Functional electrical stimulation of the ankle dorsiflexors during walking in children with unilateral spastic cerebral palsy: a randomized crossover intervention study.

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The primary objective of this study is to evaluate the effect of FES on participation level: achieving of individual goals, using the goal attainment scale (GAS)), and the Canadian Occupational Performance Measure (COPM) for the long term. Secondary...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Congenital and peripartum neurological conditions
Study type	Interventional

Summary

ID

NL-OMON55409

Source
ToetsingOnline

Brief title
Functional electrical stimulation during walking in cerebral palsy

Condition

- Congenital and peripartum neurological conditions

Synonym
infantile encephalopathy, spastic paresis

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W,Revalidatiefonds;Cornelia stichting;Stichting Vooruit

Intervention

Keyword: Ankle dorsiflexors, Cerebral palsy, Functional electrical stimulation, Spasticity

Outcome measures

Primary outcome

Participation level:

Do patients achieve individual goals, measured by the goal-attainment-scale (GAS)?

What do patients gain at the levels of activities and participation at the long term (3 years), measured using the Canadian Occupational Performance Measure (COPM)?

Secondary outcome

Activity level:

• Does FES increase the walking distance?

For this purpose we will perform a 6-minute walking test in CAREN, during both the FES and the control phase. (6) Besides that, we will use the functional mobility scale(FMS), which includes a classification of the functional mobility (1-5) and walking distance. Furthermore we will use two activity measurement devices to estimate the number of steps during 7 days at three study points (1 week before start treatment, after 3 months and at 6 months).

• Does FES have a positive effect on falls/near falls?

We will provide a questionnaire about falling a three time points (1 week

before start treatment, after 3 months and at 6 months).

• Does FES improve the stability during sustained (10-15 minutes) walking?

Function level:

• Does FES improve ankle dorsal flexion and toe clearance?

Using the gait analysis we will evaluate the ankle dorsal flexion and toe clearance using a specially developed analysis program, which allows automatic detection without user interference.

• Does the use of FES influence ankle plantar flexion force of the calf muscles during gait?

For this purpose we will use the gait analysis data to calculate net moments of push off during gait.

• Does the use of FES modulate the force of the dorsiflexors and plantar flexors of the foot (i.e anterior tibial muscle and fibular muscles)?.

For this purpose we measure strength using the Jamar hydrolic hand dynamometer. Output will be provided in kilograms (range 0.0-90 kg; sensitivity 0.1kg). The position of the dynamometer was will be standardized for each measurement. The tester will be setting a constant resistive force for 3 to 5 seconds, directed perpendicular to the long axis of the limb segment to elicit an isometric muscle contraction. A standard instruction of *push as hard as you can* was will be given to each participant for each trial. Ankle plantar flexors: Supine Knee extended and foot held in plantigrade position; resistance to plantar surface of metatarsal heads. Knee was is not allowed to flex. Ankle dorsiflexors: Supine Knee extended and foot in natural resting position;

resistance to dorsal surface of metatarsal heads. Knee was is not allowed to flex (13)

• Does long term use of FES therapy (3 years) lead to necessity of orthopaedic surgeries?

Other study parameters

• Cost-effectiveness of FES as compared to conventional treatment (e.g. physiotherapy, special shoes and/or ankle-foot orthoses)

• Donning and doffing: how is donning and doffing of FES versus donning and doffing of an orthosis? Does one of these costs significantly less time?

• Satisfaction: What is the satisfaction of patients, scored in a visual analogue scale (VAS)?

• Type of brain lesion; bodyweight; gender; age; length.

