Background: Complex regional pain syndrome (CRPS) is a multifactorial condition with complex pathogenesis characterized by spontaneous or stimulus-induced pain that is disproportionate to the inciting event. It is also commonly accompanied by a myriad of autonomic and motor disturbances in highly variable combinations. This condition has been underreported in children until recently. Consequently, the management of CRPS in the pediatric population presents an even greater challenge than in adults, partly because there is a lack of clinical data concerning the efficacy of the diverse treatment methods available, and partly because successful treatment of CRPS involves a multidisciplinary approach. There is a variety of invasive methods to the treatment of CRPS, but scarce pediatric-focused trials have been published to date.

Objective: To examine and analyze the data currently existing for the invasive management of CRPS in children. It further suggests a management algorithm based in the evidence reviewed and our team experience.

Study Design: A comprehensive review of invasive management for pediatric CRPS.

Setting: Academic hospital in Spain.

Methods: A comprehensive review of all the evidence published to date was conducted. Four databases (PubMed, Medline, Web of Science, Embase, and Cochrane databases) were searched for articles published from 1980 to 2014. The eligibility criteria were any paper published in English or Spanish where a non-conventional approach was used to manage pediatric CRPS. Two independent reviewers extracted the data.

Results: Many case series have reported the use of interventional management with positive results; however, there is not a single randomized control trial to date comparing the conservative and the invasive management in children. The largest series of pediatric cases showed that between 29% to 35% of children with CRPS needed interventional measures to manage this condition successfully. Sympathetic blocks and spinal drug infusion emerge as the most reported techniques; the spinal infusion of drugs together with the spinal cord stimulation being the most successfully employed. Based upon the available evidence with regard to effect and complications, we recommend an algorithm for the management of pediatric CRPS.

Limitations: The limitations of this study include the paucity of literature, lack of randomized trials, and lack of quality evidence.

Conclusions: Invasive techniques have been used to treat CRPS over the last few decades; however, the evidence for their use is still very weak. Invasive management should be contemplated only when high-standard conservative management has failed to work.

Key words: Pediatric pain, complex regional pain syndrome, CRPS, invasive treatment, pain management, multidisciplinary management, neurostimulation
Complex regional pain syndrome (CRPS) is a term defined by the International Association for the Study of Pain (IASP) to describe disorders primarily characterized by spontaneous or stimulus-induced pain that is disproportionate to the inciting event. CRPS has been suggested to be a multifactorial disorder that is related to an aberrant host response to tissue damage (1,2). The disease often includes a wide variety of autonomic and motor disturbances in highly variable combinations (3,4). The symptoms can be categorized into 2 groups: positive noxious symptoms, such as hyperalgesia and allodynia, and negative symptoms of sensory loss (1,2,5). Usually, patients with CRPS present following moderate or insignificant tissue damage. In the acute phase, the patient can exhibit an extremely painful, red, warm, and swollen injured limb. Other potential accompanying features are changes in sweating, hair and nail growth, allodynia and hyperalgesia, and muscle weakness. As the disorder continues, pain spreads, voluntary motor control is reduced in most patients, and negative sensory signs, namely hypoalgesia and hypoesthesia, become more apparent (1,6,7).

CRPS has been extensively studied in adults, while studies in children are scarce (1,8,9). For a long time it was doubtful that this condition even existed in children, nonetheless within the last few years numerous articles have reported CRPS at young ages (Table 1). However, due to the lack of understanding regarding its precise pathophysiology, reliable diagnostic tests are not available. CRPS diagnosis entirely depends on observable signs and reported symptoms, which have been put together into various diagnostic criteria sets for adults (4,10,11). Unfortunately these diagnostic criteria do not often agree, raising a high degree of uncertainty into a CRPS diagnosis. To date specificity and sensitivity of the standard diagnostic criteria sets have not been evaluated for pediatric patients.

