups who were developing typically demonstrated that they performed similarly on the AIMS at four months CA, 71.5 percentile (range 19th–91st percentile) and 72.5 percentile (range fourth–91st percentile), respectively (Table 4). The FT infants had a median AIMS percentile of 50 (range fourth–91st percentile). Despite the infants with normal development from both of the preterm groups performing better on the AIMS in comparison with the FT control group, the statistical test did not reach significance (p = 0.10) (Table 4). The infants with CP from the T group also had a similar median percentile rank, 43.5 percentile (range 25th–85th percentile), on the AIMS at four months CA when compared to those infants with CP in the NT group, 42nd percentile (range fourth–90th percentile) (Table 2).

**TABLE 3**

The severity of cerebral palsy in the infants from the preterm groups

<table>
<thead>
<tr>
<th>Severity of Cerebral Palsy</th>
<th>Treatment Group (N = 8)</th>
<th>Nontreatment Group (N = 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Mild</td>
<td>3</td>
<td>38</td>
</tr>
<tr>
<td>Moderate</td>
<td>2</td>
<td>24</td>
</tr>
<tr>
<td>Severe</td>
<td>3</td>
<td>38</td>
</tr>
</tbody>
</table>

**TABLE 4**

Comparison of the AIMS percentile rank between normal and cerebral palsy infants from the T group, the NT group and the FT group

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Group</th>
<th>Median AIMS Percentile Rank (Range)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral palsy</td>
<td>T group</td>
<td>43.5 (25–85)</td>
<td>0.734</td>
</tr>
<tr>
<td></td>
<td>NT group</td>
<td>42 (4–90)</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>T group</td>
<td>71.5 (16–91)</td>
<td>0.095</td>
</tr>
<tr>
<td></td>
<td>NT group</td>
<td>72.5 (7.5–91)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>FT group</td>
<td>50 (4–91)</td>
<td></td>
</tr>
</tbody>
</table>

* Significance level (two-tailed), Mann-Whitney U test.

AIMS = Alberta Infant Motor Scale; T = treatment; NT = nontreatment; FT = full-term control.
A score of ≤10th percentile on the AIMS at four months CA can be used to identify infants with abnormal motor development. At the four-month assessment, five (16%) of the NT group and two (14%) of the FT control group scored ≤10th percentile on the AIMS. None of the infants in the T group had a score ≤10th percentile on the AIMS at the four-month assessment. The differences in the number of children scoring ≤10th between the three groups approached but did not reach significance ($p = 0.09$). Of those infants who scored ≤10th percentile, three from the NT group were normal and two had CP. The number of infants classified as developing normally at 18 months CA who scored ≤10th percentile at the four-month assessment did not differ significantly between the three groups ($p = 0.25$). A comparison of the number of infants with CP from the two preterm groups who scored ≤10th percentile at four-months approached but did not reach significance ($p = 0.09$).

**Parental Compliance**

The question in the parent questionnaire relating to compliance was completed by all 28 of the parents of infants in the T group at the four-month assessment. Sixteen (57%) parents demonstrated good compliance, five (18%) had moderate compliance, and seven (25%) had poor compliance. Infants of parents with good compliance had higher percentile ranks (median 75th, IQR 37.6 percentile) on the AIMS at the four-month assessment compared to infants of parents with moderate or poor compliance (median 46th, IQR 50th percentile), this approached significance ($p = 0.05$). This result was not affected by the infant’s diagnosis.

**DISCUSSION**

The results achieved at the four-month assessment would suggest that a PT intervention provided from birth to four months CA may not affect the overall AIMS percentile rank of a group of infants born very preterm with VLBW but may reduce the number of those infants with motor delay at four months CA, based on a cutoff point of the 10th percentile. The overall median percentiles on the AIMS for the two preterm groups in this study were similar, the 10th percentile. The overall median percentiles on the AIMS at the four-month assessment did not differ significantly between the three groups ($p = 0.09$). Of those infants who scored ≤10th percentile, three from the NT group were normal and two had CP. The number of infants classified as developing normally at 18 months CA who scored ≤10th percentile at the four-month assessment did not differ significantly between the three groups ($p = 0.25$). A comparison of the number of infants with CP from the two preterm groups who scored ≤10th percentile at four-months approached but did not reach significance ($p = 0.09$).

The lack of significance in relation to the number of infants with scores ≤10th percentile at the four-month assessment may also be attributed to the small sample size because achieving zero percentage among the T group cannot be improved on. A larger sample size would be required to ascertain whether a significant result in relation to this finding could be obtained.