Study description

Background summary

Cerebral palsy (CP) is the most common upper motor neuron disorder in children and the main cause of disability in childhood (1) CP describes a group of disorders of the musculoskeletal system, which are permanently but not unchangeable. CP is caused by congenital or acquired non-progressive disorders of the developmental brain in the first year of life. (2, 3)

Children with spastic CP often walk with insufficient ankle dorsiflexion (in the swing phase) or with eversion of the foot,. A pathological gait, known as drop-foot gait, can be the result and this has 2 major complications: foot-slap during loading response and toe-drag during swing. This partlyis partly caused by weakness of the anterior tibial muscle and partly due to co-contraction of both the fibular- and anterior tibial muscle. So there is a combination of a lack of selectivity and decreased strength, making walking at various stages deviant. Furthermore, there is an imbalance noticeable while walking. In time,

the disorder appears to be progressive due to atrophy and contractures of the muscle and increasing bodyweight . For classification of gait, the Winters scale can be used (figure 1), where unilateral CP with dropfoot is classified as type I (4).
In daily life these problems cause limited walking distance and frequent falls. This can lead to restrictions in participating in daily activities at school and in leisure.
The current guideline for spastic cerebral palsy describes the different interventions in relation to the age of the child as follows:
The first step is conservative therapy, which includes physiotherapy, orthopaedic shoes and orthoses. (5)
The second step includes systemically and locally applied drugs. Diazepam, Dantrolene, Clonidine and Baclofen are the most widely used drugs. These drugs, with the exception of Dantrolene, suppress the spasticity by inhibition of excitatory neurotransmitters, or by stimulation of the inhibitory neurotransmitters. Botulinum toxin A (Bont-A) is an intramuscularly applied drug, which causes a chemical denervation at the level of the motor end plate of the muscle causing weakness. It is therefore administered in those muscles that show undesirable co-activation. Because the effect is only temporarily, the treatment has to be repeated every 3 - 9 months. Using training, the effect of Bont-A can be prolonged. To be able to administer the Bont-A injections in a muscle of a severely disabled child, general anaesthetic is required. Treatment with an orthosis can be very functional, however active movement is impossible. This is a restriction especially in patients with light symptoms; GMFCS level I and II. Furthermore, it has a proper effect in one phase of a step, but not in the other, while it is used for correction of a dynamic event. Negative effects may be muscle weakness and atrophy.
The third step includes surgical interventions, e.g. tenotomy, transposition and osteotomy. This is often followed by a conservative plaster program with good post-operative counselling (physiotherapy and splints) to prevent or postpone bone deformities. More importantly, however, is to perform soft tissue surgery at a younger age. Malformations and associated operations can therefore be prevented or postponed to a later age, when they do not interfere with the growth of the child. In each intervention, there is the risk of side effects, such as sedation with oral medications, pressure sores and atrophy in a static orthosis, temporary effect in a Bont-A treatment and surgical complications due to a result of the surgery, and on the other hand as a result of the execution(6).
Functional electrical stimulation (FES) may be an effective alternative treatment for children with spastic CP and a drop foot. By stimulating the fibular nerve or the anterior tibial muscle during the swing phase, dorsiflexion of the foot is stimulated. In contrast to bracing, FES does not restrict motion, but does produce muscle contraction, and thus has the potential to increase strength and motor control through repetitive neural stimulation over time(2). Two types of effects can be identified: 1) a direct effect of stimulation of the fibular nerve or the anterior tibial muscle (i.e *orthotic*) and 2) a therapeutic effect of repeated electrical stimulation

resulting in sustained effect on muscles and/ or joints. In preparation of this study we performed a systematic research (Moll et al. accepted) and we found that FES immediately improves ankle dorsal flexion and falls (table 1). In addition we showed longer sustained effects of FES on ankle dorsal flexion and falls (table 1). However, it should be noted only two study studies (4 articles) were of level II class evidence (small RCT) and all other studies used a single subject design.
(Table 1. see appendix) Until now, the use of FES in CP is limited and no data exist about the effects on walking distance (activity level) and participation level.
The overall objective of this study is to conduct a randomised cross-over intervention trial in children with unilateral spastic CP with 12 weeks of FES for every participant and 18-24 weeks of conventional therapy. The effectiveness of FES will be examined at an individual goal level. For every individual a goal at walking distance will be set, next to possible other goals. Next to that, results will be measured at the activity and functional level: the effect at gait kinematics (such as ankle dorsiflexion and balance), walking distance, falls, spasticity and muscle force. Both the short and mid-long term effects will be studied (initial study, 12 weeks of FES treatment) as the long-term effects (3 year follow-up of patients continuing FES treatment). We will also take in to account the type of brain damage of the patients. An addition al goal is to investigate the cost effectiveness of FES, which, in case of a positive effect, may support allowance by insurance companies.

