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ORIGINAL ARTICLE

Evaluation of a self-administered transcutaneous electrical stimulation concept for the treatment of spasticity: a randomized placebo-controlled trial

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ABSTRACT

BACKGROUND: Spasticity is a common consequence of injury to the central nervous system negatively affecting patient's everyday activities. Treatment mainly consists of training and different drugs, often with side effects. There is a need for treatment options that can be performed by the patient in their home environment.
AIM: The objective of this study was to assess the effectiveness of an assistive technology (AT), Mollii®, a garment with integrated electrodes for multifocal transcutaneous electrical stimulation intended for self-treatment of spasticity, in study participants with spasticity due to stroke or CP.
DESIGN: The study was a randomized, controlled, double-blind study with a cross-over design.
SETTING: Participants were recruited from two rehabilitation clinics. Treatments were performed in participants' homes and all follow-ups were performed in the two rehabilitation clinics.
POPULATION: Thirty-one participants were included in the study and 27 completed the study. Four participants discontinued the study. Two declined participation before baseline and two withdrew due to problems handling the garment.
METHODS: Participants used the AT with and without electrical stimulation (active/non-active period) for six weeks each, followed by six weeks without treatment. Goal Attainment Scaling (GAS), change in mobility, arm-hand ability, spasticity and pain were measured at baseline and after 6, 12 and 18 weeks.
RESULTS: Fifteen of the 27 participants fulfilled the treatment protocol in terms of recommended use. Deviations were frequent. No statistically significant differences in outcome were found between the active and the non-active treatment periods. During the active period, an improvement was seen in the 10-meter comfortable gait test, time and steps. An improvement was seen in both the active and non-active periods for the GAS.
CONCLUSIONS: Compliance was low, partly due to deviations related to the garment, complicating the interpretation of the results. Further research should focus on identifying the target population and concomitant rehabilitation strategies.
CLINICAL REHABILITATION IMPACT: The evaluated concept of multifocal transcutaneous electrical stimulation (TES) represents an interesting addition to the existing repertoire of treatments to alleviate muscle spasticity. The evaluated concept allows TES to be self-administered by the patient in the home environment. A more elaborate design of training activities directly related to patient's own rehabilitation goals is recommended and may increase the value of the evaluated concept.

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KEY WORDS: Muscle spasticity - Randomized controlled trial - Cerebral palsy - Stroke - Transcutaneous electric nerve stimulation.

Spasticity is a common consequence of injury to the central nervous system and can be a major problem for a patient's motor function and ability to perform everyday activities. There is a lack of effective therapies that can be performed by the patient, without the assistance or presence of therapists. The prevalence of spasticity differs depending on the etiology. After stroke, it appears in more than 20% of patients and, in cerebral palsy (CP),

in more than 80%.[1, 2] One major problem both clinically and in studies of epidemiology is the lack of consensus on definition. A recent review advocates the use of a broader concept presented by Pandyan *et al.*; "disordered sensorimotor control, resulting from an upper motor neuron lesion, presenting as intermittent or sustained involuntary activation of muscles." [3, 4]

The treatment for spasticity consists mainly of physiotherapy and training, sometimes in combination with pharmacological treatment in the form of oral drugs (*e.g.* baclofen, tizanidin and dantrolene), intrathecal treatment (*e.g.* baclofen), intramuscular injections (*e.g.* botulinum toxin) or peripheral nerve blocks.[5] Electrical stimulation for the reduction of spasticity has also been used [6] and is commonly referred to as therapeutic electrical stimulation (TES), or transcutaneous electrical nerve stimulation (TENS). TENS can be difficult to use in clinical practice or at home because of practical difficulties attaching the electrodes in the correct way and using TENS during training. A transcutaneous electrical stimulation application with integrated electrodes in a full-body garment, the Mollii® (formerly Elektrodress 100, Inerventions AB, Stockholm, Sweden; hereinafter referred to as "the company"), addresses this by making the TES of spastic muscles available as a self-treatment therapy in the home environment. The rationale of the Mollii® is to reduce spastic reflexes and muscle stiffness by stimulating the antagonists of the muscles affected by spasticity (reciprocal inhibition).

A number of RCT studies with blinding and placebo-TES have been published.[7-13] Generally, these studies have reported short-term improvements in spasticity and also in activity, such as improved walking. The placebo treatment most frequently used involved attaching electrodes and a TENS machine to the body, but with no electrical stimulation, *e.g.* with the electrical circuit disconnected inside.[7] A recent review concludes that there is level 1 and 2 evidence for short-term effects with TENS and that it can be considered as adjunct therapy for spasticity treatment.[14] This is the first controlled scientific study evaluating whether treatment with the Mollii® in combination with training has the intended effect.

The overall objective was to assess the effectiveness of the treatment of spasticity using Mollii® assistive technology (AT) in study participants with spasticity due to stroke or CP.

