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Effect of different durations of using a standing frame on the rate of hip migration in children with moderate to severe cerebral palsy: a feasibility study for a randomised controlled trial

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Contribution of the Paper

- It is safe and feasible to recruit to a study investigating supported standing in children with cerebral palsy. The findings of this study contribute to designing a future RCT.
- Daily standing time of an hour per day was acceptable to children, schools and families over a 12-month period.
- In children who used standing frames for 40-60 minutes per day, there was a trend towards a lower rate of hip migration than previously reported rates of spontaneous hip migration.

Key words

Standing frame; Hip dysplasia; Cerebral palsy; Children; Paediatric; Feasibility study

BACKGROUND

Cerebral palsy (CP) describes a group of non-progressive disorders of posture and movement (1) affecting 2.1 per 1000 children (2). Secondary musculoskeletal impairments such as muscle and joint contractures and bony deformity develop, particularly in those children with more impaired gross motor function(1).

The Gross Motor Function Classification System (GMFCS) (3) provides a common language to describe and predict motor development. GMFCS level III describes children use walking aids and may use wheelchairs for longer distances, and GMFCS level V describes children who require full support in wheelchairs for their mobility. This study focuses on children with GMFCS levels III -V, where standing frames are recommended as part of postural management strategies to help improve posture and function (4).

The timing and intensity (dosage) of therapies was rated as the highest research priority by health professionals and carers of disabled children (5), to enable them to make informed decisions when dedicating time and effort to therapeutic programmes. Standing in

educational settings may improve access to activities, but can detract from educational time (6) and leave the child feeling isolated (7). Children may stand when they believe that there are health benefits, despite sometimes experiencing pain or discomfort (8).

The reported benefits of using a standing frame are improving bone mineral density, managing spasticity, contractures and hip stability (9-11). Anecdotally, some physiotherapists prescribe standing frames to help reduce the risk of hip dislocation(12) but there is insufficient evidence to prove that supported standing programmes slow the rate of hip migration (13, 14). Recommendations for the frequency and duration of standing time vary between 30 to 60 minutes per day, usually 5 days per week. A feasibility study is needed to determine an acceptable dose of supported standing and comparator required for prior to a randomised controlled trial (RCT).

This study aims to explore the feasibility of conducting a RCT, doubling standing time at home and school over a 12 month period. Feasibility outcomes are reported according to the CONSORT extension for randomised pilot and feasibility trials (15, 16).

METHOD

A working group comprising patient representatives, academics, physiotherapists and orthopaedic surgeons developed the study design. The trial was registered on ClinicalTrials.gov Identifier: NCT02141802. NHS Health Research Committee, South West granted ethics approval (ref 13/SW/0228).

Eligibility criteria- Children aged 1-12 years with a diagnosis of CP, GMFCS level III-V (3), using a standing frame for at least 1.5 hours per week were eligible. Children were not eligible if they had soft tissue surgery within six months or bony surgery within twelve months before the start of the study or during the study.

Recruitment and consent- Participants were identified through local Child Development Centres, physiotherapists, paediatricians and orthopaedic clinics as well as by adverts to parents via family networks across the South West of UK.

Written informed consent was sought from the parent or guardian and assent was sought from the children, to participate in a 12-month feasibility RCT. Data were collected in the child's local physiotherapy department, home, school or nursery.

Sample size- A pragmatic sample size of n=30 was based on a previous study (11) and enabled us to assess feasibility.

Intervention and control- The children in the control group continued their usual standing time and those in the intervention group were asked to double their standing time, using their existing standing frames and orthoses provided by their physiotherapist. Children were encouraged to stand for a maximum of 60 minutes per day for the control group and 120 minutes per day in the intervention group. The intervention took place at home, school or nursery and was tailored to meet the individual needs and circumstances of the child. The child's usual paediatric physiotherapist advised carers on functional ways to use the standing frame, such as for mealtimes, cooking, craft or play activities. In both groups, carers recorded children's standing time, activities while standing and obstacles to standing.

