Serial night casting increases ankle dorsiflexion range in children and young adults with Charcot-Marie-Tooth disease: a randomised trial

Kristy J Rose\textsuperscript{1,2}, Jacqueline Raymond\textsuperscript{2}, Kathryn Refshauge\textsuperscript{2}, Kathryn N North\textsuperscript{1,2} and Joshua Burns\textsuperscript{1,2}

\textsuperscript{1}The Children's Hospital at Westmead, \textsuperscript{2}The University of Sydney

Introduction

Charcot-Marie-Tooth disease, the most common genetic nerve disorder of childhood, describes a group of clinically and genetically heterogeneous neuropathies characterised by abnormal nerve conduction, absent tendon reflexes, sensory loss, cavus foot deformity, and progressive distal muscle weakness and atrophy (Birouk et al 1997). Restricted ankle dorsiflexion range – or ankle equinus – is a common impairment in children and adolescents with Charcot-Marie-Tooth disease (Burns et al 2009a). Length-dependent neuronal degeneration in the early stages of the disease causes selective weakness of the ankle dorsiflexors, and while the ankle plantarflexors are also affected, they remain stronger by comparison and overpower the weak ankle dorsiflexors (Burns et al 2005). Over time, ankle dorsiflexion range decreases due to shortening of the gastrocnemius and soleus which in turn can limit mobility and balance (Burns et al 2009a, Newman et al 2007). These limitations have also been reported to worsen health-related quality of life (Burns et al 2010).

While there has been considerable animal research to identify a cure for Charcot-Marie-Tooth disease (Khajavi et al 2005, Passage et al 2004), it has not translated successfully to humans. Instead rehabilitative and surgical strategies are common practice. Currently, intervention for ankle equinus in Charcot-Marie-Tooth disease is preventive, symptomatic, or palliative depending on the degree of the limitation in range and its effect on activity. Orthopaedic surgery is frequently performed to lengthen the Achilles tendon. However, while surgery yields immediate results, the risk of the contracture recurring is high (Wetmore and Drennan 1989). Non-surgical stretching is frequently used clinically to increase ankle dorsiflexion range in children and young adults with Charcot-Marie-Tooth disease. Two small randomised trials (n = 12 and n = 14) in people with Charcot-Marie-Tooth disease type 1A investigated the effect of three months of prefabricated night splinting (Redmond 2004, Refshauge et al 2006). Neither study found a statistically or clinically significant effect of the intervention on any of the outcome measures which included ankle dorsiflexion range, foot posture, and ankle strength. Interestingly, participants in one of the studies anecdotally reported improvement in motor activities after wearing the splint (Refshauge et al 2006). Both studies reported technical difficulties with the prefabricated splint falling off at night, which may have resulted in insufficient duration or intensity of the stretch (Redmond 2004, Refshauge et al 2006).

Serial casting is also employed to increase ankle dorsiflexion range in children and young adults with Charcot-Marie-Tooth disease. Typically, a below-knee cast is applied to lengthen the triceps surae and worn for 24 hours a day. Cast changes are made every three to seven days, each aiming to achieve a greater range of ankle dorsiflexion than the previous cast, and continued until the desired range of ankle dorsiflexion is obtained. Although there have been no randomised trials of...
serial casting in people with Charcot-Marie-Tooth disease, there have been studies in other neurological conditions such as traumatic brain injury (Moseley 1997, Moseley et al 2008). While significant gains in ankle dorsiflexion range occurred in these studies, gains were generally lost once the cast was removed.

Clinically, serial casting is not always well tolerated by individuals with Charcot-Marie-Tooth disease. Wearing casts full-time can be uncomfortable and inconvenient, particularly for more active children and young adults (Refshauge et al 2006). In addition, many people with this disease have sensory impairment, which is thought to increase the risk of developing pressure areas if casts are worn continuously. In patients at risk of such complications, a removable serial night cast can be fabricated whereby the cast is applied according to the principles of serial casting, but bi-valved and worn only at night. However there are no data to support its use in Charcot-Marie-Tooth disease. Therefore, the specific research question for this study was:

Does 4 weeks of serial night casting followed by 4 weeks of stretching of the gastrocnemius and soleus improve ankle dorsiflexion range, mobility and balance, and reduce foot deformity, falls, and self-reported activity limitations compared with no intervention in children and young adults with Charcot-Marie-Tooth disease?

