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Interventional pain management of CRPS in the pediatric population: A literature review

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ABSTRACT

Background: Complex Regional Pain Syndrome (CRPS) is a condition that causes persistent and debilitating pain. It is often associated with physical injury but can also occur without identifiable trauma or ongoing injury. There are no published guidelines for CRPS treatment in the pediatric population, but interdisciplinary care, medication, and physical therapy are common approaches. Sometimes, interventional procedures such as regional anesthesia may be required to manage symptoms.

Objective: The objective of this literature review is to explore the different interventional pain management approaches that are currently being used and have shown effectiveness in the management of CRPS in the pediatric population.

Methods: We conducted a comprehensive search strategy with an experienced librarian and input from the study's principal investigator from January 1st, 2000 to April 2nd, 2024. The search was conducted in multiple databases using controlled vocabulary and keywords to identify studies relevant to invasive treatments for pediatric CRPS.

Results: Of 825 studies screened, 27 met inclusion criteria, predominantly case reports (70%). The analysis included 183 patients aged 7–18 years, with female predominance (81.4%). Lower extremities were most commonly affected (70.49%), and most cases (83.06%) were triggered by identifiable trauma. IASP and Budapest criteria, though not validated for pediatric populations, were inconsistently utilized across studies for CRPS diagnosis. Interventional procedures were typically implemented after failed conservative management (92.89%), which included multiple medications (e.g., pregabalin, amitriptyline, NSAIDs) combined with physical and psychological therapy. Multiple interventional procedures were often required to achieve pain relief or functional improvement. Follow-up periods were not reported in most studies and, when reported, were short, limiting the assessment of long-term intervention efficacy.

Conclusions: This review summarizes the different interventional pain management methods utilized to treat pediatric CRPS. While techniques such as continuous epidural anesthesia, lumbar sympathetic blocks, peripheral procedures, and spinal cord stimulation have been safely and successfully used as part of a multimodal treatment strategy, the lack of high-quality evidence and specific protocols for CRPS diagnosis and management in pediatric patients calls for further research.

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1. Introduction

Interventional pain management techniques have emerged as valuable alternatives for pediatric patients with Complex Regional Pain Syndrome (CRPS). The most often utilized interventional procedures for pediatric CRPS include sympathetic blocks, medial branch blocks, epidural catheters, and neuromodulation procedures [1,2]. Appropriately selected patients can derive substantial benefit from targeted pain interventions including decreased pain, enhanced functioning, and improved quality of life. These approaches are typically considered after patients have undergone unsuccessful trials of physical therapy and conservative medical management (Table 3) [1,2].

The evidence supporting the utilization and efficacy of these interventional approaches primarily derives from small case series and individual case reports, previously consolidated in other reviews [1,2]. However, significant technological and procedural advances have been made in the last decade, warranting an updated literature search of current interventional approaches and their uses and benefits.

Pediatric patients present a particular challenge in managing CRPS due to the rarity of this condition and the diverse array of motor and sensory manifestations [3]. While a known injury is commonly identified for diagnosing pediatric CRPS, cases of unknown etiology are not uncommon, leading one to consider alternative mechanisms potentially responsible for the syndrome's central sensitization and psychological components [4,5]. As studies have observed, the complexities of pediatric CRPS can lead to misdiagnosis, delaying treatment, and negatively impacting outcomes, with a significant proportion of patients requiring additional management [6,7].

This review provides an up-to-date overview of interventional pain management procedures for treating pediatric CRPS, offering a comprehensive overview of the current state of knowledge in this field.

2. Methods

2.1. Literature search

We conducted a comprehensive search strategy with an experienced librarian and input from the study's principal investigator from January 1st, 2000 to April 2nd, 2024. The databases included Ovid MEDLINE(R), Ovid EMBASE, Ovid Cochrane Central Register of Controlled Trials, Ovid Cochrane Database of Systematic Reviews, and Scopus. We used controlled vocabulary supplemented with properly designed keywords to search studies relevant to invasive treatments and procedures such as lumbar sympathetic blocks, epidural anesthesia, spinal cord stimulation, peripheral anesthesia for pediatric CRPS. We utilized recent and updated terminology for CRPS including causalgia, Sudek's atrophy, chronic pain, and algodystrophy. The actual strategy can be found in the appendix.

