Author's response to reviews

Title: Splint: The efficacy of orthotic management in rest to prevent equinus in children with cerebral palsy, a randomised controlled trial

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Version: 3 Date: 23 December 2011

Author's response to reviews: see over
Dear editor,

Thank you for the opportunity to send in a revised version of our manuscript (MS: 1351761665484255) entitled: "Splint: The efficacy of orthotic management in rest to prevent equinus in children with cerebral palsy, a randomised controlled trial". We were very pleased with the responses of the reviewer and found the comments constructive and helpful. We hope that the manuscript addresses the comments. Below you will find a point-by-point response to the comments of the referee and the corresponding changes we made to the manuscript. Regarding the request in your email to document ethical approval we added lines 173-174: “This study is approved by the Medical Ethics Committee of the VU University Medical Center and by the Institutional Review Board of the Washington University in Saint Louis.”

We hope these changes meet your requirements and we look forward to hearing from you.

Yours sincerely,

José Maas, MSc
Point by point response to the reviewer

We would like to thank the reviewer for the helpful comments and questions. Below we made a point-by-point response to the comments of the reviewer. In doing so, we interspersed our reactions in italics between the original reviews and indicated where actions have been taken.

Reviewer: Elizabeth Asztalos
Version: 2 Date: 3 November 2011

Title: Splint: The efficacy of orthotic management in rest to prevent equinus in children with cerebral palsy, a randomised controlled trial

Summary of Trial: This is a manuscript outlining the study protocol for the evaluation of splints (KAFOs) either fixed or dynamic in design compared to no splints in children with cerebral palsy. The study protocol appears to be in place over a year with the children. The primary outcome measure will be ankle dorsiflexion at full knee extension, measured with a custom designed hand held dynamometer. Secondary outcome measures will be i) maximal knee extension in stance during gait, ii) knee extension in midstance during gait, iii) ankle dorsiflexion in midstance during gait and iv) gross motor function. Furthermore, to gain more insight in the working mechanism of the orthotic management in rest, morphological parameters like Achilles tendon length, muscle belly length, muscle fascicle length, muscle physiological cross sectional area length and fascicle pennation angle will be measured in a subgroup of 18 participants a 3D imaging technique. The design of the trial is a single blind randomised controlled trial with 66 children with spastic CP, divided over three groups with each having 22 participants. Two groups will be treated for 1 year with orthoses to prevent a decrease in range of motion in the ankle (either with static or dynamic knee-ankle-foot-orthoses) and a third group will be included as a control group and will receive usual care (physical therapy, manual stretching). Measurements will be performed at baseline and at 3, 6, 9 and 12 months after treatment allocation. children with spastic CP divided over three groups with each 22 participants. Two groups will be treated for 1 year with orthoses to prevent a decrease in range of motion in the ankle (either with static or dynamic knee-ankle-foot-orthoses) and a third group will be included as a control group and will receive usual care (physical therapy, manual stretching). Measurements will be performed at baseline and at 3, 6, 9 and 12 months after treatment allocation.

Summary of Paper:

1) “It is not clear to this reviewer why this question is being asked and why the investigators feel that they need to test the use of Knee-Ankle-Foot orthosis (KAFOs) at night in children with cerebral palsy. "

Response: In children with Cerebral Palsy, the Gastrocnemius muscle is often spastic[1]. Secondary to the spasticity, this muscle is presumed to be stiffer and shorter in children with Cerebral Palsy compared to that in typically developing children [2]. It is assumed that this shortness and stiffness results in a reduced ankle dorsiflexion range of motion. A reduced ankle dorsiflexion range of motion is associated with deviated gait patterns and limitations in mobility [1,3-5]. Therefore, it is important to lengthen and/or to reduce the stiffness of the Gastrocnemius muscle
and by this increase the dorsiflexion range of motion. Sustained muscle stretch is presumed to be a condition to induce such muscular adaptations. By using a KAFO (orthotic management in rest), which is part of general management of children with Cerebral Palsy[1,6,7] the Gastrocnemius muscle is maintained in an extended position (i.e. at high length). As the Gastrocnemius muscle has its origin at the femur and its insertion at the calcaneus, this extended position is imposed by knee extension and ankle dorsiflexion. Based on joint immobilization studies of animals, it is well known that sustained muscle stretch stimulates an increase in muscle length by addition of sarcomeres in series[8-10]. In analogy with these results it is expected that the use of KAFOs as treatment of spastic calf muscles, will lengthen these muscles and in particular the Gastrocnemius muscle.

However, the evidence that sustained muscle stretch is effective in preventing reduced ankle dorsiflexion range is very limited (see for review Pin et al.[11]) and in clinical practice the physicians’ opinions about the efficacy of orthotic management in rest are conflicting. To the best of our knowledge, the only study regarding the effects of sustained stretch on the Gastrocnemius muscle is an observational study by Tardieu et al.[1986][12] including only 2 patients treated with a night splint. The study showed conflicting effects of the night splint in these two patients.