As well as posing a significant diagnostic challenge, the timely diagnosis of CRPS can substantially influence the prognosis (12-15). Additionally, prompt and accurate management is key, where the cornerstone is to restore function of the affected limb. Recognized therapies include a combination of pharmacotherapy, physical therapies, and psychotherapy where appropriate (14,16-19). Only patients who fail to progress with physical therapy may require additional or more invasive pain therapy, such as spinal cord stimulation (SCS), intraspinal analgesic infusion, or sympathetic blocks (20-23). Neurostimulation therapy and spinal cord drug infusion have been available since the 1970s and have grown in acceptance in recent years for the treatment of pain disorders of diverse etiology (21,24). Today, CRPS in adults is the second largest indication for the use of SCS in the United States, reaching success rates of up to 70% in pain reduction in CRPS sufferers treated with SCS when properly selected (25,26). However, the significance of invasive procedures during childhood and adolescence for the treatment of CRPS patients who do not respond to conventional treatments or medications continues to be unestablished (27). Several reports in the literature demonstrate success with these procedures, providing physicians (or clinicians) with more alternatives after conventional options fail (Table 3).

The focus of this article is to review the evidence for invasive pain procedures along with presenting a management algorithm for pediatric CRPS, including invasive procedures for patients who do not respond to the conventional first-line treatment.

Table 1. Invasive interventions for complex regional pain syndrome.

<table>
<thead>
<tr>
<th>Intervention</th>
<th>n studies (%)</th>
<th>n patients</th>
<th>1980 – 2000</th>
<th>2000 – 2015</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sympathetic blockade (singular or continuous)</td>
<td>15 (48%)</td>
<td>123</td>
<td>7</td>
<td>8</td>
<td>(11, 38, 40, 58, 65-75)</td>
</tr>
<tr>
<td>Spinal drug infusion or epidural catheter</td>
<td>11 (35.5%)</td>
<td>25</td>
<td>0</td>
<td>11 (100%)</td>
<td>(29, 33, 38, 51, 58, 69, 71, 74, 76-78)</td>
</tr>
<tr>
<td>Regional anesthesia</td>
<td>10 (32%)</td>
<td>36</td>
<td>1</td>
<td>8 (91%)</td>
<td>(11, 29, 38, 43, 69, 74, 79, 80)</td>
</tr>
<tr>
<td>Intravenous lidocaine</td>
<td>7 (22.4%)</td>
<td>28</td>
<td>4</td>
<td>3</td>
<td>(40, 58, 66-68, 81, 82)</td>
</tr>
<tr>
<td>Spinal Cord Stimulation</td>
<td>3 (9.6%)</td>
<td>11</td>
<td>0</td>
<td>3 (100%)</td>
<td>(28, 33, 76)</td>
</tr>
<tr>
<td>Surgery</td>
<td>3 (9.6%)</td>
<td>5</td>
<td>3</td>
<td>0 (0%)</td>
<td>(81, 83, 84)</td>
</tr>
<tr>
<td>Sympathectomy</td>
<td>2 (6.4%)</td>
<td>28</td>
<td>2</td>
<td>0 (0%)</td>
<td>(44, 81)</td>
</tr>
<tr>
<td>Total</td>
<td>31 (100%)</td>
<td>171</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Invasive Management for Pediatric CRPS

Table 2. *Adult vs. pediatric CRPS characteristics.*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adult 1</th>
<th>Pediatric 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age*</td>
<td>45</td>
<td>12.8</td>
</tr>
<tr>
<td>Gender ratio</td>
<td>Male predominance</td>
<td>Female predominance (85%)</td>
</tr>
<tr>
<td>Extremity affected</td>
<td>Upper</td>
<td>Lower (80%)</td>
</tr>
<tr>
<td>Trauma</td>
<td>Mild- Severe</td>
<td>Minor- Mild</td>
</tr>
<tr>
<td>Limb temperature</td>
<td>30% cooler</td>
<td>70% cooler</td>
</tr>
<tr>
<td>Edema</td>
<td>40%</td>
<td>75%</td>
</tr>
<tr>
<td>Prognosis</td>
<td>Variable, long term disability</td>
<td>Excellent recovery in most cases</td>
</tr>
<tr>
<td>Relapse rate</td>
<td>10%</td>
<td>30%</td>
</tr>
</tbody>
</table>

* mean age at presentation of the symptoms. 1 Data extracted from CRPS adult literature. 2 Description of patients comprised in this review.