**Method**

**Design**

A randomised trial with assessor blinding and intention-to-treat analysis was conducted. People with Charcot-Marie-Tooth disease were recruited from the neurogenetics and peripheral neuropathy clinics at a large tertiary children’s hospital in Australia. After baseline measures were collected, the treating physiotherapist telephoned the administrative assistant to obtain the participant’s random allocation. The randomisation sequence was computer-generated by an off-site administrative assistant who had no further involvement in the study. Participants were randomly allocated to either the experimental group or a control group. The experimental group received bilateral below-knee fibreglass casts which were bi-valved with a plaster saw and secured firmly to the limb with Velcro straps. Participants (and their caregivers) were instructed that the casts were to be worn while sleeping every night. No specific instructions were given regarding leg position during sleeping. New casts were made after two weeks to ensure that the stretch was maintained in the event of improved dorsiflexion range. At four weeks, the treating physiotherapist instructed the participants to stop wearing the casts and start a 4-week stretching program consisting of standardised weight-bearing stretches for the gastrocnemius and soleus. To stretch the gastrocnemius, participants were instructed to stand facing a wall or bench with feet shoulder width apart and perpendicular to the wall. They were then instructed to lean forward, keeping the back knee straight and the heel grounded. To stretch the soleus, participants were instructed to bend both knees, keeping both feet flat on the floor. Participants were asked to hold each stretch for one minute and to perform each stretch three times daily.

The control group did not receive any intervention for the duration of the study.

All participants were asked to avoid additional stretches or other specific exercises of the foot and ankle for the duration of the study. At the completion of the study, participants in the control group were offered the serial night casting and stretching. Participants and their caregivers recorded compliance with the casting and stretching regimen in a daily diary.

**Outcome measures**

The primary outcome was ankle dorsiflexion range measured using the Lunge Test (Bennell et al 1999, Burns et al 2009a). Participants stood with one foot perpendicular to a wall and were asked to lunge forward towards the wall. The foot was progressively moved further away from the wall until the maximum range of ankle dorsiflexion was obtained without the heel lifting off the ground. The angle of the tibial shaft from vertical was measured in degrees using a digital inclinometer (Bennell et al 1999). The more involved ankle (ie, with lesser dorsiflexion range) was measured (Menz 2005). The validity of this test is supported by ultrasonography, which shows elongation of the gastrocnemius and soleus fascicle lengths during
the lunge (Hallet et al 2005). Additionally, since ankle dorsiflexion range is assessed in weight bearing, it more closely approximates the range of ankle dorsiflexion during activity.

Secondary outcomes included foot deformity, mobility, balance, falls, and self-reported activity limitations. Foot deformity was measured with the Foot Posture Index – a multi-segmental screening tool that allocates a score between –2 and +2 to each of six criteria related to foot structure (Redmond et al 2006). Mobility was measured as the speed of three motor tasks: standing up from a chair (stands/s), walking (both preferred speed and fast speed in m/s), and ascending and descending stairs (stairs/s). Balance was measured as the maximum time (up to 30 s) to maintain three tasks from the Berg Balance Scale (Berg et al 1992): standing with the medial borders of the feet touching, standing with the big toe of one foot beside the heel of the other foot and standing with the toes of one foot placed directly behind the heel of the other foot (tandem stance). Falls and adverse events were recorded daily in a diary. Falls were reported as the number of falls to the ground in the week prior to scheduled visits. Self-reported activity limitations were measured with the Patient Specific Functional Scale (Westaway et al 1998). Participants were asked to nominate three activities that they had difficulty

---

**Figure 1.** Design and flow of participants through the trial.
performing and rate their ability to perform these activities on a scale from 0 to 10, with 0 indicating they were unable to perform the activity and 10 indicating they could perform the activity without any difficulty. The scores for the three activities were summed. While the validity of using the Patient Specific Functional Scale has not been established in children as young as 7 years, it has been shown that children as young as 6 years have the ability to self-report pain, disability, and activity limitation using similar visual analogue scales (Shields et al 2003). Additionally, young children have been shown to reliably answer questions regarding the impact of disease on their life (Dickinson et al 2007).

