Effects of neurolytic blocks (botulinum toxin type A and motor branch block) in patients with a Stiff Knee Gait: A systematic review

Effects of Functional Electrical Stimulation of the hamstring muscles in stroke patients with a Stiff Knee Gait: An explorative prospective cohort study

MASTER THESIS

Karen Harmelink
Studentnummer 3329070
9 juli 2010

MASTER THESIS

K.E.M. Harmelink
Studentnummer: 3329070
9 juli 2010

Eerste begeleider
Martin Tenniglo
Roessingh Research and Development
Roessinghsbleekweg 33b
7522 AH Enschede

Tweede begeleider
Dr. Tim Takken
Wilhelmina Kinderziekenhuis
Universitair Medisch Centrum Utrecht
3508 AB Utrecht

Universiteit Utrecht
Opleiding Klinische Gezondheidswetenschappen
Afstudeerrichting Fysiotherapiewetenschap

Stage-instelling
Roessingh Research and Development
Roessinghsbleekweg 33b
7522 AH Enschede

ñOndergetekende, Karen Harmelink,
Bevestigt hierbij dat de onderhavige verhandeling mag worden geraadpleegd en vrij mag worden gefotokopieerd. Bij het citeren moet steeds de titel en de auteur van de verhandeling worden vermeld.ò

K. Harmelink

DANKWOORD

Met heel erg veel plezier heb ik het afgelopen jaar op de Roessingh Research and Development afgestudeerd. Ik heb mee mogen werken aan een erg interessant onderzoek en heb in het hele onderzoeksproces vanaf de allereerste start mogen meedenken.

Ik ben begonnen met het schrijven van een METC-aanvraag. Dit heeft mij veel inzicht gegeven in het schrijven van een onderzoeksopzet. Ik vond dit dan ook een geweldige en leerzame ervaring.

Uiteindelijk heb ik een onderzoeksartikel geschreven over een interessant onderwerp binnen de CVA waar nog maar erg weinig over bekend is, namelijk een Stiff Knee Gait. Dit was voor mij een erg leuke uitdaging, mede omdat ik vanuit de fysiotherapiepraktijk een aantal patiënten behandel met een Stiff Knee Gait.

Ik wil iedereen die heeft bijgedragen aan mijn uiteindelijke master thesis ontzettend bedanken, in het bijzonder Martin Tenniglo. Hij heeft mij begeleid in het afgelopen jaar en heeft dit met veel enthousiasme en inzet gedaan. Ik heb erg veel van hem geleerd, waarvoor ik hem erg dankbaar ben. Ook wil ik Jaap Buurke bedanken voor het kritisch reviewen van de artikelen. Daarnaast wil ik Tim Takken en Marco van Brussel bedanken voor hun goede begeleiding vanuit de opleiding fysiotherapiewetenschap. Tenslotte wil ik alle collegaôs van de Roessingh Research and Development en alle medestudenten van de opleiding fysiotherapiewetenschap bedanken voor hun gezelligheid en motiverende gedachten die hebben geleid tot dit eindproduct.

All truths are easy to understand once they are discovered; the point is to discover them.

Galileo Galilei (1564 ï 1642)

INDEX

SYSTEMATIC REVIEW

Effects of neurolytic blocks (botulinum toxin type A and motor branch block) in patients with a Stiff Knee Gait:

A systematic review

Harmelink K.E.M.

Word count: 4326

Journal: Archives of Physical Medical Rehabilitation

Journal: Archives of Physical Medical Rehabilitation

Impact factor (2009): 2.184

Purpose journal:

To publish original, peer-reviewed research and clinical reports in physical medicine and rehabilitation, and to inform rehabilitation professionals of developments that affect them in the nonclinical aspect of their practices.

Word count:

Reviews should be limited to 5000 words of text, exclusive of references.

Tables and figures:

Figures, tables, and references should be limited to the number needed to clarify, amplify, or document the text.

SAMENVATTING

Achtergrond: Een Stiff Knee Gait (SKG) wordt gekarakteriseerd door een verminderde knieflexie tijdens de zwaaifase van het gaan. De meest genoemde oorzaak voor een SKG is een overactiviteit van de Rectus Femoris (RF). Neurolytic blocks zoals botox (BTX-A) en een Motor Branch Block (MBB) zouden overactiviteit van de RF kunnen verminderen en daardoor een SKG verbeteren.

Doelstelling: Primaire doelstelling van deze systematische review is het bepalen van het effect van neurolytic blocks op knieflexie tijdens de zwaaifase bij patiënten met een SKG.

Data selectie: De volgende databases werden doorzocht; PubMed, EMBASE, CINAHL en Cochrane tot november 2009.

Studie selectie: Inclusiecriteria waren: (1) volwassenen van tenminste 18 jaar met een SKG; (2) effect van neurolytic blocks bij een SKG werd bepaald; (3) uitkomstmaat knieflexie tijdens zwaaifase werd gemeten.

Data extractie: Methodologische kwaliteit werd onafhankelijk bepaald door twee reviewers door middel van de Downs en Black checklist. Er werd een Best-Evidence Synthese gebruikt volgens de criteria van Steultjens et al.

Resultaten: Zes studies werden geïncludeerd, drie studies bepaalden het effect van BTX-A en vier studies bepaalden het effect van MBB bij patiënten met een SKG.

Conclusie: Er is aantonend bewijs voor het effect van MBB en BTX-A bij patiënten met een SKG voor het verbeteren van knieflexie tijdens de zwaaifase. Om de uitkomsten uit deze systematische review te ondersteunen, is gerandomiseerd en gecontroleerd onderzoek nodig.

Sleutelwoorden: CVA ƴ Spasticiteit ƴ Rectus femoris ƴ Stiff Knee Gait ƴ Botuline toxin type A ƴ Zenuwblokkade

SUMMARY

Background: A Stiff Knee Gait (SKG) is characterised as a diminished knee flexion during swing. Most common cause of SKG is an overactivity of the Rectus Femoris (RF) muscle. Neurolytic blocks such as botulinum toxin type A (BTX-A) and Motor Branch Block (MBB) could reduce overactivity of the RF muscle and thus decrease a SKG.

Objective: The objective of this systematic review is to determine the effect of neurolytic blocks in knee flexion during swing in patients with a SKG.

Data sources: A literature search was conducted through PubMed, EMBASE, CINAHL and the Cochrane Collaboration until November 2009.

Study selection: The following inclusion criteria were applied: (1) adults over 18 years with a SKG; (2) effect of neurolytic blocks in SKG was determined; (3) outcome measure included at least knee flexion during swing phase.

Data extraction: Methodological quality was independently assessed by two reviewers using the Downs and Black checklist. Best-Evidence Synthesis was applied according to the criteria set out by Steultjens et al.

Results: Six studies were included. Three studies determined the effect of BTX-A and four studies determined the effect of MBB in SKG.

Conclusion: There are indicative findings for the effect of MBB and BTX-A in knee flexion during swing phase in patients with a SKG. Further randomized, controlled research should be done to support the findings in this systematic review.

Key words: Stroke y Muscle spasticity y Rectus femoris muscle y Stiff Knee Gait y Botulinum toxin type A y Nerve block

Introduction

Stiff Knee Gait (SKG) is characterised as a diminished knee flexion during swing[1-3] and is commonly observed in patients following stroke, traumatic brain injury and multiple sclerosis. The physiopathology of SKG is not well understood and several hypotheses are mentioned in the literature. The role of overactivity of the rectus femoris (RF) is often cited.[3-8] RF overactivity has been associated with an increased knee extension moment and decreased knee flexion velocity at toe-off, both of which potentially decrease peak knee flexion.[6] Other possible mechanisms cited in the literature are decreased ankle plantar flexor moments[1, 2] and hip flexor weakness.[4, 9]

Solutions described in the literature for the treatment of SKG are a RF release,[8, 10-12] Functional Electrical Stimulation[13, 14] and neurolytic blocks.[15] In an invasive RF release the distal insertion of the RF muscle is transferred from the patella to a site posterior to the knee. Aim of this procedure is to convert the RF from a knee extensor to a knee flexor.[16] A RF release is effective in children with Cerebral Palsy, but is as far as it is known never studied in adults. In Functional Electrical Stimulation the hamstring muscles and calf muscles will be activated at the beginning of the swing phase, which improves knee flexion during swing.[13, 14] Functional Electrical Stimulation of only the hamstring muscles in SKG is not researched.

A third intervention in the treatment of SKG are neurolytic blocks.[15] Neurolytic blocks reduce SKG, by reducing overactivity of the RF. The most common neurolytic blocks used to treat SKG are a motor branch block (MBB) and botulinum toxin type A (BTX-A) injections in the RF. A MBB is done by an injection in to a motor neuron. This denervates the particular muscle which leads to a reduction in both the efferent and afferent impulses input to a muscle from the muscle spindle which can reduce overactivity.[17] MBB is considered useful to determine the patients capability to walk with diminished activity of the RF and could be used to test the result of more long lasting effective therapy such as BTX-A injections.[17, 18] BTX-A injected in the RF blocks the release of acetylcholine at the neuromuscular junction.[8, 19] This essentially denervates the muscle and thus decreases tone. Besides the efferent effect, experimental studies provided evidence supporting an indirect action of BTX-A at the central level such as the reciprocal inhibition between agonist and antagonist muscles.[20-22]

The effect of BTX-A in other conditions than SKG in spastic patients has been described by several systematic reviews.[23-26] Two meta-analyses show reduced muscle tone after BTX-A injections in upper and lower limb spasticity after stroke.[24, 25] The effect of neurolytic blocks in the treatment of SKG is never described in a systematic review.

Neurolytic blocks could be a useful intervention in SKG. Therefore it is important to describe this in a systematic review.

Objective

The primary objective of this systematic review is to determine the effect of neurolytic blocks (MBB and/or BTX-A) in knee flexion during swing phase in patients with SKG. Secondary objective is to determine the effect of neurolytic blocks (MBB and/or BTX-A) in functional outcome parameters in patients with SKG.

Methods

Literature search

A computerized literature search was conducted in Embase, PubMed, CINAHL (Cumulative Index to Nursing and Allied Health Literature) and the Cochrane Central Register of Controlled Trials (The Cochrane Library) till November 2009. Additionally, the reference lists of all included studies were screened. In proper studies all related articles were also screened. Search strategy was done with the following (MeSH)terms: stroke, cerebrovascular disorders, hemiplegia, cerebrovascular disease, cerebrovascular accident, brain infarction, knee, botulinum toxin type A, botulinum toxins, botulinum toxin A, clostridium difficile toxin A, clostridium botulinum type A, Botox, Dysport, lidocaine, nerve block, motor nerve block, gait, walking, Range Of Motion, joint function, gait analysis and Range Of Motion, Articular. Search strategy was shown in Appendix 1.

Selection criteria

Completed and published studies were included in this systematic review. No restrictions were applied to publication language or date. Studies were considered for inclusion if patients were adults (age over 18 years) with a SKG characterized by a lack of knee flexion during swing phase of gait. Interventions included were MBB and/or BTX-A injections to reduce SKG. Outcome measure included at least knee flexion during swing phase. Exclusion criteria were not full-text published articles.

S*election of studies*

The titles and abstracts of studies retrieved following the search were reviewed by two independent reviewers (KH and JvdD), to determine whether the studies were eligible

according to the research question and inclusion criteria. When there was uncertainty regarding the eligibility of the paper from title and abstract, the full text version of the paper was retrieved and examined. The full text version of all studies that met the inclusion criteria were retrieved for assessment of methodological quality and data extraction. Disagreement was resolved by discussion. In case of permanent disagreement between two searchers, a third researcher (MT) made the final decision.

Data extraction

Data extraction was performed using forms developed by the Cochrane Collaboration. Details from in- and exclusion criteria, participants, intervention, follow-up, outcome measures and results were recorded. Data extraction was independently done by two reviewers.

Methodological quality

The methodological quality of all studies was independently assessed by two reviewers (KH and JvdD). Disagreements were resolved by discussion. If no consensus was met, a third reviewer (MT) made the final decision. To measure the agreement between the two reviewers a weighted Cohenôs Kappa was calculated. Interpretation of the Cohenôs Kappa was done according to the guidelines displayed in table 1.

Table 1: Interpretation of Cohenôs Kappa [36]

Value of Kappa	*Strength of agreement*
<0.20	Poor
0.21 – 0.40	Fair
0.41 – 0.60	Moderate
0.61 – 0.80	Good
0.81 – 1.00	Very good

To assess methodological quality the instrument developed by Downs and Black was used[27] (Appendix 2). The assessment instrument consists of 27 items measuring methodological quality and is based on epidemiological principles, reviews and existing checklists for randomized studies. Downs and Black checklist is a scale for the assessment of the methodological quality of randomized and non-randomized studies of health care interventions. Test-retest reliability and interrater reliability are good (resp. r=0.88 and r=0.75).[27] Face and content validity are also good.[27] The maximal Quality Index Score of the checklist is 32 points. There is no clear cut-off for high or low methodological quality known of the Downs & Black checklist. Downs & Black[27] evaluated ten non-randomised studies for assessing face and content validity and reliability of the Downs & Black checklist. Mean score for non-randomised studies was 11.7±4.64.[27] Brouwers et al[28] used a modified checklist of the Downs & Black. Methodological quality was defined as ôhighô when Ó7 points out of 13 were scored, which is corrected as Ó17 points for the complete Downs & Black checklist. A score of Ó17 points was therefore chosen as cut-off point for ôhigh methodological qualityô and a score of <17 was defined as ôlow methodological qualityô.

Best evidence synthesis

A qualitative approach (best evidence synthesis), based on the type of design, methodological quality and significant findings of outcome measures was performed. A best evidence synthesis (BES) was performed based on the criteria set out by Steultjens et al[29] and was based on that proposed by Van Tulder et al.[30] Subsequently, studies were categorized into five levels of evidence: strong evidence, moderate evidence, limited evidence, indicative findings and no or insufficient evidence. Levels of evidence are described in table 2.