- The primary objective was to study whether treatment with the Mollii® improved function and activity. The primary outcome was a change in goal attainment, mobility and arm-hand ability, with the secondary outcomes of self-reported pain and spasticity, change in muscular tone and self-reported health-related quality of life.
- The secondary objective was the feasibility of the treatment. Outcomes were compliance with treatment and potential adverse effects.

Materials and methods

Study design

The study was a randomized, controlled, double-blind study with a cross-over design (Figure 1). The participants used the AT during two treatment periods, each lasting 6 weeks, where the electrical stimulation differed between the two in that the TES amplitude was set at zero under control conditions, whereas the use of the garment and the training program were the same.

Study population

The target group for the study comprised participants with spasticity interfering with daily life due to stroke or CP. The participants were patients, listed at one of the two participating rehabilitation units, who fulfilled the inclusion criteria: having spasticity (at least 1+ on the modified Ashworth Scale), having preserved walking ability (with or without walking aids), having reached the age of 18 and being able to understand the treatment and instruments/interviews used. For stroke participants, two years should have elapsed since their injury to minimize the risk of spontaneous recovery affecting the result of the study. The main exclusion criterion was concomitant disease interfering with treatment, such as cardiac arrhythmia, heart infarction or unstable angina pectoris, symptomatic hyper- or hypotonia, cancer under treatment, unstable psychiatric disease, lung disease, affecting daily life, unstable epileptic

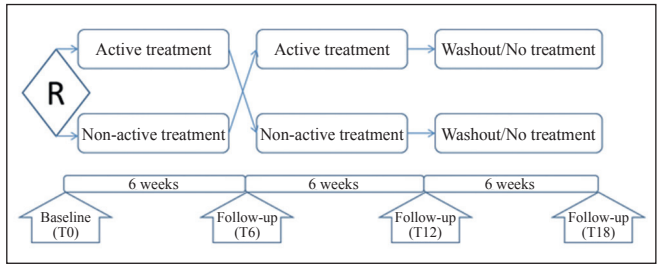

Figure 1.—Study design.

disease, orthopedic surgery during the last year, infectious disease with longstanding treatment, obesity (BMI>35), severe pain, severe cognitive dysfunctions, electronic implants, ventriculoperitoneal shunt or pregnancy. The participants should not have been treated with botulinum toxin for the past four months or during the study, but they could be receiving treatment with oral antispastic drugs with no change in doses during the intervention.

Study intervention

The AT Mollii® consists of a two-piece garment and a control unit. The garment is equipped with 58 electrodes that enable individually set electrical stimulation of the 42 separate (groups of) muscles that are indicated in Figure 2. The control unit is individually programmable, *i.e.* the amplitude of the square pulses of current, at a frequency of 20 Hz, is individually set for each muscle group based on an assessment of the spasticity pattern.

The way in which the Mollii® is offered by the company is a package with the equipment, spasticity assessment, testing for stimulation settings and a set of recommended individualized training exercises. This is performed at a session where a therapist associated with the company ("company therapist," CT) assesses the spastic condition of the user/patient.

The treatment using Mollii® can be performed where suitable but were in this study typically performed in the participants' home environment. The stimulation is said to be barely, if at all, recognizable by the user. When the Mollii® is used, the remaining time of the pre-set 60 minutes of electrostimulation is presented on the display of the control box, indicating that the stimulation is active. The suggested training exercises were mainly training of strength, stretching and co-ordination to be performed while using the Mollii®.

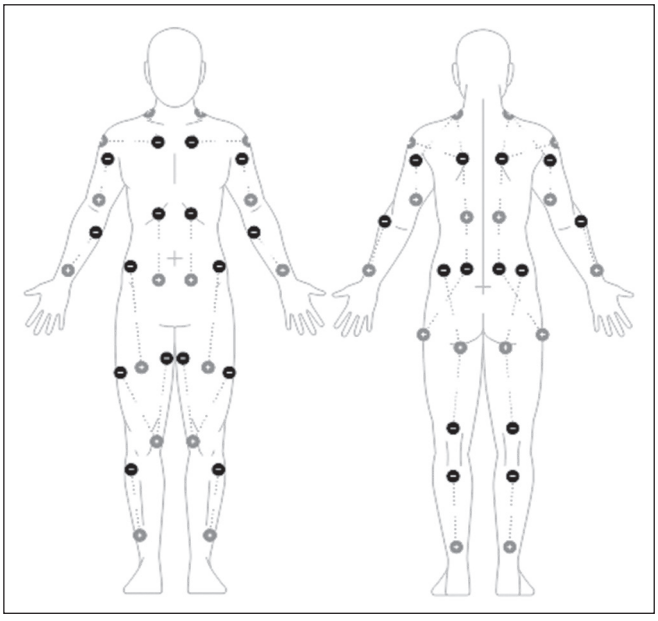

Figure 2.—Muscle groups that can be chosen for stimulation.

The aim of the present study was to match the procedure established by the company as closely as possible. Although the initial patient assessment and programming of the control box are fairly easy to perform, it was decided that they should be determined and performed by CTs in order to follow their established procedure. An observer (a research therapist) was present during the short time that the CT met the study participant at the start-up meeting (at baseline) to assess the participants and program the Mollii®. An observer protocol was used to report any deviations from the approved procedure.