Data analysis

We selected 5 degrees of dorsiflexion range a priori as the minimum clinically relevant difference, as it is used widely (Ben et al 2005, Refshauge et al 2006). The best estimate of the standard deviation of ankle dorsiflexion range in this population is 6 deg (Refshauge et al 2006). A total of 24 patients would provide an 80% probability of detecting a difference of 5 deg at a two-sided 5% significance level. To allow for loss to follow-up, we increased the total sample size to 30.

Descriptive statistics were used to characterise the sample. Normality of data distribution was assessed and the appropriate parametric or non-parametric statistical tests were applied. The mean (95% CI) between-group difference was determined at 4 and 8 weeks using analysis of covariance to adjust for baseline differences between groups (Vickers and Altman 2001). An intention-to-treat analysis was used.

Results

Flow of participants, therapists and centres through the trial

Between January 2006 and July 2009, 116 patients were screened for inclusion in the study. Of these, 30 (26%) children and young adults with Charcot-Marie-Tooth disease fulfilled the inclusion criteria and consented to participate in the study. Reasons for non-eligibility are presented in Figure 1. Fifteen participants were randomised to each group. Table 1 outlines the baseline characteristics of the participants. Twenty-nine children and young adults were independently ambulant without the need for an aide or orthosis. One participant with Dejerine-Sottas syndrome used an electric wheelchair for long distance mobility but was able to stand and walk short distances independently. One child in the experimental group had attention-deficit hyperactivity disorder. None of the other participants had coexisting conditions. All 30 (100%) participants completed the study with no participants lost to follow-up. Measures of ankle dorsiflexion range and foot deformity could not be obtained at 4 or 8 weeks from the child in the experimental group with attention-deficit hyperactivity disorder due to non-compliance, but all other outcomes were obtained from this child.

A physiotherapist with nine years of clinical experience and four years of research experience in paediatric neuromuscular disorders provided the intervention to the experimental and control groups.

The study was conducted in the Outpatient Physiotherapy Department of a large tertiary children’s hospital. Children with Charcot-Marie-Tooth disease constitute approximately 35% of yearly referrals made to the physiotherapist in the neurogenetics and peripheral neuropathy clinics at this hospital.

Compliance with trial method

Compliance was excellent during the 4-week night casting period. Participants wore the casts for an average of 24 nights (SD 4) representing 86% compliance. Five participants reported 100% compliance. When participants in the experimental group started the stretching program, compliance reduced to an average of 18 days (SD 5) representing 65% compliance. The most commonly cited reason for not doing the stretches was a lack of time due to after school/work or weekend commitments such as homework, sporting pursuits, and recreation.

Effect of intervention

Group data for all outcomes at baseline, 4 weeks, and 8 weeks for the experimental and control groups are presented in Table 2 while individual data are presented in Table 3 (see eAddenda for Table 3). By 4 weeks, serial night casting had increased ankle dorsiflexion range by a mean of 4 deg (95% CI 2 to 6) more in the experimental group than the control group. After a further 4 weeks of weightbearing stretches, the experimental group still had a mean of 3 deg (95% CI 0 to 5) more ankle dorsiflexion range than the control group. See Figure 2.

Only one of the 18 secondary outcomes showed a statistically significant between-group difference at either measurement point. By 4 weeks, serial night casting had increased preferred walking speed by a mean of 0.1 m/s (95% CI 0.1 to 0.01) more in the experimental group than the control group.

