ORIGINAL ARTICLE

Development of a Symptoms Questionnaire for Complex Regional Pain Syndrome and Potentially Related Illnesses: The Trauma Related Neuronal Dysfunction Symptoms Inventory

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ABSTRACT. Collins S, van Hilten JJ, Marinus J, Zuurmond WW, de Lange JJ, Perez RS. Development of a symptoms questionnaire for complex regional pain syndrome and potentially related illnesses: the Trauma Related Neuronal Dysfunction Symptoms Inventory. Arch Phys Med Rehabil 2008; 89:1114-20.

Objective: To develop a questionnaire to evaluate symptoms of complex regional pain syndrome type I (CRPS-I), fibromyalgia, and repetitive strain injury to determine the test-retest reliability and investigate concurrence in the clinical manifestations of CRPS-I and fibromyalgia.

Design: The Trauma Related Neuronal Dysfunction Symptoms Inventory (TSI) was developed by determining the content validity and the practical use of the questionnaire. Furthermore, the test-retest reliability was assessed on 2 identical questionnaires filled out within a 7-day interval by CRPS-I and fibromyalgia patients.

Setting: Outpatient pain clinic of a Dutch medical center.

Participants: CRPS-I (n=26; mean age, 54y) and fibromyalgia patients (n=42; mean age, 45.4y).

Interventions: Not applicable.

Main Outcome Measure: Test-retest reliability calculated with intraclass correlation (ICC).

Results: Reliability scores were good for the whole questionnaire, its categories, and domains (ICC>.75) for both CRPS-I and fibromyalgia patients. Sensory complaints (except for change in cold perception), motor complaints, and visceral complaints (diarrhea and incontinence) were reported by both CRPS-I and fibromyalgia patients. A change in cold perception, discoloration, change in skin temperature, change in sweating behavior, change in the severity of edema during exercise, and trophic changes of skin were reported significantly more often by CRPS-I patients, whereas complaints of the (upper and lower) back, constipation, urine retention, and experiencing a dry mouth were reported significantly more often by fibromyalgia patients.

Conclusions: The TSI is a reliable instrument with good content validity, which can be used in the evaluation of similarities and differences between CRPS-I and fibromyalgia. The systematic evaluation of symptoms of CRPS-I and potentially related illnesses may provide a better basis for future research into the underlying mechanism(s).

Key Words: Complex regional pain syndromes; Fibromyalgia; Questionnaires; Rehabilitation; Reliability and validity.

COMPLEX REGIONAL PAIN syndrome type I (CRPS-I), fibromyalgia, and repetitive strain injury (RSI) are chronic pain disorders with unknown pathophysiologic mechanisms. For these illnesses, no criterion standard and no objective measurement instrument for diagnosis are available; therefore, diagnosis is based on the history and observation of clinical manifestations. Similarities between these disorders have been described in different studies. Martinez-Lavin[1] suggested that fibromyalgia may reflect a generalized CRPS. He proposed that both CRPS and fibromyalgia are sympathetically maintained pain syndromes in which ongoing sympathetic hyperactivity sensitizes the primary nociceptors and induces pain and allodynia. This author claimed that the sympathetic state may also be responsible for other clinical features (eg, chronic pain, allodynia, paresthesias, vasomotor instability, response to sympathetic blockade, emotional response to chronic pain) seen in both CRPS and fibromyalgia, although more widespread in fibromyalgia. Tenderness at palpation as seen in fibromyalgia patients may reflect a state of generalized allodynia according to Martinez-Lavin.[1]

Macfarlane et al[2] considered forearm pain associated with RSI as a regional manifestation of a widespread pain and fibromyalgia-type syndrome. In a population-based prospective study, in which the epidemiology of diffuse forearm pain was examined, Macfarlane found that forearm pain commonly co-occurred with other regional musculoskeletal pain syndromes (shoulder, low back pain) or with chronic widespread pain. Macfarlane hypothesized that forearm pain may be 1 feature of a wider process of somatization, like fibromyalgia. Based on systematic literature analysis, Marinus and van Hilten[3] suggested that CRPS, fibromyalgia, and RSI may evolve through a common pathway. They found that patients with CRPS and fibromyalgia share similarities with respect to demographic characteristics and particularly occurrence of sensory symptoms. Furthermore, although less distinct, similarities were found for motor, autonomic, and trophic changes and for systemic symptoms. In addition, they have hypothesized that several other features, such as risk factors, age at onset, and sex distribution, may be similarly distributed in these complaints. This review, however, also identified methodologic differences between studies that limit the possibilities of comparison between studies. Furthermore, similar symptoms may have been

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reported differently, making accurate comparison of the symptoms difficult.

To overcome abovementioned limitations, a uniform systematic evaluation that addresses the clinical manifestations and demographic characteristics of patients with CRPS-I and potentially related syndromes like fibromyalgia and RSI is necessary. Furthermore, possible associations between CRPS-I and these syndromes may contribute to a better understanding of the involved underlying pathophysiologic mechanism(s) of these disorders. To compare disease characteristics of CRPS-I patients with syndromes like fibromyalgia and RSI, a questionnaire was developed. In this study, the development of the questionnaire is described, and the test-retest reliability of this Trauma Related Neuronal Dysfunction Symptoms Inventory (TSI) for CRPS-I and fibromyalgia patients is evaluated. Furthermore, clinical manifestations of CRPS-I and fibromyalgia will be compared.