The participants were instructed to perform self-administered treatments in their home environment, *i.e.* to use the garment for 60 minutes, any suitable time of the day but keeping to three to four times a week, which should render from 1080 to 1260 minutes of use for each six-week period. The control unit displayed the time of use, independently of whether or not electrical stimulation was given. The participants continued their normal life with no study-related restrictions.

Assessments were made at the rehabilitation clinic at baseline and at the end of each 6-week cycle, *i.e.* week 6, 12 and 18 from study start. For consistency in the study assessment, a regular treatment using the garment should be performed the day before the follow-up assessments after six and 12 weeks (the intervention periods). Treatment was not allowed on assessment days.

Ethical approval including a full description of the study protocol was obtained from the Regional Ethical Review Board of Linköping, Sweden in July 2013 (Dnr 2013/150-31). All participants signed a written informed consent in accordance with the Declaration of Helsinki. The study is registered in Clinicaltrials.gov (trial no: NCT02261142).

Randomization and blinding procedure

Due to the relatively small number of participants and the fact that the study was performed at two clinics, a block

randomization procedure was applied to arrive at comparable sizes of groups starting with active and non-active intervention at both clinics. Further, in order to limit the influence of any seasonal variation, block randomization was used for each clinic to arrive at a balanced intervention sequence within four participants (four participants would typically start study participation in a time frame of two weeks). The blocking restrictions were not known by those having direct contact with the participants. The randomization was based on a computer generated sequence and performed by the study coordinator (last author) who was excluded from contact with the participants. The information about allocation to intervention groups was generated and kept by the coordinator and concealed to all involved by means of color-coded information produced and provided by the coordinator in sealed envelopes addressed to the company representative (the CT) and the research therapist/clinic respectively. As each study participant was assigned two control units at baseline, one active and one placebo, the concealed allocation could be achieved by varying the color of self-adhesive labels attached to the active and "placebo" control unit according to information provided in the envelope sent to the company representative. The envelope sent to the clinic contained information on which of the color-coded units should be handed out to the participant for the first and second intervention periods respectively (*i.e.* the intervention assignment). By keeping these two randomization activities separated, the CTs did not know which unit was used in which intervention period and the research therapists and personnel at the clinic collecting data and assessing outcomes did not know which unit that was active. The procedure ensured that no one but the coordinator had access to information about when participants had active respective placebo intervention. Prior to starting the study, the participants had been informed that they would have different treatments during the two six-week periods that would differ in that one of the periods would not include electrical stimulation. The blinding was kept for all involved until the analysis commenced after the study protocols had been completed.

Outcome measures

The theoretical framework when choosing outcome measures was based on "The International Classification of Functioning, Disability and Health" (ICF).[15] The study protocol aimed to capture activities important in daily life and relevant to the treatment under investigation, as presented in Table I.

Goal attainment

To set and evaluate individual patient-relevant treatment goals, Goal Attainment Scaling (GAS) [16] was used. This instrument has been found to be sensitive and patient relevant.[17] There are, however, concerns about its construct validity, team dependence in goal-setting and a learning period to set adequate goals.[18]

In the present study, the goals were defined by the participant in discussion with the study team. The original scale was used, where GAS goals are "scaled" in relation to two end-points, the starting point, -2, and the most favorable outcome, +2, with 0 being the most likely outcome (Table II). For each participant, one to three goals could be defined. The individual goals were weighted for importance and difficulty and an aggregated T-score was calculated.[19]

Change in mobility

The ten-metre walking test, divided into the fast gait test (FGT) and comfortable gait test (CGT),[20] was chosen for the present study. These tests have good test-retest reliability [21] and are responsive to change.[22] In order to study more complex movements, the Timed Up & Go (TUG), which includes rising from a chair, walking three meters,

TABLE I.—*Study schedule for assessments.*

Data	Baseline	Week 6	Week 12	Week 18
Descriptive data				
Demographic data	X			
NIH stroke scale (only stroke)	X			
GMFCS (only CP)	X			
Effect measurements				
Expectations/fulfilment	X	X	X	X
Goal attainment scaling (GAS)	X	X	X	X
Action research arm test (ARAT)	X	X	X	X
Wolf motor function test (WMFS), parts 1-2	X	X	X	X
Timed up & go (TUG)	X	X	X	X
Ten-meter walking test (CGT + FGT)	X	X	X	X
Modified Ashworth Scale (MAS)	X	X	X	X
Range of motion (ROM)	X	X	X	X
Numerical rating scale – pain	X	X	X	X
Numerical rating scale – spasticity	X	X	X	X
SF-36v2/SF-6D	X	X	X	X
EQ-VAS	X	X	X	X

TABLE II.—*The version of the Goal Attainment Scale (GAS) chosen for the study, with one example from the study.*

	Definition of level	Example
+2	Goal achieved (much better than expected level of outcome)	Manages to walk ≥800 meters before becoming tired
+1	Goal achieved (better than expected level of outcome)	Manages to walk ≥600 meters before becoming tired
0	Goal achieved (expected level of outcome)	Manages to walk ≥400 meters before becoming tired
-1	Goal not achieved (less than expected level of outcome)	Manages to walk ≥200 meters before becoming tired
-2	Goal not achieved (much less than expected level of outcome) – baseline	Gets tired after walking 100 meters

turning, walking back and sitting down again on the chair, was added to the protocol.[21, 23] Walking aids and ankle-foot orthoses were permitted,[24] if used on a daily basis by the participant.