Minor adverse events were reported by two (13%) children in the experimental group. One child experienced mild bruising on her upper right calf muscle corresponding with the upper rim of the cast. The child was not clear how this
Table 2. Mean (SD) outcomes for each group, mean (SD) difference within groups, and mean (95% CI) difference between groups.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Exp</th>
<th>Con</th>
<th>Exp</th>
<th>Con</th>
<th>Exp</th>
<th>Con</th>
<th>Exp</th>
<th>Con</th>
<th>Exp ~ Con</th>
<th>Exp ~ Con</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Week 0</td>
<td>Week 4</td>
<td>Week 8</td>
<td>Week 0</td>
<td>Week 4</td>
<td>Week 8</td>
<td>Week 0</td>
<td>Week 0</td>
<td>Week 4</td>
<td>Week 8</td>
</tr>
<tr>
<td></td>
<td>(n = 15)</td>
<td>(n = 15)</td>
<td>(n = 15)</td>
<td>(n = 15)</td>
<td>(n = 15)</td>
<td>(n = 15)</td>
<td>(n = 15)</td>
<td>(n = 15)</td>
<td>(n = 14)</td>
<td>(n = 14)</td>
</tr>
<tr>
<td><strong>Ankle dorsiflexion (deg)</strong></td>
<td>14 (6)</td>
<td>15 (6)</td>
<td>19 (6)</td>
<td>15 (7)</td>
<td>19 (6)</td>
<td>17 (6)</td>
<td>4 (6)</td>
<td>0 (7)</td>
<td>5 (4)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Foot deformity</td>
<td>1.7 (6.2)</td>
<td>–2.5 (4.6)</td>
<td>1.7 (5.5)</td>
<td>–1.9 (4.5)</td>
<td>1.4 (5.9)</td>
<td>–1.8 (4.5)</td>
<td>0.0 (1.5)</td>
<td>–0.6 (2.1)</td>
<td>–0.3 (1.9)</td>
<td>0.7 (2.0)</td>
</tr>
<tr>
<td>FPI (~12 to 12)</td>
<td>0.0 (7)</td>
<td>–4.0 (6)</td>
<td>0.0 (5)</td>
<td>–2.0 (4)</td>
<td>0.0 (3)</td>
<td>–3.0 (3)</td>
<td>–0.6 (3.0)</td>
<td>–0.0 (2.1)</td>
<td>–0.6 (2.0)</td>
<td>0.0 (2.1)</td>
</tr>
<tr>
<td><strong>Mobility</strong></td>
<td>1.0 (0.3)</td>
<td>1.0 (0.3)</td>
<td>0.8 (0.3)</td>
<td>0.9 (0.4)</td>
<td>0.8 (0.3)</td>
<td>0.8 (0.4)</td>
<td>–0.2 (0.3)</td>
<td>–0.1 (0.2)</td>
<td>–0.1 (0.2)</td>
<td>–0.1 (0.2)</td>
</tr>
<tr>
<td>Standing up speed (stands/s)</td>
<td>0.8 (0.1)</td>
<td>0.9 (0.1)</td>
<td>0.8 (0.1)</td>
<td>1.0 (0.1)</td>
<td>0.5 (0.1)</td>