Table 3. *Relevant publications, selection by the authors.*

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Intervention</th>
<th>n</th>
<th>Outcome measur.</th>
<th>Length</th>
<th>Previous medication</th>
<th>Adverse effects</th>
<th>Improvement (% patients)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rodriguez et al (33)</td>
<td>2015</td>
<td>LA Spinal inf. SCS</td>
<td>10 (6)*</td>
<td>Yes</td>
<td>52 w</td>
<td>Opioids (67%) NSAIDs (83%) Anticonvul (100%) Antidepress (67%) Capsaicin (100%)</td>
<td>No</td>
<td>100%</td>
<td>This study showed successful results after applying a multimodal and progressive approach including invasive measures as well as physical management and novel medication as the capsaicin 8% patch.</td>
</tr>
<tr>
<td>Olsson et al (28)</td>
<td>2012</td>
<td>SCS</td>
<td>7</td>
<td>Yes</td>
<td>52/250 w</td>
<td>Opioids NSAIDs Anticonvul Antidepress Ketamine (14%) Epidural L.A (28%)</td>
<td>Yes, Local infection</td>
<td>Full recovery (72%)</td>
<td>Olsson’s study comprised 7 girls, presenting with severe, incapacitating and therapy-resistant CRPS-I, who were subjected to SCS. Good technique description but poor methodology.</td>
</tr>
<tr>
<td>Meier et al (42)</td>
<td>2009</td>
<td>Cont Lumbar sympath block Lidocaine iv</td>
<td>23</td>
<td>Yes</td>
<td>-</td>
<td>“6-week trial of aggressive physical, bio-behavioral, and pharmacological therapies”</td>
<td>Minor</td>
<td>LSB: Complete (29%). Adequate (41%) Minimal (32%) Lido iv: Minimal (84%) Adequate (16%)</td>
<td>The purpose of this study is to compare the efficacy of lidocaine administered by lumbar sympathetic to IV route. Excellent methodology and clear results. No follow-up period.</td>
</tr>
<tr>
<td>Kachko et al (38)</td>
<td>2008</td>
<td>Epid cath (1) Stellate gang block (1) Regional anesth. (2)</td>
<td>14 (4)*</td>
<td>Poorly</td>
<td>8 w</td>
<td>NSAIDs Anticonvulsive Antidepressant</td>
<td>-</td>
<td>Full (78%) Partial (15%) Recurrence (29%)</td>
<td>Retrospective study that aimed to assess the efficiency of the multimodal management of CRPS. Limited but illustrative of the actual clinical set up of many pain treatment units.</td>
</tr>
<tr>
<td>Stanton et al (11)</td>
<td>1993</td>
<td>Sympath block Regional anesth</td>
<td>36 (x)*</td>
<td>Poor</td>
<td>-</td>
<td>NSAIDs Anticonvulsive Antidepressant Opioids</td>
<td>-</td>
<td>Moderate or poor</td>
<td>Review of the experience at this center. They aimed to present diagnostic criteria for pediatric CRPS. Management and outcomes poorly described.</td>
</tr>
<tr>
<td>Wilder et al (75)</td>
<td>1992</td>
<td>Sympath block</td>
<td>70 (37)</td>
<td>Yes</td>
<td>20 w</td>
<td>NSAIDs Antidepressant</td>
<td>-</td>
<td>Full (71%) Moderate (13%)</td>
<td>Wilder retrospective study reported his experience with a multimodal treatment, using more than 50% invasive techniques.</td>
</tr>
</tbody>
</table>

(1) Outcome measure carefully described. (2) Length of the follow-up – weeks. (3) Medication prior invasive treatment. * Number of patients treated with invasive measures within the total of patients.
Literature Selection

A literature search identified studies relevant to invasive treatments for CRPS in children. Databases used included PubMed, Medline, Web of Science, Embase, and Cochrane. Because of the small volume of literature on the pediatric population, database-specific controlled vocabulary (subject headings or index terms) was not used, and keyword searching produced a comprehensive and manageable yield. The following search strategy was used: ((complex regional pain syndrome) OR (CRPS) OR (reflex dystrophy) OR (algodystrophy) OR (causalgia) OR (Sudeck's atrophy) AND (sympathetic OR neurovascular)) OR ((amplified OR complex OR chronic) AND (neuralgia OR pain) AND musculoskeletal)) AND (therapy OR therapies OR therapeutic)) OR (transcranial AND magnetic AND stimulation) OR (spinal cord stimulation OR neurostimulation OR spinal drug infusion OR intra-spinal therapy OR epidural infusion OR epidural catheters OR sympathetic block OR sympathetic blockade OR peripheral blocks OR surgery) AND (child OR adolescent OR pediatric). Initial search results were limited to English and Spanish language articles. The references in the selected articles were used to identify additional relevant sources. In addition, the authors identified a limited number of articles or chapters from personal readings.

