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ORIGINAL STUDY

Prevention of Complex Regional Pain Syndrome type 1 after conservative reatment of a distal radius fracture with a home exercise program: A proof-of-concept study

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Prevention of CRPS-1, a post-traumatic pain syndrome, after a distal radius fracture is important as this syndrome might lead to chronic pain and serious disabilities. In several studies, it was shown that CRPS-1 can be cured with exercise and graded activities.

In a prospective cohort study, a home exercise program with progressive loading exercises was applied immediately after cast removal in patients with a distal radius fracture. After three months, patients were interviewed by telephone using the subjective Budapest diagnostic criteria for CRPS-1.

In our study, 56 patients were included and 9 patients (16%) scored positive on the subjective diagnostic criteria. None of the 9 patients was diagnosed with CRPS-1.

This study indicates that a home exercise program after conservative treatment of distal radius fracture is a safe and effective option to prevent CRPS-1. A larger study is needed to prove the preventive power of this home exercise program.

Ethics approval : approved by the local ethics committee of the Radboudumc.

Level of evidence : 3.

Keywords : complex regional pain syndrome ; reflex symptomatic dystrophy ; distal radius fracture ; home exercise program ; prevention.

INTRODUCTION

Complex regional pain syndrome type 1 (CRPS-1), formally known as reflex sympathetic dystrophy (RSD), may occur after trauma and is characterized by excessive pain (allodynia and/or hyperalgesia), oedema, changes in skin blood flow or abnormal sudomotor activity *(2)*. The incidence of CRPS-1 after a distal radius fracture varies from 1% to 37% *(2,6,10,22)*, and approximately 75% of CRPS-1 patients experience serious disabilities related to general activities (74.2%), mood (74.2%), work (74.2%) and recreational activities (77.4%) *(5)*.

The diagnosis of CRPS-1 is difficult as there is no diagnostic 'gold standard' and the pathophysiology

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is unclear due to the low specificity of diagnosis. There are hardly any studies with a sufficient evidence level to make recommendations for treatments for CRPS-1; therefore, treatment is based on symptom management. There is a strong need for a method to prevent CRPS-1, as it can occur after trauma, can potentially cause chronic disability, and has limited available treatment options.

Vitamin C is currently used as an effective prevention for CRPS-1 after a wrist fracture *(1,12,17,23)*. However, recently a publication by Evaniew et al. indicated that it is doubtful whether vitamin C has a significant effect on the prevention of CRPS-1 *(4)*.

Recent studies have indicated that disuse and kinesiofobia might play a role in the development of CRPS-1 and chronic muscluloskeletal pain syndromes *(3,14,20)*. For example, pain exposure in physical therapy (PEPT treatment), which is a countermeasure of disuse and kinesiofobia, has been proven to be effective in the treatment of acute and chronic CRPS-1 *(14)*. This result begged the question whether management of disuse and kinesiofobia could be used to prevent CRPS-1. Rehabilitation using a home exercise program is a validated method after distal radius fracture *(11,13,18)*. The aim of this pilot study is to explore whether a home exercise program aiming to reduce disuse and kinesofobia after trauma can prevent CRPS-1. Our hypothesis is that a home exercise program, with a fixed schedule of progressive loading exercises, can prevent CRPS-1.

PATIENTS AND METHODS

The trial was designed as a proof of concept cohort study and was performed between December 2012 and November 2014 in the Radboudumc, Nijmegen, the Netherlands. 81 Patients were available to participate in the study. The local ethical committee of the Radboudumc approved the study, NL2014-1361.

After removal of the plaster cast, all patients with a distal radius fracture were consecutively screened by one investigator for the inclusion and exclusion criteria (Table I). The inclusion criteria were as follows: conservative treatment of a distal radius fracture and an age of 18 years and older. Patients predisposed to unreliably answering questions regarding the subjective diagnostic Budapest criteria due to dementia were excluded. The Orthopaedic Trauma Association (OTA) system was used for the classification of the distal radius fracture.