Given the potential beneficial effects of the use orthotic management in rest and the fact that this is not an evidence based treatment, the use of KAFOs and the optimization of this treatment requires further investigation.

Manuscript changes:

2nd and 3rd paragraph (lines 49 – 65) are rephrased as follows:

“Range of motion (ROM) deficits in one or more limb joints are present in many children with spastic cerebral palsy with about the half of the children having ROM deficits in the ankle, knee and hip[13]. In clinical practice, it is assumed that a reduced ROM in a joint is caused by a relative shortness of the muscle tendon complex compared to the length of the bone and/or by enhanced stiffness of the muscle tendon complex[14,15].

The Gastrocnemius muscle is often spastic in children with CP[1]. As the Gastrocnemius muscle has origin at the femur and his insertion at the calcaneus, this muscle is a major determinant of the ankle and knee ROM. The Gastrocnemius muscle was found to be shorter and stiffer in children with CP (having reduced ankle dorsiflexion) compared to typical developing children[2] and is expected to play a major role in the cause of limited ankle dorsiflexion ROM (measured at full knee extension). This ankle dorsiflexion ROM may lead to equinus deformities in the ankle[16]. Furthermore, a short and stiff Gastrocnemius muscle may lead to a gait pattern with increased ankle plantar flexion and increased knee flexion in midstance[3,5]. Compared to children with typical gait patterns, children with deviated gait patterns are impaired in mobility[1] and are metabolically less efficient and less resistant to fatigue during walking[4]. To prevent equinus contractures and less efficient gait patterns, it is important to treat and prevent impaired ankle dorsiflexion[1]."

Lines 68-73 are added to the manuscript

“It is recommended not to use surgical interventions to improve gait (and thus not to treat impaired ankle dorsiflexion ROM by using surgical intervention) until gait is matured [1]. Based on joint immobilization studies of animals, it is well known that sustained muscle stretch stimulates an increase in muscle length by addition of sarcomeres in series[8-10]. In analogy with these results it is expected sustained muscle stretch as treatment of spastic calf muscles, will lengthen these muscles and in particular the gastrocnemius.”

Lines 87-88 are added to the manuscript
“Although sustained stretch is not an evidence based treatment, it is often applied by the use of night splints that are part of the general management of children with CP [1,6,7].”

Lines 101-109 were included in the original manuscript as well and describe the limited amount of literature.

“To the best of our knowledge, Tardieu et al.[12] is the only study that evaluates the efficacy of orthotic management in rest in children with CP. It reports the effectiveness of orthotic treatment at night in two children, but these results are not confirmatory, due to the limited study design: 1) the number of treated subjects (2) was small, 2) there was no control group, and 3) the subject’s ankle dorsiflexion was measured in knee flexion rather than extension which is more consistent with a measure of the Soleus muscle length instead of the Gastrocnemius muscle. Therefore, more research is needed to establish whether their conclusions were correct and whether the Gastrocnemius muscle will adapt in the same way to sustained stretch as the Soleus muscle.

2) “They include the limited amount of literature in this area but do not explain why that is the case.”

Response: Indeed, the amount of literature with respect to the efficacy of orthotic management in rest is limited and to our knowledge, no new studies have been published in the last six months. It is not clear why there is such limited amount of literature available on this topic. Possibly, in clinic the efficacy of KAFOs is accepted as general knowledge, as KAFOs are part of the general management[1,6,7] of children with CP.

Manuscript changes:

Lines 109 - 111 are added to the manuscript

“Despite the reported limited evidence in the literature, the efficacy of orthotic management in rest is probably considered as general knowledge.”

Line 87-88 are added to the manuscript

“Although sustained stretch is not an evidence based treatment, it is often applied by the use of night splints that are part of the general management of children with CP [1,6,7].”

In addition, to indicate that the use of KAFOs is general practice we now have cited several papers [1,6,7], which do mention that orthotic management in rest is part of general treatment of children with CP.

3) “There is also not a very clear reason why this should be done at night. Are there potential proposed benefits that warrant this exploration?”

Response: We would like to clarify that we are proposing orthotic management (for stretching) during rest. This does not necessarily have to be during sleep or at night. Wearing a KAFO with fixed knee joints (used in this study) may interfere with mobility and is not easy to wear during the active parts of the day. Other orthoses, like Ankle Foot Orthosis(AFOs) that are often used during active parts of the day, do not necessarily stretch the Gastrocnemius Muscle as the knee is allowed to flex. Knee flexion will occur during, for example, walking and sitting. Therefore, it is questionable whether these AFOs apply sustained strain to the Gastrocnemius Muscle. In this regard, the use of KAFOs at night is expected to be more effective.
Manuscript changes:

Line 96 - 101 are added to the manuscript

"Using KAFOs in rest could be more effective compared to using KAFOs during active moments of the day. It might be presumed that a KAFO with fixed knee joints limits mobility, and therefore, will likely not be worn during active moments of the day. Other orthoses, like AFOs that are often used during active parts of the day, do not necessarily stretch the Gastrocnemius Muscle as the knee is allowed to flex. Knee flexion will occur during, for example, walking and sitting."