Thirty-one studies met the criteria to be included in this review (Table 1). Their full texts were analyzed for retrieving information such as the invasive treatment –used – including prior and concurrent conservative interventions, outcomes measured, type of study, patient characteristics, quality of the study, design, and methodology.

Review of the Evidence

Conservative Management

Although reviewing CRPS non-invasive therapy is not the goal of this article, we have considered it appropriate to briefly describe the most accepted model of management for this condition. CRPS in children and adolescents seems to respond favorably to conservative multimodal inpatient therapy (34,35). In the largest pediatric trial reported to date, 92% of children and adolescents were free of symptoms after an intensive physical therapy program (36). Other smaller series identified in the literature have presented recovery rates of 70% as well after applying conservative management (25,37,38), however recovery or resolution is not always well-defined.

Invasive Pain Therapy

The relevance of invasive therapies in children who otherwise do not respond to conservative management or medications after a few weeks of treatment has not been established in pediatric patients (27,28,33,40). There is not a single randomized control trial to date comparing the conservative and the invasive management of this particular group of patients. The largest series of pediatric cases showed that between 29% to 35% of children with CRPS needed interventional measures to manage this condition successfully (14,38,41).

Within this review we have identified 31 publications published between 1980 and 2015. Most studies were case series and case reports (n = 28), including a total of 108 patients. One randomized control trial of 23 patients and 2 controlled studies of 40 patients in total complete the collection of studies of this review (Table 1). The entire collection of publications contained data of 171 patients. The characteristics of the population who received invasive procedures correlates with the characteristics of the children shown in other publications affected by this syndrome who do not receive this sort of treatment (Table 2) (23,39). Spontaneous pain and functional disability were the 2 outcomes measured with more assiduity. The overall improvement for spontaneous pain was documented in 79% of cases; 16% of patients showed no change. Functional disability was reported in 25 publications, 24 of them showed improvement after treatment.

This study reveals that the most used procedure was the sympathetic blockade (Table 1). Singular or continuous sympathetic blocks were used in 15 studies, 123 patients. Within this group of studies we found the only randomized control trial (42) and 2 controlled studies (43,44). Numerous types of blocks are included in this group, for example: the sympathetic blocks of the ganglion stellatum for CRPS in the arm, the block of the lumbar truncus sympathicus for CRPS in the leg, or the thoracic block of the Kuntz’s nerve. Local anesthetic blockade of the sympathetic chain has been widely
used to treat CRPS in adults, however the empirical data is confusing (45,46). A systematic review revealed the paucity of published evidence to support the use of local anesthetic sympathetic blockade as the “gold standard” treatment for CRPS (32,47,48). Likewise, we can conclude that its efficacy has not been proven for the treatment of CRPS in adults. The data in children is far scarcer and uncertain, that is why this treatment has been relegated to a more tentative choice in pediatric CRPS. Additionally, most of the publications analyzed revealed that multiple invasive procedures were needed during the period of treatment with this technique, increasing the risks of side effects (11,38).

The spinal drug infusion of local anesthetics was used in 11 studies, all of them in the last 15 years. Spinal drug infusion through epidural catheter has been largely used in this group of patients when the physiotherapy program needs to be supported or when the symptoms do not decrease with conservative management. Epidural drug infusion with local analgesics is a viable alternative when conventional treatments do not achieve acceptable results, it also has the advantage of supplementation with opiates to the local anesthetics to offer better analgesia. The complications and risks of this technique (e.g., respiratory depression, motor block, sympathetic block resulting in hypotension, and urinary retention) can be avoided by careful titration of the infused medications and adequate patient and family education. To date there is no randomized trial for spinal drug infusion in CRPS, however there are numerous reports supporting this technique. Of 37 adult CRPS patients treated with continuous epidural infusion of bupivacaine and fentanyl, nearly 90% had a reduction in their symptoms when treated within 12 months after onset. However, the success rate diminished considerably when treatment was started more than a year after onset (49). In the pediatric literature, reports are fewer yet analogous to those found in adults which would suggest a favorable outcome (33,38,50,51). Some authors highlight the importance of avoiding delay for treating CRPS invasively (33,50). Therefore, we conclude that early treatment with continuous epidural anesthesia may be promising when initial non-invasive management is ineffective.