Study objective

The primary objective of this study is to evaluate the effect of FES on participation level: achieving of individual goals, using the goal attainment scale (GAS)), and the Canadian Occupational Performance Measure (COPM) for the long term. Secondary objectives are to study effects at the body and function level; improvement of gait characteristics, improvement of balance and muscle force, and also effects on activity level like walking distance and number of falls. Next to this, the donning and doffing of FES versus conventional treatment (e.g. ankle-foot orthoses) and patient satisfaction will be studied.

In the end evidence should be provided about whether FES is a feasible treatment option for foot drop in children with sCP, and if yes, for which specific patients. This evidence could be used to apply for insurance reimbursement for the FES apparatus.

Study design

The study will be a randomised controlled crossover study. Patients will be randomised for the
conventional or the FES group, to decide with which treatment they will start.

FES group
This group will start with FES treatment: 4 weeks *adaptation phase* and 8 weeks *FES phase*. During the adaption phase, the stimulus (in Volt) will gradually be increased up to an effective level. The participants have to increase the wear time during this phase from 30 minutes to 6 hours a day. During the 8 weeks FES phase, the participants have to wear the FES device for minimal 6 hours a day during walking. After the FES phase, this group will enter the *wash-out* period of 6 weeks. This period is meant to let the therapeutic effects of FES fade, to prevent disturbance of the assessments during the conventional therapy. After this period, 12 weeks of conventional therapy will follow (orthoses/shoes and usual physiotherapy)

Conventional (control) group
This group will be instructed to wear their orthoses/shoes on a daily basis for the first 12 weeks of the study. Usual physiotherapy can be continued. After the first 12-week period, the control group will enter a 6 week wash-out period (second baseline) and then be switched to FES treatment for 12 weeks in total. (see fig 1 for a diagram of the study design).

Long term clinical follow-up
For patients who continue FES therapy after they completed the study, the long term follow-up will be described. This long term follow-up resembles the follow-up in the case of conventional orthotic therapy . However, because little literature reports on the long term effects of FES, we specifically aim to collect and publish data on the long term effects. The follow-up will consist of 4 visits: at the start of the follow-up and 3 visits each a year later (3 years follow-up in total). The assessments are mostly the same as the assessments of the initial study, but a bit shorter.

Assessments
Patients will undergo four complete assessments. A complete assessment will exist of: physical examination, gait analysis, strength analysis, 7 day activity measurement, goal attainment score and the CPQoL questionnaire. These assessments include the 1) assessments at baseline (time 0) with current intervention (week 0), 2) at week 12), 3) at week 18 at the end of wash-out and start of next treatment 4) at week 30, the end of the last treatment phase. (see fig. 1 for a diagram of the study design). In the case of continuation of FES therapy, a 3-year follow-up will follow, including 4 measurements in total.

Intervention

Current (control) treatment: Individuals suffering from stroke and other neurological disorders often experience inadequate dorsiflexion during swing phase of the gait cycle due to dorsiflexor muscle weakness. This type of pathological gait, mostly known as drop-foot gait, has two major complications: foot-slap during loading response and toe-drag during swing. Physiotherapy and