Table 2: Best-evidence synthesis set out by Steultjens et al[29]

Strong evidence
Provided by consistent, statistically significant findings in outcome measures in at least two high quality RCTs*
Moderate evidence
Provided by consistent, statistically significant findings in outcome measures in at least one high quality RCT and at least one low quality RCT or high quality CCT*
Limited evidence
Provided by statistically significant findings in outcome measures in at least one high quality RCT* *or* Provided consistent, statistically significant findings in outcome measures in at least two high quality CCTs* (in the absence of high quality RCTs)
Indicative findings
Provided by statistically significant findings in outcome and/or process measures in at least one high quality CCT or low quality RCT* (in the absence of high quality RCTs) *or* Provided by consistent, statistically significant findings in outcome and/or process measures in at least two Other Designs with sufficient quality (in absence of RCTs and CCTs)*
No or insufficient evidence
In the case that results of eligible studies do not meet the criteria for one of the above stated levels of evidence *or* In the case of conflicting (statistically significant positive and statistically negative) results among RCTs and CCTs *or* In the case of no eligible studies
** If the number of studies that show evidence is <50% of the total number of studies found within the same category of methodological quality and study design (RCTs, CCTs, or Other Designs), there is no evidence*

Results

Literature search

Literature search using multiple databases yielded 91 articles. After removal of duplicates 62 articles were assessed for eligibility at title. After applying the in- and exclusion criteria 50 articles were ineligible. After reviewing twelve articles on abstract, five articles were excluded as they did not met inclusion criteria. Examination of the reference lists of the remaining seven relevant studies added one other study,[17] making a total of eight possibly relevant studies. The full-text version of these articles was reviewed to determine whether they met the inclusion criteria. This process led to the exclusion of two studies.[31, 32] The study of Bleyenheuft et al[31] was excluded because outcome measures did not include knee flexion in swing phase[31] and the study of Pisters et al[32] was excluded because there was no SKG.[32] Six relevant studies were included in this systematic review.[15, 17, 18, 33-35] There was no

disagreement in study selection between the two searchers. The flow diagram of study retrieval and selection is presented in figure 1.

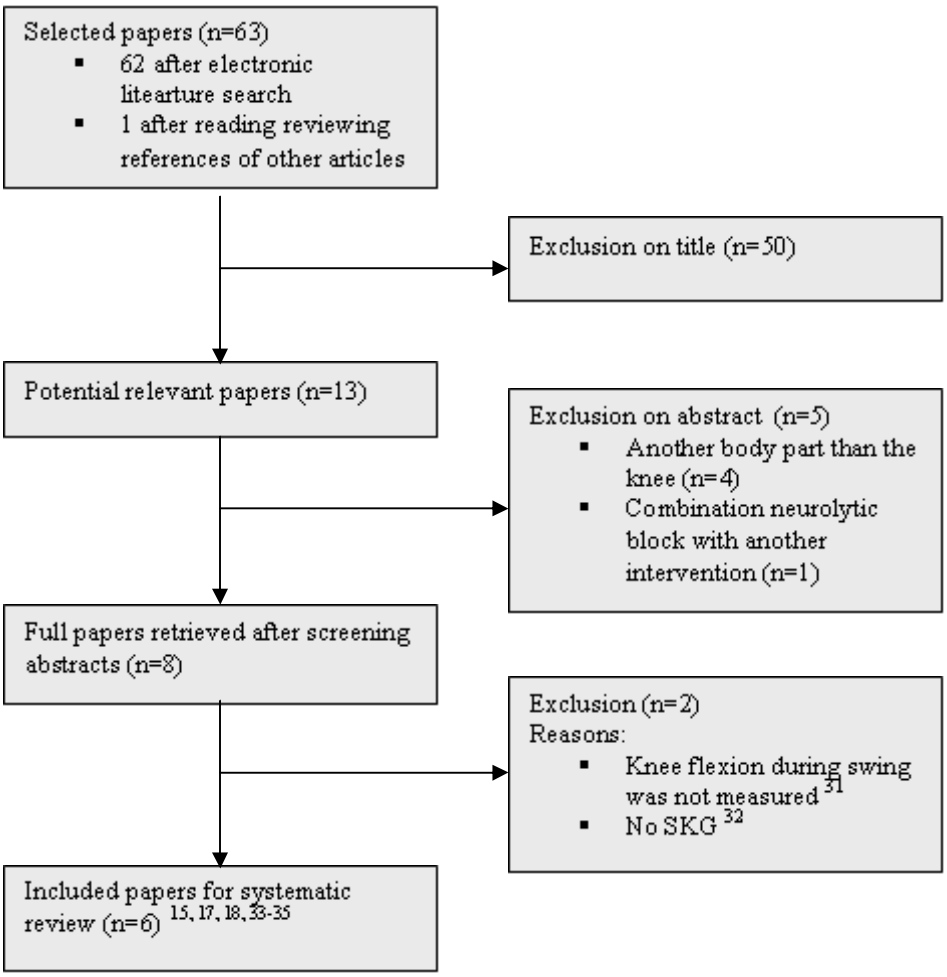

Figure 1: Flow chart of the study selection

Description of studies

Six studies found in the literature search examined the effect of MBB or BTX-A in patients with SKG.[15, 17, 18, 33-35] Study characteristics of the included studies are described in table 3. The number of the participants varied among the included studies and ranged from six[18] to 31.[17] Three studies[18, 33, 34] reported that there were no adverse events. All other studies included in this review did not mention the presence or absence of adverse events.[15, 17, 35]

Table 3: Study characteristics of the studies

STUDY	PARTICIPANTS			INTERVENTION			KNEE FLEXION DURING SWING PHASE			FUNCTIONAL OUTCOME MEASURES			
	N	M/F	Age mean (sd)	Neuro-lytic block	lokalisation	dosage	Pre mean (sd)	Post mean (sd)	p-value	Instrument	Pre mean (sd)	Post mean (sd)	p-value
Caty, 2008	20	15/5	52.3 (16.1)	BTX-A	RF ST TS	200u (RF) 100u (ST) 200u (TS)	22 (19)	27 (16)	p=0.003*	SIAS DE	56.5 2	56.5 0	p<0.001 p<0.001
Stoquart, 2008	19		53 (15)	BTX-A	RF	6x33u (RF)	26 (13)	31 (14)	p<0.001*	SIAS DE	53 3	57 1	p=0.005 p<0.001
Robertson, 2009	10	8/2	40 (10)	BTX-A	RF	200u (RF)	27.4 (8.2)	35.0 (8.8)	p<0.05*	 10MWT 6MWT TUG	BTX-A 0.87 (0.4) 306.7 (125.2) 14.2 (3.5)	BTX-A 0.93 (0.29) 320.3 (96.5) 13.2 (2.8)	 NS NS NS
				MBB	RF	0.5 ml / 2% / LC	27.4 (8.2)	38.2 (10.7)	p<0.05*	 10MWT 6MWT TUG	MBB 0.87 (0.4) 306.7 (125.2) 14.2 (3.5)	MBB 0.92 (0.28) 322.0 (97.1) 17 (6.3)	 NS NS NS
Chantraine, 2005	6	3/3	55 (18)	MBB	RF	1 ml / 2% / LC 1 ml / 2% / BV	38,5 (15.2)	40,4 (14.8)	P=0.502 NS				
Albert, 2002	12	9/3	49.8 (11.3)	MBB	FN	2 cm^2 / 1% / EC	21	32	P=0.06 NS				
Sung, 2000	31		50 (12.7)	MBB	RF	0.5 ml / 2% / LC	25.7 (13.7)	41.1 (16.2)	P<0.05*				

M/F = male/female
BTX-A = botulinum toxin type A
MBB = motor branch block
RF = rectus femoris
ST = semitendinosus
TS = triceps surae
FN = femoral nerve
LC = Licocaïne
BV = Bupivacaïne
EC = Etidocaïne
** p<0,05 (statistically significant)*
NS = not significant
SIAS = Stroke Impairment Assessment Set
DE = Duncan-Ely
TUG = Timed Up and Go test
10MWT = 10 meter walk test
6MWT = 6 minutes walk test
AS = Ashworth Scale

Methodological quality

Methodological quality of the included studies ranged from 19 to 25 points. A score of Ó17 points is considered as óhigh methodological qualityô, so methodological quality of all included studies is high. The results are presented in table 4. Downs and Black[27] scored four items; reporting, internal validity which consists of bias and confounding and external validity. All articles score five points out of ten for reporting (questions 1, 2, 3, 4 and 6) and five points out of seven for bias (questions 16, 17, 18, 19 and 20) Weighted Cohenôs Kappa was calculated as an estimate of agreement between the two assessors for methodological quality of studies. Kappa was 0.72, which is considered a ógoodô strength of agreement (table 1).[36] After discussion all disagreements were solved.

Table 4: Methodological quality of the studies

Item Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Caty	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	U	U	Y	N
Stoquart	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	U	U	Y	N
Robertson	Y	Y	Y	Y	N	Y	Y	N	Y	N	Y	Y	U	N
Chantraine	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	U	Y	N
Albert	Y	Y	Y	Y	N	Y	N	N	Y	N	Y	Y	Y	N
Sung	Y	Y	Y	Y	P	Y	Y	N	Y	N	U	U	U	N

Item Study	15	16	17	18	19	20	21	22	23	24	25	26	27	Score
Caty	N	Y	Y	Y	Y	Y	U	U	N	N	U	Y	5	**23**
Stoquart	U	Y	Y	Y	Y	Y	Y	Y	N	N	U	Y	5	**25**
Robertson	N	Y	Y	Y	Y	Y	U	Y	N	N	U	N	4	**19**
Chantraine	N	Y	Y	Y	Y	Y	Y	U	N	N	U	Y	3	**21**
Albert	N	Y	Y	Y	Y	Y	Y	U	N	N	Y	Y	4	**21**
Sung	N	Y	Y	Y	Y	Y	U	U	N	N	U	Y	5	**19**

Score item 1-4, 6-26: Y=yes (1 point); N=no (0 points); U=unable to determine (0 points)
Score item 5: Y=yes (2 points); P=partially (1 point); N=no (0 points)
Score item 27: 0-5 points

Primary outcome measure

Five studies[15, 17, 18, 33, 34] evaluated knee flexion during swing with three-dimensional gait analysis (*Vicon* Oxford Metrics, Limited, Oxford, England; *ExpertVision* Motion Analysis, Incorporated, Santa Rosa, CA, USA; *Elite system* BTS, Italy). Reflective markers were positioned on specific anatomic landmarks and angular displacement of the knee was computed based on the determination of Euler angles.[37-39] Albert et al[35] registered knee flexion with a goniometer during five strides at a normal pace and five strides at a fast pace. Knee flexion during swing improved in all studies, varying from 1.9 till 15.4 degrees. In four[15, 17, 33, 34] out of five studies in which knee flexion with three-dimensional analysis was measured, knee flexion improved statistically significant. Knee flexion registered with a goniometer improved not statistically significant.[35] Results are described in table 3.

Secondary outcome measures

All three studies who determined the effect of BTX-A in SKG measured functional outcome measures.[15, 33, 34] Caty et al[34] and Stoquart et al[33] examined the Stroke Impairment Assessment Set (SIAS) and the Duncan-Ely. The scores of the SIAS and the Duncan-Ely test improved statistically significant in both studies.[33, 34] In the study of Caty et al[34] the median SIAS value did not change after BTX-A injections, but the neurological impairments improved significantly, shown by the increase in the lowest values (56.5 [48 to 63] to 56.5 [52.5 to 63]). Robertson et al[15] measured functional outcome measures in BTX-A and MBB, namely the 10 meter walk test, 6 minutes walk test and Timed Up and Go (TUG). There was no significant improvement in functional outcome measures. In MBB functional outcome measures even tended to worsen. Other studies who determined the effect of MBB did not measure secondary outcome measures. Results are presented in table 3.

Intervention

Three studies examined the effect of BTX-A in SKG.[15, 33, 34] Stoquart et al[33] and Robertson et al[15] injected only the RF, Caty et al[34] injected also the Semitendinosus and Triceps Surae. Knee flexion increased statistically significant in all three studies, varying from five[33, 34] till 7.6 degrees.[15]

Four studies determined the effect of MBB in SKG.[15, 17, 18, 35] Three studies injected the RF[15, 17, 18] and one study injected the femoral nerve.[35] In all studies knee flexion during swing improved. In two studies which determined the effect of MBB the improvement in knee flexion was statistically significant ($p<0.05$).[15, 17]

Dosage, localization and solution of injection

In five studies the RF muscle was injected.[15, 17, 18, 33, 34] Caty et al[34] injected the Semitendinosus and the Triceps Surae besides the RF. Caty et al[34] and Stoquart et al[33] used the same method of BTX-A injection, namely 200U BTX-A through three punctures into the RF, respectively at the junction between the proximal and the middle third, at the midpoint, and at the junction between the middle and the distal third. One proximal and one distal injection were performed at each site (6 injections of 33U). Robertson et al[15] injected 200U BTX-A in four anatomical points into the RF. All studies injected the clinically available botulinum toxin Botox (Allergan). In all studies who injected BTX-A in the RF knee flexion during swing improved significantly. Three studies injected a MBB in the RF[15, 17, 18] and Albert et al[35] injected a solution of etidocaïne in the femoral nerve, which did not improve

knee flexion during swing significantly (p=0.06). Sung et al[17] and Robertson et al[15] injected 0.3 to 0.5 mL of 2% lidocaïne solution in the RF. Chantraine et al[18] injected following the same method as Sung et al[17] and Robertson et al,[15] but used a mixture of 1 mL of 2% lidocaïne and 1 mL of bupivacaïne solution. Knee flexion increased in all four studies,[15, 17, 18, 35] but the increase was statistically significant ($p<0.05$) in only two studies.[15, 17]

Diagnosis

Three studies included only stroke patients.[18, 33, 34] Robertson et al[15] included patients after stroke and traumatic brain injury and Albert et al [35] included patients with stroke, head injury, spinal cord lesion and multiple sclerosis. Sung et al[17] included patients with traumatic brain injury, stroke, multiple sclerosis, hereditary spastic paraplegia and idiopathic thoracic myelopathy. In three of four studies who included only patients with stroke or traumatic brain injury the increase in knee flexion was statistically significant.[15, 33, 34]

Best Evidence Synthesis (BES)

All three studies which examined the effect of BTX-A in knee flexion during swing improved statistically significant. BES set out by Steultjens et al[29] showed that there are indicative findings for the effect of BTX-A in knee flexion during swing in SKG. Four studies determined the effect of MBB in knee flexion during swing.[15, 17, 18, 35] Robertson et al[15] and Sung et al[17] found a significant improvement in knee flexion during swing. BES showed that there is no evidence for the effect of MBB in knee flexion during swing. Studies which measured the SIAS and Duncan-Ely test in BTX-A found a statistically significant improvement.[33, 34] BES set out by Steultjens et al[29] showed that there are indicative findings for the effect of BTX-A in the improvement of SIAS and Duncan-Ely test. Functional outcome parameters of MBB were only measured in the study of Robertson et al.[15] There was no statistically significant improvement after MBB in functional outcome parameters measured. BES showed that there is no evidence for the effect of MBB in functional outcome parameters.