Randomisation- The child's mean baseline standing time was measured using a standing diary recorded for two weeks by the child's family and school. A computer-generated programme (MINIM- York University) was used to randomise the participants into two groups at a ratio of 1:1 using the minimisation algorithm:

Age (<6 years vs >6 years)

Functional ability (GMFCS level III and IV vs GMFCS level V)

Average baseline standing time/day (<30 minutes vs>30 minutes)

The chief investigator (CI) performed randomisation and allocation after baseline assessment

Assessments and outcome measures- The feasibility of conducting a RCT was assessed by collecting recruitment and attrition rates, baseline characteristics, the acceptability of

77 increasing standing dose, the blinding of the assessor, the percentage of outcome
78 measurements achieved at each stage, and adverse events.

79 The potential primary clinical outcome measure was Reimers' hip migration percentage
80 (HMP)(17). Routine hip surveillance radiographs at baseline, 12 and 24 months were used
81 to avoid additional exposure to radiation. The start time of the treatment phase was
82 scheduled to begin up to 4 weeks before or after a routine hip x-ray. During the analysis,
83 radiographs taken up to 4 weeks before or after specified time points were accepted for
84 analysis. The HMP was reported by two paediatric consultant orthopaedic surgeons to
85 ensure that HMP was measured reliably and to a consistent standard (18).

86 Secondary clinical outcomes were measured at 0, 6 and 12 months by a research
87 physiotherapist blinded to group allocation. These were: Gross Motor Function Measure Item
88 set (GMFM-66-IS) (19), a battery of lower limb function measures described previously (20)
89 that included the modified Tardieu scale (21) measuring spasticity and range of movement of
90 gastrocnemius, hamstrings and hip flexors, ultrasound depth of rectus femoris, thigh girth
91 and myotonometer measurement of gastrocnemius muscle tone. Parents and guardians
92 were asked to complete the Caregivers Priorities and Child Health Index of Life with
93 Disabilities (CPCHILD)(22) questionnaire and the Paediatric Pain Profile (PPP)(23).

94 ***Analyses-*** The feasibility objectives were analysed using descriptive statistics according to
95 the group they were originally assigned (intention to treat analysis).

RESULTS

Recruitment and retention

Twenty-five children were recruited to the study between April 2014 and 2015, at a rate of three per month, reaching 25/30 (83%) of the recruitment target (Figure 1).

<insert figure 1 here>

The two groups were of similar age, but there were more females in the control group (Table 1). The intervention group stood for longer at baseline and had two participants GMFCS III.

<insert table 1 here>

Intervention and feasibility outcomes

Diaries were completed for a mean of 29.2 (SD 18.4) weeks in the control and 19.3 (SD 10.5) weeks in the intervention group. Thirty-eight adverse events were recorded in the diaries, most frequent events were colds (n=28 control, n=7 intervention) or tiredness (n=0 control, n=3 intervention) Three serious adverse events were recorded in the intervention group due to unplanned admissions to hospital with epilepsy (n=2) and respiratory illness (n=1) and were not attributed to standing.

The control group stood for a daily mean of 36.6 (SD 33.8) minutes (mon-sun) with a mean of 43.2 (SD 36.2) minutes during the weekdays (Mon-Fri). This was a 4% decrease in mean standing time compared to baseline, but with 13% increase during weekdays. The intervention group stood for a daily mean of 49.0 mins (SD 39.1) (mon-sun) and a mean of 58.1 (SD 44.1) minutes during the weekdays. This represented an overall 2% increase in standing with 21% increase from baseline during weekdays.