4) “The inclusion criteria are not clear. Are they planning to include children with varying degrees of cerebral palsy as determined by the GMFCS score? Children with a GMFCS score of 2 or less may have a totally different response than those with GMFCS score of 3, 4, or 5. In addition, age and growth are not taken into consideration”

Response: Indeed, GMFCS level, age and growth are important to describe the specific group of children including. In the original manuscript, the GMFCS levels of the children to be included were mentioned in table 1 (see below), which is referred to in the text. We will only include children with GMFCS level 1, 2 and 3 (all able to walk) and within the age between 4 and 12 years.

To take effects of growth into consideration, we will measure the body and lower leg lengths. Particularly, lower leg length will be measured to correct for the amount of growth that the children will undergo during the study. These details were mentioned in the original manuscript and are now described at lines: 332 – 334

"Patient characteristics will be recorded using an intake form and will include age, gender, race, ethnicity, weight, length, localisation of CP (uni- or bilateral) and Gross Motor Function Classification System (GMFCS)[17] class."

And lines 340 – 345

"Variables to be measured are: 1) Position of the foot in standing, 2) transmalleolar axis position[18], 3) gait pattern classification according to Rodda[19] and Becher[20], 4) ROM of the ankle and knee joints, 5) spasticity, by measuring the angle of catch (AOC)[21] of the ankle and knee, 5) selective motor control, using the Selective Control Assessment of the Lower Extremity (SCALE)[22] and 6) lower leg length."

And lines 463 – 465

"Covariates will be: 1) KAFO wearing time, 2) lower leg growth, 3) use of an AFO by day, 4) stretching exercises and 5) level of spasticity."
### Table I: Inclusion and exclusion criteria

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
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<tbody>
<tr>
<td>Children must have:</td>
<td>Children must not:</td>
</tr>
<tr>
<td>1. a clinical diagnosis of unilateral or bilateral spastic CP</td>
<td>1. have had surgery of the Gastrocnemius and/or Soleus muscle</td>
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<tr>
<td>2. an age between 4-12 years old</td>
<td>2. have had Selective Dorsal Rhizotomy</td>
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<tr>
<td>3. at least 0° ankle dorsiflexion with extended knee</td>
<td>3. have had Intrathecal Baclofen therapy</td>
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<tr>
<td>4. a GMFCS class I, II or III</td>
<td>4. have had Botulinum toxin A treatment in the lower extremity less than 6 months ago</td>
</tr>
<tr>
<td>5. has been treated for reduced ankle dorsiflexion (&lt; 5° dorsiflexion) before the start of the study by:</td>
<td>5. have had casting of the lower extremity less than 3 months ago</td>
</tr>
<tr>
<td>a. and/or serial casting at least 3 months ago</td>
<td>6. have knee contractures (less than 0° knee extension)</td>
</tr>
<tr>
<td>b. and/or Botulinum toxin A injections in the Gastrocnemius and/or Soleus muscle at least 6 months ago</td>
<td>7. have more than 20° ankle dorsiflexion at full knee extension</td>
</tr>
<tr>
<td>c. orthotic management in rest with a knee-ankle-foot orthosis to prevent for decreasing ankle dorsiflexion</td>
<td>8. have behavioural problems (like mental retardation)</td>
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<tr>
<td>6. a stable social family situation</td>
<td>9. have significant sleeping problems</td>
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<td></td>
<td>10. be institutionalised</td>
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<tr>
<td></td>
<td>11. be suffering from co-morbidity interfering with mobility that prevents them from walking adequate distance.</td>
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<tr>
<td></td>
<td>12. have problems with understanding either the Dutch (for subjects in the Netherlands) or English language</td>
</tr>
</tbody>
</table>

### Reference List


5) “I realize that this is a project currently or possibly underway in the future but justification as to why this is being proposed would be helpful. KAFOs are used in the general management of children with cerebral palsy for a variety of reason and the reasons vary depending on the capabilities of the child. In this study, it is not clear as to whether a specific group of children are included however; a clearer justification would be most valuable.”

   *Response:* We hopefully have addressed these issues in our responses to comment 1-4.

**Level of interest:** An article of limited interest  
**Quality of written English:** Acceptable  
**Statistical review:** No, the manuscript does not need to be seen by a statistician.