Discussion

The primary objective of this systematic review was to determine the effect of neurolytic blocks in the RF in knee flexion during swing phase in patients with SKG.

This systematic review revealed that only six studies have been published so far that attempt to evaluate this in intervention studies.[15, 17, 18, 33-35] Results are therefore based on these six studies with a total of 98 participants. Knee flexion during swing increased in all studies, but in only the study of Albert et al[35] and Chantraine et al[18] the increase was not statistically significant. According to the BES set out by Steultjens et al[29] it can be conclude that there are indicative findings for the effect of BTX-A in knee flexion during swing. There is no evidence for the effect of MBB in knee flexion during swing.

Secondary objective was to determine the effect of neurolytic blocks in functional outcome parameters in patients with a SKG. In the study of Caty et al[34] and Stoquart et al[33] SIAS score and Duncan-Ely score improved significant after BTX-A.[33, 34] According to the BES set out by Steultjens et al[29] it can be conclude that there are indicative findings for the effect of BTX-A in functional outcome parameters. There is no evidence for the effect of MBB in fuctional outcome measures.

There is no systematic review known to the effects of neurolytic blocks in SKG. The effect of BTX-A in stroke is examined in varies systematic reviews.[24, 25] Cardoso et al[24] and Rosales et al[25] described in a systematic review an improvement in muscle tone in upper and lower limb spasticity following stroke. These systematic reviews are in agreement with the studies of Stoquart et al[33] and Caty et al[34] included in our review which measures spasticity with the Duncan-Ely test. The Duncan-Ely score improved statistically significant in both studies, which means that spasticity in the RF decreased. The decrease in RF spasticity after BTX-A injection is expected and corresponds to the well known chemodenervation effect of the BTX-A injection.[40, 41] It is plausible that an improvement in knee flexion, which was in all included studies to the effect of BTX-A statistically significant, was caused by a decrease in muscle tone. The effect of BTX-A is namely decreasing muscle tone. Therefore the results in this systematic review are in accordance with the results of the systematic reviews to the effect of BTX-A in spasticity following stroke.[33, 34]

The effect of MBB in spasticity was not earlier described in a systematic review. The effectiveness of MBB in improving knee flexion during swing and functional outcome measures in SKG is not clear. The duration of effect in MBB is very short. In MBB there is a loss of afferent information and adaptation in walking and functional activities is not possible. In BTX-A the adaptation time is quite longer than that of MBB. Possibly functional activities

increased after BTX-A of the afferent information or the fact that a period of longer adaptation is possible after BTX-A.

Included studies that determined the effect of neurolytic blocks on SKG described the administered intervention well, so reproducibility of the intervention is maximizing. Nene et al[42] showed that in healthy subjects the RF is active during the stance-to-swing transition and the activity during swing-to-stance transition found in other studies[43, 44] is very probably due to cross-talk from the vastii. To determine an overactivity of the RF it is therefore necessary to measure both the RF and the vastii with surface EMG. When fine wire EMG was used, only RF activity is adequate.[42] Goldberg et al[45] found in all patients with SKG an excessive RF activity during swing and/or a positive score in Duncan-Ely and support therefore the findings of Nene et al.[42] Robertson et al[15] based inclusion on RF and vastii activity established with EMG. In all other studies included in this systematic review inclusion was not based on RF and vastii activity. Therefore these studies could not certainly include participants with RF overactivity for which the neurolytic block is effective. Possibly, in the other studies participants have a SKG not caused by RF overactivity but caused by hip flexor weakness or decreased ankle plantar flexor moments. Recommendation for inclusion is therefore RF overactivity established with EMG and/or positive Duncan-Ely score for quadriceps spasticity.

All included studies used Botox (Allergan), which is effective in improving knee flexion during swing, SIAS score and Duncan-Ely score in SKG. No statements can be done about Dysport, the other clinically available preparation of BTX-A.

Injection in the RF seems to be more effective for treating SKG than injection in the femoral nerve. In the study of Chantraine et al[18] the increase in knee flexion was not statistically significant after injection in the RF, plausibly due to the small sample size (n=6) or the variety of neurological conditions included in this study. Sung et[17] al included more diagnose groups and found well a statistically significant improvement in knee flexion during swing, but 74% of the participants included had stroke or traumatic brain injury. Neurolytic blocks seems to be effective in stroke and traumatic brain injury more than in other neurological conditions causing SKG.

All included studies in this review are observational designs. Observational designs are useful as preliminary studies. If preliminary studies show a positive effect of this new therapy, this effectiveness should then be confirmed by a Randomized Controlled Trial (RCT).[46, 47] In the case of neurolytic blocks in SKG, RCTs should be confirmed. But it is not

probable that results from observational studies differ from the results of RCTs.[48, 49] Therefore BTX-A seems to be a useful intervention in the treatment of SKG.

Adverse events

Three studies described that there were no adverse events,[18, 33, 34] all other studies included in this review not mentioned the presence or absence of adverse events.[15, 17, 35] In other studies which determined the effect of BTX-A mild adverse events were reported, like pain in the injected region.[50, 51] A systematic review of the efficacy and safety of BTX-A in post-stroke spasticity showed that the odds ratio of having an adverse event after BTX-A injections did not show any significant difference between placebo and BTX-A.[25] Neurolytic blocks seems therefore a safe intervention.

Methodological quality

There is no known valid and reliable cut-off point for high and low methodological quality on the Downs & Black checklist. In this study the choice of a cut-off point was based on two studies.[27, 28] The choice of a cut-off point of 17 points for high methodological quality is arbitrary. There is also a study which considered a score of Ó15 points on the checklist as a ôhigh methodological quality studyõ.[52] The choice of a cut-off point of Ó17 points is based on stern demands to ensure a study defined as ôhigh methodological qualityô is really a study which described reporting, internal validity (bias and confounding) and external validity good.

Bias

Caty et al[34] reported that the Botox used as intervention was sponsored by Allergan. There could be pressure to show that neurolytic blocks causes a favorable outcome when it was done by sponsored research. Systematic reviews of the impact of financial conflicts on biomedical research found that studies financed by industry, although as rigorous as other studies, always found outcomes favorable to the sponsoring company.[53, 54] This lead to funding bias; biases in the design, outcome and reporting of industry-sponsored research to show that a drug shows a favorable outcome.[55]

Gage et al[16] found in children with SKG in Cerebral Palsy a reduction of knee flexion during swing of at least 20 percent, which is less than 45 degrees knee flexion during swing. In stroke patients there is no clear definition known about amount of degrees of diminished knee flexion during swing. Definitions of SKG also not mention the phase of measured diminished

knee flexion. This is important information, because diminished knee flexion is different in different phases during swing. Recommendations for a more specific definition in stroke patients with SKG should be done.

Practical recommendations

Chantraine et al[18] and Sung et al[17] advised a MBB before BTX-A injection. This could be done to avoid falls due paresis and knee buckling after the BTX-A treatment and to predict BTX-A results. Robertson et al[15] found knee flexion during swing in MBB to be significantly correlated with knee flexion during swing in BTX-A, but if inappropriate RF activity has already been identified by EMG, MBB give no more prediction in BTX-A results. Therefore Robertson et al[15] challenge the relevance of performing a MBB, when inappropriate activity of the RF has already been established. Dependent from established inappropriate activity BTX-A should immediately be given or first a MBB should be given in patients with SKG due to the improvement in knee flexion during swing and functional outcome measures. When RF overactivity was shown by EMG activity or Duncan-Ely test, BTX-A could be given in stroke patients with a SKG.

Future research

Although most studies show a significant effect of neurolytic blocks there are indicative findings for the effect of neurolytic blocks in SKG because of the absence of randomized controlled trials. Authors of observational studies of the effect of neurolytic blocks in SKG patients recommend future research with larger sample sizes and randomized controlled studies. Future research should be focus on double-blind, controlled, randomized studies to further validate the results of the included observational studies.

To determine the effects in activity- and participation level functional outcome measures should be studied in further research. Future research should also focus on the long-term benefits of BTX-A injections.

Research with homogenous populations must be done in other neurological conditions to determine the effectiveness of neurolytic blocks. The effect of habituation in BTX-A and MBB should also be researched.

Knee flexion improved in all studies but did not reach normal values. Studies have suggested that normal ankle mechanics[1] and hip flexion[17] are necessary for knee flexion. Possible explanation for the not fully improved knee flexion are problems with the ankle mechanics or hip flexion. Further research to these causes of SKG is very important. When

other causes of SKG are found, neurolytic blocks could be combined with other interventions to improve SKG.

Further research is also important to determine the effect of neurolytic blocks in patients with knee flexion smaller than 10 degrees. This may be related to the other causes of SKG, namely hip flexor weakness and insufficient push-off as result of underactivity of the gastrocnemius muscle.[56] BTX-A seems to be not effective in SKG smaller than 10 degrees.

Conclusion

There are indicative findings for the effect of BTX-A in the RF in knee flexion during swing phase and functional outcome parameters in patients with SKG. No effect is found in knee flexion during swing and functional outcome parameters for MBB. There are no known adverse events reported of the neurolytic blocks. Further randomized, controlled research should be done to support the findings in this systematic review.

Conflicts of interest

There are no known conflicts of interests.

Reference List

(1) Kerrigan DC, Burke DT, Nieto TJ, Riley PO. Can toe-walking contribute to stiff-legged gait? American Journal of Physical Medicine and Rehabilitation, 2001;80(1):33-37.

(2) Kerrigan DC, Karvosky ME, Riley PO. Spastic paretic stiff-legged gait: joint kinetics. American Journal of Physical Medicine and Rehabilitation, 2001;80:244-249.

(3) Sutherland DH, Davids JR. Common gait abnormalities of the knee in cerebral palsy. Clinical Orthopaedics and Related Research, 1992;288:139-147.

(4) Kerrigan DC, Roth RS, Riley PO. The modelling to assess stiff-legged gait swing period based on actual kinematic data. Gait and Posture, 1998;7:117-124.

(5) Perry J. Gait analysis: normal and pathological function SLACK. 1992. Thorofare (NJ): Slack.

(6) Piazza SJ, Delp SL. The influence of muscles on knee flexion during the swing phase of gait. Journal of Biomechanics, 1996;29:723-733.

(7) Riley PO, Kerrigan DC. Torque action of two-joint muscles in the swing period of stiff-legged gait: a forward dynamic model analysis. Journal of Biomechanics, 1998;31:835-840.

(8) Waters RL, Garland DE, Perry J, Habig T, Slabaugh P. Stiff-legged gait in hemiplegia: surgical correction. Journal of Bone and Joint Surgery ï American volume, 1979;61:927-933.

(9) Kerrigan DC, Bang MS, Burke DT. An algorithm to assess stiff-legged gait in traumatic brain injury. Journal of Head Trauma Rehabilitation,1999;14:136-145.

(10) Chambers H, Lauer A, Kaufman K, Cardelia M, Sutherland DH. Prediction of outcome after rectus femoris surgery in cerebral palsy: the role of cocontraction of the rectus femoris and vastus lateralis. Journal of Pediatric Orthopaedics, 1998;18:703-711.

(11) Perry J. Distal rectus femoris transfer. Developmental Medicine and Child Neurology, 1987;29:153-158.

(12) Sutherland DH, Larsen LJ, Mann R. Rectus femoris release in selected patients with cerebral palsy: a preliminary report. Developmental Medicine and Child Neurology, 1975;17:26-34.

(13) Burridge JH, Wood D. Two channel stimulation for hemiplegic gait. Control algorithms, selection of muscle groups and the results of a preliminary clinical trial. *6th Internet World Congress for Biomedical Sciences, February 2000.*

(14) Mann GE, Burridge JH, Ewins DJ, McLellan DL, Swain ID, Taylor PN, Wood DE, Wright PA. Optimising two channel stimulation to improve walking following stroke. 5*th Annual Conference of the International FES Society*, (ISBN 87-90562-01-1), pp. 452-455, Aalborg, Denmark, June 2000.

(15) Robertson JV, Pradon D, Bensmail D, Fermanian C, Bussel B, Roche N. Relevance of botulinum toxin injection and nerve block of rectus femoris to kinematic and functional parameters of stiff knee gait in hemiplegic adults. Gait and Posture, 2009;29(1):108-112.

(16) Gage JR, Perry J, Hicks RR, Koop S, Werntz JR. Rectus femoris transfer to improve knee function of children with cerebral palsy. 29 Developmental Medicine and Child Neurology, 1987;29:159-166.

(17) Sung DH, Bang HJ. Motor branch block of the rectus femoris: its effectiveness in stiff-legged gait in spastic paresis. Archives of Physical Medicine and Rehabilitation, 2008;81(7)910-915.

