ABSTRACT

EXAMINING EFFECTIVE SHORT-TERM INTERVENTIONS FOR CHILDREN WITH IDIOPATHIC TOE-WALKING IN ANKLE RANGE OF MOTION AND NORMALIZATION OF GAIT: A META-ANALYSIS

Context: Idiopathic toe-walking (ITW) is present in 7-24% of the children's population without identifiable orthopedic or neurologic conditions. Because of the unknown etiology, there are a myriad of treatment options and minimal evidence on the most effective intervention for improving toe-walking in these children.

Objective: To determine if short-term serial casting is an effective intervention in improving heel contact during the gait cycle in children ages 2-14 years presenting with ITW and making meaningful changes in ankle dorsiflexion (DF) range of motion when compared to natural history management.

Data Sources: Search procedures followed PRISMA guidelines using the databases Medline, CINAHL, PubMed, Cochrane and PEDro from their earliest record to October 7, 2014. The search was limited to randomized controlled trials, prospective studies and retrospective studies from 2000 to the present in the English language.

Study Selection: Children ages 2-14 years with a preliminary diagnosis of ITW, estimated to toe-walk ≥50% and achieved independent walking by 12 months of age were included. Exclusion criteria included the presence of a known neurological, orthopedic, psychiatric condition, a unilateral difference in DF ROM of >5 degrees or a Peabody Developmental Motor Score greater than 1.5 standard deviations below mean. Outcome measures collected were passive ankle DF and

the presence of toe-walking post-intervention. Initially 13 retrospective and prospective studies met the inclusion criteria.

Data Extraction: Titles, abstracts and full text articles were screen by 1 reviewer.

Results: A fixed effect Forest plot compared effects of serial casting versus natural history in improving ankle DF, p-value 0.940, Q-value of 0.0056, moderate grand effect size -0.61 favoring natural history. Grand effect size of 95% confidence interval was insignificant. Odds-ratio analyzed persistence of toe-walking following intervention; EER 48% continued to toe-walk after serial-casting, CER 80% continued after natural history.

Conclusion: The major finding of this meta-analysis was that there is currently no intervention effective in the reduction of toe-walking and demonstrated improvements in ankle dorsiflexion.

Jessica Lee Thompson
May 2015

EXAMINING EFFECTIVE SHORT-TERM INTERVENTIONS FOR CHILDREN WITH IDIOPATHIC TOE-WALKING IN ANKLE RANGE OF MOTION AND NORMALIZATION OF GAIT: A META-ANALYSIS

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BACKGROUND

Toe-walking, also referred to as equinus gait, is classified as absence of heel-strike at initial contact and absence of full foot contact during stance phase of the gait cycle with majority of weight-bearing occurring through the forefoot.[1-3] Toe-walking is considered normal in emerging gait for children less than 2-years of age. However, when children continue to demonstrate this gait pattern beyond the age of 3 years, it may be suggestive of developmental abnormalities and pose a clinical problem. [1,2,4-6] Habitual, idiopathic toe-walking (ITW) is diagnosed when children present with bilateral equinus in the absence of contributing neurologic, orthopedic, or psychological conditions.[6] A diagnosis of ITW is one of exclusion; children are first screened for identifiable medical conditions that may lead to this gait pattern such as cerebral palsy, muscular dystrophy, talpes equniovarus, Charcot-Marie-Tooth Disease or autism spectrum disorders.[7,8] Parental concern regarding persistent ITW often sparks referral to pediatric orthopedic surgeon or pediatric neurologist, given the deviations of physical performance from the norm, the presence of pain, and/or resultant limitations in participation in school-aged children.[9] Literature from 1982 to 2011 documents a wide prevalence of ITW, ranging from 7% to 24% of school-aged children.[8,10,11] Toe-walking is a normal transient stage of development and therefore is difficult to accurately identify the incidence of this condition in the population.[12]

Prolonged or habitual toe walking has been linked with an increased risk in the development of more serious musculoskeletal complications. These complications have been considered to be a result of progressive limitations in ankle mobility, specifically range of motion restrictions in ankle dorsiflexion and presence of structural abnormalities that increase with age.[13] Children with ITW

also demonstrate poor static and dynamic balance, increased risk of falls, and foot pain.[12,14] Of concern is a development of an equinus contracture, a limitation of passive ankle dorsiflexion (knee extended) of at least 10 degrees resulting from persistent plantar flexion position.[12,15] This range of motion limitation results in various compensations of the lower extremity to maintain gait such as pes planus, excessive out-toeing, external tibial torsion and genu recurvatum.[12-14] Literature has linked equinus contractures to the development of adult acquired flatfoot, metatarsalgia, diabetic foot ulceration and plantar fasciitis.[14,16,17] The presence of equinus contractures often results in the need for more aggressive treatment approaches, such as Achilles' tendon resection and Botulinum Toxin A injections.[14]

The etiology of ITW in these otherwise healthy children is unknown. Many conflicting hypotheses exist proposing various orthopedic, neurologic, and sensory dysfunctions that cause children to adopt this gait pattern. Some researchers hypothesize a muscular or structural origin, whereas others propose an underlying neurological or motor control component. [7,8,18-20] One study[8] found that a majority of children had complaints of musculoskeletal pain and stiffness, demonstrated decreased ankle range of motion and generalized joint hypomobility.[8] An additional study[21] examined calf musculature and heel cord restriction[21] and discovered that when a child possessed adequate dorsiflexion range, a well timed heel-strike could be obtained with verbal cueing and would be sustained throughout the time of observation.[21] These 2 investigations reveal the opposing depictions of ITW, 1 hypothesizing muscular restrictions and loss of passive ankle dorsiflexion ROM, and the other suggesting an equinus posture in gait adopted in spite of the presence of adequate dorsiflexion ROM.