<td>0.6 (0.1)</td>
<td>0.0 (0.1)</td>
<td>0.0 (0.1)</td>
<td>0.0 (0.1)</td>
<td>–0.09 (0.03)</td>
</tr>
<tr>
<td>Walking speed–preferred (m/s)</td>
<td>0.5 (0.1)</td>
<td>0.6 (0.1)</td>
<td>0.5 (0.1)</td>
<td>0.6 (0.1)</td>
<td>0.5 (0.1)</td>
<td>0.6 (0.1)</td>
<td>0.0 (0.1)</td>
<td>0.0 (0.1)</td>
<td>0.0 (0.1)</td>
<td>–0.46 (0.28)</td>
</tr>
<tr>
<td>Walking speed–fast (m/s)</td>
<td>1.2 (0.2)</td>
<td>0.9 (0.2)</td>
<td>1.1 (0.2)</td>
<td>0.9 (0.2)</td>
<td>1.1 (0.2)</td>
<td>1.0 (0.2)</td>
<td>–0.1 (0.2)</td>
<td>0.0 (0.2)</td>
<td>0.0 (0.2)</td>
<td>0.04 (0.08)</td>
</tr>
<tr>
<td>Stairs speed (stairs/s)</td>
<td>27.2 (7.3)</td>
<td>28.1 (7.2)</td>
<td>27.1 (7.5)</td>
<td>28.2 (7.1)</td>
<td>28.4 (6.3)</td>
<td>27.9 (7.4)</td>
<td>–0.1 (0.4)</td>
<td>0.1 (0.1)</td>
<td>1.2 (0.8)</td>
<td>–0.2 (5.2)</td>
</tr>
<tr>
<td>Feet together side by side</td>
<td>24.6 (9.3)</td>
<td>26.4 (9.1)</td>
<td>23.5 (10.2)</td>
<td>26.0 (8.5)</td>
<td>26.3 (6.2)</td>
<td>26.8 (8.7)</td>
<td>–1.1 (6.3)</td>
<td>–0.4 (4.2)</td>
<td>1.7 (0.9)</td>
<td>0.4 (6.2)</td>
</tr>
<tr>
<td>Standing with big toe touching heel</td>
<td>19.5 (11.2)</td>
<td>23.8 (9.8)</td>
<td>19.2 (11.7)</td>
<td>23.4 (10.5)</td>
<td>24.9 (9.8)</td>
<td>24.9 (9.8)</td>
<td>–0.3 (7.6)</td>
<td>–0.4 (7.6)</td>
<td>5.4 (10.8)</td>
<td>1.1 (6.9)</td>
</tr>
<tr>
<td>Tandem stance</td>
<td>11.6 (4.2)</td>
<td>13.3 (5.2)</td>
<td>15.4 (3.3)</td>
<td>15.1 (5.4)</td>
<td>16.7 (5.0)</td>
<td>17.2 (6.6)</td>
<td>3.8 (3.9)</td>
<td>1.8 (3.8)</td>
<td>5.1 (5.3)</td>
<td>3.9 (3.1)</td>
</tr>
<tr>
<td>Falls (n)</td>
<td>6 (6)</td>
<td>8 (6)</td>
<td>2 (13)</td>
<td>4 (9)</td>
<td>1 (1)</td>
<td>2 (3)</td>
<td>–4 (5)</td>
<td>–4 (12)</td>
<td>–5 (13)</td>
<td>–6 (13)</td>
</tr>
<tr>
<td>Self-reported activity limitations</td>
<td>13.6 (10)</td>
<td>13.3 (10)</td>
<td>15.4 (15)</td>
<td>15.1 (15)</td>
<td>16.7 (15)</td>
<td>17.2 (15)</td>
<td>3.8 (3.8)</td>
<td>1.8 (3.8)</td>
<td>5.1 (5.3)</td>
<td>3.9 (3.1)</td>
</tr>
</tbody>
</table>