(18) Chantraine F, Detrembleur C, Lejeune TM. Effect of the Rectus Femoris motor branch block on post-stroke stiff-legged gait. Acta Neurologica Belgica, 2005;105:171-177.

(19) Kao I, Drachman D, Price D. Botulinum toxin: mechanism of presynaptic blockade. Science, 1976;193:1256-1258.

(20) Caleo M, Anonucci F, Restani L, Mazzocchio R. A reappraisal of the central effects of botulinum neurotoxin type A: by what mechanism? Journal of Neurochemistry, 2009;109:15-24.

(21) Currà A, Trompetto C, Abbruzzese G, Berardelli A. Central effects of botulinum toxin type A: evidence and supposition. Movement Disorders, 2004;19(Suppl. 8):S60-S64.

(22) Gilio F, Currà A, Lorenzano C, Modugno N, Manfredi M, Berardelli A. Effects of botulinum toxin type A on intracortical inhibition in patients with dystonia. Annals of Neurology, 2000;48:20-26.

(23) Ade-Hall R, Moore P. Botulinum toxin type A in the treatment of lower limb spasticity in cerebral palsy. Cochrane Database of Systematic Reviews, Issue 1. Art.No.:CD00140.DOI:10.1002/14651858. CD001408. 2000.

(24) Cardoso E, Rodrigues B, Lucena R, Oliveira JR de, Pedreira G, Melo A. Botulinum toxin type A for the treatment of the upper limb spasticity after stroke. Arquivos de Neuro-psiquiatria, 2005;63(1):30-33.

(25) Rosales RL, Chua-Yap AS. Evidence based systematic review on the efficacy and safety of botulinum toxin-A therapy in post-stroke spasticity. Journal of Neural Transmission, 2008;115:617-623.

(26) Wasiak J, Hoare BJ, Wallen MM. Botulinum toxin A as an adjunct to treatment in the management of the upper limb in children with spastic cerebral palsy. Cochrane Database of Systematic Reviews, Issue 4. Art.No.:CD003469 DOI:10.1002/14651858 CD003469. pub3. 2004.

(27) Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. Journal of Epidemiology and Community Health, 1998;52:377-384.

(28) Brouwers MC, Johnston ME, Charette ML, Hanna SE, Jadad AR, Browman GP. Evaluating the role of quality assessment of primary studies in systematic reviews of cancer practice guidelines. BMC Medical Research Methodology, 2005;5-8.

(29) Steultjens EMJ, Dekker J, Bouter LM, Nes JCM van de, Cup EHC, Ende CHM van den, Landi F, Bernabei R. Occupational therapy for stroke patients: a systematic review. Stroke, 2003;34:676-687.

(30) Tulder MW van, Cherkin DC, Berman B, Lao L, Koes BW. The effectiveness of Acupuncture in the Management of Acute and Chronic low back pain. A systematic review within the framework of the Cochrane Collaboration Back Review Group. Spine, 1999;24(11):1113-1123.

(31) Bleyenheuft C, Cockx S, Caty GD, Stoquart GG, Lejeune TM, Detrembleur C. The effect of botulinum toxin injections on gait control in spastic stroke patients presenting with a stiff knee. Gait and posture, 2009;30(2):168-172.

(32) Pisters MF, Blois D de, Bernards ATM, Bakx WGM. Effect of botulinum toxin injections, on gait and comfort during walking in a hemiparetic patient with lower extremity spasticity following stroke. Nederlands Tijdschrift voor Fysiotherapie, 2004;114(2):41-44.

(33) Stoquart GG, Detrembleur C, Palumbo S, Deltombe T, Lejeune TM. Effect of botulinum toxin injections in the rectus femoris on stiff-knee gait in people with stroke: a prospective observational study. Archives of Physical Medicine and Rehabilitation, 2008;1(89)56-61.

(34) Caty GD, Detrembleur C, Palumbo S, Deltombe T, Lejeune TM. Effect of simultaneous botulinum toxin injections into several muscles on impairment, activity, participation, and quality of life among stroke patients presenting with a stiff knee gait. Stroke, 2008;39(10):2803-2808.

(35) Albert TA, Yelnik A, Bonan I, Lebreton F, Bussel B. Effectiveness of femoral nerve selective block in patients with spasticity: preliminary results. Archives of Physical Medicine and Rehabilitation, 2002;83(5):692-696.

(36) Cohen J. Weighted kappa: nominal scale agreement with provision for scaled disagreement or partial credit. Psychological Bulletin, 1968;10(70):213-220.

(37) Davis RB, Ounpuu S, Tyburski D, Gage JR. A gait analysis data collection and reduction technique. Human Movement Science, 1991;10:575-587.

(38) Greenwood DT. Principles of dynamics. Englewood Cliffs, NJ: Prentice-Hall1965.

(39) Kadaba MP, Ramakrishnan HK, Wootten ME. Measurement of lower extremities kinematics during level walking. Journal of Orthopaedic Research, 1990;8389-8392.

(40) Mancini F, Sandrini G, Moglia A, Nappi G, Pacchetti C. A randomised, double blind, dose-ranging study to evaluate efficacy and safety of three doses of botulinum toxin type A (Botox) for the treatment of spastic foot. Neurological Sciences, 2005;26:26-31.

(41) Pittock SJ, Moore AP, Hardiman O, Ehler E, Kovac M, Bojakowski J. A double-blind randomised placebo-controlled evaluation of three doses of botulinum toxin type A (Dysport) in the treatment of spastic equinovarus deformity after stroke. Cerebrovascular Diseases, 2003;15:289-300.

(42) Nene A, Byrne C, Hermens H. Is rectus femoris really a part of quadriceps? Assessment of rectus femoris function during gait in able-bodied adults. Gait and Posture, 2004;20:1-13.

(43) Winter DA, Yack HJ. EMG profiles during normal walking: stride to stride and inter-subject variability. Clinical Neurophysiology, 1987;67:402-411.

(44) Yang JF, Winter DA. Electromyographic amplitude normalisation methods: Improving their sensitivity as diagnostic tools in gait analysis. Archives of Physical Medicine and Rehabilitation, 1984;65:517-521.

(45) Goldberg SR, Ounpuu S, Delp SL. The importance of swing-phase initial conditions in stiff-knee gait. Journal of Biomechanics, 2003;36(8):1111-1116.

(46) Horn SD, Jong G de, Ryser DK, Veazie PJ, Teraoka J. Another look at observational studies in rehabilitation research: going beyond the holy grail of randomized controlled trial. Archives of Physical Medicine and Rehabilitation, 2005;86(12 Suppl. 2):S8-15. 2005.

(47) Tate DG, Findley T Jr, Dijkers M, Nobunaga AI, Karunas RB. Randomized clinical trials in medical rehabilitation research. American Journal of Physical Medicine and Rehabilitation, 1999;78:486-499.

(48) Benson K, Hartz AJ. A comparison of observational studies and randomized, controlled trials. New England Journal of Medicine, 2000;342:1878-1886.

(49) Concato J. Observational versus experimental studies: what's the evidence for a hierarchy? Neuroradiology, 2004;1:341-347

(50) Corry IS, Cosgrove AP, Duffy CM, McNeill S, Taylor TC. Botulinum toxin A compared with stretching casts in the treatment of spastic equinus: a randomised prospective trial. Journal of Pediactric Orthopaedics, 1998;18:304-311.

(51) Gormley ME, Herring GM, Gaebler-Spira DJ. The use of botulinum toxin in children: a retrospective study of adverse reactions and treatment of idiopatic toe-walking. European Journal of Neurology, 1997;4(Suppl.4(Suppl.2)):S27-S30.

(52) Albernaz E, Victoria CG. Impact of face-to-face counselling on duration of exclusive breast-feeding: a review. Revista Panamericana de Salud Publica/Pan American Journal of Public Health, 2003;14(1):17-24.

(53) Bekelman JE, Li Y, Gross CP. Scope and impact of financial conflicts of interest in biomedical research: a systematic review. Journal of the American Medical Association, 2003;289:454-465.

(54) Lexchin J, Bero LA, Djulbegovic B, Clark O. Pharmaceutical industry sponsorship and research outcome and quality: systematic review. British Medical Journal, 2003;326:1167-1170.

(55) Tricco AC, Tetzlaff J, Sampson M, Fergusson D, Cogo E, Horsley T, Moher D. Few systematic reviews exist documenting the extent of bias: a systematic review. Journal of Clinical Epidemiology, 2008;61:422-434.

(56) Goldberg SR, Anderson FC, Pandy MG, Delp SL. Muscles that influence knee flexion velocity in double support: implications for stiff-knee gait. Journal of Biomechanics, 2004;37:1189-1196.

ARTICLE

Effects of Functional Electrical Stimulation of the hamstring muscles in stroke patients with a Stiff Knee Gait:

An explorative prospective cohort study

Harmelink K.E.M.

Word count: 4102

Journal: BMC Neurology

Journal: BMC Neurology

Impact factor (2009): 2.109

Purpose journal:

To publish original peer-reviewed research articles in all aspects of the prevention, diagnosis and management of neurological disorders, as well as related molecular genetics, pathophysiology, and epidemiology.

Word count:

There is no explicit limit on the length of articles submitted.

Authors are encouraged to be concise.

Tables and figures:

There is no restriction on the number of figures, tables or additional files.

SAMENVATTING

Introductie: Een Stiff Knee Gait (SKG) is een veelvoorkomend probleem bij CVA-patiënten. Een SKG wordt gedefinieerd als een verminderde knieflexie tijdens de zwaaifase van het gaan. Meest voorkomende oorzaak van een SKG is overactiviteit van de m. rectus femoris. Activatie van de hamstrings kan de knieflexie tijdens de zwaaifase verbeteren. Functionele Elektrische Stimulatie (FES) van de hamstrings zou daardoor een SKG kunnen verminderen.

Doelstelling: Bepalen van het effect van Functionele Elektrische Stimulatie bij CVA-patiënten met een SKG.

Methode: Zeventien CVA-patiënten met een SKG werden geïncludeerd in deze studie. Na de voormeting is er vijf weken getraind met FES van de hamstrings, waarna een nameting is gedaan. Om het effect van FES te bepalen werden de uitkomstmaten geanalyseerd, middels een gepaarde t-toets.

Resultaten: FES van de hamstrings verbetert knieflexie tijdens de zwaaifase, loopsnelheid, heupflexie, stride lengte, steplengte en cadans bij CVA-patiënten met een SKG. Een statistisch significant verschil is niet aangetoond voor VAS score en Duncan-Ely test.

Discussie: FES zorgt voor een statistisch significante verbetering van knieflexie tijdens de zwaaifase. FES van de hamstrings kan een reciprocale inhibitie van de m. rectus femoris geven, wat ook een mogelijke oorzaak is voor de verbeterde knieflexie tijdens de zwaaifase. Beperking van de studie is het ontbreken van een randomisatieprocedure en de afwezigheid van een controlegroep.

Conclusie: FES van de hamstrings lijkt effectief bij CVA-patiënten met een SKG. Er zijn geen bijwerkingen gerapporteerd. Deze resultaten moeten verder worden onderzocht met een gerandomiseerde, gecontroleerde studie.

SUMMARY

Introduction: A Stiff Knee Gait (SKG) is a common problem in stroke patients. A SKG is defined as a diminished knee flexion during swing phase. Most common cause of SKG is an overactivity of the rectus femoris muscle. Activation of hamstring muscles could increase knee flexion during swing. Therefore Functional Electrical Stimulation (FES) of the hamstring muscles could improve SKG.

Objective: To determine the effect of FES of the hamstring muscles in stroke patients with a SKG.

Methods: Seventeen stroke patients presenting with a SKG were included in this study. After a pre-test there was a training period of five weeks, which has been completed with a post-test. Statistical analysis was done by a paired t-test.

Results: This study showed that FES of the hamstring muscles in stroke patients improved knee flexion, hip flexion, walking speed, stride length, step length and cadence measured with three-dimensional gait analysis. There is no improvement in VAS and Duncan-Ely score.

Discussion: FES improves knee flexion during swing significantly. FES of the hamstring muscles could decrease spasticity of the RF via reciprocal inhibition, which is a possible cause for the improvement in knee flexion during swing. The lack of a control group and a randomisation procedure are limitations of this study.

Conclusion: This study demonstrates that FES of the hamstring muscles seems to be effective in stroke patients presenting with a SKG. There were no adverse events reported. To make definitive recommendations, a randomized controlled trial with a large sample size should be carried out.

Introduction

The number of stroke patients is rising worldwide. In The Netherlands the prevalence of stroke is 190.000. Problems after stroke are diverse. Cognitive, visual and motor problems may appear. A very important activity of daily life in stroke patients is walking. 50 percent of the stroke patients experience problems with walking and in 11 percent walking is impossible after stroke.[1] Remaining gait deficits can result in elevated energy cost, poor endurance and falling. Falling has been reported as a major cause of morbidity, hospitalization and mortality among stroke patients.[2, 3]

Regaining the ability to walk is a major goal in rehabilition.[4-6] One of the causes of walking problems is insufficient footclearance. About 18.000 patients in the Netherlands experience problems with walking caused by insufficient footclearance.[7] Footclearance problems in swing phase are caused by a combination of lack of hip flexion, knee flexion and dorsal flexion at the ankle.[8] Lack of dorsal flexion at the ankle can be solved by prescribing an ankle foot orthosis (AFO) or Functional Electrical Stimulation (FES). No assistive devices exist to overcome the problems of lack of knee and hip flexion.