A 2010 study[19] also posit that the cause of ITW may be more complicated than simply muscular restriction.[19] They suggested the cause of ITW could be attributed to a dysfunction in the processing of sensory information. Based on the Sensory Processing Theory, normal body movement relies on the integration of the vestibular, proprioceptive and tactile systems.[22] These 3 systems rely on environmental input to organize and direct motor control; this sensory feedback occurs throughout and after movement sending knowledge of results to specific regions of the brain, where it allows the movement to be modified in order to gain the desired result.[22-24] Based on the results of an additional study[25] children with ITW and concurrent developmental delays, demonstrated mixed responses (hypersensitivity and hyposensitivity) to tactile stimulation of their feet. Furthermore, if these children were provided vestibular stimulation therapy, they were able to obtain short-term heel-toe gait.[25] This supports that ITW may be a result of sensory processing dysfunction.[25] Furthermore, a 2013 study[26] concluded that the presence of ITW may suggest an immaturity or mild impairment at the cerebellum or motor cortex level, thus posing the question that this ,gait anomaly is not in fact idiopathic by nature.[26]

A study in 1997[18] examined a group of full-term children with seemingly unremarkable medical and motor developmental histories who presented with toe-walking.[18] They found that these children actually demonstrated delays in multiple developmental areas, with language development being the most prevalent and severe. Another study[11] examined 799 children and found that severity of toe-walking correlated with the severity of language impairments.[11] Based upon their findings, they concluded that idiopathic toe-walking should be viewed as a marker for developmental problems.[7,11,18,19]

Other theories of etiology for ITW relate to motor maturity of the child. Toe walking is a natural stage in the development of gait; toddlers under the age of 3 develop a propulsion strategy that utilizes whole-body displacements and stepping strategies to maintain upright position.[27] They also use lower extremity antagonist co-activation (gastrocnemius and anterior tibialis) without push-off to compensate for decreased muscular strength.[27,28] In typically developing gait in children, heel-strike with active dorsiflexion occurs after 2 years of age and use of the plantarflexor complex for push-off evolves at 4 to 5 years of age.[27] The current hypothesis is the acquisition of reciprocal ankle activation, along with upright trunk posture, that significantly contributes to the achievement of heel-toe gait. Furthermore, that delayed attainment of upright posture and reciprocal activation may be the causative factor in ITW.[29]

Motor control interventions, therefore are centered on these causative variables such as range of motion, strength, coordination or coactivation. These variables change movement capacity, or the regulation of the mechanisms that control movement, and also take into account orthopedic interventions that address range of motion deficits of the ankle joint.[29] Nonsurgical management of ITW has been shown to improve ankle ROM and gait; however, it is unknown what patient characteristics yield the best outcomes in nonsurgical interventions. Less severe cases of ITW with a baseline ankle dorsiflexion range of greater than zero degrees have shown the best success with conservative measures.[2]

Given the lack of agreement on the etiology of ITW, there is also a lack of agreement on the most effective intervention to improve or decrease the occurrence of bilateral equinus gait. Treatment approaches for ITW include both conservative to invasive treatment procedures that vary in focus from orthopedic to neurologic. These treatment approaches include: observation, serial-casting,

gait-retraining, orthotics, botulinum toxin injections and surgical Achilles tendon lengthening. No consensus has been reached among clinicians because no single treatment has resulted in long-term resolution of toe-walking gait. Some clinicians believe that toe walking resolves spontaneously in many children and medical intervention is unnecessary.[14,30,31]

The necessity and effectiveness of surgical treatment for ITW has recently been questioned due to the continued presence of ITW post-surgery.[14,30,32,33] A 2014 systematic review[14] including 174 children that were treated by serial-casting or surgical interventions and found no statistical difference in the reduction of toe-walking between groups.[14] Thirty-four percent of children treated with surgical means continued to toe-walk at a 4.1 mean year follow-up compared to 52.1% of children treated with serial-casting at a 3.6 mean year follow-up.[14] With the paucity of evidence guiding interventional strategies in ITW, it has been suggested that it may be more beneficial to the child to exhaust conservative treatment options before pursuing invasive surgical procedures.[2] Conservative treatment of ITW typically includes physical therapy with a focus on passive stretching of the plantar flexors and posterior calf musculature, prescription and long term use of ankle foot orthosis to maintain positioning and serial casting.[34,35] In addition, physical therapists also provide post-surgical, post-casting and post-injection treatment, including ROM, gait training, and patient/family education.

"Natural history" treatment of ITW consists of observation of the child, recommendation of special shoe-wear and/or heel-cord stretching exercises.[15] Evidence is lacking to confirm treatment is necessary due to the lack of long-term follow-up studies in adulthood.[36] Some researchers found support for natural history treatment of children with ITW.[30] They found that children left untreated for 3-years demonstrated significant improvements in their ankle ROM, and gait,

demonstrating decreased time spent toe-walking at follow-up.[30] Studies have shown that in the pediatric and adult population, footwear provides tactile input that influences the neurological system and leads to changes in gait.[34,35] Footwear can also affect stride length and motion of the subtalar, midtarsal and ankle joint which also contribute to gait variances.[34,35]

Serial casting is a widely used intervention for ITW. Serial casting is designed to stretch the plantarflexor muscles and has been used in children with and without neurological involvement to resolve toe-walking.[37] Although research is lacking in examining outcome measures in ITW, recent studies have shown increase in muscle length, muscle strength and gait parameters following a short-term casting intervention(ref). In serial casting, with the subtalar joint positioned in neutral with the forefoot aligned with the hindfoot in the sagittal plane. The knee is placed in 90-degrees of flexion and slight overpressure is provided at the foot to promote dorsiflexion. The angle of casting occurs at the midway point from initial resistance to passive stretch and the maximal end range. A below-knee fiberglass cast is applied for a period of 1 to 2 weeks, at which point the cast is removed and if there are increases in ankle dorsiflexion ROM, the ankle is again immobilized. The total casting period is typically 3 to 6 weeks based on passive stretch and determined by the referring clinician.[37] The theory behind serial casting is that it will improve passive ankle dorsiflexion during the gait cycle, allowing the child to achieve heel-to-toe gait and resolve ITW.[37]

The purpose of this meta-analysis is to determine the most effective short-term intervention for the resolution of toe-walking gait and the increase in ankle PROM. The efficacy of serial casting interventions in children presenting with idiopathic toe walking will be investigated and discussed. This investigation will fill a gap in the literature, as there are currently no meta-analyses comparing serial

casting to the ‘watch and wait’ of a natural history treatment approach using the outcome with measures of gait and ankle ROM.

This study will determine if short-term serial casting is an effective intervention for children (ages 2-14 years) presenting with idiopathic toe walking, resulting in improved ankle range of motion and gait. The alternative hypothesis is there will be a measurable, clinically significant improvement in passive ankle range of motion and/or gait parameters using a parental dichotomous statement following a short-term serial casting intervention for children with idiopathic toe walking. The null hypothesis is there will be no statistically significant difference between serial-casting or natural history in ankle range of motion or improvements in toe-walking gait.