Table I. — Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Above eighteen years old	Dementia
Distal radius fracture type*	
Conservative treatment	
Instruction leaflet provided	

* OTA classification
Abbreviations: OTA; Orthopaedic Trauma Association

After removal of the plaster cast, patients were taught how to exercise their fingers, forearm, and wrist and were allowed to resume normal activities gradually increasing the amount of weight and force based on fracture healing explained by a leaflet (Figure 1). The instructions notified the patients of the importance of using and strengthening the arm and/or wrist for proper healing of the fracture as well as optimize arm hand function. The patients were strictly instructed to perform all exercises at home on a daily basis for a 6-week period without involvement of a physiotherapist. Three months after the distal radius fracture, the patients were interviewed by the attending (independent) physician over the telephone. Compliance with the exercise program was evaluated by telephone interview using the question: “Have you been performing all the exercises from the instruction leaflet.” Moreover, the interview included a scoring of the subjective items of the Budapest diagnostic criteria for CRPS-1 (Figure 2) (8). Patients scored positive when they answered ‘yes’ on the first question and when they answered ‘yes’ on one or more of the other questions. Patients scoring positive on the subjective items of the Budapest criteria for CRPS-1 were invited to visit the specialized CRPS-outpatient clinic of our centre. During the consultation at the outpatient clinic,

8	**Lift a filled glass**	
9	**Knead a stress ball/sponge**	
Week 5 and 6	Do all the exercises (1-9)	• Use your hand by performing daily exercises (washing, eating, getting dressed etc.)
10	**Lift a water bottle filled with ½ liter of water**	
11	**Squeeze a tennis ball**	
12	**Lift a grocery bag filled with one and a half liter bottles (building up from 1 bottle to 3 bottles). Lift the bag for one minute. Repeat this exercise 3 times.**	

Fig. 1. — Example of a page from the instruction leaflet (English version). In this leaflet the home exercise program is explained. Patients need to perform the exercises every day and the exercises are intensified over the three months

Telephone interview leaflet (fill in 4 months after the wrist fracture)

Is the leaflet "Exercises at home after a wristfracture" clear?	yes/no
Have all the exercises from the instruction leaflet been performed?	yes/no
Did you receive physiotherapy because of the wrist fracture?	yes/no

Budapest criteria for CRPS

1. Do you have continously disproportionate pain in the wrist/hand? (fracture side)	yes/no
2. Is the hand/wrist oversensitive for touching?	yes/no
3. Is your wrist swollen and/or is there a difference in transpiration between L and R?	yes/no
4. Is there a difference in skincolor and/or temperature between L and R?	yes/no
5. Is there a difference in body hair and/or nailgrowth between L and R?	yes/no
6. Is there a difference in range of motion of the wrist between L and R?	yes/no

Budapest positive: If the Budapect criteria question 1 and one or more from questions 2 till 6 is answered with yes → refer to CRPS-outpatient clinic

Fig. 2. — The subjective items of the Budapest criteria are shown. These items were used to score the patients during the telephone interview. The items are translated to English

an x-ray of the wrist was performed and the objective Budapest criteria were assessed (Table II). Variables that could potentially be associated with the occurrence of pain and CRPS-1 were obtained from the patient's medical file (Table III).

Statistical analysis was performed with SPSS version 20.0 (IBM Amsterdam, The Netherlands) and SAS (Huizen, The Netherlands). The primary outcome was defined as having CRPS-1 diagnosed on the CRPS-outpatient clinic. The secondary outcome was scoring positive on the subjective Budapest diagnostic criteria. The incidence of CRPS-1 was calculated by the amount of patients with CRPS-1 divided by the total number of patients. The 95% confidence interval was calculated from the CRPS-1 incidence. The results and confidence intervals were compared with incidence numbers and confidence intervals of CRPS-1 after a distal radius fracture treated with plaster cast immobilization in the literature.