2.2. Study selection and inclusion criteria

To be included in this review, the studies had to meet the following criteria.

1. Clinical trials, cohort studies, case-control studies, cross-sectional studies, case series, case reports, retrospective studies, and prospective studies.
2. Age range: pediatric population (0–18 years)
3. Publication years: 2000–2024.
4. Language restrictions: English only.
5. Include any of the following interventions (in isolation or any combination): lumbar sympathetic block, epidural catheters, continuous sympathetic block, continuous epidural anesthesia, peripheral regional anesthesia, intravenous blocks, sympathetic nerve blocks, chemical sympathectomy, spinal cord stimulation, intrathecal anesthesia.

We identified 825 articles, and three independent reviewers performed title and abstract screening. Discrepancies that could not be resolved by consensus were resolved by the senior author. We identified 103 articles for full-text review, and 80 were excluded for multiple reasons (Fig. 1). Citation searching contributed to the addition of four studies that met the inclusion criteria. Finally, 27 articles were included in this review (Fig. 2).

2.3. Data extraction

We created an Excel spreadsheet after consensus was reached on important variables and outcomes relevant to this review. Two independent authors extracted and scrutinized the information. Discrepancies were resolved with the input of the principal investigator. Our data extraction focused on the following information: 1) research design, 2) patient characteristics, 3) CRPS characteristics such as type of CRPS, principal cause for CRPS development, diagnostic criteria and clinical findings, 4) treatment including prior and current treatment and indication for intervention, 5) characteristics of the intervention, such as the location of the intervention, medication used, and dosage, 6) concomitant treatments that may affect the outcome, 7) study outcome measures, including efficacy, pain assessment, follow-up, and procedure-related adverse events, and 8) resolution of symptoms.

3. Results

Most included studies were case reports (70%) and case series (19%) (Fig. 1). We identified a total of 183 patients aged 7–18 years, with the majority being female patients (81.4%). In 70.49 % of the cases, the lower extremities were the most affected part of the body, and in 83.06% of cases, CRPS was attributed to a known injury or trauma event of a specific body region (Table 1).

3.1. Interventional pain management therapies

Interventional pain management procedures for pediatric CRPS intend to mitigate pain and improve symptoms, facilitating engagement in rehabilitation [11].

In 92.89 % of cases included in this review, interventions were used after more conservative management was proven ineffective. The most common non-invasive treatment approaches before resorting to interventional procedures involved the use of various pain medications, including pregabalin, amitriptyline, and nonsteroid anti-inflammatory drugs (NSAIDs), in combination with physical and psychological therapy. We identified that 68.23% of the studies did not provide follow-up details after the procedures, especially in case reports (Table 2). Most studies evaluated the success of the intervention based on pain scale improvement, physical capability, or engagement in activities. From the studies that reported a follow-up, either immediate post-procedure or long-term, complete resolution of the symptoms was reported in 26.78% of the studies included (Fig. 3).

A retrospective chart review that analyzed 102 pediatric CRPS patients over an 11-year period who underwent regional anesthesia procedures (epidural and peripheral catheters, peripheral blocks, epidural blocks, and sympathetic blocks) combined with rehabilitation showed statistically significant and clinical improvements maintained during the intervention and persisting after 4 months [11]. Other observational studies, including 14 pediatric cases of CRPS, found that 28% of patients required interventional procedures (including lumbar epidural catheter placement, stellate ganglion blocks, and ankle blocks not otherwise specified).

Pediatric referral times showed notable variation, with a mean of 4.46 weeks, though some cases experienced significant delays averaging 63 weeks [6]. Despite these delays, pediatric outcomes were generally favorable, with 78.5% achieving full recovery and 14.5% partial recovery [6]. In contrast, adult CRPS typically presents with