In healthy people knee flexion during swing is approximately 60 degrees.[8]A diminished knee flexion during swing is defined as a Stiff Knee Gait (SKG).[9-11] The physiopathology of SKG is not well understood and several hypotheses are mentioned in the literature. The role of overactivity of the rectus femoris (RF) is often cited.[12-16] RF overactivity has been associated with an increased knee extension moment and a decreased knee flexion velocity at toe-off, both of which potentially decrease peak knee flexion.[14] Other possible mechanisms cited in the literature are decreased ankle plantar flexor moments[9, 10] and hip flexor weakness.[17, 18]

Solutions for the treatment of SKG are botulinum toxin injections,[19-21] a RF release[22-25] and FES of the hamstring muscles.[26] Botulinum toxin injections in the RF blocks the release of acetylcholine, which denervates the RF and thus decrease the overactivity of the RF.[27, 28]
In a RF release the distal insertion of the RF is transferred from the patella to a site posterior to the knee to convert the RF from knee extensor to a knee flexor.[8] A RF transfer is carried out in children with Cerebral Palsy, but is not researched as a treatment option in stroke patients. A possible alternative and non-invasive intervention for stroke patients which is not much researched is FES of the hamstring muscles.

The use of FES is expanding the last years. Functional Electrical Stimulation was first described by Levine in 1952.[29] FES elicits a contraction of the stimulated muscles.

Physiological effects that have been ascribed to FES include muscle strengthening, inhibition of antagonist spasticity, reduced muscle tone and increased passive range of motion.[30-33] FES of a combination of the hamstring muscles and calf muscles in stroke patients was reported by Burridge et al[34] and Mann et al.[35] These studies are unpublished congress presentations. They both found positive results on walking speed using FES of the hamstring muscles in combination with calf muscles in stroke patients. However, a problem of stimulating two muscles in order to influence kinematics is timing. Providing adequate timing is easier in one muscle and in addition, stimulating one muscle is more feasible in clinical practice. FES of only the hamstring muscles therefore could even be better to improve knee flexion during swing compared to FES of a combination of muscles. Activation of the hamstring muscles at the end of the stance phase possibly improves knee flexion during swing. This leads to the hypothesis that FES of the hamstring muscles at the end of the stance phase increases knee flexion during swing which improves SKG.

Objective

Primary objective of this study is to determine the effect of Functional Electrical Stimulation (FES) of the hamstring muscles in stroke patients with a SKG on knee flexion during swing phase of gait.

Secondary objective is to determine the effect of FES of the hamstring muscles in stroke patients with a SKG on walking speed, hip flexion, stride length, step length, cadence, tone, disutility, spasticity and subjective findings.

If knee flexion during swing improves statistically significant, correlations between knee flexion and walking speed, hip flexion and subjective knee flexion are determined.

Methods

Subjects

Seventeen stroke patients walking with a SKG were recruited from the rehabilitation department from óthe Roessinghô in Enschede, the Netherlands. Patients were enrolled in the present study between August 2008 and November 2009. Patients were included at least 3 months after stroke when they were over 18 years and had sufficient cognitive abilities to understand and follow the instructions. Inclusion was based on clinical examination and observation of gait; lack of knee flexion during swing phase of gait and the ability to walk independently with and without FES. The exclusion criteria were the presence of a pacemaker and/or metal implantations, skin defects, problems with handling an electrical stimulation unit, other neurological conditions causing SKG, a progressive syndrome which influences walking and a diminished knee flexion based on an orthopaedic cause. After given their informed consent all patients participated freely in the study. The study was approved by the Medical Ethics Committee of the Roessingh Rehabilitation Centre.

Characterisation of patient population

To determine the characteristics of the participantsô age, weight, height, hemiparetic side, onset of stroke, Functional Ambulation Categories (FAC) score, Rivermead Mobility Index (RMI) score and Motricity Index (MI) were measured.

FAC measures the level of independent walking.[36, 37] A FAC score of ó0ô means not able to walk or only walk with the help of two persons and FAC score of ó5ô means that the participant walks independent. Reliability and validity of the FAC are good.[38] The RMI is a questionnaire with fourteen questions about activities of daily life.[39] Reliability[39] and construct validity[40] of the RMI are good. The MI gives a rapid overall indication of a patientôs limb impairment. The MI measures the possibility of voluntary movements and maximal isometric strength of arm and leg in stroke patients. In the leg the three movements tested are ankle dorsiflexion, knee extension and hip flexion. A higher MI score correlates with more muscle strength. Interrater reliability of the MI of the leg is 0.87. In this study only the score of the leg is measured.

Measurements

Before and after the intervention the kinematics during walking were measured using a three-dimensional gait analysis system (Vicon 370 system[b]) Sixteen reflective markers were placed on specific anatomic landmarks, according to the ñplug in gait Lower Body Modelò of Kadaba[41] and six cameras recorded the three-dimensional spatial location of each marker as the participant walked at a self-selected comfortable speed. Knee flexion during completed gait cycle was determined. Other parameters measured were walking speed, hip flexion, stride length, step length, and cadence. To determine these gait parameters at least ten strides were collected for the analysis.

Tone and disutility were measured with a Visual Analogue Scale (VAS).[42] The VAS is a valid and reliable measurement tool in rating pain intensity.[43] The measurement tool consists of a 100-mm horizontal VAS with anchor points for tone of ólowest tone possibleô (score 0) and óhighest tone possibleô (score 100) and for disutility of óno disutilityô (score 0) and ómaximal disutilityô (score 100). Participants marked the VAS with a line. The score was taken at the point where the centre of the cross transacted the VAS line. Muscle tone was also measured with the Duncan-Ely test.[44] The Duncan-Ely tests the velocity-dependent spasticity of the rectus femoris muscle by a rapidly, passive flexion of the knee while the patient lies prone in a relaxed state. The Duncan-Ely test was shown to have a good positive predictive value for rectus femoris dysfunction during gait.[44]

After the intervention a self-reported questionnaire was examined. Six questions about possible effects of FES were answered by the participants. Five answers can be given on a Likert scale, varying from ófully agreeô, óagreeô, óneutralô, ódisagreeô and ófully disagree.ô Questions asked deal with the effect of FES on walking, fatigue, muscle tone, knee flexion, walking distance and automatism of walking. The seventh question concerns the most important reasons to use FES. In this question more answers are possible.

Experimental set-up and procedures

After inclusion in the study and given informed consent the protocol started with the first set of measurements, the gait analysis followed by the functional assessments and the subjective questionnaire (pre-test). After this first evaluation the training period started. FES was given for five weeks. The second evaluation to assess the effect of FES was performed after the intervention (post-test). In the post-test the participants walked with FES of the hamstring muscles.

FES was given using the Odstock Two Channel Stimulator (O2CHS).[a] This is an electronic device, designed to assist people who have difficulty in walking due to neurological damage. An indifferent and an active surface electrode were placed. The indifferent electrode was placed at the bottom of the hamstring muscles, just above the poplitea. The active electrode was placed over the centre of the muscle, about two hand widths above the indifferent electrode.

Triggering of the stimulation was done by a foot switch. The foot switch measures the pressure of the foot. When the pressure disappears the hamstring muscles are activated. Depending on the individual walking pattern the foot switch is either set on the heel or fore foot. In this way it was possible to stimulate the hamstring muscles in every individual patient at the end of the stance phase. FES parameters like frequency, pulse duration and delay time were individually optimalised for each participant.

Individual training was given three times a week during five weeks by the same physical therapist. Each session took 1.5 till 2 hours. Training consisted of walking exercises at comfortable walking speed with FES. All FES sessions were given by an experienced physical therapist/researcher. The same researcher performed all gait analysis, functional assessments and subjective questionnaires. Figure 1 shows the study design of this explorative prospective cohort study.

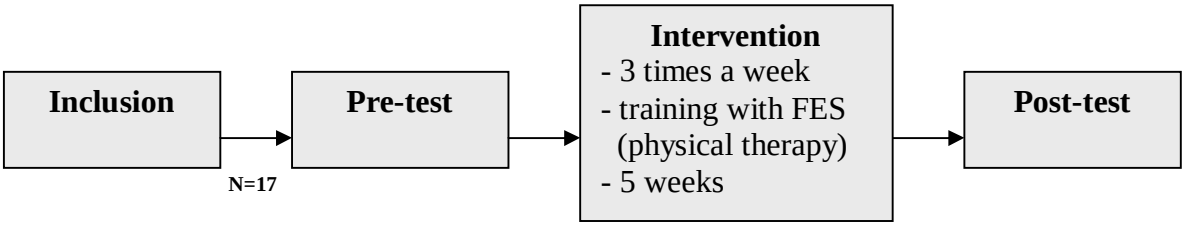

Figure 1: Study design

Statistical analysis

A paired *t* test was computed for normal distributed data to compare pre- and post-test (mean ± SD) and identify the effect of FES. A Wilcoxon test was used to compare non-parametric data (median [interquartile range]). All statistical analyses were performed using SPSS 16.0 for Windows. A $p < 0.05$ was regarded as significant. Correlations between knee flexion and walking speed, hip flexion and subjective knee flexion were analysed Pearsons correlation. Correlation is significant at the 0.05 level.

A calculation of the sample size was not possible. There were no known reference data in FES by stroke patients with a SKG.

Results

Study characteristics

Seventeen stroke patients were included, 15 males and 2 females. Due to a migration one male stopped after the pre-test, therefore sixteen patients were analysed. Age of the participants ranged from 38 to 79 years. The mean age was 57.3 ± 10.3 years. Time since stroke was 67 ± 64 months. Seven participants had right side hemiplegia and nine participants had left side hemiplegia. Seven patients scored FAC 4 and nine patients scored FAC 5. RMI score varies from 11 to 14. Eight patients walked with a splint. Seven patients used a crutch. Subject characteristics are described in table 1. The intervention was well tolerated by all 16 patients. No side effects were reported.

Table 1: Subject characteristics

Participant	Sexe (M/F)	Age (years)	Weight (kg)	Height (m)	Hemiparetic side (R/L)	Time since stroke (months)	FAC	RMI	MI
1	M	46	90.0	1.89	L	24	5	12	83
2	M	49	92.0	1.78	L	17	5	13	75
3	F	65	68.9	1.57	R	151	4	11	75
4	M	65	97.9	1.77	L	34	5	13	63
5	M	59	105.6	1.81	R	81	4	12	75
6	M	61	95.4	1.86	L	73	5	13	72
7	M	38	91.4	1.90	R	82	4	13	39
8	M	46	83.7	1.81	R	73	4	12	59
9	M	48	61.1	1.77	R	17	4	12	75
10	M	52	58.5	1.70	L	23	5	14	75
11	F	54	67.5	1.80	R	55	5	13	69
12	M	72	67.7	1.71	R	115	4	11	28
13	M	59	77.5	1.85	L	9	5	13	69
14	M	79	80.3	1.73	L	51	5	14	83
15	M	53	95.3	1.84	L	255	4	12	28
16	M	60	92.5	1.72	L	14	5	13	64
Total	**14/2**	**57.3 (10.3)**	**82.8 (14.4)**	**1.78 (0.084)**	**7/9**	**67 (64)**	**5 [1]**	**13 [3]**	**70.5 [55]**

FAC = Functional Ambulation Categories; RMI = Rivermead Mobility Index; MI = Motricity Index leg

Total data are described as mean (standard deviation) or median [range]

Kinematics

All kinematic measures improved statistically significant. Data are shown in table 2. Average knee flexion during swing significantly increased 8.3 degrees after FES, knee flexion before the intervention varied from 12 to 46 degrees and after the intervention from 17 to 61 degrees. Figure 2 shows a typical example of knee flexion before and after FES in one participant. Before FES (figure 2 A) knee flexion is decreased at the beginning of the swing phase. After FES (figure 2 B) knee flexion during swing clearly increased.

Table 2: Effects of FES

	Before FES	After FES	p-value
Knee flexion (degrees)	29.1 (8.7)	37.4 (10.9)	0.001* ÿ
Hip flexion (degrees)	35.6 (8.3)	39.7 (8.2)	0.001* ÿ
Walking speed (m/s)	0.86 (0.22)	0.97 (0.23)	0.001* ÿ
Spatiotemporal measures:			
- **Stride (m)**	1.10 (0.19)	1.20 (0.20)	0.001* ÿ
- **Step (m)**	0.54 [0.48]	0.61 [0.51]	0.001* **À**
- **Cadens**	92.7 (12.1)	96.4 (11.3)	0.025* ÿ
Duncan-Ely	1.63 (0.72)	1.63 (0.72)	1.00ÿ
VAS tone	4.36 (1.63)	4.82 (1.59	0.26 ÿ
VAS disutility	3.54 (2.47)	3.54 (2.26)	1.00 ÿ

** p<0.05 = statistically significant;* ***ÿ*** *paired t-test (data are expressed as mean (standard deviation);* ***À****Wilcoxon signed rank test (data are expressed as median [range])*

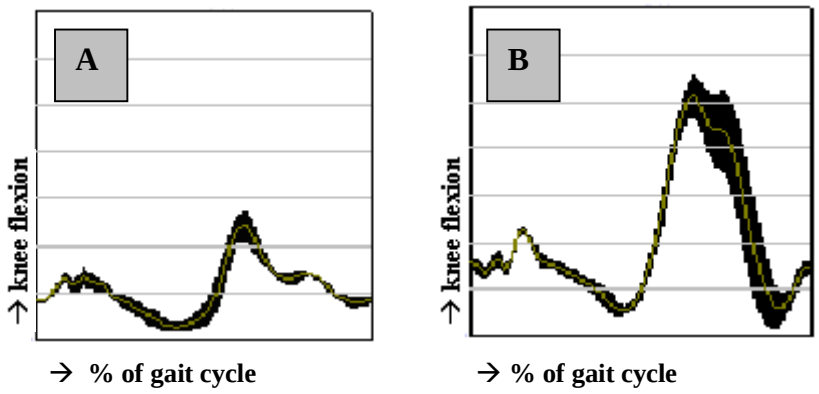

Figure 2: Knee flexion during swing in a male with SKG before (A) and after (B) FES

In table 3 the improvement in knee flexion during swing is shown for three different ranges of knee flexion. From this table it becomes clear that a moderate (5°-10°) to good (< 10°) improvement in knee flexion is seen in respectively 7 and 4 patients.