RESULTS

Between December 2012 and November 2014, we enrolled 56 patients with 57 fractures in this proof-of-concept study (one patient had a bilateral fracture).Twenty-five patients were excluded based on the exclusion criteria or because they could not be reached by telephone (n=4). Sixteen patients were called at the end of the study, and 40 patients were called on time, i.e., after three months. The baseline characteristics of the included patients are shown in Table IV. The average age was 58

Table II. — Budapest diagnostic criteria for complex regional pain syndrome (Harden et al., 2013)

Continuing pain, which is disproportionate to any inciting event		yes/no
Must report at least one symptom in three of the four following categories (subjective)		yes/no
	Sensory: Reports of hyperalgesia and/or allodynia	+ -
	Vasomotor: Reports of temperature asymmetry and/or skin color changes and/or skin color asymmetry	+ -
	Sudomotor/Edema: Reports of edema and/or sweating changes and/or sweating asymmetry	+ -
	Motor/Trophic: Reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)	+ -
Must display at least one sign* at time of evaluation in two or more of the following categories (objective)		yes/no
	Sensory: Evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or deep somatic pressure and/or joint movement)	+ -
	Vasomotor: Evidence of temperature asymmetry and/or skin color changes and/or asymmetry	+ -
	Sudomotor/Edema: Evidence of edema and/or sweating changes and/or sweating asymmetry	+ -
	Motor/Trophic: Evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)	+ -
There is no other diagnosis that better explains the signs and symptoms		yes/no
Diagnosis CRPS-1		yes/no

* A sign is counted only if it is observed at time of diagnosis.
Abbreviation: CRPS-1; complex regional pain syndrome type 1

(SD 18.15) years, and 76.8% of the patients were female. Of the 57 fractures, 33 (57.9%) were on the left side. Seventeen patients had a type 23A fracture (29.8%), 16 had a type 23B fracture (28.1%), and 24 had a type 23C fracture (42.1%). During the plaster cast immobilization period, 12(21.1%) patients complained of pain. The compliance with the exercise program was 100%.

Nine patients (16%) scored positive on the subjective Budapest diagnostic criteria. None of the 9 patients were diagnosed with CRPS-1 when the objective symptoms of the Budapest criteria were assessed, resulting in an incidence of 0% (95% CI of 0.00%-6.38%) (Table V).

DISCUSSION

In this proof-of-concept study, it was found that a home exercise program was safe and potentially effective in preventing CRPS-1 after distal radius fracture. Our incidence of 0% (0.00%-0.06%) is different from other studies. A comparable

Table III. — Variables used for analysis

Variables
Age
Classification of the fracture (OTA classification)
Gender
Side of fracture
Complaints during cast period
Positive score on the subjective criteria of the Budapest criteria
CRPS-1

Abbreviation: CRPS-1; complex regional pain syndrome type 1 : OTA; Orthopaedic Trauma Association.

Table IV. — Patient characteristics

Characteristics	Patients n =56
Gender, n(%)	
Female	43 (76.8)
Male	13 (23.2)
Age, mean (SD)	58.13 (18.15)
	Fractures n =57
Side fracture, n(%)	
Left	33 (57.9)
Right	24 (42.1)
Fracture type, n(%)*	
23 A	17 (29.8)
23 B	16 (28.1)
23 C	24 (42.1)
Complaints cast, n(%)**	
Yes	12 (21.1)
No	45 (78.9)

* Fracture classification by OTA classification
** Complaints during treatment with plaster cast
Abbreviation: SD; standard deviation: OTA; Orthopaedic Trauma Association.

Table V. — Incidence CRPS-1

	fractures n =57
CRPS-symptoms, n(%)*	
Yes	9 (15.8)
No	48 (84.2)
CRPS-1, n(%)	
Yes	0 (0)
No	57 (100)

* CRPS symptoms means when a patients scored positive on the subjective items of the Budapest criteria with an interview by telephone.
Abbreviation: CRPS-1; complex regional pain syndrome type 1

prevention study with vitamin C showed a CRPS-1 incidence of 7% (0.07%-14%) after distal radius fracture *(22)*.

The difference in incidence between CRPS-1 prevention studies most likely depends on how CRPS-1 is determined. For example, CRSP-1 designation can depend on which diagnostic criteria, trauma type and prevention method are used. In the literature, incidence numbers in prevention studies vary between 1 and 37% *(2,6,10,22)*. The vitamin C prevention study is a randomized trial comparing vitamin C with placebo and reducing the incidence of CRPS-1 from 22% (18%-32%) to 7% (0.07%-14%) *(22)*. These incidence numbers might be biased because in this vitamin C study, only the subjective Veldman criteria were used for the diagnosis of CRPS-1. It might be that incidence numbers in the vitamin C study could have been lower when objective criteria for CRPS-1 were used in the diagnostic process. Furthermore, a recent meta-analysis failed to demonstrate a statistically significant effect for vitamin C to prevent CRPS. Thus, the use of vitamin c for the prevention of CRPS-1 is doubtful *(4)*.

