English Version of "Bitte nicht noch mehr verletzen! Plädoyer gegen eine invasive Schmerztherapie bei Kindern mit komplexem regionalem Schmerzsyndrom (CRPS)".
DOI 10.1007/s00482-012-1164-2-z

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Please don't hurt me!

A plea against invasive procedures in children and adolescents with complex regional pain syndrome (CRPS)

Introduction

Complex regional pain syndrome type I (CRPS I) is characterized by a pain syndrome of the hands or feet that is associated with sensory, motor, and autonomous symptoms. This syndrome occurs irrespective of age. There may also be related changes to body representations, joint and bone metabolism, as well as edema. In almost all cases, a previous physical trauma can be recalled, although the severity of symptoms is not related to the severity of trauma. The pathophysiology of CRPS remains unclear; however, a combination of peripheral inflammatory dysregulation [16] and processing of signals in the central nervous system, especially the sensory and motor cortex and basal ganglia, are currently proposed [19]. The diagnosis of CPRS requires the presence of several objective signs, and subjective symptoms [10]. Exclusion of other possible causes of the signs and symptoms is critical. A distal generalization of the symptoms is characteristic, e.g., pain as a result of nerve damage (this is called CRPS type II) extends into areas outside the area that is innerved by the affected nerve. The therapies of choice for an ascertained CRPS are glucocortocoids in the early phase, physio- and ergotherapy, as well as medications in the later phase. There are very few specific studies on medication use in CRPS. Consequently, guidelines are based on recommendations for neuropathic pain (see AWMF Leitlinie 2011). Of the invasive procedures, spinal cord stimulation has resulted in positive outcomes in some studies. The relevance of sympathetic blockade is still under debate despite anti-hyperalgesic effects [1, 24]. A Cochrane analysis challenges the long-term utility for this therapy of CRPS in adults [4].

Children and adolescents can also show signs and symptoms that suggest CRPS I (Morbus Sudeck). Several authors have highlighted differences in the presentation of adolescent compared to adult CRPS [30]. The diagnostic criteria for CRPS were developed and validated in adults. In this paper, we use the term CRPS for all children and adolescents who fulfill the relatively broad criteria of the IASP [21]. CRPS affects more girls than boys in adolescence, and a lower extremity is more commonly affected than an upper extremity. The mean age is between 11 and 13 years [3, 33]. Present knowledge about CRPS is based on case series [2, 3, 29]. The largest centers in the US and Europe, such as Harvard Medical School (Boston), Children's Hospital (Seattle), and the Medical Center (Nijmegen), treat between 1 and 9 pediatric CRPS in-patients per year—more often than not as part of multimodal interventions that use invasive procedures when conventional treatments do not result in quick improvements. Outside of these centers, invasive and experimental treatments are used in affected children, despite problems in forming a definite diagnosis and therapy. The literature supporting these treatments consists mainly of unmatched case reports. The effectiveness of spinal cord stimulation [23], lumbar sympathetic blocks [22], and regional nerve blocks [27] or catheters [14] in CRPS are reported. The success rates of such invasive treatments are invariably described as excellent [5].

In contrast to these, the authors are faced with a growing number of children in whom invasive treatments have been tried. In order to describe the relevance of a multimodal conventional treatment in patients who seem refractory to therapy, the authors' experiences are described and discussed in the following contribution.

Methods and design

Treatment setting

Each year about 450 new patients are admitted to the German Paediatric Pain Centre for chronic pain. Of these, about 10–12 children and adolescents suffer from CRPS. The diagnostic and therapeutic procedure, including a referral to the