METHODS

Eligibility Criteria

The study design was developed following PRISMA guidelines. Peer-reviewed, randomized control trials, prospective and retrospective studies comparing serial-casting and natural history (conservative physical therapy treatment) of idiopathic toe-walking from 2000 to the present in the English language were included. Idiopathic toe-walking was defined as a child greater than 2 years old that demonstrated a bilateral equinus gait pattern: lack of heel-strike during initial contact and full-foot contact in stance phase of the gait cycle with no known neurological, orthopedic or psychological deficits. Children (male and female) aged 2-14 years, who were walking independently by 12 months of age and were diagnosed with ITW with a parent estimate of toe-walking frequency greater than 50% of the time were included within the analysis. The exclusion criteria for this study included the presence of neurological, cognitive, orthopedic conditions, a unilateral difference of greater than 5 degrees ankle dorsiflexion, or motor skill development lower than 1.5 standard deviations below mean according to the Peabody Development Motor Scale.

Identification of Studies

The following databases were systematically searched: CINAHL, MEDLINE, Physiotherapy Evidence Database (PEDro), PubMed and Cochrane from their earliest record to October 7, 2014. The following search terms were used: idiopathic toe-walking, toe-walking gait, serial casting, natural history idiopathic toe-walking, conservative treatment idiopathic toe-walking, habitual toe-walking, serial casting idiopathic toe-walking. Titles, abstracts and full text articles were screen by 1 reviewer.

Quality Appraisal

A methodological quality evaluation of included studies was conducted using the PEDro scale, an 11-point scale that addresses external and internal validity. The first criterion evaluates external validity and is not considered as part of the overall scoring. Criteria 2-11 address internal validity which contribute to an overall score out of 10. Please refer to the Appendix for PEDro scoring of articles included in this meta-analysis.

Outcome Measures

Two different measures were collected across 5 studies, with the evaluation of passive ankle dorsiflexion with knee extended being the most common. Normal ankle dorsiflexion ranges from 0 to 20 degrees and measured using a goniometer with knee flexed and extended. If available range of motion is less with knee extended, that indicates a gastrocnemius muscle length deficit as opposed to a structural dorsiflexion limitation with knee flexed.[38] Good intra-test reliability of goniometer measurement of dorsiflexion has been documented but is dependent upon standardized measurements.[39] A dichotomous scale (yes/no), for clinician-determined presence of continued toe-walking following intervention was also consistent among studies.

Statistical Analysis

A random-effects model was used to compare serial-casting pre and post-intervention and natural history pre and post-intervention in improvements in ankle DF. A fixed-effect model was used to compare serial-casting versus natural history. Grand effect size (ES) using a 95% confidence interval was determined. Studies were determined to be homogeneous or heterogeneous by Chi Square distribution (p-value). Variance of studies determined by Q-value statistic.

An odds-ratio was performed to compare serial-casting and natural history in resolving toe-walking gait examining experimental event rate (EER) and control event rate (CER).

RESULTS

The search strategy identified 2,226 studies, of which 25 required further full-text screening, see Figure 1. Thirteen studies met the inclusion criteria. Twelve studies were excluded because they did not present means or standard deviations for ankle dorsiflexion, leaving 6 studies remaining for meta-analysis. The studies were conducted across 4 countries: United States[29, 33], United Kingdom[32], Canada[37], and Sweden[21]. These studies were evaluated for quality and scored according to the PEDro scales as mentioned above, see Appendix and Table 1. The studies ranged in score from 4 to 5 out of a 10-point total. Study characteristics for each individual study may be located in Table 2.

Evidence for Conservative Therapies

A retrospective study[21] that examined the long-term follow-up of 14 children mean aged 6.4 years with ITW who were treated conservatively ("natural history").[21] Baseline and follow-up measures of presence/absence of toe walking (determined by clinician and video-analysis) and passive ankle dorsiflexion (knee extended) were included. Patient files were retrieved from the Department of Physiotherapy, St Goran's Children's Hospital from time of treatment 1979-1988.[21] The mean follow-up time was 14.5 years after initial evaluation and each patient had reached the age of 13 years or more by follow up. The natural history intervention consisted of physical therapy; passive exercises to promote length of calf musculature and Achilles' tendon, as well as a home exercise program of stretching exercises. Five children were given below-knee serial casting for 2-4 weeks with subsequent physical therapy targeting passive stretching of posterior calf musculature and Achilles tendon. Three children were not clinically examined

at follow-up and instead answered a questionnaire to determine they were no longer toe walking and these children were not included in data analysis. For purposes of this study, the 6 children that were clinically examined at follow-up and were only treated conservatively were included in the analysis for natural history. The 5 children that had additional serial casting were included in the serial casting data.[21]

A 2010 study[29], examined a group of 5 children with ITW who received a motor control intervention.[29] The motor control intervention focused on achieving upright postural control and increasing calf muscle length in standing position. Children self-selected play as a physical therapist emphasized activities that influenced muscle activation and focused the child on maintaining center of gravity over their feet. Participants were selected based on convenience, were aged 30-72 months and had neutral (0 degrees) or greater of passive ankle dorsiflexion. Passive ankle dorsiflexion measurements were taken at baseline, during weekly intervention and at 2 follow-up visits, 1 and 4 weeks post-intervention. Motor skill development was assessed at eligibility screening and at 2 follow-up visits using a portable in-shoe gait detector to evaluate heel-strike. All 5 children had improvement in passive ankle DF ($p=0.002$) and these improvements were maintained at 4-week follow-up. There were minimal changes in toe-walking according to parental reports, with no complete resolution following treatment achieved.[29]