Table 3: Improvement in knee flexion during swing

Improvement in knee flexion (degrees)	Number of participants (n=16)
0-5 degrees	5
5-10 degrees	7
<10 degrees	4

Spatiotemporal parameters improved significantly after FES of the hamstring muscles. On average stride length improved with 10 cm after FES and step length improved with 5 cm after FES. Walking speed was 0.86 ± 0.22 m/s and increased significantly ($p<0.001$) after FES to 0.97 ± 0.23 m/s. Cadence improved four steps. No change in Duncan-Ely score was observed.

A significant correlation between knee flexion and hip flexion was found ($r=0.54$, $p=0.031$). There was no significant correlation between walking speed and knee flexion ($p=0.98$). Correlations are presented in table 4.

Table 4: Correlation coefficients between knee flexion and walking speed, hip flexion and subjective knee flexion

	Walking speed	Hip flexion	Subjective knee flexion
Knee flexion	0.006	0.54*	-0.38

There was no difference in experienced muscle tone ($p=0.26$) and disutility ($p=1.00$) before and after FES measured with a VAS questionnaire. VAS scores are shown in table 2.

Fourteen participants fully completed the self-reported questionnaire. The results are presented in table 5 and table 6. Two participants did not answer the questionnaire, because of aphasia. The self-reported questionnaire showed that 75 percent of the participants experienced improvement in knee flexion during walking, but only four patients mentioned improved knee flexion as one of the most important reasons to use FES. There was no significant correlation between measured knee flexion with VICON and self-reported knee

flexion experienced by the participants (r=-0.38, p=0.149). FES positively influences walking in general in 87.5 percent of the participants and ñautomatism of walkingò in 75 percent of the participants. Increased automatism of walking is also the most important reason for the participants to use FES.

Table 5: Self-reported questionnaire

Question	**Positive (%)**	**Neutral (%)**	**Negative (%)**
Use of FES has influence in walking	87.5	12.5	0
Use of FES has influence in fatigue in walking	18.75	68.75	12.5
Use of FES has influence in tone/stiffness sensation in the leg	18.75	68.75	12.5
Use of FES has influence in knee flexion during walking	75.0	25.0	0
Use of FES has influence in walking distance	12.5	87.5	0
Use of FES has influence in automatism of walking	75.0	18.75	6.25
Total effect	**47.91**	**46.88**	**5.21**

Table 6: Most important reason to use FES

Most important reason to use FES*		
Walking is less tiredness	0	0%
Walking is more automatically	7	50%
It gives a reduction in stiffness of the knee	1	7.1%
Knee flexion is easier	4	28.6%
Increasing of walking distance	1	7.1%
Walking is easier	4	28.6%
Balance is better	0	0%
** more answers are possible*		

Discussion

The aim of this study was to determine the effect of FES in stroke patients presenting with a SKG. The present study demonstrates that FES of the hamstring muscles in stroke patients improves knee flexion, hip flexion, walking speed, stride length, step length and cadence measured with three-dimensional gait analysis. There is no change in tone measured with the VAS and the Duncan-Ely test. Average knee flexion increases significantly with 8.3 degrees. Four of 14 participants found improvement in knee flexion an important reason to use FES.

Knee flexion during swing

Average knee flexion improved statistically significant with 8.3 degrees (p=0.001). 75 percent of the participants reported positive influence of FES on knee flexion during swing on a self-reported questionnaire. The objective measured improvement in knee flexion during swing is not self-reported in all patients. There is no positive significant correlation between objective knee flexion during swing and self-reported improvement of knee flexion during swing after FES (r=-0.38, p=0.149). Myers et al[45] found a good correspondence between self-reported and performance based activities in elderly between 60 and 92 years for only one third of the matching. In the other two third a bad correspondence was described between the self-reported and performance based activities. This is in agreement with the results in the present study. An explanation for this phenomenon might be that a significant improvement of 8.3 degrees in knee flexion is not clinically noticeable or relevant for the participants. However all other interventions treating SKG in stroke patients like botulinum toxin report less than 8.3 degrees. Caty et al[19] and Stoquart et al[21] described an improvement of five degrees in knee

flexion during swing after botulinum toxin injections. Robertson et al[20] described an improvement of eight degrees after botulinum toxin injections. In eleven of eighteen participants in the present study, knee flexion during swing improved more than five degrees (table 3). At this moment FES seems therefore the best intervention to improve knee flexion during swing in SKG.

Walking speed

Mean comfortable walking speed in stroke patients varies from 0.18 to 1.03 m/s.[46-48] Stroke subjects walk at slower speeds compared with age-matched controls.[47] Decreased walking speed is an important functional limitation in persons with stroke patients.[47, 49, 50] Therefore in many stroke patients improving walking speed is an important goal during rehabilitation.[4, 51] Walking speed increased significantly after FES of the hamstring muscles (0.86 ± 0.22 m/s before intervention and 0.97 ± 0.23 m/s, p=0.001), but did not reach normal values. In normal healthy subjects comfortable gait speed is 1.25 ± 0.18 m/s in males and 1.11 ± 0.10 m/s in females.[52] It appears likely that other factors like spasticity or paresis of other muscles, balance problems and the severity of stroke play an important role in this.

In the literature, walking speed is positively correlated with knee flexion during swing.[53, 54] In this study there was no significant correlation between walking speed and knee flexion during swing (r=0.006, p=0.98). The studies that reported a significant correlation between walking speed and knee flexion during swing involved healthy normal subjects.[53, 54] Possibly walking speed and knee flexion are correlated in healthy subjects, but not in stroke patients. A possible explanation might be that increased walking speed correlates with increased spasticity in the rectus femoris which in turn prevents the increase in knee flexion.

Mechanism of FES

Burridge et al[34] and Mann et al[35] first described FES in stroke patients presenting SKG. No other studies were found that reported the effect of FES in SKG.

Burridge et al[34] used two stimulation channels to identify selection criteria for subjects who would benefit from using two channel stimulation during walking. The common peroneal nerve and the hamstring muscles or calf muscles were stimulated. Results showed that stimulating the hamstring muscles or calf muscles in addition to the common peroneal nerve increased walking speed. Furthermore stimulation of the calf muscles is more likely to result in an increase in walking speed than stimulation of the hamstring muscles. Burridge et al[34]

included participants with predominant calf spasticity. It is therefore plausible that the participants benefit most from calf muscles stimulation.

Mann et al[35] found a significant improvement on walking speed by using a second channel stimulation. Selection of the second muscle group in addition to the common peroneal nerve was based on clinical observation. In inadequate swing hamstring muscles were stimulated from mid-stance to mid-swing to improve swing. From the six participants using hamstring stimulation one showed an improvement in the gait problem treated and three achieved an improvement in knee flexion. This is in agreement with the results of the present study.

Activation of the hamstring muscles with FES in the beginning of swing phase, causing a concentric contraction of the hamstring muscles, improves knee flexion during swing. This mechanism, the concentric contraction, is in agreement to what is reported by Burridge[34] and Mann.[35]

Levine et al[29] described another mechanism for the effect of FES. They applied electrical stimulation to the antagonist of the spastic muscle. An explanation reported by Levine et al[29] for the improvement of knee flexion is the effect of reducing spasticity of the RF, being a common cause of SKG.[25, 55-57] Hamstring stimulation may decrease spasticity of the RF via reciprocal inhibition. In reciprocal inhibition the antagonistic muscle group is simultaneously inhibited via inhibitory postsynaptic potentials. In FES of the wrist, this effect of reciprocal inhibition was shown by Chae et al.[58] However, Chae et al[58] used a pulse of ten seconds, which is much longer than the pulse of only 300 ms used in the present study. Therefore it is not sure that the effect of FES in the present study is an effect of reciprocal inhibition. In addition, the unchanged VAS and Duncan-Ely scores are in agreement with the presumption that the reported effects in this study are not caused by the mechanism of reciprocal inhibition.

Another mechanism which might explain the effect of FES is the withdrawal reflex. Withdrawal reflexes were first described as a typical flexion of the limb when applying electrical stimulation on different aspects of the leg, except when stimulating directly extensor muscles.[59] Emborg et al[60] and Spaich et al[61] stimulated different parts of the foot and evaluated the withdrawal reflex in healthy subjects. Stimulation at heel-off evoked the largest knee flexion response.[60, 61] The study of Quintern et al[62] support these findings. They included 38 patients with hemiparesis after acute stroke that had a positive withdrawal reflex response on electrical stimulation below the pain threshold. This appeared to be true for about 70% of the tested patients. FES of the withdrawal reflex afferents enhances the recovery of gait function in patients with hemiparesis after acute stroke. In patients with a positive withdrawal

reflex FES of the hamstring muscles probably works better than in patients without withdrawal reflex.

Limitations of this study

The lack of a control group and a randomisation procedure are the major limitations of this study. Future studies to the effect of FES in SKG should be randomized and controlled. Furthermore in this study there was no blinding of the intervention. This of course might cause a bias, especially in this study where treatment and assessment was done by one and the same therapist. In this study FES improved knee flexion, hip flexion, walking speed, stride length, step length and cadence.

Clinical implications and implications for further research

FES improves knee flexion, hip flexion, walking speed, stride length, step length and cadence in stroke patients presenting with a SKG. Therefore FES can be recommended in stroke patients with a SKG.

FES is compared to other available interventions, like botulinum toxin injections, an effective treatment in the reduction of SKG. Application of FES is simple and every physical therapist should be able to apply FES to patients.

Future research should focus on the determinants for success of FES in SKG. A possible determinant may be found in the correlation between the first FES application and the result after a certain training period. If positive correlation is found between the first FES application and the result after a training period, the choice whether or not to use FES can be made after one session with FES of the hamstring muscles.

Future studies concerning the effect of FES in SKG should be double-blinded and placebo-controlled. Different combinations of treatment duration and number of training sessions are suggested to explore any difference in the effectiveness of the intervention. The effects of FES on fall incidence and quality of life is also important.

In this study no significant correlation between walking speed and knee flexion and a moderate correlation between walking speed and hip flexion was found. Further research might focus on a new combined parameter of knee flexion and hip flexion such as step height as an outcome measure for the treatment of these complex movement patterns in stroke patients.

Conclusion

This study demonstrates that FES of the hamstring muscles improves knee flexion during swing, hip flexion, walking speed, stride length, step length and cadence in stroke patients presenting with a SKG. No adverse events were reported. In order to make definitive recommendations, a randomized controlled trial with a large sample size should be carried out.

Acknowledgments

The author likes to thank the stroke subjects for their participation in this study. There are no conflicts of interest.

a. **Department of Medical Physics and Biomedical Engineering, Salisbury District Hospital, Salisbury, Wiltshire, SP2 8BJ, United Kingdom**
b. **Oxford Metrics Ltd, 14, Minns Estate, West Way, Oxford OX2 OJB, United Kingdom**

Reference List

(1) Jorgensen HS, Nakayama H, Raaschou HO, Olsen TS. Recovery of walking function in stroke patients: The Copenhagen Stroke Study. Archives of Physical Medicine and Rehabilitation, 1995;76:27-32.

(2) Cryfe CI, Amies A, Asbley MS. A longitudinal study of falls in an elderly population: incidence and morbidity. Age Ageing, 1977;6:201-210.

(3) Lau YC, Wong MK. Traumatic bone fracture in CVA patients. Journal of Rehabilitation and Medicine Association, 1989;17:34-37.

(4) Bohannon RW, Horton MG, Wikholm JB. Importance of four variables of walking to patients with stroke. International Journal of Rehabilitation Research, 1991;14:246-250.

(5) Duncan PW, Sullivan K, Behrman A, et al. Protocol for the Locomotor Experience Applied Post-stroke (LEAPS) trial: a randomized controlled trial. BMC Neurology, 2007;7-39.

(6) Mayo NE, Wood-Dauphinee S, Ahmed S, Gordon C, Higgings J, McEwen S, Salbach N. Disablement following stroke. Disability and Rehabilitation, 1999;21:258-268.

(7) Kottink AIR, Oostendorp LJ, Buurke JH, Nene AV, Hermens HJ, IJzerman MJ. The orthotic effect of functional electrical stimulation on the improvement of walking in stroke patients with a dropped foot: A systematic review. Artificial Organs, 2004;28(6):577-586.

(8) Gage JR. Surgical treatment of knee dysfunction in cerebral palsy. Clinical Orthopaedics and Related Research, 1990;253:45-54.

(9) Kerrigan DC, Burke DT, Nieto TJ, Riley PO. Can toe-walking contribute to stiff-legged gait? American Journal of Physical Medicine and Rehabilitation, 2001;80(1):33-37.

(10) Kerrigan DC, Karvosky ME, Riley PO. Spastic paretic stiff-legged gait: joint kinetics. American Journal of Physical Medicine and Rehabilitation, 2001;80:244-249.

(11) Sutherland DH, Davids JR. Common gait abnormalities of the knee in cerebral palsy. Clinical Orthopaedics and Related Research, 1993;288:139-147.

(12) Kerrigan DC, Roth RS, Riley PO. The modelling to assess stiff-legged gait swing period based on actual kinematic data. Gait and Posture, 1998;7:117-124.

(13) Perry J. Gait analysis: normal and pathological fiunction SLACK. Thorofare (NJ): Slack. 1992

(14) Piazza SJ, Delp SL. The influence of muscles on knee flexion during the swing phase of gait. Journal of Biomechanics, 1996;29:723-733.

(15) Riley PO, Kerrigan DC. Torque action of two-joint muscles in the swing period of stiff-legged gait: a forward dynamic model analysis. Journal of Biomechanics, 1998;31:835-840.

(16) Waters RL, Garland DE, Perry J, Habig T, Slabaugh P. Stiff-legged gait in hemiplegia: surgical correction. American Journal of Bone and Joint Surgery, 1979;61:927-933.

(17) Kerrigan DC, Roth RS, Riley PO. The modelling to assess stiff-legged gait swing period based on actual kinematic data. Gait and Posture, 1998;7:117-124.

(18) Kerrigan DC, Bang MS, Burke DT. An algorithm to assess stiff-legged gait in traumatic brain injury. Journal of Head Trauma Rehabilitation, 1999;14:136-145.