Tab. 1 Overview of the medications taken before admission

Drugs	Number	Percent
Opioids		
High-potency (morphine, hydromorphone, oxycodone, buprenorphine)	7	19
Low-potency (codeine, tilidine, tramadol)	22	59
Non-opioids		
Ibuprofen	22	59
Paracetamol	17	46
Metamizol	17	46
NSAIDs		
COX-2 inhibitors (celecoxib, etoricoxib, parecoxib)	7	19
Other (naproxen, diclofenac)	6	16
Adjuvants		
Gabapentin/pregabalin	24	65
Amitriptyline	10	27
Calcitonin NS	8	22
Other (oxcarbazepine; clonidine, prednisolone, promethazine, tolperisone, flupirtine, trimipramine, duloxetine, clomipramine, amlodopine, lidocaine topical)	22	59

pain clinic at Bochum, is standardized and has been extensively evaluated [7, 11]. An admission to the inpatient ward is made when pain results in severe impairment. Treatment in the inpatient ward consists of six modules:

- goal setting and education,
- training of coping strategies,
- therapy of comorbid emotional problems,
- family interventions,
- other interventions (ergo- and physiotherapy, analgesics), and
- relapse prevention, therapy completion, and follow-up care [7].

Module five (ergo- and physiotherapy) is extremely important for CRPS. It consists of a gradual exposition and increase of strain, mirror therapy, and other ergo- und physiotherapeutic interventions. Invasive pain-related procedures are not used. Existing pre-medications are stepwise reduced and, if possible, stopped completely.

Design

All patients with CRPS admitted as inpatients and treated between 2004 and 2010 were reviewed with regard to invasive pretherapy and changes after conventional therapy. Several children are presented as case reports to highlight points of interest.

Results

Between 1 October 2004 and 30 September 2010, 37 patients, of which 35 were girls, with CRPS were admitted for inpatient therapy. All children fulfilled the diagnostic criteria for CRPS of the IASP [21]. There were 6 patients (16%) who could not remember an initial trauma. The mean age was 14.3 years. A lower extremity was involved in 17 patients (46%), an upper extremity in 15 patients (41%), and in 5 patients (14%) both lower and upper extremities were affected. The mean duration of the disease before admission was 37 (range 3–160) weeks. At admission, pain ratings on the 11-point numerical rating scale was 9.2 (7–10) for maximal pain and the 7.8 (range 5–10) for average pain. All patients reported an increase in pain during activity. Three patients used a wheel chair and 16 patients used other medical devices (crutches 11; arm splints 4; compression stocking 1). Using the Pediatric Pain Disability Index (PPDI) [12] which ranges from 12–60, pain-related disability during everyday activities was on average 38 (range 17–60). On a five-point scale (1= never impaired; 5= always impaired), the average impairment due to pain during physical activity (sports) was 5 (range 3–5).

The pediatric patients used on average 4.4 different oral, sublingual, intranasal, or topical medications (range 1–10). Most of the 29 different drugs were neither approved for use in this age group nor for this indication. The most frequent medications were low-potency opioids, ibuprofen, gabapentin, or pregabalin (**Tab. 1**).

In 16 children and adolescents (43%), invasive procedures were performed prior to admission, including operations for pain treatment (3 patients), singular sympathetic blocks (10 patients), and continuous sympathetic blocks with catheter (1 patient). Regional anesthesia was used in 8 children, of these 5 patients had perineural catheters and 3 had peridural catheters. Individual children received up to five difference pain catheters and three "single" shot sympathetic bocks. Furthermore, 1 patient received corticosteroids, 2 botulinum toxin injections, and 1 child received intraspinal opioids.

Follow-up

There were 26 patients who participated in a follow-up visit. The last ambulant follow-up was on average 6.7 (2–41) months after discharge from inpatient therapy. At follow-up both maximal pain score of 5.0 (0–10) and the mean pain of 3.9 (0–10) were significantly lower than at admission (paired t-tests: $p<0.001$). Both pain-related disability (PPDI) during overall everyday activities as well as in sports were reduced significantly in the 26 patients from 35 (range 17–60) to 19 (12–56) and from 5 (3–5) to 2 (1–5), respectively (paired t-tests $p<0.001$). The majority (18 of 26; 69%) were able to use the affected limb without any limitations. None of the children required a wheelchair. Only 2 patients (5%) still required a medical device (McNemar's $\chi^2=7.11$, $p<0.01$). Analgesics and co-analgesics were only taken by 3 patients (McNemar's $\chi^2=21.04$, $p<0.01$). The first patient took tramadol plus etoricoxib, the second took gabapentin plus amitriptyline, the third duloxetine plus amitriptyline, all with decreasing doses and an aim to completely stop medication intake.