Table 2 shows the number of outcomes recorded for each participant at each time point. Routine clinical hip surveillance radiographs were available in 37% of all possible data points and 25 % of the CPCHILD and 18% PPP questionnaires were returned by parents. Of the secondary clinical outcomes, 93% measures of leg function and 86% of GMFM were collected. The outcome assessor was accidently un-blinded to group allocation on one occasion, and guessed four out of the remaining 18 allocations correctly.

<insert table 2 here>

Results of the pilot RCT within the feasibility study

Table 3 shows the differences in outcome measures at baseline and 12 months. The mean increase in hip migration (12 months – baseline) was larger in the control group (5% SD 17, n=5) than the intervention group (2% SD 3, n=3) in the eight children who had hip x-rays at 12-months. Two in each group had x-rays at 24 months and the mean increase in HMP was 4% in both groups. Improvements were seen in range of movement in the gastrocnemius in the control group, hamstrings in both groups, and hip flexors in the intervention group. The intervention group showed a reduction of spasticity in hamstrings and hip flexors at 12 months. The ultrasound measure of depth of rectus femoris reduced in both groups over 12 months. Mean GMFM -Item Set scores improved at 6 months from 16.5 (10-33) to 21 (5-54) in the control group and 26 (6-69) to 29 (7-62) in the intervention group.

<insert table 3>

DISCUSSION

This study has shown that it is safe and feasible to recruit to an RCT to investigate the effect of the daily duration of using a standing frame on hip migration in non-ambulant children with cerebral palsy.

Recruitment and retention

Families and children were willing to participate in this study. Initial recruitment was slow where physiotherapists perceived parents as already overburdened. However, contrary to clinicians' fears, parents often do want to be approached, even during difficult circumstances (24). An increased recruitment rate was achieved following advice from expert parents on the steering committee and training offered to therapy teams.

Schools and families were generally enthusiastic about participating. Administrative delays experienced while obtaining permission and insurance to carry out research activities in schools could be reduced by involving education partners in the design, planning and management of the study (25). A checklist has been produced to address these potential barriers in future community-based studies (25).

This study had a high rate of attrition. In a previous study assessing the effects of increasing standing time over 9 months on bone mineral density, the investigators achieved 52% of the initial recruitment target and only one participant withdrew (11). Our intervention took place over 12 months, with 24-month follow up of the HMP, in order to reflect the timescale for changes in hip migration shown in previous studies (26, 27). Allocation after routine hip surveillance radiographs caused delays in starting the treatment phase and was the reason that four participants dropped out of the study before allocation. Surgery and botulinum toxin injections contributed to high rates of exclusion and loss to follow-up.

Intervention

Patient and public involvement during the design phase raised concerns over stopping usual standing practice for 12 months, and so the control was set at usual standing time. The intervention group were able to increase their standing time during the school week up to a mean of 58 minutes per day over the 12-month trial, however, the target daily standing time of 120 minutes was unrealistic. Adherence to standing during the week was good, while use

at home was variable due to the multiple pressures of family life. The mean standing time achieved is similar to a study that aimed at increasing standing time by 50% (11).

Goodwin et al (28) explored the acceptability to parents, physiotherapists and other stakeholders of a pilot RCT exploring the effect of standing frames. They concluded that a pilot of 6-12 weeks of standing 3 days per week for 30-60 minutes compared to no standing would be acceptable (29). It is unlikely that changes in hip development will be detectable over such a short period (11). Whilst comparison to no standing is more likely to highlight differences between groups, it is only likely to be acceptable to stake holders over a short period, such as the six-week school holidays. Therefore, a future RCT should compare an hour of standing 5 days per week to 30 minutes of standing 3 times per week for 12 months. This would enable comparison of two durations of standing at a ratio of 10:3, which should enable detection of differences between groups.

Outcomes

The blinding of the assessor to allocation was largely successful and could be used in a multi-site RCT. The primary clinical outcome was measured using routine hip surveillance x-rays, to ensure that children were not exposed to additional radiation or procedures. However, guidelines were applied inconsistently resulting in routine hip surveillance proving inadequate for the primary outcome. Pelvic radiographs may need to be included as a research cost in a full RCT to ensure consistency and timeliness.