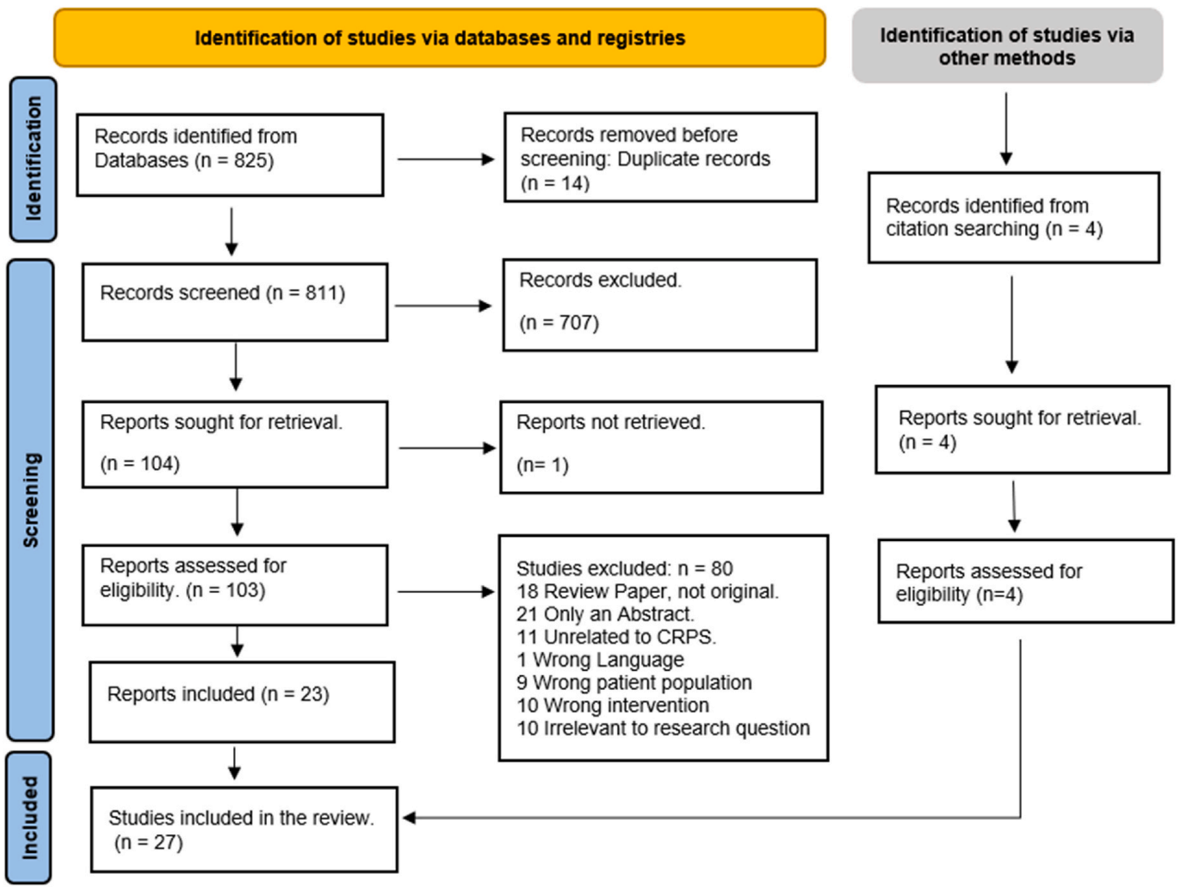

Fig. 1. Flowchart of the systematic literature review.