Case reports

Patient 1

A 15-year-old female child (**Fig. 1**, photograph taken at admission) developed progressive pain and increasing edema in the right foot after a sprain. Five different regional anesthetic procedures were performed at two different hospitals on three separate admissions. One "pain catheter" had to be removed due to local infection. On admission to the German Paediatric Pain Centre, the patient used crutches. She complained of pain in her foot with

distal generalization of 10 on the numerical rating scale (NRS; range 0–10). The right foot was only covered in a sock due to the intense pain and swelling to 1 cm above the upper ankle. The skin was discolored, marbled, and very touch-sensitive. When touched, the patient reported a sudden increase in pain; this pain could also be triggered by a breeze of air. Furthermore, the affected foot was warmer and grew less hair. The active range of motion was severely limited. She showed a club foot (dorsal extension–plantar flexion 0–15–30°). Medication consisted of oxycodone, codeine, paracetamol, ibuprofen, diclofenac, and pregabalin per os as well as intranasal calcitonin.

During the inpatient and outpatient multimodal pain therapy, medications were stepwise reduced and finally stopped. During inpatient treatment, the patient spoke about severe psychiatric trauma in her past for the first time and symptoms improved markedly after therapy. This therapy was complicated due to suicidal crisis, which required close monitoring (i.e., a foster home). At follow-up, 3.5 months after treatment (8 weeks inpatient therapy in three separate admissions), she is able to walk without crutches and move the joint freely.

Case 2

In the 11-year old female, the CRPS began without any incident being reported. Over the course of 2 months, several stellate ganglion blocks were performed without any long-lasting analgesic effect. Medication consisted of ibuprofen per os and transdermal lidocaine. Physio- and ergotherapy were used repeatedly. In the 3 months prior to admission to the German Paediatric Pain Centre, she had 35 visits to doctors and therapists and had been admitted to a 1-week inpatient pain treatment. At admission, she had edema (**Fig. 2**), a total lack of mobility in the right hand and all finger joints. She complained of intense pain (NRS 10) and dysesthesia.

Six months after multimodal conservative treatment that involved two 4-week inpatient admissions, the hand was mobile and could be used in an age-adequate fashion.

Abstract · Zusammenfassung

Schmerz 2012 · DOI 10.1007/s00482-012-1164-2

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Please don't hurt me! A plea against invasive procedures in children and adolescents with complex regional pain syndrome (CRPS)

Abstract

Background. Complex regional pain syndrome (CRPS; formerly known as Morbus Sudeck/reflex dystrophy) is diagnosed in children and adolescents, but the clinical presentation is often atypical. Unfortunately, potentially harmful, invasive treatments are used in pediatric patients.

Patients and methods. A retrospective chart study of pediatric chronic pain patients with CRPS was performed.

Results. Over the course of 6 years, 37 (35 girls) children and adolescents took part in a multidisciplinary chronic pain inpatient program. At admission, patients took on average 4.4 (range 1–10) different medications and 29 different pharmaceuticals were used overall. Prior to admission, invasive pain treatments were performed without success in 16 of the children (43%). At least 13 children received two or more invasive treatments. Although sympathetic blocks were most prevalent, operations and regional anesthesia were also used.

Conclusion. Despite a lack of evidence for invasive procedures, these continue to be used in children and adolescents with CRPS, who later respond positively to conventional treatment.The English full-text version of this article is available at SpringerLink (under "Supplemental").