Change in arm-hand ability

The Action Research Arm Test (ARAT) [25, 26] was chosen as the primary hand function test and was complemented by the first two tasks in the Wolf Motor Function Test (WMFT) measuring active abduction of the shoulder joint.[27] Both instruments have been shown to be reliable, valid and responsive to change.[28]

Spasticity assessment

The version of the modified Ashworth scale with six steps (numbered from 0-5) was chosen for the present study. Although there are doubts about the reliability [29] and the content validity of the scale,[30] it is still frequently used as a measurement of muscular tone in a clinical setting. For presentation the sum score of the 20 measured muscles were used. Spasticity in the feet were not included in Ashworth scoring, but registered as degree of clonus.

Self-reported pain and spasticity

Self-reported pain and spasticity were registered using the Numerical Rating Scale (NRS) that has been shown to be valid and reliable for use with both pain and spasticity.[31]

Self-reported health-related quality of life

Health-related quality of life (HRQoL) was measured using the SF-36 instrument.[32] The SF-36 is a frequently used instrument that includes 36 questions divided into eight domains. The instrument is presented on two overall dimensions: Mental Component Summary (MCS) score and Physical Component Summary (PCS) Score. This instrument was complemented by the EQ-VAS,[33] where participants are asked to rate their current health on a vertical visual analogue scale, ranging from 0 (worst imaginable state) to 100 (perfect health).

Compliance and adverse effects

For measurements of compliance with the instructed time of using the AT, total time of use was electronically registered in the control unit for each treatment period. Deviations in AT use were continuously registered in a separate protocol if subjects contacted the study team and they were also asked about any deviations at follow-ups. Adverse effects were described in free text and subsequently categorized for analysis.

Sample size

The sample size was determined based on the number of available garments (Mollii® systems) from the company. From a clinical perspective the aim was to include at least 12 participants from each of the two study sites/rehabilitation clinics. This can be considered a small sample, though the instruments used in the present study have been shown to be sensitive in studies with similar small study populations. The crossover design means that each participant will be included in both the intervention and control group which increases the power of the statistical evaluation by allowing paired tests.

Statistical analyses

Changes during the active and non-active periods and differences between the two periods (treatment effect) were studied using a paired *t*-test for outcome with continuous variables. A paired-sample Wilcoxon signed-rank test was used for non-parametric data. SPSS version 23 (SPSS Inc., Chicago, IL, USA) was used for the analyses.

The analysis was based on intention to treat (ITT) including all participants. An *ad-hoc* "per protocol (PP)" analysis was also performed to handle variations in compliance with the study protocol. To be included in the PP analysis, the participants had to have used the equipment for at least 2/3 of the expected time in both treatment cycles.

Results

Thirty-one participants were included in the study and 27 completed the study. Four participants discontinued the study. Two declined participation before baseline and two withdrew due to problems handling the garment. Enrolment started in September 2013 and continued through March 2014 when the targeted number of participants had completed the two intervention periods (Figure 3).

Twelve participants had CP and 15 participants had a post-stroke disability. Baseline characteristics relating to age, gender and the severity of disease did not differ significantly between the intervention groups (Table III). The NIHSS score for the stroke group was 5.40 on average and all the CP participants had a Gross Motor Function Classification System (GMFCS) Score of 1 to 3. The distribution of functional impairments between the left and right side was fairly even (Table IV). All post-stroke participants had hemiplegia with functional impairment of both the upper and lower extremities on the affected side. Of the participants with CP, seven of 12 had spastic diplegia with normal or close-to-normal arm function but functional impairment of the lower extremities. Ashworth score at baseline varied with a range from 0-23 and a median of 11. Seventeen of the 27 patients had clonus. Participants own average rating of their spasticity at baseline according to NRS was 5/10 (range 1-9), and for pain 3/10 (range 0-9).

Compliance with treatment

The total time using the AT, as registered by the control unit, was typically lower than the instructed 1080-1260 minutes. The mean time was 870 (range 48-1332) minutes and did not differ between the active and the non-active period or between the first and the last six-week intervention period. Six of the 27 participants used the garment for 1080 minutes or more in both treatment cycles. A total of 15 participants fulfilled the criteria for being included in the PP analysis. Figure 4 illustrates the variation in use between participants.