SCS has demonstrated efficacy in CRPS type 1 in adults (30,52,53). In SCS in adults, as in pediatrics, an electrode is placed in the epidural space on the dorsal aspect of the spinal cord at the level of the nerve roots innervating the painful area. Electrical current from the electrode brings about paresthesia, a sensation that suppresses the pain. This technique has become more popular during the last decade for the management of CRPS in adults, obtaining successful results in most cases (21,53-55). In the pediatric population it has been suggested as a possible option when the patient is resistant to all conventional treatments (30,55-57), but only a few examples of successfully treated CRPS in children have been presented to date, 3 case series with 11 people in total (16,28,33). Therefore, to the best of our knowledge SCS can be a useful and promising treatment for CRPS in pediatric patients who do not respond to conventional treatment. Nevertheless, due to the small and non-controlled design of these case series, further studies are needed to verify that SCS can be recommended for its use in this group of patients.

There are others invasive techniques that have been considered when conventional therapy has failed in pediatric CRPS. Regional anesthesia has been tried in 36 patients during the last years, mostly during the last 10 years, however the results do not appear to be as good as with some of the techniques mentioned previously. Similarly, intravenous regional blocks with lidocaine show unsatisfactory or unclear results in general: the decrease in spontaneous pain and functional disability improvement less than with any other procedure, 55% and 50%, respectively.

**Discussion**

CRPS is characterized by complex clinical presentations and a pathophysiology that seems to be multifactorial in nature, characterized by an aberrant host response to tissue damage (1,5,58). Most of the clinical features of this condition can be explained by the confluence of 3 major pathophysiological pathways: vasomotor dysfunction, aberrant inflammatory mechanisms, and maladaptive neuroplasticity. The clinical heterogeneity of the disorder is indicative of the interindividual variability in the activation of these pathways after tissue injury (1,59,60).

The recommendations of the special interest group in Neuropathic Pain (NeupSIG) of the IASP for the pharmacological management of neuropathic pain (NP) only considered treatments with at least 2 high-quality randomized clinical trials (61). Nonetheless, there is limited evidence evaluating interventional treatments for NP, and many interventions used in clinical practice to manage NP in refractory patients are supported by weak, if any, evidence (62). This evidence is even more fragile when talking about the management of CRPS,
and completely exiguous when referring to the management of pediatric CRPS.

Nonetheless, the scientific consensus is that the cornerstone of CRPS management should be the restoration of function. Acknowledged therapies include a combination of pharmacotherapy, physical therapies, and psychotherapy where appropriate (14,17-19). Several studies highlight that early mobilization of the affected limb assisted with cognitive behavioral techniques is the most important part of the management process in children (14,16). In our experience this is highly important but so is the use of medication and the early diagnosis of the disorder, which substantially influence the prognosis of the condition (12-15). Low et al (37) showed that children who received a prompt diagnosis (less than 12 weeks), and therefore were offered treatment more rapidly, achieved a quicker and more successful remission of CRPS when compared to those whose diagnosis was delayed (10.6 and 21.5 weeks).

Unfortunately a significant percentage of children who suffered CRPS do not respond to conservative treatments. Only those patients who do not improve successfully after being treated with a complete pain management plan during a reasonable time are candidates for invasive pain therapies (33). Unfortunately the evidence supporting the use of these procedures is weak. This review shows that the methodological quality of the existing data is low as most of the publications found are case series or case reports representing level IV evidence. On top of that, a very low percentage of publications used the established diagnostic criteria for CRPS from the IASP. Additional negative aspects of this group of publications are that validated outcome tools were not used in most cases and that the follow-up periods were usually not reported or rather too short.

Within the invasive techniques described in these publications, we must highlight the continuous epidural infusion and the SCS. They seem to have an important effectiveness and to be minimally invasive and reversible, besides in adults, they have been shown to be very effective for certain forms of NP (49,62,63). Olsson et al (28) concluded that SCS was successful for treating CRPS in all their pediatric patients; however, this conclusion is questionable from our point of view as in one of the patients the symptoms ceased after the patient had not responded well to any stimulus of SCS and another patient in the same series developed an infection which seriously compromised the treatment. Rodriguez et al (33) had a great experience with SCS, abolishing the symptoms in 3 children with a well-defined history of uncontrollable CRPS. This study, together with the positive experience of Wilder (16), encourages the need for a better understanding and use of SCS in CRPS. Likewise, the use of an epidural catheter for the infusion of local anesthetics has been implemented in the last years. The majority of publications agreed that the treatment diminishes the pain and improves functionality of the limb affected. Regrettably, very few of these publications described the process (the space where the catheter was implanted, the concentration, the dose, etc.), the outcome, or the side effects, if any.