The parent reported questionnaires yielded important data about how the child's disability affected family life. Parents were asked to return the questionnaire by post. However, some parents found answering the same questionnaire emotionally challenging when it exposed a lack progress in the child's development. This, along with lack of administrative support, may have contributed to the poor return of these questionnaires. There was poorer completion of the paper diaries in the intervention group. This may reflect situations where both parents

and school completed paper diaries. Online diary and questionnaire collection, with automated reminders, would simplify and improve diary returns.

The magnitude of change in the primary outcome measure

A full set of primary outcome measures (HMP) was available at 0, 12 and 24 months for five participants, which can gives little indication of effect, and provides inadequate data for a power calculation. A power calculation should be made ahead of an RCT using the standard error of measurement of +/- 10% (30) and a clinically significant change of >10%(31) for Reimers' Hip migration percentage(17). Our results showed a small increase in HMP in both groups, but lower in the intervention group over 12 months. Both groups compare favourably with the median annual10% rate of spontaneous hip migration previously reported (17). Hip migration of >40% is an indication for surgical, rather than conservative intervention, to prevent dislocation. Therefore, HMP > 40 should be an additional exclusion criterion for a future RCT and would reduce the number of participants lost to surgery.

A large battery of potential secondary clinical outcome measures were explored. Potential indicators of muscle strength showed a decrease in depth of rectus femoris in both groups and an increase in the cross-sectional area in the intervention group. Studies have shown that muscle thickness increases in relation to weight in typically developing children of this age (32) and that the thickness of this muscle is significantly smaller in children with CP (33). Height and weight should therefore be recorded serially in a future RCT to account for growth. Hamstring range improved in both groups in line with previous work (10). The Myotonometer (an indicator of muscle tone) and thigh girth (an indicator of muscle strength) were not useful outcomes.

Limitations to the study

One limitation of this study was the small sample size, resulting in differences between groups at baseline. In an adequately powered RCT the minimisation criteria of age and GMFCS level should create equivalence between the groups.

Another limitation of this trial was the large attrition rate. Standing frames are part of a complex management plan for children with CP and therefore a RCT may not be able to control all factors (34). Hip adductor tenotomies, proximal femoral osetotomies and hip adductor botulinum toxin injections are common interventions known to affect the primary outcome measure of HMP and should remain exclusion criteria. However, botulinum toxin and soft tissue releases of other lower limb muscles e.g. hamstrings are common and may be indicated for comfort or functional benefit without influencing the primary outcome. In a future RCT these should not be exclusion criteria but should be noted as possible confounding factors. This may help reduce the rate of attrition.

Missing data was a limitation of this study, particularly for the primary outcome and diaries. A proportion of the HMP was not reported due to inadequate routine surveillance radiographs or inability to retrieve radiographs from hospital records. In a future RCT, it would be necessary to establish the inter- and intra-observer reliability of the raters in order to calculate the standard error of measurement (18).

An important limitation to this trial was the failure to establish distinctly different standing times in the two arms of the trail. This resulted in the control group being too similar to the intervention group. Recommendations are made to specify the dosage for a future study.

Conclusions

This study assessed the acceptability and adherence of a standing programme at home and school and feasibility of a RCT design. It explored barriers and facilitators to recruitment, documented the individualised standing programmes through diaries and assessed the use of a range of outcomes (35).

It is safe and feasible to conduct a RCT to assess the clinical effectiveness of comparing two duration times of standing on the rate of hip migration in children with CP. To facilitate a clear distinction in doses between the two groups, recommended dosages of one hour, five times per week would be compared to a control group standing for 30 minutes three times per week, over twelve months. Hip x-rays should be included as a research cost to improve the consistency and timing of the hip xray surveillance as a source of the primary outcome.

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