The absence of CRPS-1 after a distal radius fracture treated with plaster and a home exercise program is a promising finding and helps elucidate the pathogenesis of nonspecific post traumatic pain disorders such as CRPS-1. Guo et al. showed in an animal study that cast immobilization, with or without a fracture, induces CRPS-1-like changes including increased hindlimb nociceptive sensitization, increased skin temperature, edema and inflammatory mediator expression. Early mobilization after fracture inhibited these changes *(7)*. That animal study demonstrates that immobilization of a limb may cause pain and an inflammatory response,

which are comparable with the typical CRPS-1 signs and symptoms. Experiments in healthy volunteers showed similar results: plaster immobilization of an extremity for four weeks caused transient changes in skin temperature, mechanosensitivity and thermosensitivity *(19)*.

If disuse caused by immobilization plays a role in the development of CRPS-1 signs and symptoms, then treatment of disuse should restore these disuse related signs and symptoms. In chronic musculoskeletal pain, disuse and pain avoidance behaviour are prominent behavioural characteristics *(20)*. In 2009, pain exposure physical therapy (PEPT) was developed as a countermeasure for disuse and pain-avoidance behaviour. PEPT is based on the assumption that behavioural and psychological factors can exacerbate pain and dysfunction and might help to maintain the condition (CRPS-1) in some patients *(3,14)*.

If disuse caused by immobilization and pain avoidance behaviour is an important contributor in the development of CRPS-1, then the incidence of CRPS-1 should be higher in patients treated conservatively compared to patients treated operatively. Compared with operative treatment, conservative treatment often leads to a longer immobilization period of an extremity. In the randomized controlled trial of Zollingers' study, it was found that the incidence of CRPS-1 after distal radius fracture was higher after conservative treatment (4.5%) compared to that after operative treatment (2.1%) *(21)*.

Several limitations of this pilot study need to be acknowledged:

1. This is a small study (n=56) of patients with a distal radius fracture. Larger studies are necessary to obtain more accurate incidence numbers. However as a proof of concept, these numbers are sufficient to test safety and feasibility.

2. A telephone interview may result in an under- or overestimation. However, a telephone interview as a (screening) tool for CRPS-1 in patients with a wrist fracture is an accepted method, and little discrepancy was found between the telephone interview and in-person assessments *(15,22)*. In our study, we did not only rely on the subjective criteria; the diagnosis of CRPS-1 was confirmed by an objective assessment, which reduces the possibility of under- or overestimation.

3. The patients who were treated in our hospital did not receive a prescription of vitamin C. It may be possible that patients used vitamin C on their own. Vitamin C is usually taken in a lower dose than the dose prescribed for CRPS-1 prevention; therefore, this issue will likely not influence our incidence data.

4. The specificity of the CRPS-1 diagnosis remains a weak aspect. There is no gold standard for diagnosing CRPS-1, which limits the results. We used the CRPS-1 diagnostic criteria based on the most recent CRPS diagnosis consensus meeting in Budapest *(8)*. These criteria have the highest sensitivity (0.99) and specificity (0.68) and are generally accepted as first choice for diagnosing CRPS-1 in research projects *(9,16)*. In addition, the Budapest criteria have been used in the CRPS-outpatient clinic in the Radboudumc for several years and are well known by the clinic's physicians. Based on these advantages, we chose to use the Budapest criteria.

CONCLUSION

A home exercise program focusing on the prevention of disuse after a plaster immobilization of a distal radius fracture is safe and a feasible concept in preventing CRPS-1. Future studies are needed to prove the preventive power of this home exercise program compared to standard preventive measures.

Author contributions: E.Z. Boersma contributed to the conception and design of the study, the collection of data, analysis and interpretation of data, drafting the article and final approval of the version to be published.
H. van de Meent contributed to the conception and design of the study, the analysis and interpretation of the data, revised the article critically and approved the final version to be published.
J.P.M. Frölke contributed to the conception and design of the study, the analysis and interpretation of the data, revised the article critically and approved the final version to be published.

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