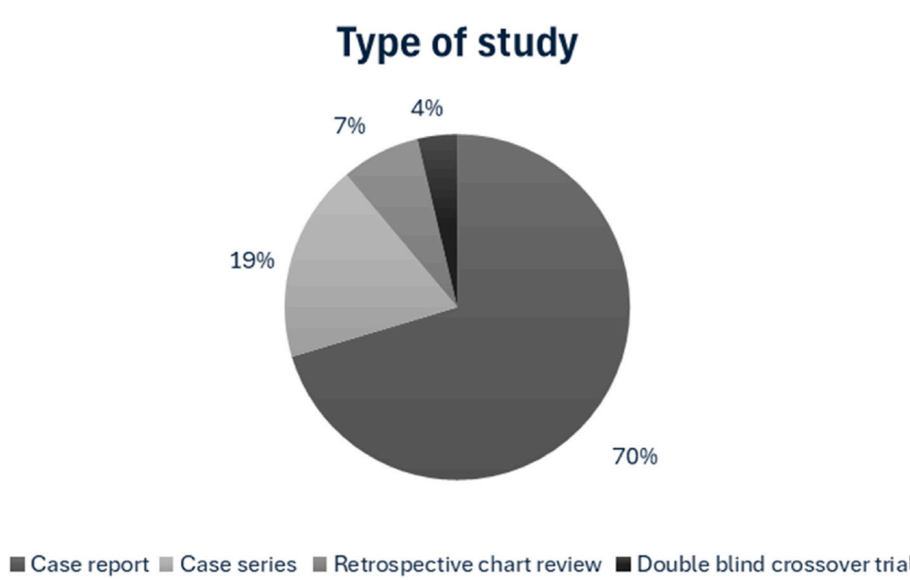

Fig. 2. Study types.

disproportionate pain and swelling distal to the injury site within 8 weeks post-injury, but referral delays can extend up to 50 weeks [34, 35]. This stark difference in referral patterns and outcomes between pediatric and adult populations highlights the importance of age-specific diagnostic and treatment approaches.

3.1.1. *Lumbar sympathetic block*

Lumbar sympathetic blocks are utilized in pediatric patients with CRPS, showing positive results in reported cases [8–10]. Theoretically, the expected benefit provided by LSBs is accomplished via the temporary interruption of sympathetic nerve signals, provoking a consequent change in efferent outflow. The rationale for the use of LSBs is based on the proposed pathophysiology of CRPS, which associates sympathetic

Table 1
Description of patients and CRPS characteristics.

	(n)
Total of patients	183
	(Range)
Age	7–18 years
Sex	n (%)
Female	149 (81.42 %)
Male	34 (18.58 %)
Affected part of the body	n (%)
Upper body	17 (9.29 %)
Lower body	129 (70.49 %)
Both extremities	13 (7.10 %)
Other	1 (0.55 %)
Not reported	23 (12.57 %)
Registered cause for CRPS	n (%)
Trauma	152 (83.06 %)
Spontaneously development	28 (15.30 %)
After IV. in the arm	1 (0.55 %)
Developed after surgery	2 (1.09 %)

CRPS: Chronic regional pain syndrome, IV: intravenous

Table 2
Interventions characteristics.

Indication for intervention	**n (%)**
Failed conventional management	170 (92.89 %)
Failed previous blocks or stimulators	12 (6.56 %)
First approach because of the severity of the symptoms	1 (0.55 %)
Physical Therapy after procedure	**n (%)**
Yes	155 (84.7 %)
Not mentioned	28 (15.3 %)
Follow up	**n (%)**
Long-term follow-up	52 (28.42 %)
Immediate post-procedure response follow-up	6 (3.28 %)
Not reported	125(68.3 %)
Resolution of symptoms	**n (%)**
Complete resolution	49 (26.78 %)
Partial improvement	7 (3.83 %)
No pain improvement	2 (1.09 %)
Not reported	125 (68.30 %)

dysregulation as responsible for the trophic and vasomotor symptoms in the affected limb [36–39].

Case reports have demonstrated the utility of LSB in achieving significant pain reduction. These reports document positive outcomes and varying degrees of pain relief following single or multiple blocks, with results sustained for up to five months [8,9].

A double-blind placebo crossover trial, which included 23 pediatric patients aged 10–18 years, evaluated the efficacy of LSB with lidocaine, administered intravenously (IV) versus via epidural catheters in children with CRPS. The study found that LSB produced greater reductions in verbal pain scores, brushed allodynia, and pinprick temporal summation compared to IV administration of lidocaine [10]. However, the authors noted an overall low success rate attributed to several factors: the lower lidocaine dose used, the lack of objective methods to evaluate appropriate LSB completion and possible difficulties associated with the indwelling catheters [10].

Table 3
Interventional pain management interventions.