A prospective study[32] of 44 children (mean age 73±42 months) with the preliminary diagnosis of ITW, who were evaluated at the Paediatric Orthopaedic Clinic in Blackburn, United Kingdom between December 1999 and September 2003.[32] All children were treated with bilateral below-knee serial casting with revisions/progression every 2 weeks. Collected outcome measures of passive ankle

dorsiflexion and physician-determined presence of toe walking were taken at baseline, 3 months and 6 months post-casting. Following intervention, 66% (29) children demonstrated complete cessation toe walking or improved enough to satisfy their parents to cease treatment. At post-casting there was significant improvement in ankle DF in both groups of patients; those who improved toe walking and those who did not ($p<0.0001$ and $p=0.01$). Comparing pre-casting ankle DF in children who improved toe walking and those who did not, there was no significant different in either knee extension ($p=0.97$) or knee flexion ($p=0.79$). Comparing post-casting DF in children who improved toe walking and those who did not, there was a highly significant change in knee flexed ($p=0.001$) but not knee extended ($p=0.23$).[32]

One prospective study[37] examining 16 children, 8 with the diagnosis of ITW and 8 with the diagnosis of cerebral palsy.[37] For the purposes of this meta-analysis, only the information for children with ITW was utilized; the children with ITW (3 males/5 females, aged 5-10 years) with a mean dorsiflexion angle of -5 degrees at baseline (range -20 to 10 degrees). Objective measures collected were ankle dorsiflexion ROM, neuromuscular function using electromyographic analysis of the reflex threshold of the soleus and tibialis anterior muscle, and gait video analysis (sagittal plane) of barefoot stride length and gait velocity averaged over 3 trials. Each participant underwent serial casting to promote increased dorsiflexion, wearing the below-knee serial cast for a 1-2 week periods with a total casting period of 3-6 weeks based upon clinical judgment. A casting technician carried out all casting protocols. Objective measures were collected immediate post-casting and at a 6-week follow up. Upon cast removal, all children demonstrated gains in dorsiflexion and decreased resistance to passive stretch of the plantarflexor groups ($p<0.01$). No changes occurred in stride length or gait

velocity post-casting ($p>0.05$). The reflex threshold in children with ITW did not change significantly from baseline, immediate post-casting or at 6-week follow up (-8.5±2.4degrees, -8.7±3.4degrees, -8.2±3.4 degrees, respectively). The children with ITW all achieved heel-strike after serial casting; 2 children made a foot-flat contact immediately post-casting and only 1 child continued foot-flat contact at the 6-week follow-up.[37]

In one retrospective study[33], researchers examined 13 skeletally mature subjects who had previously been treated for ITW either with serial casting (n=6, 3 female, 3 male) or percutaneous tendo-Achilles lengthening/Baker's gastroc-soleus lengthening surgery (n=7) from 1984 to 1990.[33] Passive ankle DF at baseline was 9±3 degrees, mean age at serial casting 5.1±1.5 years, mean age at follow-up 16.2±0.4 years and average length of follow-up 10.9±1.4 years. Children treated with serial casting had 3 sets of cast changes over a 6-week period, with a final target ankle DF of 10-degrees. Subjects were given a stretching program to continue post-casting. At follow-up, there was no significant difference in passive ankle DF for the serial casting group (mean 9.5±5 degrees).[33]

In another retrospective study[30], researchers examined 136 children with ITW that had been previously treated with observation (n=49), serial-casting (n=41) or surgical lengthening of Achilles (n=46) from January 1968 to December 1990 at the Royal Children's Hospital in Melbourne, Australia.[30] The children in the observation group initially presented to the hospital at a median of 4 years, toe-walked 90% of their gait cycle and had a male to female ratio of 27:22. The observation group had a follow-up period of a median of 3.2 years. The casted group initially presented at a median age of 3.3 years, toe-walked 100% of their gait cycle and had a male to female ratio of 25:16. Their median follow-up time was 3.7 years. At follow-up, 6% of the observation group and 9% of the serial-

casting group had resolved toe-walking gait according to a physician-determined outcome. There was no difference between the serial-casting and the observation group in toe-walking outcome at initial presentation or follow-up.[30]

Results of Statistical Analysis

Combined effect size and confidence intervals for effects of passive ankle DF following serial casting are shown in Table 3. The data are represented as a forest plot in Figure 2. There was a large effect size (ES combined=0.94) favoring serial-casting for the improvement of ankle DF. The grand effect size was statistically significant. The Q-total variance is 18.988 with a Chi Square distribution, p=0.0002749 indicating the presence of significant heterogeneity following a serial-casting intervention. Heterogeneity indicates a variation of study outcomes between all serial casting studies and the results cannot be applied as a whole for treatment of children with ITW.

Combined effect size and confidence intervals for effects of passive ankle DF following natural history are shown in Table 4. The data are represented as a forest plot in Figure 3. There was a moderate grand effect size (ES combined=0.40) favoring natural history for the improvement of ankle DF. The grand effect size does cross midline, suggesting that this effect size is not statistically significant. The Q-total variance is 1.40798 with a Chi Square distribution (p=0.23539) indicating the presence of homogeneity. Homogeneity indicates minimal variation of study outcomes between all natural history studies and the results can be applied as a whole for treatment of children with ITW.

Combined effect size and confidence intervals for effects of passive ankle DF comparing natural history and serial-casting are shown in Table 5. The data are represented as a forest plot in Figure 4. There was a moderate effect size (ES

combined: -0.61) in favor of natural history for the improvement of passive ankle DF. The grand effect size does cross midline, suggesting that some children did benefit more from serial-casting intervention. The Q-total variance is 0.005642 with a Chi Square distribution (p=0.940125) indicating that the studies included were homogeneous.

An odd-ratio comparing 5 studies examining serial-casting[21,30,32,33,37] and 2 studies examining natural history[21,30] was performed to determine if toe-walking persisted post-treatment using a dichotomous yes/no outcome, seen in Table 6. It was found that ITW continued in 48% of children treated with serial casting and 80% of children treated with natural history.

DISCUSSION

The major finding of this study was that there is no statistically significant intervention that resolved toe-walking and demonstrated improvements in ankle dorsiflexion. Based upon the results of Figure 4 and Table 6 the alternative hypothesis was rejected and the null hypothesis accepted. There was no statistically significant improvement in ankle DF and improvements in gait between serial-casting and natural history in children with ITW. It appears from the results of this meta-analysis, natural history had greater improvements in ankle DF following intervention and serial-casting had greater effects on gait improvement.