The trend for early PT intervention from birth to four months CA to reduce the number of preterm infants who scored ≤10th percentile provides support for authors who have been postulating for several decades that some of the motor disorders evident among the preterm population may be preventable. However, the literature also suggests that promoting muscle balance and flexor development in the neonatal period and in the months post-term for infants at high risk should optimize their motor development. Additionally, providing movement experiences is considered important in the formation and selection of the appropriate neural networks thought to contribute to the process of motor development. Therefore it is surprising that improving the neonatal motility and providing early motor experiences for the infants in the T group did not have an effect on the motor development of the whole group of infants but only those who were at risk of motor delay.

Previous researchers who investigated the effect of early PT interventions on the motor outcome in the first year of infants born preterm who are at high risk also found no effect of their PT interventions, however, the literature also suggests that one of the factors that contributed to their lack of significance was that the assessment tools used were not sensitive enough to detect motor changes brought about by PT intervention. The current study produced a result similar to those previous studies despite using a motor assessment, the AIMS, considered to be sensitive to changes in motor performance brought about by PT interventions.

One reason for finding no significant effect of the PT intervention may be the frequency of the intervention, in particular with those infants who were classified as usual and who were only seen once between discharge and four months CA. Of the available literature, only one study, conducted by Lekskulchai and Cole, found that early PT had a significant effect on the motor outcome at four months CA for a group of infants born preterm. The PT intervention of Lekskulchai and Cole was provided on a monthly basis from term age for all infants in the intervention group regardless of their developmental progress. With that frequency of intervention, the intervention group had a significantly higher score than the nonintervention group on the TIMP when assessed at four months CA. The PT intervention in the current study was based on similar principles and contained similar activities to that provided by Lekskulchai and Cole. In addition, the TIMP and the AIMS are both motor assessments recognized to be sensitive to small differences in motor development that may be brought about by a PT intervention. Therefore, one difference between the current study and that of Lekskulchai and Cole, which may explain the different results
obtained, was the frequency of the intervention provided between term and four months CA. The result of the intervention provided by Lekskulchai and Cole suggests that an increased frequency of PT intervention for the normally developing infants in the T group in the current study may have led to greater effect on those infants' motor development at the four-month assessment.

Another factor that possibly contributed to the non-significant result was the level of parental compliance of the parents whose infants were in the T group, particularly as infants whose parents had high compliance levels performed better than those with lower compliance levels \((p = 0.05)\). In the current study, 38% of the parents had poor compliance levels. The study by Lekskulchai and Cole, which investigated a monthly early PT intervention, only included infants in their study if the parents could demonstrate the previous month's prescribed activities in at least three of the four PT sessions, ie, they demonstrated good recall and thus potentially good compliance levels. The significant effect of the early PT developmental intervention provided by Lekskulchai and Cole reinforces the possible importance of achieving high levels of parental compliance to a developmental PT intervention. The findings of this study also suggest that regular contact between the physical therapist and the parent may be required to achieve high levels of compliance with a PT intervention program. To enhance compliance with the PT intervention, future researchers should contact participants on a regular basis to remind them of the activities that should be carried out at home.

Aside from the low frequency of intervention for the infants classified as usual or unusual and the influence of parents with poor compliance levels, additional factors related to the study design may have affected the result obtained. One factor was the potential for cross-contamination between the T and NT groups. Parents of infants in the T group may have informed parents of infants in the NT group of some of the advice and activities provided by the physical therapist. During the neonatal period, parents of infants in the NT group may have observed the physical therapist providing demonstration or advice to parents of infants in the T group. Further studies should ensure that parents involved in providing PT treatment are not instructed with parents from a NT group within observational distance. Parents of infants in a treatment group should also be asked not to communicate the advice or interventions to other parents.

The short duration of the intervention may also have influenced the result because the motor skills of infants at four months of age are still limited. Assessing the infants at six months of age may have demonstrated more of a treatment effect and should be considered by investigators in future studies evaluating an early developmental intervention. Additionally, assessing the infants from both groups at repeated periods between birth and four months CA may have provided more information on the effects of a neonatal and early developmental PT intervention. This would be of particular importance if the researcher has control over the frequency and duration of the intervention before discharge from the neonatal unit.