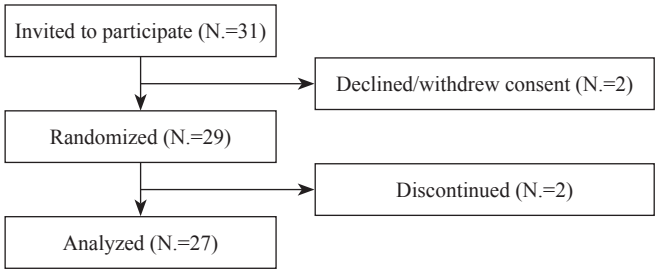

Figure 3.—Study flowchart.

TABLE III.—*Demographic description of the participants.*

Demographic variables	All (N.=27)	Active treatment first period (N. =14)	Active treatment second period (N.=13)
Age, mean years (range)	49.9 (26-70)	47.9 (26-67)	51.9 (26-70)
Gender, male/female	15/12	7/7	8/5
Diagnosis, CP/stroke	12/15	6/8	6/7
CP (N.=12) GMFCS 1, N.	2	2	0
GMFCS 2, N.	4	1	3
GMFCS 3, N.	6	3	3
GMFCS ≥4, N.	0	0	0
Stroke (N.=15) NIHSS, mean (range)	5.40 (1-11)	5.00 (2-8)	5.86 (1-11)

The number of deviations from the recommended/intended use was relatively high throughout the study. The deviations mainly consisted of problems with the garment and the control unit (Table V). No deviations from the approved procedure were noted for the period when the CT met the participants.

Adverse effects

Six participants reported pain related to treatment. Of these participants, four had CP and two had stroke, three were female and three were male. The pain differed between the participants and no systematic pattern could be seen. The average use of the equipment in these 6 participants was 807 minutes in the non-active phase and 688 minutes in the active phase.

Outcomes

For the 27 participants, a total of 56 treatment goals were formulated and evaluated using the GAS. Eight participants had three goals defined, 11 had two goals and eight

TABLE IV.—*Description of extremity impairment at baseline.*

Distribution of extremity impairment at baseline (N., all=27, CP=12, stroke=15)	Normal/close to normal functioning	Moderate functional impairment	Severe functional impairment
Right arm (CP/stroke)	15 (8/7)	8 (4/4)	4 (0/4)
Left arm (CP/stroke)	16 (8/8)	4 (3/1)	7 (1/6)
Right leg (CP/stroke)	8 (1/7)	16 (9/7)	3 (2/1)
Left leg (C/stroke)	9 (1/8)	13 (9/4)	5 (2/3)

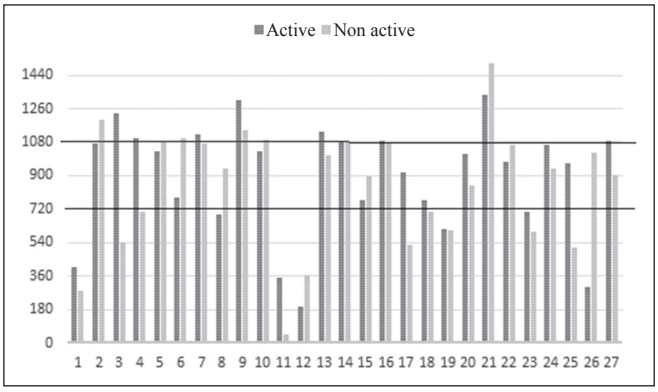

Figure 4.—The use of the AT in minutes per six-week period, showing the active and non-active period for each participant. The expected time if used according to protocol is 1080-1260 minutes and the lower limit of 1080 and the cut-off for the PP analysis (720 min) are highlighted with horizontal lines.

had one goal defined. All goals were classified into ICF codes. The most frequent ICF codes were walking (d450), followed by fine hand use (d440). The complete list is presented in Table VI.

There were no differences between the active and the non-active intervention periods in any of the outcomes, Table VII, VIII.

The T-score for goal attainment increased during both the active and non-active conditions (T-score increase by 3.9 and 5.1 respectively), indicating that the individual goals set by each participant improved at group level. However, the increase in T-score did not differ between the two conditions (Table VII).

The PP analysis did not change this picture, but the increase in T-score was only significant during the active condition (T-score increase by 5.7 [SD 7.6], P=0.011).

Regarding change in mobility, improvements were found during the active period for the 10 m comfortable gait test, showing a reduction in time of 1.65 seconds and 0.70 fewer steps, but this change did not differ significantly from the non-active condition. The FGT and Timed Up & Go did not change during either of the two conditions (Table VII).

The PP analysis showed an improvement in CGT time (-1.5 s [SD 2.3], P=0.026) and steps (-1.1 steps [SD 1.7], P=0.027) during the active condition, an improvement with a reduced TUG time (-1.8 s [SD 3.0], P=0.037) during the non-active condition and no change in the FGT test in either of the conditions.