Side effects were infrequently reported. Infections only occurred in 2 patients and minor side effects were reported only in 10 studies. Sixteen of 83 reported cases experienced a relapse. From our perspective, based on our experience and the literature behind these procedures, we believe that the side effects in this collection are underreported.

**Recommendation**

Based upon the available evidence with regard to effect and complications, we recommend the following algorithm for the management of pediatric CRPS (Fig. 1).

A crucial first step for the management of this condition appropriately consists of making an accurate and early diagnosis. We strongly encourage basing the diagnosis in the CRPS criteria from the IASP (10), despite that this set of criteria has been made for adults. The real goal of the physician must be the restoration of the normal function of the affected limb, using every possible management tool to achieve this. Initially, physical therapy, psychological support, and adequate pharmacological treatment should be used together, complementing one another and aiming to make the condition resolve within a few weeks. Pharmacological measures are prescribed on a symptom-oriented basis. However, new approaches should be adopted when fitting within a mechanism-based management (8). Analgesics, anti-inflammatory therapy, and antidepressant and antiepileptic drugs have been used to date. However, new topical drugs such as the high-concentration capsaicin patch have been tried within the past few years with excellent results (33).

Based on our experience (33), the heterogeneity found in the literature regarding the duration of the conservative management for treating CRPS together with the lack of knowledge of its precise pathophysiology, we recommend that after a reasonable time of 4 to 5 weeks under intensive multimodal therapy with-
Invasive Management for Pediatric CRPS

Fig. 1. Clinical algorithm for the management of pediatric CRPS. The first crucial step is the correct and early diagnosis. Immediately after, a multimodal approach must be taken. Active physical therapy, psychological support, and the correct pharmacological approach must be planned. Initially a sign and symptom oriented pharmacological treatment is engaged. Patients who do not respond successfully to the conservative management carried out during a period of 25 to 40 days can be treated with invasive techniques. First LA continuous epidural infusion for 2 weeks and then SCS can be recommended after multidisciplinary evaluation.
out successful results, more invasive options should be considered. Before failure of conservative management is taken as a reason to contemplate invasive measures as the following step, only high-quality conservative treatment should be implemented. Therefore, knowledge concerning such treatment needs to be increased. Patients with CRPS with severe pain, allodynia, or with a measurable skin temperature difference compared to the non-affected limb that do not respond to the multi-modal conservative management should be put forward for therapies such as spinal infusion of drugs, sympathetic blockades, or SCS. In our opinion, after reviewing the literature on the topic, the initial option for children who do not respond successfully to conservative management is the continuous epidural infusion of local anesthetics (33). This technique provides analgesia and sympathetic blockade throughout the time the catheter is attached. This is usually enough to control the condition and prevent the reappearance of symptoms (33). We recommend its use for 10 to 14 days. Having the catheter in for more time could increase the risk of infection (64) or further side effects secondary to the drug infusion or the catheter itself. However, this technique can fail or the symptoms can re-emerge after the catheter is removed. In this case, SCS can be recommended after multidisciplinary evaluation and a successful trial stimulation. SCS is a minimally invasive and reversible technique that facilitates physical therapy and helps decrease medication (28).

**Conclusion**

This article proposes a multidisciplinary management approach to the treatment of CRPS in children for whom the standard treatment has not been successful. Because of the severity and rapid progression of the symptoms in CRPS, we consider that an early diagnosis of the condition together with comprehensive and individualized multidisciplinary treatment offers children with CRPS the best opportunity for a complete recovery. Within this approach we encourage clinicians to consider invasive procedures as a reliable option of treatment. Unfortunately the type of technique that should be applied when high quality multimodal conservative treatment fails cannot yet be based on empirical data. Therefore, since there is significant limitations of the evidence, interventional treatments for the management of CRPS in children should ideally be offered in clinical and research settings with experience and ability to understand and report the outcomes. This will make it possible to substantially improve the evidence on which forthcoming recommendations are established.

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