special shoes are the first treatment options. Also ankle foot orthotic (AFO) devices are prescribed to resolve these complications. Existing AFOs are designed with or without articulated joint with various motion control elements like springs, dampers, four-bar mechanism, series elastic actuator, and so forth. (10) In the first assessment we will analyze the current treatment of the children; for instance whether they have properly aligned and fitted orthoses and shoes. If the orthosis or shoes are not well fitting, we will first adjust and optimize this before starting the trial. We will use a systematic approach as described by Kerkum et al (11) using the *shank-to-vertical* angle. This tibia inclination angle is responsive to changes in heel height of the AFO-footwear combination and reflects the accompanying changes in the lower limb angles and movements. In addition we will look at pre-positioning, the ankle angle at heelstrike and knee extension in mid-stance. Of course the type of orthoses will influence the assessment.
FES intervention: The FES device used (WalkAide; Innovative Neurotronics, Austin, Texas, USA) delivers asymmetrical biphasic surface electrical stimulation to the common fibular (formerly common peroneal) nerve, triggered by an individually programmed tilt sensor, to improve foot clearance during the swing phase of gait. The major dorsiflexor of the ankle is the tibialis anterior muscle, which lifts and inverts the foot. The fibular (formerly peroneal) muscle group primarily everts the foot, with some contribution to plantar flexion. (12) Minor adjustments in placement of the stimulating electrodes can more selectively activate the anterior tibial and * or the fibular muscles to achieve the desired motion in both the sagittal and frontal planes. In addition to the user-controlled amplitude dial, the stimulation parameters that are adjustable by the clinician include pulse frequency (16.7-33 Hz), pulse width (25-300ms), tilt angles to trigger stimulation off and on, presence of ramps up or down, minimum and maximum stimulation times, and a wait time in between consecutive stimulations. Software provided with the device is able to record walking data to guide decision making around these parameters.
Initial setup of the FES device will be done after the baseline assessment. In the first 4 weeks the settings of the FES will be adapted. Participants will be instructed to increase wear time from 30 minutes per day to 6 hours per day.
During the following 8 weeks FES phase, participants will be asked to wear the device daily for at least 6 hours, during the times when they are walking the most. During this period, patients can continue their conventional therapy (except for AFO), for example physiotherapy if they are used to do so.
After the initial 12 weeks the FES group will be reassigned to the orthosis - after a 6 week wash-out period - and the orthosis group to the FES group.

After completion of the initial study, patients can choose to continue FES therapy - a decision that will be made together with the treating physician.

Study burden and risks

Most AFOs (current treatment) induce mobility restriction. By restricting ankle movement, AFOs may exacerbate muscle weakness and atrophy, potentially leading

to further loss of function over time. Furthermore, especially patients treated with AFOs may suffer from pressure sores. FES does not restrict motion, but does produce muscle contraction, and thus has the potential to increase strength and motor control through repetitive neural stimulation over time. The risk of this treatment is negligible and the burden minimal. The study can only be done using this patients group.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

- Unilateral foot drop of central origin, particularly the absence of initial heel contact
- Participants are currently treated with ankle-foot orthoses or (adapted)

shoes to wear on a daily basis
- Participants ambulate independently, and thus classified as Gross Motor Function Classification System (GMFCS) levels I or II and have a gait type 1 according to Winters et al (4).
- Participants are able to walk for at least 15 minutes
- Confirmed cerebral abnormality with MRI (showing medial infarction, maldevelopment of the brain, or porencephaly).
- Participants are aged 4-18 years
- In the case that more than 3 dropouts occur, more than 25 patients will be included, in order to have at least 22 patients finishing the study.

Exclusion criteria

- Plantarflexion ankle contracture of more than 5 degrees plantarflexion with the knee extended
- Botulinum toxin A injection to the plantar or dorsiflexor muscle groups within the 6 months before the study
- Orthopaedic surgery to the legs in the previous year
- Uncontrolled epilepsy with daily seizures

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-08-2018
Enrollment:	25
Type:	Actual

Medical products/devices used

Generic name:	WalkAide
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	25-01-2018
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	14-09-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
Other	clinicaltrials.gov, volgt
CCMO	NL63250.068.17