Changes were not found in arm-hand ability, the spasticity assessment, any of the self-reported pain and spasticity measurements (Table VIII) or in the HRQoL instruments (Table VII). The PP analysis showed improvements in the EQ-VAS (8.2 [SD 11.4], P=0.014) and SF-36, MCS (3.8 (SD 6.2), P=0.034), during the non-active condition.

TABLE V.—*Deviations and adverse effects reported during the study, divided according to the number of reports and the number of participants reporting adverse effects and deviations.*

Deviations and adverse effects Categories	Number of reported adverse effects and deviations	Number of participants reporting adverse effects and deviations
Pain [1]	8	6
Technical problem – garment [2]	26	16
Technical problem – control unit [3]	23	17
Contact, logistical and/or comfort problems [4]	14	13
Increased need for assistance [5]	2	2

[1]Feeling pain or discomfort while using the garment; [2]mainly problems with zippers breaking or getting stuck; [3]includes problems with battery and unit not working properly; [4]includes problems with finding the right size of garment, lack of a manual and poor reply from company; [5]includes the need for assistance to put the garment on.

Discussion

This study was designed to assess the effectiveness of a self-treatment concept for spasticity, based on individual-

TABLE VI.—*ICF coding for all GAS goals with frequency of occurrence.*

Description	ICF code	Frequency
Walking	d450	11
Fine hand use	d440	7
Dressing	d540	7
Gait pattern function	b770	6
Structure of upper extremity	s730	5
Sensation of pain	b280	4
Muscle tone function	b735	4
Hand and arm use	d445	4
Moving around in different locations	d460	4
Moving around using equipment	d465	4
Exercise tolerance function	b455	3
Moving around	d455	3
Sleep functions	b134	2
Changing basic body position	d410	2
Doing housework	d640	2

Goals with only one occurrence were mobility of joint function b710, involuntary movement reaction function b755, control of voluntary movement function b760, sensations related to muscles and movement functions b780, writing d170, maintaining a body position d415, transferring oneself d420, lifting and carrying objects d430, moving objects with lower extremities d435, caring for body parts d520, toileting d530, eating d550, drinking d560, looking after one's health d570, preparing meals d630, structure of trunk s760.

TABLE VII.—*Outcome from the ITT analysis for parametric data.*

Variable	Baseline (T0)	Active period	Non-active period	Difference active – non-active		Change active period		Change non-active period		Difference, change active – non-active		Follow-up (T18)
	Mean (SD) Median (range)	Mean (SD) Median (range)	Mean (SD) Median (range)	Mean (SD) Median (range)	P value	Mean (SD) Median (range)	P value	Mean (SD) Median (range)	P value	Mean (SD) Median (range)	P value	Mean (SD) Median (range)
GAS	26.2 (2.7) 25 (23-30)	32.9 (9.9) 30 (23-58)	33.1 (8.7) 30 (23-60)	-0.3 (9.4) 0 (-30-20)	0.880	3.9 (7.1) 0 (-10-24)	0.009	5.1 (8.6) 0 (-10-30)	0.005	-1.2 (11.9) 0 (-30- 34)	0.610	34.2 (9.5) 30 (23-56)
CGT, time (s)	19.8 (24.0) 12 (7-132)	17.6 (21.3) 11 (6-117)	18.7 (24.4) 11 (7-135)	-1.1 (4.1) 0 (-18-6)	0.174	-1.6 (3.9) -1 (-18-3)	0.037	-0.1 (2.7) 0 (-6-8)	0.779	-1.5 (5.3) 0 (-21 - 9)	0.155	19.0 (24.3) 11 (6-131)
CGT, steps	23.4 (11.2) 22 (15-74)	22.0 (11.4) 19 (14-75)	22.8 (11.6) 20 (15-72)	-0.8 (4.1) 0 (-20-3)	0.328	-0.7 (1.7) 0 (-4-3)	0.044	0.2 (4.2) -1 (-3-20)	0.786	-0.9 (5.1) 0 (-22 - 5)	0.351	22.9 (12.7) 19 (15-79)
FGT, time (s)	17.1 (25.1) 10 (5-136)	16.3 (23.9) 9 (5-130)	16.0 (21.6) 9 (5-117)	0.3 (3.8) 0 (-11-13)	0.686	0.1 (3.3) 0 (-5-13)	0.841	-0.9 (4.6) 0 (-19-11)	0.320	1.0 (7.0) 0 (-7 - 32)	0.457	16.9 (23.2) 10 (6-124)
FGT, steps	21.1 (12.3) 19 (13-78)	20.9 (13.1) 18 (13-82)	21.5 (12.2) 18 (13-73)	-0.6 (5.2) 0 (-24-9)	0.559	0.0 (2.4) 0 (-5-9)	0.938	0.6 (5.0) 0 (-5-24)	0.541	-0.6 (5.9) -1 (-23 - 14)	0.582	21.4 (12.4) 19 (13-77)
TUG (s)	23.4 (26.5) 14 (8-147)	21.7 (24.5) 14 (7-135)	21.6 (24.4) 14 (8-133)	0.1 (2.9) 0 (-4-7)	0.844	-0.9 (2.8) -1 (-8-7)	0.117	-1.0 (4.3) 0 (-14-7)	0.221	0.1 (6.2) -1 (-12 - 16)	0.902	24.0 (33.8) 15 (7-183)
EQ-VAS	65.7 (16.5) 65 (30-99)	66.1 (18.6) 69 (20-95)	64.7 (19.9) 70 (20-98)	1.3 (20.5) 1 (-70-43)	0.738	-1.7 (22.0) 0 (-70-31)	0.684	-0.7 (16.8) 3 (-43-35)	0.821	-1.0 (30.2) 0 (-80 - 63)	0.865	66.6 (16.6) 70 (35-94)
SF-36. PCS	43.6 (8.5) 44 (28-67)	43.9 (8.2) 45 (27-62)	42.2 (7.5) 41 (31-59)	1.7 (4.7) 2 (-10-10)	0.065	0.8 (4.9) 0 (-10-11)	0.414	-1.7 (4.4) -2 (-10-9)	0.056	2.5 (7.9) 1 (-18 - 21)	0.116	42.0 (7.8) 41 (30-64)
SF-36. MCS	53.1 (9.9) 53 (27-67)	52.9 (11.2) 56 (25-66)	55.3 (8.8) 57 (33-67)	-2.4 (10.7) 0 (-37-21)	0.254	-1.3 (10.9) 1 (-37-15)	0.536	1.1 (8.4) 1 (-21-15)	0.496	-2.45 (16.5) -1 (-51 - 29)	0.448	49.9 (13.9) 54 (23-65)