The PT intervention reduced the number of preterm infants with abnormal motor development at the four-month assessment; based on a cutoff point of the 10th percentile on the AIMS, this result neared significance \((p = 0.09)\). Significance may be reached with a larger sample size. However, it could be debated that this result may be considered clinically or meaningfully significant. Establishing what is meaningful when testing a healthcare intervention is considered an important element of healthcare research. A nonsignificant result may still have important implications in the clinical setting, eg, in this case, for the infants and their families. The significance level chosen by the researcher is dependent on several factors such as the mortality and morbidity rates associated with the intervention and the resources required to implement the intervention. Neonatal PT interventions have not demonstrated any adverse effects, although there is little research in this area. This intervention may be considered cost-effective because preventing motor problems in early infancy for the infant born very preterm with VLBW may reduce the need for PT and other developmental resources later in the child's life. In addition, preventing motor delays for infants born very preterm with VLBW at four months CA may reduce family stress, improve the quality of life for the infant and the family, and have additional hidden effects. Therefore, it may be meaningful to accept a significance level of \(p < 0.1\) in this case. However, before a conclusion is reached as to the appropriate significance level for neonatal PT interventions, further studies need to investigate additional nonmotor effects of early PT programs. There is also a need for research to firmly conclude that neonatal developmental interventions have no adverse effects.

A surprising finding of this study was that, at the four-month assessment, the FT group performed less well on the AIMS than either of the preterm groups' normal infants. It is generally accepted that correcting for prematurity until approximately the age of two to two and a half years or later is necessary when assessing the preterm infant's development using assessments that have determined normal values on full-term samples. However, in recent decades, there have been several studies that have demonstrated that this rule should perhaps not be applied to all aspects of the infants' development. The findings in this study would suggest that when assessing motor development, correction for prematurity at four months CA may not be justified and is certainly an issue requiring further study.

**Study Limitations**

One of the limitations of the current study was the sample size. The sample size recruited was smaller than the principal researcher estimated, primarily because the researcher underestimated the number of parents who would not consent to participate in the study. Literature on recruitment that can be used to guide such estimation is generally incomplete. However, the fact that the study...
involved randomization and required active parental participation and follow-up \cite{57, 69} may have influenced the parents' decision to decline participation. The adverse media attention surrounding the medical profession in the United Kingdom in relation to the Bristol Heart scandal \cite{69} and subsequently the Alder Hey organ scandal \cite{57} during the recruitment period of the study in 1998 to 2001 may also have contributed. The recruitment figures of the current study highlights the difficulty in recruiting a vulnerable group to a clinical trial involving PT interventions. Future researchers in this field should consider conducting a multicentered trial in order to obtain an adequate sample size. In addition, a research assistant responsible for and dedicated to the recruitment of infants to a trial of this nature may enhance recruitment.

In conducting this trial, there were several weaknesses as a result of being carried out in the highly controlled clinical environment of neonatal intensive care. As a result, the number of PT treatments could not be standardized as each infant's medical status dictated how much PT they received. Another factor, due to financial and logistical considerations, was the number of therapists involved in providing the intervention both before and after discharge. Despite the efforts of the principal researcher to provide education and information, the variability of the physiotherapists in providing assessment and treatment was not measured to ascertain the success of these strategies; future research should aim to standardize variability in the provision of the intervention. However, it may also be seen as a strength of this study that the results obtained can be directly applied to the typical clinical situation \cite{80}.

This study has also demonstrated that at four months CA, the AIMS only detected two (17%) of the 12 infants with CP from the preterm group, highlighting that its use in the detection of preterm infants with abnormal motor development at four months CA may be limited. This is contradictory to the findings of Darrah et al. \cite{57} The use of additional or alternative motor assessments (eg, the TIMP) in future studies is recommended.

Research is required to reinforce the findings of this study with a larger sample of infants born very preterm with VLBW. Future research should increase the intensity of the follow-up developmental intervention offered to this group of infants; this would also potentially enable the researcher to enhance parental compliance levels, although further strategies may be required to address this issue. Future research should also consider a longer duration of developmental intervention with repeated measures between the start and the final measurement to further inform the effects and timing of neonatal and early developmental PT. Further follow-up of this sample to school age would be important to ascertain whether preventing motor delay at four months CA prevents later appearing motor difficulties for this group of infants. This research, in addition to investigations into the nonmotor effects of neonatal and early PT interventions and clarification of the physiological effects of neonatal PT techniques, would further inform the debate on continued resource allocation in neonatal and early PT interventions.

CONCLUSIONS

This study was designed to investigate the effects of a developmental neonatal and early PT intervention, tested in this study, on the motor outcome of the infant born very preterm with VLBW at four months CA. PT intervention does not have a significant effect on the motor performance of infants born preterm at four months CA. However, this study has provided preliminary evidence that the neonatal and early PT program tested in this study might reduce the incidence of motor delay among infants born very preterm with VLBW at four months CA. Further research is required to establish the clinical significance associated with this result. This study has also highlighted the difficulties in recruiting an adequate sample size of infants born very preterm with VLBW when studying a PT intervention.