Keywords

Children and adolescents · Chronic pain · Complex regional pain syndrome · Hospitalization · Invasive procedures

Bitte nicht noch mehr verletzen! Plädoyer gegen eine invasive Schmerztherapie bei Kindern mit komplexem regionalem Schmerzsyndrom (CRPS)

Zusammenfassung

Hintergrund. Das komplexe regionale Schmerzsyndrom (CRPS; früher M. Sudeck) wird auch bei Kindern und Jugendlichen diagnostiziert. Die klinische Präsentation ist nicht immer typisch. Potenziell schädliche invasive schmerztherapeutische Maßnahmen kommen bei betroffenen Kindern zu häufig zum Einsatz.

Material und Methoden. Eine retrospektive Analyse stationär behandelter Kinder mit CRPS wurde durchgeführt.

Ergebnisse. In 6 Jahren wurden stationär 37 Kinder und Jugendliche (35 weiblich, mittleres Alter: 14,3 Jahre) multimodal konservativ schmerztherapeutisch behandelt. Bei der Nachuntersuchung von 26 Patienten (70%) zeigte sich eine signifikante Verbesserung der Erkrankung auf den Ebenen Schmerz, Beeinträchtigung und Medikamenteneinnahme. Zuvor hatte jeder Patient im Mittel 4,4 verschiedene Medikamente erhalten (Spanne: 1–10). Dabei waren 29 verschiedene Pharmaka eingesetzt worden. Invasive schmerztherapeutische Maßnahmen hatten 16 Patienten (43%) frustran durchlitten, 13 Kinder mehrfach. Am häufigsten kamen Sympathikusblockaden zum Einsatz, aber auch Operationen und regionalanästhesiologische Verfahren wurden durchgeführt.

Schlussfolgerung. Bei Kindern und Jugendlichen mit CRPS, die auf eine konservative multiprofessionelle Schmerztherapie in der Regel positiv reagieren, werden zu häufig invasive schmerztherapeutische Maßnahmen eingesetzt, ohne dass deren Nutzen belegt ist.Die englische Volltextversion dieses Beitrags ist in SpringerLink (unter „Supplemental") verfügbar.

Schlüsselwörter

Kinder und Jugendliche · Chronische Schmerzen · Komplexes regionales Schmerzsyndrom · Stationäre Therapie · Invasive Therapie

Case 3

A 14-year-old girl with learning disabilities developed CRPS at the age of 12 years after a minor trauma. In the 2 years preceding admission to the German Paediatric Pain Centre the following therapies had been tried: 21 weeks (partly) inpatient treatment in hospitals for pain therapy (once), rheumatology (once), psychosomatics (twice), rehabilitation (once); several regional an-