TABLE VIII.—*Outcome from the ITT analysis comparing active with non-active treatment for non-parametric data.*

Variable	Baseline (T0)	Active period	Non active period	Difference active – non-active		Change active period		Change non-active period		Difference change active – non-active		Follow-up (T18)
	Median (range)	Median (range)	Median (range)	Median (range)	P value	Median (range)	P value	Median (range)	P value	Median (range)	P value	Median (range)
ARAT	86 (57-114)	81 (57-114)	83 (57-114)	0 (-8-13)	0.819	0 (-12-13)	0.549	0 (-6-8)	0.299	0 (-19-12)	0.468	82 (57-114)
MAS	11 (0-23)	11 (0-22)	10 (1-21)	-1 (-5-13)	0.690	-1 (-7-13)	0.211	-1 (-13-5)	0.467	-1 (-8-26)	0.914	10 (1-31)
WMFT. FAS	18 (11-20)	18 (11-20)	18 (11-20)	0 (-1-3)	1.000	0 (-2-2)	0.408	0 (-3-1)	1.000	0 (-3-3)	0.670	17 (11-20)
NRS pain	3 (0-9)	3 (0-10)	2 (0-8)	0 (-4-3)	0.831	0 (-4-3)	0.307	0 (-6-5)	0.731	0 (-7-6)	0.378	2 (0-10)
NRS spasticity	5 (1-9)	5 (0-10)	6 (2-10)	0 (-5-4)	0.658	0 (-6-4)	0.985	0 (-4-4)	0.366	0 (-9 - 8)	0.579	6 (0-10)

ized electrical stimulation administered by means of a full-body garment, intended for use in the home environment. The participants had moderate to severe functional impairment in their legs and/or arms due to spasticity from CP or stroke but with maintained walking ability either with or without walking aids.

No significant differences were found between the active and the non-active treatment periods. Improvements in goal attainment were seen during both the active and non-active period of the intervention, when all 27 participants were included in the analysis, but only during the active period when considering the 15 participants reaching the compliance threshold. A similar pattern was found in mobility, measured by the comfortable gait test, time and number of steps, where improvements were seen during the active period of the intervention regardless of whether all 27 participants or only those 15 reaching the compliance threshold in the analysis were included. Improvements found during the non-active period related to the Timed Up-and-Go test, EQ-VAS and SF-36 MCS in the PP analysis based on the 15 participants reaching the compliance threshold. The interpretative value of these findings is low, as neither of the improvements differs significantly from what is seen during the comparative period of the intervention.

There are issues that need to be considered when interpreting the results. For this study, both stroke and CP were chosen as target groups for intervention. This mimics an everyday clinical situation in which these two diagnostic groups are major groups for anti-spastic interventions.

This also results in a diverse study population, reducing the power of the study. For instance, the low incidence of impairment in arm function for the CP group limits the potential for finding differences in the chosen arm function tests and also in measurements of hypertonicity in the arms.