(19) Caty GD, Detrembleur C, Palumbo S, Deltombe T, Lejeune TM. Effect of simultaneous botulinum toxin injections into several muscles on impairment, activity, participation, and quality of life among stroke patients presenting with a stiff knee gait. Stroke, 2008;39(10):2803-2808.

(20) Robertson JV, Pradon D, Bensmail D, Fermanian C, Bussel B, Roche N. Relevance of botulinum toxin injection and nerve block of rectus femoris to kinematic and functional parameters of stiff knee gait in hemiplegic adults. Gait and posture, 2009;29(1):108-112.

(21) Stoquart GG, Detrembleur C, Palumbo S, Deltombe T, Lejeune TM. Effect of botulinum toxin injections in the rectus femoris on stiff-knee gait in people with stroke: a prospective observational study. Archives of Physical Medicine and Rehabilitation, 2008;1(89):56-61.

(22) Chambers H, Lauer A, Kaufman K, Cardelia M, Sutherland DH. Prediction of outcome after rectus femoris surgery in cerebral palsy: the role of cocontraction of the rectus femoris and vastus lateralis. Journal of Pediatric Orthopaedics, 1998;18:703-711.

(23) Perry J. Distal rectus femoris transfer. Developmental Medicine and Child Neurology, 1987;29:153-158.

(24) Sutherland DH, Larsen LJ, Mann R. Rectus femoris release in selected patients with cerebral palsy: a preliminary report. Developmental Medicine and Child Neurology, 1975;17:26-34.

(25) Waters RL, Garland DE, Perry J, Habig T, Slabaugh P. Stiff-legged gait in hemiplegia: surgical correction. American Journal of Bone and Joint Surgery, 1979:61(61A):927-933.

(26) Daly JJ, Roenigk K, Holcomb PJ, Rogers JM, Butler K, Gansen J, McCabe J, Fredrickson E, Marsolais EB, Ruff RL. A randomized controlled trial of functional neuromuscular stimulation in chronic stroke subjects. Stroke, 2006;37:172-178.

(27) Dolly JO. Therapeutic and research exploitation of botulinum neurotoxins. European Journal of Neurology, 1997;4(suppl 2):S5-S10.

(28) Jankovic J, Brin MF. The therapeutic uses of botulinum toxin. New England Journal of Medicine, 1991;324:1186-1194.

(29) Levine MG, Knott M, Kabat H. Relaxation of spasticity by electrical stimulation of antagonist muscles. Archives of Physical Medicine, 1952;33:668-673.

(30) Carnstam B, Larsson LE, Prevec TS. Improvement of gait following functional electrical stimulation, 1: investigations on changes in voluntary strength and proprioceptive reflexes. Scandinavian Journal of Rehabilitation and Medicine, 1977;9:7-13.

(31) Gerrits HL, Hopman MT, Sargeant AJ, et al. Effects of training on contractile properties of paralyzed quadriceps muscle. Muscle & Nerve, 2002;25:559-567.

(32) Glanz M, Klawansky S, Stason W, et al. Functional electrostimulation in post-stroke rehabilitation: a meta-analysis of the randomized controlled trials. Archives of Physical Medicine and Rehabilitation, 1996;77:549-553.

(33) Winchester P, Carollo JJ, Habasevich R. Physiologic costs of reciprocal gait in FES assisted walking. Paraplegia, 1994;32:680-686.

(34) Burridge JH, Wood D. Two channel stimulation for hemiplegic gait. Control algorithms, selection of muscle groups and the results of a preliminary clinical trial. *6th Internet World Congress for Biomedical Sciences*, February 2000.

(35) Mann GE, Burridge JH, Ewins DJ, McLellan DL, Swain ID, Taylor PN, Wood DE, Wright PA. Optimising two channel stimulation to improve walking following stroke. *5th Annual Conference of the International FES Society*, (ISBN 87-90562-01-1), pp. 452-455, Aalborg, Denmark, June 2000.

(36) Kallra L, et al. An integrated system for multidisciplinary assessment in stroke rehabilitation. Stroke, 1994;25:2210-2214.

(37) Wade DT. Measurement and clinical rehabilitation. 1990.

(38) Kwakkel G, et al. Effects of intensity of lower and upper extremity training after primary middle cerebral artery stroke: A randomised clinical trial. Lancet, 1999;354:191-196.

(39) Collen FM, et al. The Rivermead Mobility Index: a further development of the Rivermead Motor Assessment. International Disability Studies, 1991;13:50-54.

(40) Hsueh I, Wang C, Sheu C, Hsieh C. Comparison of psychometric properties of three mobility measures for patients with stroke. Archives of Physical Medicine and Rehabilitation, 2003;34:1741-1745.

(41) Kadaba MP, Ramakrishnan HK, Wootten ME. Measurement of lower extremities kinematics during level walking. Journal of Orthopaedic Research, 1990:8389-8392.

(42) Pomeroy VM, Dean D, Sykes L, Faragher EB, Yates M, Tyrrell PJ, Moss S, Tallis RC. The unreliability of clinical measures of muscle tone: implications for stroke therapy. Age and Ageing, 2000;29(3):229-233. 2000.

(43) Price DD, Bush FM, Long S, Harkins SW. A comparison of pain measurement characteristics of mechanical visual analogue and simple numerical rating scales. Pain, 1994;56:217-226.

(44) Marks MC, Alexander J, Sutherland DH, Chambers HG. Clinical utility of the Duncan-Ely test for rectus femoris dysfunction during the swing phase of gait. Developmental Medicine and Child Neurology, 2003;45:763-768.

(45) Myers AM, Holliday PJ, Harvey KA, Hutchinson KS. Functional performance measures: are they superior to self-assessments? Journal of Gerontology, 1993;48(5):M196-206.

(46) Olney SJ, Griffin MP, McBride ID. Temporal, kinematic, and kinetic variables related to gait speed in subjects with hemiplegia: a regresssion approach. Physical Therapy, 1994;74:872-885.

(47) Turnbull GI, Charteris J, Wall JC. A comparison of the range of walking speeds between normal and hemiplegic subjects. Scandinavian Journal of Rehabilitation and Medicine, 1995;27:175-182.

(48) Wade DT, Heller WA, Maggs J, Hewer RL. Walking after stroke. Scandinavian Journal of Rehabilitation and Medicine, 1987;19:25-30.

(49) Dettman MA, Linder MT, Sepic SB. Relationship among walking performance, postural stability, and functional assessments of the hemiplegic patients. Scandinavian Journal of Rehabilitation and Medicine, 1987;66:77-90.

(50) Nadeau S, Arsenault AB, Gravel D, Boubonnais D. Analysis of the clinical factors determining natural and maximal gait speeds in adults with stroke. American Journal of Physical Medicine and Rehabilitation, 1999;123-130.

(51) Bohannon RW, Andrews AW, Smith MB. Rehabilitation goals of patients with hemiplegia. International Journal of Rehabilitation and Research, 1988;11:181-182.

(52) Oberg T, Karsznia A, Oberg T. Basic gait parameters; Reference data for normal subjects, 10-79 years of age. Journal of Rehabilitation Research and Development], 1993;30(2):210-223.

(53) Lelas JL, Merriman GJ, Riley PO, Kerrigan DC. Predicting peak kinematic and kinetic parameters from gait speed. Gait and Posture, 2003;17:106-112.

(54) Oberg T, Karsznia A, Oberg K. Joint angle parameters in gait: reference data for normal subjects, 10-79 years of age. Journal of Rehabilitation Research and Development, 1994;31:199-213.

(55) Perry J. Gait analysis normal and pathological function SLACK. 525pp. 1992. Incorporated Thorofare, NJ.

(56) Piazza SJ, Delp SL. The influence of muscles on knee flexion during the swing phase of gait. Journal of Biomechanics, 1996;29:723-733.

(57) Riley PO, Kerrigan DC. Torque action of two-joint muscles in the swing period of stiff-legged gait: a forward dynamic model analysis. Journal of Biomechanics, 1998;31:835-840.

(58) Chae J, Bethoux F, Bohinc T, Dobos L, Davis T, Friedl A. Neuromuscular stimulation for upper extremity motor and functional recovery in acute hemiplegia. Stroke, 1998;29:975-979.

(59) Haghbarth KE. Spinal withdrawal reflexes in human lower limbs. Journal of Neurology Neurosurgery and Psychiatry, 1960;23:222-227.

(60) Emborg J, Spaich EG, Andersen OK. Withdrawal reflexes examined during human gait by ground reaction forces and gait phase dependency. Medical & Biological Engineering & Computing, 2009;47:29-39.

(61) Spaich EG, Emborg J, Collet T, Arendt-Nielsen L, Andersen OK. Withdrawal reflex responses evoked by repetitive painful stimulation delivered on the sole of the foot during late stance: site, phase, and frequency modulation. Experimental Brain Research, 2009;194;359-368.

(62) Quintern J, Krewer C, Bisle G, Husemann B, Heller S. Enhancement of gait retraining by Electrical Stimulation of flexor reflex afferents in acute stroke patients: a randomized, controlled clinical study. *9th annual conference of the international FES society*, Bournemouth, UK. 2004.

APPENDIXES

Appendix 1: Search strategy Systematic Review

Appendix 2: Methodological quality instrument Systematic Review (Downs & Black)

Appendix 3: Data extraction table Systematic Review

Appendix 1: Search strategy Systematic Review

	PubMed	EMBASE	CINAHL	Cochrane
Population	#1 stroke [MeSH] 147455	#1 stroke [EMTREE] 164213	#1 stroke [CINAHL Headings] 27411	#1 stroke [MeSH] 242
	#2 cerebrovascular disorders [MeSH] 218150	#2 cerebrovascular disease [EMTREE] 288988	#2 cerebrovascular disorders [CINAHL Headings] 1423	#2 brain infarction [MeSH] 19
	#3 hemiplegia [MeSH] 11609	#3 hemiplegia [EMTREE] 12663	#3 hemiplegia [CINAHL Headings] 2368	#3 cerebrovascular disorder [MeSH] 7
	#4 (stroke OR cerebrovascular disorder OR hemiplegia) AND knee 220193	#4 cerebrovascular accident [EMTREE] 35467	#4 stroke OR cerebrovascular disorders OR hemiplegia 29379	#4 hemiplegia [MeSH] 1
	#5 knee [MeSH] 83428	#5 stroke OR cerebrovascular disease OR hemiplegia OR cerebrovascular accident 351111	#5 knee [CINAHL Headings] 15956	#5 stroke OR brain infarction OR cerebrovascular disorder OR hemiplegia 255
		#6 knee [EMTREE] 103724		#6 knee [MeSH] 86
Intervention	#6 botulinum toxin type A [MeSH] 3993	#7 botulinum toxin [EMTREE] 15128	#6 botulinum toxins [CINAHL Headings] 1548	#7 botulinum toxins [MeSH] 24
	#7 botulinum toxins [MeSH] 8765	#8 botulinum toxin A [EMTREE] 7849	#7 lidocaine [CINAHL Headings] 1796	#8 botulinum toxin type A [MeSH] 14
	#8 lidocaine 23630	#9 clostridium difficile toxin A [EMTREE] 736	#8 nerve block [CINAHL Headings] 1704	#9 clostridium botulinum type A [MeSH] 1
	#9 nerve block 21139	#10 lidocaine [EMTREE] 52660	#9 botox 294	#10 lidocaine [MeSH] 25
	#10 botox 4320	#11 nerve block [EMTREE] 35680	#10 dysport 31	#11 nerve block [MeSH] 31
	#11 dysport 4142	#12 motor nerve block [EMTREE] 6304	#11 botulinum toxins OR lidocaine OR nerve block OR botox OR dysport 4851	#12 botox 8
	#12 botulinum toxin type A OR botulinum toxins OR lidocaine OR nerve block OR botox OR dysport 51931	#13 botox 7977		#13 dysport 4
		#14 dysport 7878		#14 botulinum toxins OR botulinum toxin type A OR clostridium botulinum type A OR lidocaine OR nerve block OR botox OR dysport 76
		#15 botulinum toxin OR botulinum toxin A OR clostridium		

		difficile toxin A OR lidocaine OR nerve block OR motor nerve block OR botox OR dysport 35680		
Outcome	#13 gait [MeSH] 12535 #14 walking [MeSH] 11196 #15 Range Of Motion [MeSH] 21714 #16 gait OR walking OR Range Of Motion 42042	#16 gait [EMTREE] 29336 #17 walking [EMTREE] 52182 #18 joint function [EMTREE] 10460 #19 range of motion [EMTREE] 16195 #20 gait OR walking OR joint function OR range of motion 86809	#12 gait analysis [CINAHL Headings] 2529 #13 gait [CINAHL Headings] 5668 #14 walking [CINAHL Headings] 10280 #15 Range Of Motion [CINAHL Headings] 8482 #16 gait analysis OR gait OR walking OR Range Of Motion 21376	#15 gait [MeSH] 19 #16 walking [MeSH] 120 #17 Range Of Motion, Articular [MeSH] 47 #18 gait OR walking OR Range Of Motion, Articular 166
Articles	#17 = #4 AND #5 AND #12 AND #16 **21**	#21 = #5 AND #6 AND #15 AND #20 **30**	#17 = # 4 AND #5 AND #11 AND #16 **7**	#19 = #5 AND #6 AND #14 AND #18 **33**

62 articles are selected after screening reference lists and correction on double articles

Appendix 2: Methodological quality instrument (Downs & Black)

Appendix

Checklist for measuring study quality

Reporting

1. *Is the hypothesis/aim/objective of the study clearly described?*

yes	1
no	0

2. *Are the main outcomes to be measured clearly described in the Introduction or Methods section?*
   If the main outcomes are first mentioned in the Results section, the question should be answered no.

yes	1
no	0

3. *Are the characteristics of the patients included in the study clearly described ?*
   In cohort studies and trials, inclusion and/or exclusion criteria should be given. In case-control studies, a case-definition and the source for controls should be given.

yes	1
no	0

4. *Are the interventions of interest clearly described?*
   Treatments and placebo (where relevant) that are to be compared should be clearly described.

yes	1
no	0

5. *Are the distributions of principal confounders in each group of subjects to be compared clearly described?*
   A list of principal confounders is provided.

yes	2
partially	1
no	0

6. *Are the main findings of the study clearly described?*
   Simple outcome data (including denominators and numerators) should be reported for all major findings so that the reader can check the major analyses and conclusions. (This question does not cover statistical tests which are considered below).

yes	1
no	0

7. *Does the study provide estimates of the random variability in the data for the main outcomes?*
   In non normally distributed data the inter-quartile range of results should be reported. In normally distributed data the standard error, standard deviation or confidence intervals should be reported. If the distribution of the data is not described, it must be assumed that the estimates used were appropriate and the question should be answered yes.

yes	1
no	0

8. *Have all important adverse events that may be a consequence of the intervention been reported?*
   This should be answered yes if the study demonstrates that there was a comprehensive attempt to measure adverse events. (A list of possible adverse events is provided).

yes	1
no	0

9. *Have the characteristics of patients lost to follow-up been described?*
   This should be answered yes where there were no losses to follow-up or where losses to follow-up were so small that findings would be unaffected by their inclusion. This should be answered no where a study does not report the number of patients lost to follow-up.

yes	1
no	0

10. *Have actual probability values been reported(e.g. 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?*

yes	1
no	0

External validity

All the following criteria attempt to address the representativeness of the findings of the study and whether they may be generalised to the population from which the study subjects were derived.