Serial-Casting Intervention

The serial-casting studies that were used to examine pre and post-serial casting intervention on improvements in ankle DF (Figure 2) were statistically different from one another ($p=0.0002$); even though the grand effect size suggested positive outcomes following serial-casting, these results cannot be extrapolated to the general population. There were only 2 studies [21, 33] that did not show a positive effect for gains in ankle DF following a serial-casting intervention.[21,33] Possible reasons for this discrepancy are that both of these studies were retrospective, with varying follow up times (mean 14.5yrs and 10.9±1.4yrs) with sample sizes of 5 and 6 children. These results suggest that serial-casting may have greater short-term benefits and little or no long-term benefits on gains of ankle DF for ITW; as there were positive effect sizes for the prospective studies.[32,37] Despite both studies assigning a home exercise program to continue passive stretching of posterior calf musculature, stricter adherence to a continued

stretching program or continued physical therapy may be needed to maintain gains in ankle mobility.

Referring to Figure 2, one study[37] had a greater positive effect for improvements in ankle DF following a serial-casting intervention program compared to any other serial-casting studies.[37] This study[37] differed from the other studies in that they included a smaller age range of children (5-10 years old) and 1 subject (8-year old girl) began with -20 degrees of ankle DF at baseline.[37] This child may be the contributing factor to a large standard error of effect size, 1.02. This outlier may have also contributed to why this study showed such a positive effect on improving ankle DF following a 3-6 week serial-casting intervention.

Natural History Intervention

Referring to Figure 3, the 2010 study[29] showed a greater positive effect size compared to Hirsh et al.[21] Hirsh et al.[21], utilized a tradition physical therapy program for the children treated with natural history: consisting of passive stretching posterior calf musculature and a home exercise flexibility program.[21] In contrast, the 2010 study[29] focused on motor control to facilitate a more erect standing and walking postures in an effort to secure ground reaction forces relative to the ankle joint.[29] All 5 children demonstrated improvements in ankle DF post-intervention that was maintained; however, parents reported minimal improvements in toe-walking when the child was unaware of being observed. The results of this study further suggest a developmental delay component in children with ITW.[29] Characteristics of a mature gait pattern include a narrowed base of support, minimal oscillations of center of gravity, reciprocal arm swing and heel-to-toe contact.[27,28] The children in this study demonstrated co-contraction of the gastrocnemius and anterior tibialis with decreased upright postural control,

hindering their ability to maintain center of gravity when ambulating. Although Clark et al.[29], identified improvements in postural reactions following a motor control intervention; additional intervention components are necessary to attain heel-to-toe gait and resolve toe-walking.[29]

Comparing Natural History vs. Serial-Casting

Figure 4 demonstrates the difficulty in selecting treatment interventions for children with ITW. The 4 studies included were comparable and statistically categorized as homogeneous. The results of this forest plot showed improvements in ankle DF favoring natural history over serial-casting intervention. These results illustrate the clinical perils and difficulty clinicians' face when approaching this diagnosis. The mixed results demonstrate that ITW is multi-dimensional, there are several factors that need to be clinically addressed than merely decreased muscular length.

Continued Presence of Toe-Walking

Examining the results of the odds-ratio (Table 6) it appears that serial casting is more effective than natural history in resolution of toe-walking gait. Of the children treated with serial-casting interventions, 48% continued toe-walk, compared to children treated with natural history, 80% continued to toe-walk. The studies included in the odds ratio included both prospective and retrospective studies, indicating a long-term benefit of serial-casting on resolution of toe-walking gait. However, neither intervention showed significant improvement of gait in a vast majority of the children. The results of the odd-ratio further illustrate the complexity of the problem and suggest the need for a multi-faceted treatment approach.

Improvements in Ankle Dorsiflexion

A 2006 study[32] had an interesting result, as children who improved in ITW and those that did not improve, both showed significant improvements in gains in ankle DF with knee extended.[32] However, the children who improved their gait parameters had a significant improvement in ankle DF with knee flexed ($p=0.0001$), compared to those who did not improve ($p=0.36$). This finding suggests that the restrictions in both the gastrocnemius and soleus, which comprise the posterior calf musculature, may play a role in ITW. This finding also suggests that ankle DF with knee flexed may be a more appropriate outcome measure because it mimics the demands of the gait cycle. Also, the children who did not improve in toe walking were older when they presented at the clinic, median 67 months compared to median 58 months.[32] This suggests that a delay in intervention for ITW may be the cause for the continued gait. This continued gait pattern in older children may be due to the neuromuscular system losing plasticity as children age; similar children of greater age did not respond as favorably as younger children.

Development of Gait

Mature gait pattern is identified as a narrowed base of support, development of reciprocal activation of lower extremities, a reciprocal arm swing and the presence of a heel-to-toe gait pattern. In children with ITW, they demonstrate a narrowed base of support with a reciprocal arm swing; yet fail to achieve a heel-to-toe gait and demonstrate co-contraction of anterior tibialis and gastrocnemius resulting in plantarflexed position at initial contact.[27,40] There is emerging speculation that ITW may be a result of developmental delays and disruption of neuromuscular activation patterns. A 2014 study[7] attributes the

presence of ITW to immaturity or a mild impairment at the cerebellum or motor cortex level.[7] According to the theory of reciprocity, information is regulated between at least 2 neural networks.[41] These networks can represent specific brain centers such as the cerebellum and basal ganglia, working together to coordinate movement patterns.[41] If a child has an impairment at the cerebellum, it could possibly lead to disruption in gait patterns and result in ITW. Clark et al.[29], further states that children with ITW have a delay in motor skills that hinder their ability to achieve heel-to-toe gait because they are lacking ankle reciprocal activation and are unable to achieve upright posture control.[29]

Researchers found that in children who walked on their toes, the increased plantarflexion angle was likely reducing the force generating capacity of their plantarflexor muscles.[27] Another group of researchers found that toe-walking may provide a benefit for those with have distal lower extremity weakness; as toe-walking requires lower plantarflexion strength compared to a heel-to-toe gait pattern.[42] These findings suggest that plantarflexion weakness seen in children with ITW may be two-fold: weakness may be a secondary to prolonged toe-walking gait and/or secondary to prolonged immobilization, such as serial-casting intervention. Although serial-casting interventions may address decreased muscle length; the resulting PF weakness needs to be addressed in an effort to achieve long-term resolution of ITW.