METHODS

Development of the Questionnaire

Over a period of 2 years (2003–2004), a generic questionnaire for the evaluation of signs and symptoms was developed in 3 sequential stages, during which the content validity, other clinimetric properties, and the practical use of the questionnaire were addressed.

In the first stage of development, literature was searched for studies that evaluated the clinical spectrum described for CRPS, fibromyalgia, and RSI. Literature was obtained from Medline, PubMed, and the Cochrane database over the period between 1980 and 2003, whereby the following search terms were used: *complex regional pain syndrome*, *CRPS*, *posttraumatic dystrophy*, *PTD*, *reflex sympathetic dystrophy*, *RSD*, *Sudeck's dystrophy*, *dystonia*, *repetitive strain injury*, *refractory cervicobrachial pain syndrome*, *cumulative trauma disorder*, *work-related upper-limb disorders*, *occupational overuse syndrome*, *occupational cervicobrachial disorder*, *work-related upper-extremity musculoskeletal disorders*, *chronic upper-limb pain*, *fibromyalgia*, *fibromyalgia syndrome*, and *fibrositis*. These search terms were subsequently combined with the following key words: *epidemiology*; *female*, *male*, *women*, and *men*; *incidence*, *prevalence*, and *occurrence*; *age*; *gender* and *sex*; *hereditary* and *heredity*; *risk factors*; and *disease course*, *longitudinal course*, *symptoms*, and *signs*. After screening 526 publications, 240 articles were included.

Based on aforementioned reviews, the second phase was started, which led to the development of the first trial version of the questionnaire. A 47-item set list was constructed, which was divided into domains reflecting the presence of sensory, autonomic, motor, trophic, and visceral symptoms. Clinical signs were evaluated in the extremity in which the complaints started. The provisional item list was first tested as a standardized interview questionnaire in 19 CRPS-I and 5 fibromyalgia patients to improve the quality and content of the questionnaire and to remove redundant items.

Because features such as neck and back problems were only marginally addressed in the previously mentioned version of the questionnaire, a new search was performed with *spine* and *spinal column*, as additional key words. This resulted in a 57-item interview questionnaire, in which the frequency and severity of sensory, autonomic, motor, and trophic symptoms were assessed both in the extremity in which complaints first started as well as in the upper back and/or neck and lower back regions. The interrater reliability between 3 interviewers was good (mean intraclass correlation [ICC]=.90; n=38 CRPS-I patients), whereas the intrarater reliability with a 2-week interval was moderate (mean ICC=.70; n=12 CRPS-I patients), which was due to changes in complaints over the evaluation period. Because the frequency and severity data showed high agreement (mean ICC=.89), these questions were combined to reduce redundancy. Finally, the questionnaire was adapted to be used as a written questionnaire that could be completed by patients.

In this final version of the TSI, complaints were evaluated in all extremities, resulting in a questionnaire with 164 items. The TSI is a Dutch questionnaire that consists of 10 categories. Categories 1 and 2 (9 items) address general (disease) characteristics (medication use, disease duration, cause of complaints, and other disorders). Categories 3, 4, 5, and 6 (128 items) address sensory, autonomic, trophic, and motor symptoms in the right arm, left arm, right leg, and left leg, respectively. Categories 7 and 8 (12 items) address the neck and/or upper back and lower back. Category 9 (1 item) consists of a body picture to record the region of complaints. Category 10 (14 items) addresses the visceral domain and includes a miscellaneous domain for symptoms that do not fit in the aforementioned categories. Questions addressed the frequency of complaints, and response options were presented on an ordinal scale (1–4). A preliminary translation of a section of the questionnaire can be found in appendix 1.

Study Population

CRPS-I patients were recruited at the outpatient pain clinic of the VU University Medical Center, Amsterdam, The Netherlands. CRPS-I patients had to meet the following inclusion criteria: (1) diagnosis of CRPS-I according to the International Association for the Study of Pain criteria,[4] (2) minimum age of 18 years, (3) command of the Dutch language, and (4) no history of psychiatric abnormalities as registered in the patient's medical record.

Fibromyalgia patients were recruited from a fibromyalgia patient organization. The diagnosis of fibromyalgia had to be made by a specialist or general practitioner, and patients had to meet inclusion criteria 2 through 4.

Test-Retest Reliability

Patients received 2 identical questionnaires to test the test-retest reliability. Both patient groups received the first questionnaire with an accompanying letter with instructions in addition to oral instructions. Patients were requested to fill out the questionnaire alone on the day of receipt and to return it the following week. The second questionnaire was sent by mail after 7 days with the request to complete it exactly 7 days after completing the first. To control for possible changes in general health and/or the specific complaints of the patient, an additional 5-point rating scale evaluating changes in general health and CRPS-I or fibromyalgia complaints was completed together with the second questionnaire. To assess whether the questionnaire was user-friendly, a short questionnaire, inquiring after the clarity of questions and response options and the terminology used in the questionnaire, was added.

Statistical Analysis

The data were processed and analyzed with SPSS.[a] Questions about the patient's general (disease) characteristics were not included in the test-retest analyses. Test-retest reliability between the first and second measurement was calculated for all individual items by using the ICC,[5,6] which was subsequently used to calculate the mean overall test-retest reliability, the mean category reliability (ie, body areas), and the mean domain reliability (type of symptom). The following cutoff