11. *Were the subjects asked to participate in the study representative of the entire population from which they were recruited?*
    The study must identify the source population for patients and describe how the patients were selected. Patients would be representative if they comprised the entire source population, an unselected sample of consecutive patients, or a random sample. Random sampling is only feasible where a list of all members of the relevant

population exists. Where a study does not report the proportion of the source population from which the patients are derived, the question should be answered as unable to determine.

yes	1
no	0
unable to determine	0

12. *Were those subjects who were prepared to participate representative of the entire population from which they were recruited?*
The proportion of those asked who agreed should be stated. Validation that the sample was representative would include demonstrating that the distribution of the main confounding factors was the same in the study sample and the source population.

yes	1
no	0
unable to determine	0

13. *Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?*
For the question to be answered yes the study should demonstrate that the intervention was representative of that in use in the source population. The question should be answered no if, for example, the intervention was undertaken in a specialist centre unrepresentative of the hospitals most of the source population would attend.

yes	1
no	0
unable to determine	0

Internal validity - bias

14. *Was an attempt made to blind study subjects to the intervention they have received ?*
For studies where the patients would have no way of knowing which intervention they received, this should be answered yes.

yes	1
no	0
unable to determine	0

15. *Was an attempt made to blind those measuring the main outcomes of the intervention?*

yes	1
no	0
unable to determine	0

16. *If any of the results of the study were based on "data dredging", was this made clear?*
Any analyses that had not been planned at the outset of the study should be clearly indicated. If no retrospective unplanned subgroup analyses were reported, then answer yes.

yes	1
no	0
unable to determine	0

17. *In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls ?*
Where follow-up was the same for all study patients the answer should yes. If different lengths of follow-up were adjusted for by, for example, survival analysis the answer should be yes. Studies where differences in follow-up are ignored should be answered no.

yes	1
no	0
unable to determine	0

18. *Were the statistical tests used to assess the main outcomes appropriate?*
The statistical techniques used must be appropriate to the data. For example non-parametric methods should be used for small sample sizes. Where little statistical analysis has been undertaken but where there is no evidence of bias, the question should be answered yes. If the distribution of the data (normal or not) is not described it must be assumed that the estimates used were appropriate and the question should be answered yes.

yes	1
no	0
unable to determine	0

19. *Was compliance with the intervention/s reliable?*
Where there was non compliance with the allocated treatment or where there was contamination of one group, the question should be answered no. For studies where the effect of any misclassification was likely to bias any association to the null, the question should be answered yes.

yes	1
no	0
unable to determine	0

20. *Were the main outcome measures used accurate (valid and reliable)?*

For studies where the outcome measures are clearly described, the question should be answered yes. For studies which refer to other work or that demonstrates the outcome measures are accurate, the question should be answered as yes.

yes	1
no	0
unable to determine	0

Internal validity - confounding (selection bias)

21. *Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?*
For example, patients for all comparison groups should be selected from the same hospital. The question should be answered unable to determine for cohort and case-control studies where there is no information concerning the source of patients included in the study.

yes	1
no	0
unable to determine	0

22. *Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?*
For a study which does not specify the time period over which patients were recruited, the question should be answered as unable to determine.

yes	1
no	0
unable to determine	0

23. *Were study subjects randomised to intervention groups?*
Studies which state that subjects wererandomised should be answered yes except where method of randomisation would not ensure random allocation. For example alternate allocation would score no because it is predictable.

yes	1
no	0
unable to determine	0

24. *Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?*
All non-randomised studies should be answered no. If assignment was concealed from patients but not from staff, it should be answered no.

yes	1
no	0
unable to determine	0

25. *Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?*
This question should be answered no for trials if: the main conclusions of the study were based on analyses of treatment rather than intention to treat; the distribution of known confounders in the different treatment groups was not described; or the distribution of known confounders differed between the treatment groups but was not taken into account in the analyses. In non-randomised studies if the effect of the main confounders was not investigated or confounding was demonstrated but no adjustment was made in the final analyses the question should be answered as no.

yes	1
no	0
unable to determine	0

26. *Were losses of patients to follow-up taken into account?*
If the numbers of patients lost to follow-up are not reported, the question should be answered as unable to determine. If the proportion lost to follow-up was too small to affect the main findings, the question should be answered yes.

yes	1
no	0
unable to determine	0

Power

27. *Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%?*
Sample sizes have been calculated to detect a difference of x% and y%.

	Size of *smallest* intervention group	
A	$<n_1$	0
B	n_1–n_2	1
C	n_3–n_4	2
D	n_5–n_6	3
E	n_7–n_8	4
F	n_9+	5

Appendix 3: Data extraction table

First author	No. of participants	Inclusion / exclusion criteria	Participants	Intervention	Follow-up	Outcome measures	Authorôs conclusion
Caty, 2008 Intervention study	20	Inclusion criteria: - spastic hemiparesis secondary to stroke - >6 months since stroke - lack of knee flexion during swing phase - ability to walk independently without an assistive device Exclusion criteria: - inability to walk on a treadmill for sufficient time to complete a metabolic analysis -any cognitive deficit that would prevent the completion of the questionnaires	N=20 - 15 males - 5 females Age: (mean (sd)) 52,3 (16,1) Time since stroke: (mean(sd)) 45,9(32,9)	Botulinum toxin type A (BTX-A) injections: - 200u rectus femoris - 100u semitendinosus - 200u triceps surae Botox, allergan	2 months after BTX-A injections	Impairments: - Ashworth scale - Duncan-Ely test - Stroke Impairment Assessment Set - 3D gait analysis - knee flexion Activities: - Functional Ambulation Categories - Functional Walking Category - ABILOCO - 10 m walktest Participation: - 36-item Short-Form Health Survey - SATISPART-Stroke	Results BTX-A injections: - reduction rectus femoris muscle tone - reduction semitendinosus muscle tone - increasing knee flexion during swing phase - decreasing external mechanical work - lower energy cost BTX-A injections in several muscles improved the stiff knee gait and the locomotion ability in adult stroke patients

First author	No. of participants	Inclusion / exclusion criteria	Participants	Intervention	Follow-up	Outcome measures	Authorôs conclusion
Stoquart, 2008 Intervention study	19	Inclusion criteria: - >6 months since stroke - lack of knee flexion during swing - ability to walk independently (without any assistive device) on a treadmill for sufficient time to complete a metabolic analysis Exclusion criteria: - presence of significant impairments in other joints that restrained walking - presence of other significant neurologic conditions - knee contracture	N=19 Age (mean(sd)) 53(15) Time since stroke (mean(sd)) 52(56)	Botulinum toxin type A injections (BTX-A) - 200u rectus femoris (6 injections of 33u) Botox, allergan	2 months after BTX-A injections	- Stroke Impairment Assessment Score (SIAS) - Duncan-Ely test - 3D gait analysis - knee flexion	Results BTX-A injections: - Improving median SIAS score - Improving Duncan-Ely score - Improving maximum knee flexion during swing phase - Improving knee flexion speed at toe-off - Improving knee negative joint power (eccentric muscular contraction) 4 patients who almost did not flex the knee (<10º) before the BTX-A rectus femoris injection did not improve after injection BTX-A rectus femoris injection may be beneficial in patients with a stiff knee gait after stroke, particularly in patients with some knee flexion (>10º)

First author	No. of participants	Inclusion / exclusion criteria	Participants	Intervention	Follow-up	Outcome measures	Authorôs conclusion
Robertson, 2009	10	Inclusion criteria: - >18 years - >6 months post stroke or traumatic brain injury - decrease in peak knee flexion of more than 2 standard deviations (normal =58,3 ± 3,8 degrees) - ability to walk 10m without walking aids - RF EMG activity in mid swing (considered as inappropriate) - successful nerve block	N=10 - 8 males - 2 females Age: Range 27-58 Time since onset: Range 0.5-36 years	Botulinum toxin type A injections (BTX-A): - 200u in 4 anatomical points into the rectus femoris muscle belly under electrical stimulation (5mA) Botox, Allergan Nerve block was performed according to the technique described by Sung et al using lidocaïne 2%.	1 month post BTX-A Half an hour after nerve block	- 3D gait analysis - Timed Up and Go test - 10m walk test - 6 min walk test - time taken to ascend and descend a flight of stairs - knee flexion	BTX-A is an effective treatment for stiff knee gait in adult hemiplegic subjects, with a significant increase in peak knee flexion, no reduction in hip flexion and a tendency towards functional improvements The effect of the nerve block on peak knee flexion was significantly correlated with the effect of BTX-A (11 degrees average increase in peak knee flexion after nerve block)

First author	No. of participants	Inclusion / exclusion criteria	Participants	Intervention	Follow-up	Outcome measures	Authorôs conclusion
Chantraine, 2005	6	Inclusion criteria: - able to walk independently irrespective of the walking surface - familiar with walking on a treadmill - able to give informed consent Exclusion criteria: - other major ongoing medical disorders	N=6 -3 males - 3 females Age: range 27-78 Onset of stroke (months): range 11-240	Motor branch block of the rectus femoris (MBB): - method of Sung and Bang - A Teflon-coated nerve block needle was inserted around 1 cm lateral and 3 to 4 cm distal to the point of an arterial pulsation and alongside the medial border of the RF - mixture of 1 ml of 2% Lidocaïne and of 1 ml of 1% Bupivacaïne solution		- Duncan-Ely test - knee flexion - range of knee motion - knee extension moment	- improved Duncan-Ely test (p<0,05) - mean maximum knee flexion did not change significantly (p=0,502) - increased mean range of knee flexion (p<0,05) - unchanged mean extension knee moment (p=0,764)

First author	No. of participants	Inclusion / exclusion criteria	Participants	Intervention	Follow-up	Outcome measures	Authorôs conclusion
Albert, 2002 Case design	12	Inclusion criteria: - Patients with spastic paresis, disabled by overactivity of the quadriceps impairing knee flexion - able to walk 10m or more, with or without a cane - Overactivity of the quadriceps was considered disabling when it resulted in an inability to flex the knee during the swing phase despite a good motor test of knee flexion while sitting or standing Exclusion criteria: - anticoagulant therapy - previous anesthetic allergy - skin lesion of the thigh	N=12 - 9 male - 3 female Age: Mean 49,8 Range 35-72 8 patients with diagnosis stroke, other diagnoses are head injury, spinal injury and multiple sclerosis	Femoral nerve selective block Two cubic centimetres of a 1% diluted solution of etidocaine	Immediately after nerve block	- assessment of spasticity - voluntary knee extension velocity - speed of gait - knee flexion when walking	Phenol or alcohol block of the vastus lateralis nerve or of both the vastus lateralis and the vastus intermedius nerves can be easily achieved by using cutaneous coordinates, with a decrease in quadriceps spasticity and without any dramatic effect on voluntary knee extension velocity

First author	No. of participants	Inclusion / exclusion criteria	Participants	Intervention	Follow-up	Outcome measures	Authorôs conclusion
Sung, 2000 Intervention study	31	Inclusion criteria: - walk with a stiffly extended knee at swing phase in the observational gait analysis - show clinical signs of stiff-legged gait, such as toe dragging or excessive wear of anterior tip of a shoe - community ambulators with or without a walking aid - more than 6 months after the onset of spasticity or primary neurologic injury Exclusion criteria: - impaired balance - not able to walk independently in outdoor ambulation - significant cognitive deficits	N=31 Age: Range 27-71 Mean (sd) 50(12,7) - Traumatic brain injury (n=2) - ischemic or hemorrhagic stroke (n=21) - multiple sclerosis (n=3) - hereditary spastic paraplegia (n=1) - idiopathic thoracic myelopathy (n=4)	Motor branch block of the rectus femoris A couple of wheals were made with 1% lidocaine for the superficial anesthesia around 1 cm and 3 to 4cm distal to the point of an arterial pulsation and alongside the medial border of the rectus femoris 0,3 to 0,5mL of 2% lidocaine solution was injected slowly Repeating until visible contraction of the rectus femoris by the electrical stimulation disappeared	Immediately after the nerve block, before the lidocaine effect disappeared	- 3D gait analysis with the Vicon 370 system - Dynamic EMG - subjective assessment - knee flexion	Results: - 74% of patients felt an improvement - increased maximal knee flexion at swing phase (p<0,05) - increased slope of knee flexion curve at toe off (p<0,05) Motor branch block of the rectus femoris can be an effective treatment in stiff-legged gait. Its effect is varied with hip flexor strength and dynamic electomyographic findings of quadriceps.

BTX-A = botulinum toxin type A
MBB = motor branch block
RF = rectus femoris