Exp = experimental group, Con = control group, shaded row = primary outcome, * = ANCOVA-adjusted for baseline, PSFS = Patient Specific Functional Scale, FPI = Foot Posture Index
had occurred but thought that the upper border of the cast had probably bruised the calf when she turned in bed and her leg made contact with their bedroom wall. The parent of another child reported a blister on the left fifth toe due to an exposed edge of the cast, which irritated the skin. Both children continued wearing the casts with the application of additional padding over the problem areas. There were no serious adverse events.

Discussion

This is the first randomised controlled trial to examine the effect of serial night casting on ankle dorsiflexion range of motion in children and young adults with Charcot-Marie-Tooth disease. Four weeks of serial night casting significantly increased ankle dorsiflexion range by, on average, 4° compared with no intervention, but at 8 weeks there was no significant difference between groups. Besides reduced time to walk 10 m at preferred speed favouring night casting at 4 weeks, no other outcomes differed between groups at either measurement point. It remains unclear if the effect size achieved in this study is functionally relevant.

The results of this study concur with previous investigations of various stretching interventions for the ankles in other neurological conditions such as spinal cord injury (Ben et al 2005, Harvey et al 2000, Harvey et al 2009) and traumatic brain injury (Moseley 1997). We did, however, find larger improvements in ankle dorsiflexion range than the previous two studies of prefabricated night splints in Charcot-Marie-Tooth disease (Redmond 2004, Refshauge et al 2006). There may be a number of reasons for this. We used a different type of intervention from the previous studies. In this study the night casts were custom made for each participant with their ankle positioned in maximal passive dorsiflexion and then replaced at 2 weeks to further increase the stretch. The casts could not be adjusted and there was no opportunity to reduce the amount of stretch given, as in previous studies. While the previous studies reported similar compliance with prefabricated night splints, these detached during the night in some participants. As we did not encounter this problem, our study participants may have received a stretch of greater intensity and duration.

We anticipated that increases in ankle dorsiflexion range might translate to improvements in activity, since restricted ankle dorsiflexion flexibility is a significant independent predictor of activity limitations in children with Charcot-Marie-Tooth disease (Burns et al 2009). However, study participants may not have gained enough ankle dorsiflexion range to significantly affect function. It is also possible that some of the outcome measures used to assess motor function were lacking in sensitivity and responsiveness to change for the less affected children and young adults. For example, it is likely that the balance tasks were not challenging enough considering the 30 participants obtained an average balance time of 25 s at baseline and 8 children achieved the 30 s ceiling for all three balance tasks providing little or no room for improvement. A 1 min ceiling, or more challenging balance and motor tasks might have been more sensitive to change and yielded different results. This should be considered in the future when selecting functional outcome measures for children and young adults with Charcot-Marie-Tooth disease, especially for those with less severe Charcot-Marie-Tooth disease phenotypes.

The primary outcome in this study was ankle dorsiflexion range which, after much consideration, was assessed using the weightbearing lunge test. This method was selected as it is the most reliable, feasible and widely published clinical method for quantifying ankle dorsiflexion range in children. As in previous studies, we did not intend to measure underlying tissue mechanics or passive properties of associated soft tissues, which would have necessitated the use of a torque-controlled device (Harvey et al 2003). The simplicity of the lunge test reflects our desire to measure clinically and functionally meaningful outcomes that can be interpreted and targeted by the practising clinician.

We found that 4 weeks of serial night casting resulted in statistically significant but small increases in ankle dorsiflexion range compared with no intervention. However, these effects were not maintained with stretching at 8 weeks. This does not mean we should abandon stretching interventions in children and young adults with Charcot-Marie-Tooth disease. We found serial night casting to be safe and well tolerated. Many of the participants commented that the intervention was worthwhile and continued to wear the casts after they had completed the study. Participants also appreciated having to wear the casts only at night, as they could participate in their regular daytime activities and avoid feeling self-conscious about wearing serial casts to school, university, or work. Further investigation into the efficacy of serial night casting for children and young adults with Charcot-Marie-Tooth disease is required. Such studies should be designed to allow for a greater number of cast changes, to control for leg position while sleeping and be conducted over a longer period of time in order to assess the effect of the intervention on functional and meaningful outcomes such as walking distance, fatigue, balance, pain, and activity participation.


Addenda: Table 3 available at jop.physiotherapy.asn.au

Ethics: The Human Research and Ethics Committee of The Children’s Hospital at Westmead, Australia, approved this study. Informed consent was obtained for all participants before data collection began.

Competing interests: None declared.
Support: KJR is supported by a scholarship from the Medical Foundation of The University of Sydney and JB is supported by an Australian Clinical Research Fellowship from the National Health and Medical Research Council of Australia (NHMRC#336705). Grant obtained from the Australian Podiatry Education and Research Foundation Research.

Acknowledgements: We thank Stephanie Wicks for study co-ordination, Annie Soo for participant randomisation, and Roger Adams for statistical advice.

Correspondence: KJ Rose, Institute for Neuroscience and Muscle Research, The Children’s Hospital at Westmead, Locked Bag 4001, Westmead NSW 2145 Australia. E-mail: KristyR2@chw.edu.au

References