ACKNOWLEDGMENTS

We thank the medical and nursing staff from the neonatal unit at Aberdeen Maternity Hospital for their help with recruitment; Dr. D.J.L. Lloyd, who carried out the follow-up clinics; and the pediatric physiotherapists from the Royal Aberdeen Children's Hospital and Community Child Health for helping provide the neonatal and follow-up developmental programs.

REFERENCES

### APPENDIX A

The Neonatal Developmental Intervention

<table>
<thead>
<tr>
<th>Aim</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>To promote symmetry and midline</td>
<td>Position the infant with limbs flexed and supported, if required, in supine, prone, or side lying position.</td>
</tr>
<tr>
<td>To encourage head symmetry</td>
<td>Support the infant in supine position in the cot or on the therapist's/parent's lap, head midline, limbs flexed. Using visual or auditory stimulation, encourage eye following from midline to the left and from midline to the right. Encourage head control in midline. Advocate symmetrical positioning and symmetrical stimulation (ie, to both left and right sides). In a fully supported semiprone position on the therapist's/parent's lap or in the cot. Stabilize the infant's shoulders in flexion. With full support, gently shift infant's weight to aid head righting. Repeat to both sides using visual or auditory stimuli.</td>
</tr>
<tr>
<td>To strengthen neck and trunk flexors</td>
<td>In a fully supported sitting position, the infant is tilted from an upright supported posture to a 10–30-degree backward tilt. This movement is graded depending on ability and will stimulate flexor activity of the neck and trunk flexors. In upright supported sitting position, encourage eye following using visual or auditory stimulation. In this position, gentle bouncing up and down on the therapist's/parent's lap to stimulate concontraction of the neck muscles.</td>
</tr>
<tr>
<td>To encourage hand to mouth</td>
<td>Facilitate hand-to-mouth activity in any posture. Provide stimulation by stroking across the infants pectoral muscles to encourage antigravity upper limb movement. Compression downward through the shoulders in the supine position to activate anterior chest and shoulder muscles.</td>
</tr>
<tr>
<td>To strengthen leg flexors</td>
<td>Facilitate kicking in the supine position by moving the limbs reciprocally into flexion and extension. Stroke diagonally across the infant's abdomen and legs to encourage active kicking.</td>
</tr>
<tr>
<td>To promote rotation</td>
<td>In the supine position with the lower limbs held in flexion, gently rock the knees from side to side. Encourage independent rotation of the head with this movement.</td>
</tr>
<tr>
<td>To promote movement experience</td>
<td>Encouraging touch and stimulation in a variety of postures, if stable, in prone, supine, sitting, or side-lying position.</td>
</tr>
<tr>
<td>To prevent contractures</td>
<td>Supported position changes from supine to side lying and to prone. Positioning the infant with the lower limbs held in flexion, the hips supported in a neutral position, and the ankles supported in mid-position. The upper limbs are supported in flexion. Passive movements of the limbs: lower limbs fully flexed to the chest, head flexed to the chest, upper limbs flexed across the chest.</td>
</tr>
</tbody>
</table>

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## APPENDIX B

### Follow-up Developmental Intervention

<table>
<thead>
<tr>
<th>Aims</th>
<th>Activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Promote symmetrical movement</td>
<td>Midline activities in supine and alternate side-lying positions (term to four months). Promotion of symmetrical head turning (term to four months) and facilitation of symmetrical reaching in prone (three to four months) and supine (one to four months) positions.</td>
</tr>
<tr>
<td>Strengthen flexor muscle groups</td>
<td>Facilitate upper limb reaching and midline activities in supine (term to four months) and sitting (two to four months) positions. Facilitate hands to midline, hands to mouth, hands to feet in supine position and supported sitting position in a seat (term to four months). Supported sitting, encourage head turning on trunk (term to four months). Supported sitting, incline the infant backward to encourage flexor control (term to four months).</td>
</tr>
<tr>
<td>Strengthen extensor muscle groups</td>
<td>Prone, weight-bearing; promote head extension (term to four months). Prone, facilitate weight transference and promote head righting on the body (term to four months). Prone, facilitate reaching (three to four months).</td>
</tr>
<tr>
<td>Promote rotation</td>
<td>Facilitating rolling from supine to side lying to prone positions (two to four months).</td>
</tr>
<tr>
<td>Promote movement experience</td>
<td>Awareness of play in supine, prone, sitting, side-lying (term to four months) and rolling (two to four months) positions.</td>
</tr>
<tr>
<td>Prevent contractures</td>
<td>Stretching of muscle groups if required (term to four months)</td>
</tr>
</tbody>
</table>

The support, degree of facilitation, and position are modified based on corrected age and ability.