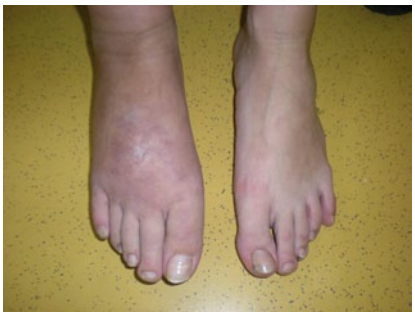

Fig. 1 ▲ Patient 1

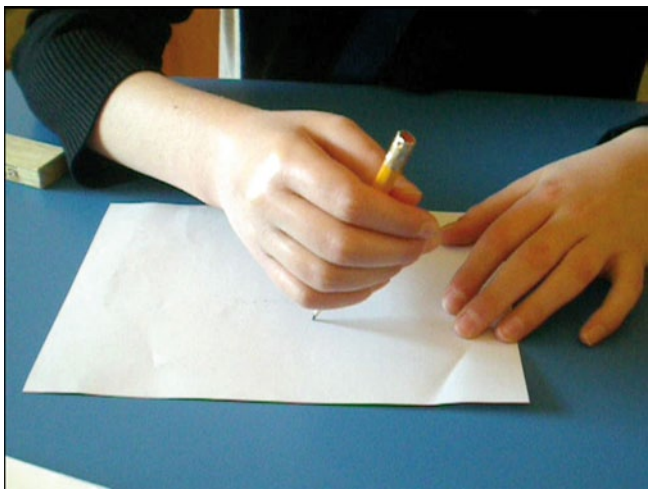

Fig. 2 ◀ Patient 2

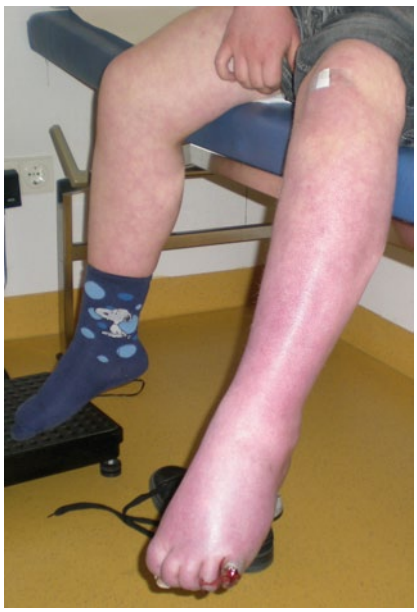

Fig. 3 ▲ Patient 3 at presentation

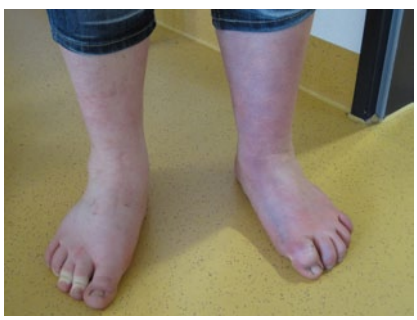

Fig. 4 ▲ Patient 3 after therapy

algesic catheters; CT-guided sympathicolysis; oral medical treatments (with tramadol, codeine, paracetamol, ibuprofen, amitriptyline, duloxetine, gabapentin per os; calcitonin intranasal), physiotherapy; ergotherapy; manual lymphatic drainages.

The state of the affected limb at presentation is shown in ◘ **Fig. 3**. The pain rating was 8 on the NRS. The child was confined to a wheelchair because the leg was not usable. She bit her lip to distract from the pain. Because of the possible infection associated with this biting she wore dental splints. Previous therapists described the family situation as "extremely complex".

A multimodal pediatric pain treatment was initiated and with the help of the childcare services continued over 32 months (6 weeks inpatient therapy, 17 outpatient visits). The outcome of the therapy after 26 months is depicted in ◘ **Fig. 4**. The affected limb has regained use in an age-adequate fashion within the past 6 months.

Discussion

Reports concerning complex regional pain syndrome (CRPS) concerning children starting from the age of 2.5 years can be found in the literature [9]. A sentinel traumatic trigger is not always reported. CPRS after immunizations is reported [8]. The pain intensity at first admission is between 8 and 10 (NRS/VAS 0–10) for most patients. The affective expression is often incongruent to the high reported pain intensities; children report extreme pain intensities with a smile on their faces [25]. A lower limb is more commonly involved in children than in adults. Cold and mechanical allodynia, burning pain, dysesthesia and paresthesia are leading symptoms. Signs of autonomous dysfunction (e.g., edema, cold skin, discolorations, changes in hair-growth, and sweating) and movement problems (e.g., dystonia and limited range of motion) are often present. Cognitive and emotional problems are common in children. Many children report a feeling that the limb does not belong to the body (neglect of the affected extremity). This feeling may become so intense that the child wishes to "cut off" the affected limb.

The signs and symptoms often do not conform to the classical symptoms in adult CRPS patients [29, 31]. Thus, it remains unclear whether CRPS in childhood and adolescence is the same disease as CRPS in adults. The existence of two entities with similar symptoms is possible.

Psychological factors

Severe psychological problems are present in almost all CRPS patients and they are more prevalent in children with relapsing courses [25, 26, 28]. Critical life-events are often elicited in adolescents. In a study by Sherry [26], about 20% of the patients reported sexual abuse. Suicidal tendencies before the onset of CRPS were risk factors for a relapse [25]. If children only receive body-oriented treatment, there is a real risk of symptom transversal and onset of psychiatric diseases, e.g., eating disorders, self-mutilation, and suicide [25].