Study Limitations

There were several limitations of this investigation. First, there were limited number of studies and limited and non-proportional number of children evaluated. Only 104 children were evaluated for serial-casting and 60 children for natural history. Second, only retrospective and prospective studies were found; these are

lower level of evidence compared to randomized controlled trials (RCTs). From the exhaustive literature search, there are no RCT's that examine children with ITW in respect to changes in ankle ROM and gait following serial-casting or natural history interventions. Third, the time of follow-up was not consistent among studies. Some studies collected outcome measures immediately following intervention[29,32,37] whereas other studies had longer follow-up times[21,30,33]. These discrepancies of methodological quality may have contributed to the acceptance of the null hypothesis.

Conclusion

Serial-casting and natural history are not effective therapeutic options for resolution of toe-walking gait and improvements in available ankle DF for children with ITW. From the results of this meta-analysis in addition to an exhaustive literature search, ITW reveals a multifaceted problem that involves additional systems that are not typically addressed. For example, recent literature has suggested that children with ITW may have a sensory processing dysfunction. Researchers in 1988[43] found that in children with ITW compared to typically developing children had difficulty normalizing postural responses to challenges and they were less proficient on the Bruininks-Oseretsky Test.[43] ITW may be considered a marker for developmental delays based on the involvement of motor control dysfunction, sensory processing dysfunction, and language impairments and delays[7,25,26,29,43]. Currently, treatment for children with ITW is not addressing developmental delays that are disturbing motor control. It is quite possibly the faulty motor control: increased co-contraction of the anterior tibialis and gastrocnemius that leads to weakness in the PF's, decreased gastrocnemius and soleus muscle length and decreased ankle ROM.

Clinically, the etiology of this disease must be properly identified to enable health-care providers to understand the pathogenesis and possible progression of the condition, in order to effectively select treatment for children with ITW.

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TABLES

Table 1. PEDro Scoring Scale

	Brouwer et. al, 2000	Clark et. al, 2010	Eastwood et. al, 2000	Fox et. al, 2006	Hirsch & Wagner, 2004	Stott et. al, 2004
Random allocation of subjects	-	-	-	-	-	-
Allocation concealment	-	-	-	-	-	-
Similar groups at baseline	+	+	+	+	+	+
Subjects blinded	-	-	-	-	-	-
Therapists administering treatment blinded	-	-	-	-	-	-
Assessors blinded	-	-	-	-	-	-
One key outcome obtained from 85% of subjects initially allocated to groups	+	+	+	+	+	+
'Intention to treat' used for analysis of one key outcome	+	+	+	+	+	+
Between-group statistics for one key outcome reported	+	+	+	+	+	+
Point measures and measures of variability for one key outcome	+	-	+	+	-	+
Total Score	5/10	4/10	5/10	5/10	4/10	5/10

Table 2. Study Characteristics

Study	Design	Sample Size	Intervention	Outcome Measure
Stott et. al, 2004	Level IV; retrospective study (10.8yrs post-intervention)	n=6 (3-6yo)	Below knee serial casting; 3-6wks	1. Ankle DF 2. Presence of toe-walking 3. 3-D gait analysis
Fox et. al, 2006	Level IV; prospective study	n=44 (2-14yo)	Below knee serial casting; 3-10wks	1. Ankle DF 2. Presence of toe-walking 3. Gillette functional assessment
Brouwer et. al, 2000	Level IV; prospective study	n=8 (5-10yo)	Below knee serial casting; 3-6wks	1. Ankle DF 2. Presence of toe-walking 3. Isometric PF strength 4. Neuromuscular function
Eastwood et. al, 2000	Level III; prospective study	n=49 control n=41 serial casting (2-14yo)	Below knee serial casting; 3-6wks or natural history	1. Ankle DF 2. Presence of toe-walking 3. Wet footprint analysis
Hirsch & Wagner, 2004	Level III; retrospective study	n=5 serial-casting n=6 natural history	Below knee serial-casting; 3-6wks or natural history/physical therapy	1. Ankle DF 2. Presence of toe-walking
Clark et. al, 2010	Level IV; prospective, multiple-case series design	n=5	Natural history/motor control	1. Ankle DF 2. Gross motor development

Table 3. Combined Effect Size (ES) and Confidence Intervals (CI): Ankle DF Following Serial-Casting

Study	Lower CI	Upper CI	Combined ES
Fox et. al, 2006	0.49	1.36	0.93
Brouwer et. al, 2000	3.01	6.99	5.00
Hirsh & Wagner, 2004	-0.70	1.82	0.56
Stott et. al, 2004	-1.13	1.13	0
Grand Effect Size	0.55	1.32	0.94

Table 4. Combined Effect Size (ES) and Confidence Intervals (CI): Ankle DF Following Natural History

Study	Lower CI	Upper CI	Combined ES
Clark et. al, 2010	-0.29	2.35	1.03
Hirsch & Wagner, 2004	-1.02	1.05	0.02
Grand Effect Size	-0.41	1.22	0.40

Table 5. Combined Effect Size (ES) and Confidence Intervals (CI): Ankle DF Following Natural History vs. Serial-Casting

Study	Lower CI	Upper CI	Combined ES
Fox et. al, 2006/ Clark et. al, 2010	-1.50	0.36	-0.57
Brouwer et. al, 2000/ Hirsch et. al, 2004	-1.69	0.47	-0.61
Grand Effect Size	-1.69	0.47	-0.61

Table 6. Odds-Ratio Comparing Resolution of Toe-Walking Gait Following Natural History or Serial-Casting Intervention

	Toe-Walking Present	Toe-Walking Absent	Total number of children
Natural History	44	11	55
Serial-Casting	50	54	104
Total number of children	94	65	159