Crucial study design decisions were related to the intended use of the commercial Mollii® product and how it is offered to potential customers. As the study was designed to mimic the company's established procedure for spasticity assessment and setting up the individualized therapy, while keeping to restrictions necessary to fulfil a double-blind RCT study, the CTs had some limitations in their interaction with the participants. This may have affected the try-out and fine-tuning of the treatment, as well as not allowing modifications to the individualized programming during the study period. Two six-week treatment periods without a wash-out between the periods were chosen mainly from a practical/logistical standpoint, as this allowed a reasonable throughput of study participants based on the limited number of available Mollii® systems. This decision was based on the firm belief that six weeks of training sessions every other day would create a contrast between the active and non-active treatment period and that the 6-week periods in themselves would compensate for not having a wash-out between the treatment periods. In retrospect, this raises questions about whether a wash-out period between the periods would have limited a possible carry-over effect between the two conditions and thereby increased the opportunity to detect differences between the active and non-active treatment. Another question is whether six weeks is long enough to obtain the gains in function for which the study was designed. Further, assessments were made the day after treatment to avoid the immediate treatment effects and focus on the long-term effects on function. This may have affected the effect size of the assessments, thereby increasing the risk of missing relevant changes.

The study size was comparable to that in earlier RCT studies of TENS and spasticity, but the diverse study population and the problem with the lack of use of the garment in adherence with the study protocol decreases the power of the study. Participant use of the garment varying from 48 minutes to 1332 minutes and only six participants reaching the lower intended time of 1080 minutes of use for both treatment cycles complicate the interpretation of the ITT analysis. For this reason, a PP analysis was performed with a cut-off level of 720 minutes of use in both treatment cycles. Fifteen participants fulfilled this criterion and were included in the PP analysis. One cause of these deviations in usage levels is related to issues with the AT or logistics associated with the AT. Taken as a whole, this reduced the power of the study, as many participants missed out on the prescribed number of treatment opportunities and the number of participants who actually followed the protocol may be too low to show treatment effects. Technical problems with the AT, difficulties for the hemiparetic participants to put on the clothing without assistance and pain problems while using the AT might also have affected participant motivation. The manufacturer of the Mollii® has reported that improvements have been made in order to overcome the shortcomings of the garment encountered in the present study. Future studies will evaluate the success of these attempts.

Numerous studies have previously shown that TES has an effect on spasticity.[7-14] Compared with other studies, our study differs in a number of respects. First of all, our intention was to evaluate a commercial product intended for use in the home without the need for therapist involvement in the daily treatment, with minimal interference from the study team, thereby relying more on the participants' own motivation to complete the treatment, in contrast to a more experimental design performed at the clinic. This might have affected compliance with the treatment protocol. Secondly, in previous studies, stimulation frequencies have varied from 20 to 200 Hz.[34, 35] with 100 Hz being the most common frequency. A recent study implies that stimulation frequencies for maximum reciprocal inhibition differ between healthy subjects and post-stroke, where the latter group requires higher frequencies for maximum reciprocal inhibition.[36]

Finally, in the presented study, the intensity of concurrent training has to be regarded as low, consisting of limited exercises recommended by the CT during electrotreatment three times a week for six weeks. Compared with many other studies, this was of less intensity and less goal directed. The CT who was responsible for suggesting suitable training activities in relation to the CT's spasticity assessment of the user/patient and individual programming of the Mollii® did not participate in the discussion and definition of the rehabilitation goals that were evaluated by GAS. Some studies have daily training (as well as electro-stimulation) and more goal-directed training,[7, 11, 13] *i.e.* task-related training. Recent studies of the importance of high-intensity, goal-directed training suggests that this might be of importance to the outcome.[37] The question of

how to optimize treatment, considering stimulation frequency, the frequency of treatment cycles and optimizing concurrent training, needs to be further explored.

Our study is a double-blind RCT. Using this study design in assessments of AT is associated with challenges. This study ran into unexpected problems related to the AT being tested, which led to some modifications being made to the garment during the study. RCTs tend to be less applicable to evaluating AT in general, as there is no way of defining a control condition that can be blinded. TES is a rare exception, as it can be tested as active and non-active. Although the blinding aspects of placebo-controlled trials are essential, there is typically no discussion about the extent to which RCT studies of ATs are successful in this respect. The blinding aspects of the present study will be studied further.

In the present study, no differences were found between the active and the non-active treatment. The absence of a clear result at group level does not rule out the possibility that certain individuals benefited from the intervention. This is supported by individual observations and participant reports, although the blind design make this kind of input difficult to assess in the present study. We intend to make further analyses to study this, as further research should focus on methods for identifying the target population that will benefit from multifocal transcutaneous electrical stimulation combined with training. In retrospect, considering the shortcomings of the newly developed garment, the fact that only 15 of 27 reached the recommended use of the garment and the diversity of the study population, the current study could be looked upon as a pilot study providing valuable information for further studies of AT for the treatment of spasticity in the home environment.

Limitations of the study

There are limitations to the study, mostly related to deviations from the protocol due to technical problems with the AT, and the results should therefore be interpreted with caution.

Conclusions

This study found no differences between the active and the non-active treatment periods, although changes were seen within groups during the study in some outcomes. The absence of a significant result at group level does not rule out the possibility that certain individuals benefited from the intervention, which is supported by observations indicating that some participants experienced improvements when using the Mollii®. Further research should focus on methods for identifying the target population that will benefit from electrostimulation and the optimal mode of integrated rehabilitation strategies.

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