Multimodal therapy

CRPS in childhood and adolescents seems to respond favorably to conservative multimodal inpatient therapy, with an emphasis on physiotherapy and gradual desensitization. In about 20–60% of the children,

one or more relapses will occur [3, 18, 31]. The long-term prognosis is unclear [3, 17, 18, 25, 28, 31, 34].

The most recent study with the longest follow-up (median of 12 years) found that 52% of the former pediatric CRPS patients still have pain; in 57% of these patients, pain increases during movement [31]. About half of the former CRPS patients complain 2–22 years after therapy of differences in skin temperature and limited range of motion of the affected limb.

Invasive pain therapies

The relevance of invasive therapies [22, 23] in children who otherwise do not respond to conventional treatments or medications is not established in pediatric patients and a positive publication bias must be assumed. In one study from the Children's Hospital in Boston, 35% of the pediatric CRPS patients received an invasive therapy, e.g., continuous lumbar sympathetic blocks and/or peridural catheters [17]. In the case series of Kachko et al. [13], these were 29% and in the series of Kesler et al. [15] 33%.

Review of case reports on invasive pain therapy for children with CRPS suggests that unusual clinical presentations are common and that children endure many different treatments over a long period of time. For example, Dangel et al. [6] describe four cases. In the first patient, both the right upper and lower extremities as well as the thorax and neck were affected. The second child with left and right lower extremities CRPS was treated for 3 years with four intravenous phentolamine tests, nine intravenous, and unknown number of single shot and three continuous sympathetic blocks. Finally, five different chemical sympathectomies were performed, which resulted in neuralgia of the genitofemoral nerve, but no significant improvement in outcome. In the third child, extensive invasive treatments resulted in an exacerbation of pain; the fourth patient had no positive outcome reported. Olsson et al. [23] judged the success of invasive spinal cord stimulation (SCS) as positive in all of their pediatric CRPS patients: twice a partial and five times a complete remission was reported. Of note, but not discussed in any detail by the authors, is the fact that at least 3 of the 7 suffered from a severe psychological disease (sexual abuse with suicide attempt, anorexia nervosa, obsessive–compulsive disorder, conversion disorders). One child suffered from five relapses and 1 child improved despite but not because of the SCS. The child reported no effect from the stimulation even at high voltages but overcame the disease during the subsequent 6 weeks. One child had an infection and the stimulator had to be extracted. Before a second system could be implanted, spontaneous remission occurred.

Wilder [32] summarized his experiences with SCS in children: "I know of least a half-dozen children who have undergone SCS for CRPS. Results have been mixed, ranging from modest improvement in pain and function to a worsening of pain, with explantation of the system (…)". Concerning his successes with sympathectomy in childhood he notes: "The three patients undergoing these procedures did not have improvement in pain scores despite improvement in circulation and edema (…)" ([32], page 446). In addition, no improvements were found with regard to spontaneous pain in a randomized-controlled trial of sympathicolysis [20].

Recommendations for practice

- **Taken together the published studies cannot establish the effectiveness of invasive procedures for CRPS in childhood and adolescence.**
- **The patients who are described as nonresponders to conventional therapy are very similar to the patients who improved markedly from a conventional noninvasive therapy delivered in a pediatric inpatient pain therapy setting.**
- **Considering the low incidence of the disease and the massive loss of quality of life in addition to the unclear long-term outcomes, only a few centers should specialize in the treatment of CRPS in childhood and adolescence in Germany.**
- **In children with CRPS, a conservative procedure is demanded, including abstinence from invasive pain therapies and medications, especially those treatments that are not even proven to be effective in adults with CRPS and/or any other pediatric disease.**

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Conflict of interest. The corresponding author states that there are no conflicts of interest.

Acknowledgment. The help of Brian Anderson with the English translation is very much appreciated.

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