FIGURES

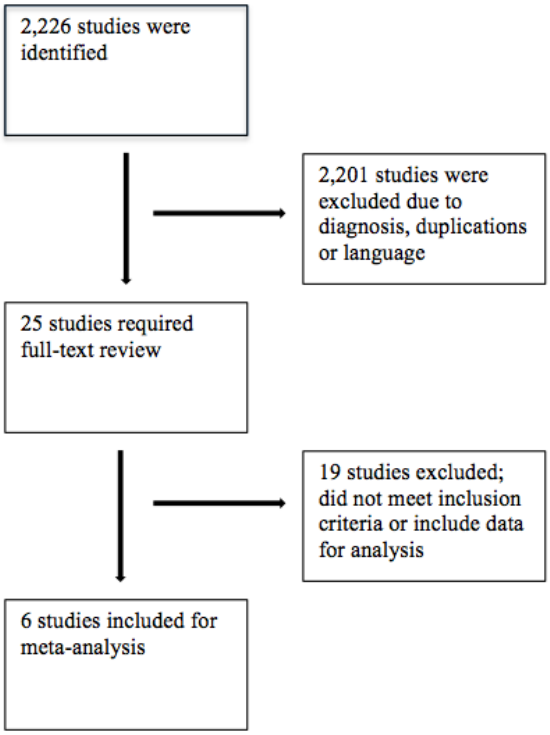

Figure 1. Selection of Studies

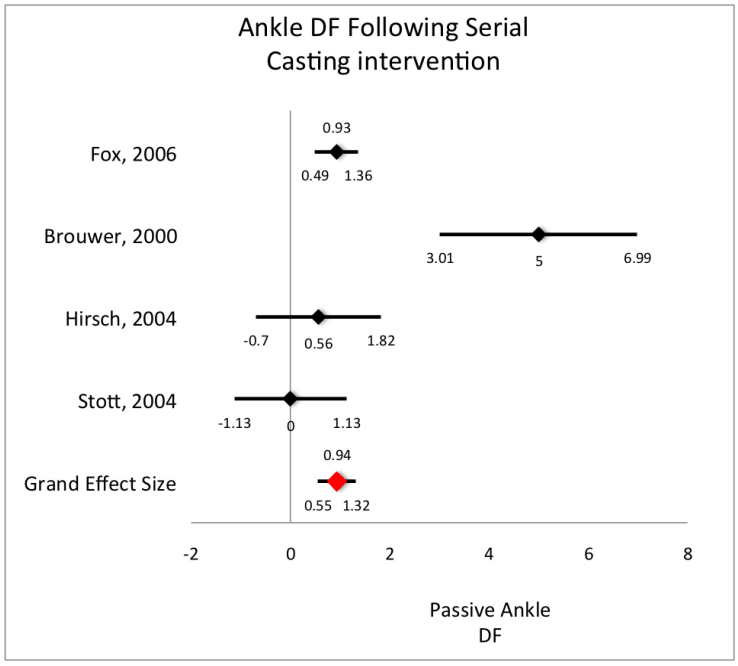

Figure 2. Forest plot: Improvements in ankle DF following serial-casting

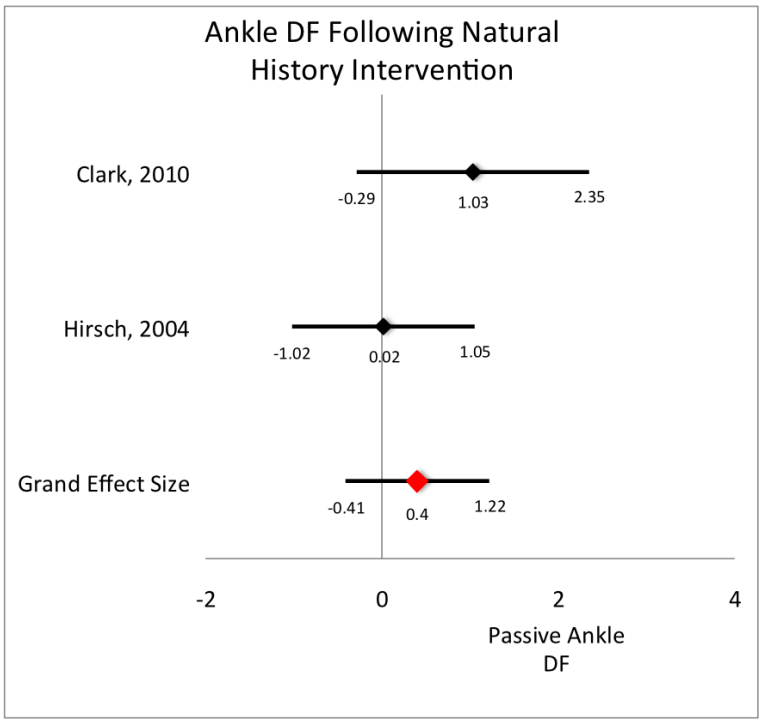

Figure 3. Forest plot: Improvements in ankle DF following natural history

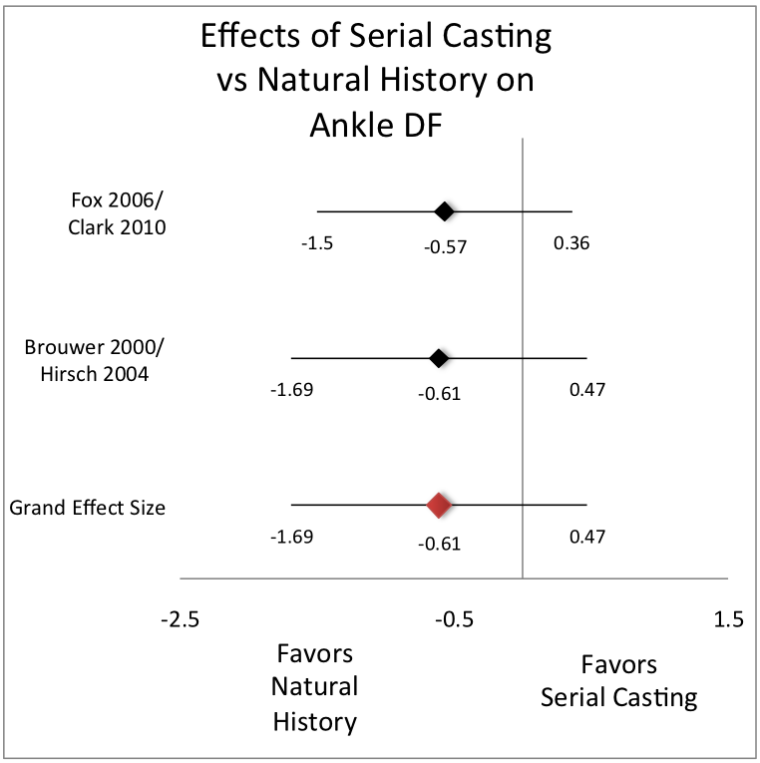

Figure 4. Forest plot: Improvements in ankle DF following natural history vs. serial-casting

APPENDIX: PEDro SCALE

PEDro scale

1.	eligibility criteria were specified	no ❑ yes ❑ where:
2.	subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received)	no ❑ yes ❑ where:
3.	allocation was concealed	no ❑ yes ❑ where:
4.	the groups were similar at baseline regarding the most important prognostic indicators	no ❑ yes ❑ where:
5.	there was blinding of all subjects	no ❑ yes ❑ where:
6.	there was blinding of all therapists who administered the therapy	no ❑ yes ❑ where:
7.	there was blinding of all assessors who measured at least one key outcome	no ❑ yes ❑ where:
8.	measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups	no ❑ yes ❑ where:
9.	all subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analysed by "intention to treat"	no ❑ yes ❑ where:
10.	the results of between-group statistical comparisons are reported for at least one key outcome	no ❑ yes ❑ where:
11.	the study provides both point measures and measures of variability for at least one key outcome	no ❑ yes ❑ where:

The PEDro scale is based on the Delphi list developed by Verhagen and colleagues at the Department of Epidemiology, University of Maastricht (*Verhagen AP et al (1998). The Delphi list: a criteria list for quality assessment of randomised clinical trials for conducting systematic reviews developed by Delphi consensus. Journal of Clinical Epidemiology, 51(12):1235-41*). The list is based on "expert consensus" not, for the most part, on empirical data. Two additional items not on the Delphi list (PEDro scale items 8 and 10) have been included in the PEDro scale. As more empirical data comes to hand it may become possible to "weight" scale items so that the PEDro score reflects the importance of individual scale items.

The purpose of the PEDro scale is to help the users of the PEDro database rapidly identify which of the known or suspected randomised clinical trials (ie RCTs or CCTs) archived on the PEDro database are likely to be internally valid (criteria 2-9), and could have sufficient statistical information to make their results interpretable (criteria 10-11). An additional criterion (criterion 1) that relates to the external validity (or "generalisability" or "applicability" of the trial) has been retained so that the Delphi list is complete, but this criterion will not be used to calculate the PEDro score reported on the PEDro web site.

The PEDro scale should not be used as a measure of the "validity" of a study's conclusions. In particular, we caution users of the PEDro scale that studies which show significant treatment effects and which score highly on the PEDro scale do not necessarily provide evidence that the treatment is clinically useful. Additional considerations include whether the treatment effect was big enough to be clinically worthwhile, whether the positive effects of the treatment outweigh its negative effects, and the cost-effectiveness of the treatment. The scale should not be used to compare the "quality" of trials performed in different areas of therapy, primarily because it is not possible to satisfy all scale items in some areas of physiotherapy practice.

Last amended June 21st, 1999

Notes on administration of the PEDro scale:

All criteria	**Points are only awarded when a criterion is clearly satisfied**. If on a literal reading of the trial report it is possible that a criterion was not satisfied, a point should not be awarded for that criterion.
Criterion 1	This criterion is satisfied if the report describes the source of subjects and a list of criteria used to determine who was eligible to participate in the study.
Criterion 2	A study is considered to have used random allocation if the report states that allocation was random. The precise method of randomisation need not be specified. Procedures such as coin-tossing and dice-rolling should be considered random. Quasi-randomisation allocation procedures such as allocation by hospital record number or birth date, or alternation, do not satisfy this criterion.
Criterion 3	*Concealed allocation* means that the person who determined if a subject was eligible for inclusion in the trial was unaware, when this decision was made, of which group the subject would be allocated to. A point is awarded for this criteria, even if it is not stated that allocation was concealed, when the report states that allocation was by sealed opaque envelopes or that allocation involved contacting the holder of the allocation schedule who was "off-site".
Criterion 4	At a minimum, in studies of therapeutic interventions, the report must describe at least one measure of the severity of the condition being treated and at least one (different) key outcome measure at baseline. The rater must be satisfied that the groups' outcomes would not be expected to differ, on the basis of baseline differences in prognostic variables alone, by a clinically significant amount. This criterion is satisfied even if only baseline data of study completers are presented.
Criteria 4, 7-11	*Key outcomes* are those outcomes which provide the primary measure of the effectiveness (or lack of effectiveness) of the therapy. In most studies, more than one variable is used as an outcome measure.
Criterion 5-7	*Blinding* means the person in question (subject, therapist or assessor) did not know which group the subject had been allocated to. In addition, subjects and therapists are only considered to be "blind" if it could be expected that they would have been unable to distinguish between the treatments applied to different groups. In trials in which key outcomes are self-reported (eg, visual analogue scale, pain diary), the assessor is considered to be blind if the subject was blind.
Criterion 8	This criterion is only satisfied if the report explicitly states *both* the number of subjects initially allocated to groups *and* the number of subjects from whom key outcome measures were obtained. In trials in which outcomes are measured at several points in time, a key outcome must have been measured in more than 85% of subjects at one of those points in time.
Criterion 9	An *intention to treat* analysis means that, where subjects did not receive treatment (or the control condition) as allocated, and where measures of outcomes were available, the analysis was performed as if subjects received the treatment (or control condition) they were allocated to. This criterion is satisfied, even if there is no mention of analysis by intention to treat, if the report explicitly states that all subjects received treatment or control conditions as allocated.
Criterion 10	A *between-group* statistical comparison involves statistical comparison of one group with another. Depending on the design of the study, this may involve comparison of two or more treatments, or comparison of treatment with a control condition. The analysis may be a simple comparison of outcomes measured after the treatment was administered, or a comparison of the change in one group with the change in another (when a factorial analysis of variance has been used to analyse the data, the latter is often reported as a group × time interaction). The comparison may be in the form hypothesis testing (which provides a "p" value, describing the probability that the groups differed only by chance) or in the form of an estimate (for example, the mean or median difference, or a difference in proportions, or number needed to treat, or a relative risk or hazard ratio) and its confidence interval.
Criterion 11	A *point measure* is a measure of the size of the treatment effect. The treatment effect may be described as a difference in group outcomes, or as the outcome in (each of) all groups. *Measures of variability* include standard deviations, standard errors, confidence intervals, interquartile ranges (or other quantile ranges), and ranges. Point measures and/or measures of variability may be provided graphically (for example, SDs may be given as error bars in a Figure) as long as it is clear what is being graphed (for example, as long as it is clear whether error bars represent SDs or SEs). Where outcomes are categorical, this criterion is considered to have been met if the number of subjects in each category is given for each group.

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