Procedure/Intervention		Authors
Lumbar Sympathetic Block		[8–10]
Epidural Anesthesia	Epidural Block	[11,12]
	Epidural Catheter	[6,11,12–20]
Peripheral Procedures	Bier Block	[21]
	Stellate Ganglion block	[6,22,23]
	DRG block	[24,25]
	Peripheral blocks	[11,26,27]
	Clavicular catheters	[23]
	Axillary nerve block	[28]
	Continuous brachial plexus catheter	[29]
	Popliteal nerve block	[28,30,31]
	Ankle nerve block	[6]
Spinal cord stimulation		[17,32,33]
Intravenous Lidocaine		[10]

Some studies used multiple procedures; this classification was based on the last procedure used to achieve improvement.

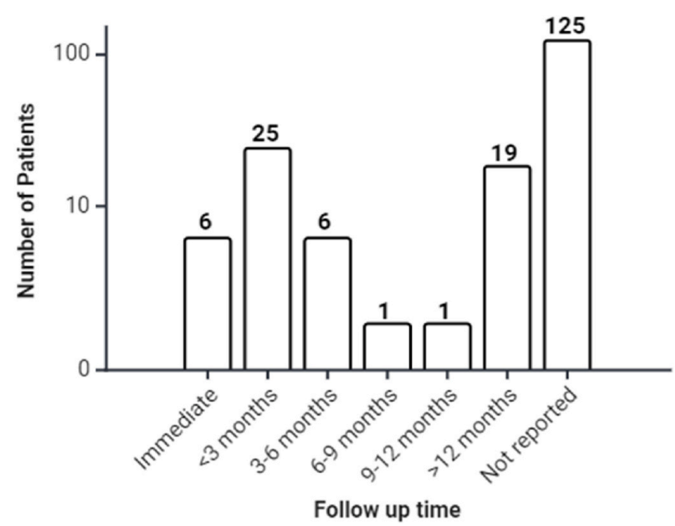

Fig. 3. Follow-up rate.

3.1.2. *Epidural anesthesia*

Epidural nerve blocks and catheters have demonstrated efficacy in managing pediatric CRPS, particularly in those unable to tolerate physical therapy [12,16,40]. Some reported cases have shown that these interventions can provide 50% prolonged pain relief and improve symptoms after continuous epidurals [12].

However, the response to epidural interventions varies. While some patients experience substantial pain reduction, as seen in cases where a continuous epidural infusion of bupivacaine led to significant improvement [14,16], others may exhibit resistance. Maneksha et al. described a case of a 12-year-old with CRPS who did not respond to epidural block, suggesting potential alterations in the dorsal horn cells and N-methyl-D-aspartate (NMDA) receptor activation as contributing factors [13].

Combining epidural therapy with comprehensive rehabilitation often enhances outcomes. Neuraxial analgesia was found to be effective in 50% of pediatric CRPS patients who failed conservative treatment, with additional improvements achieved through spinal cord stimulation in some cases [17]. Moreover, innovative approaches, such as the simultaneous use of multiple nerve block catheters have shown promise in rapidly improving severe CRPS symptoms [20].

3.1.3. *Peripheral procedures*

Peripheral interventional procedures have demonstrated considerable efficacy in managing pain associated with CRPS and other chronic pain conditions. These procedures encompass peripheral nerve blocks, continuous peripheral nerve catheters, intravenous regional anesthesia (IVRA), dorsal root ganglion (DRG) stimulation, and high-dose ketamine infusions [21,27,29].

One commonly employed approach involves peripheral nerve blocks and continuous catheters. For instance, one case report highlighted the successful use of continuous peripheral nerve catheters in a child with CRPS, leading to a significant reduction in pain intensity, from 10/10 on a Visual Analog Scale (VAS) to 0–2/10 [27]. Combining these blocks with glucocorticoids has shown to potentiate pain relief, reducing pain scores from 10/10 to 2/10 on VAS [31].

Dorsal root ganglion (DRG) stimulation has emerged as another therapeutic option based on the concept of targeting peripheral nerves. While studies reported that a substantial proportion of patients experienced significant pain reduction (≥50%) and improved functional status with DRG stimulation [23], the technical aspects of these interventions were poorly documented. Most publications, being case reports, failed to specify critical procedural details such as lead placement locations, stimulation parameters, or technical considerations specific to the pediatric population [25].

In addition to nerve-based interventions, intravenous regional anesthesia (IVRA) has been explored as a potential treatment for CRPS. The documented protocol involved exsanguination of the affected extremity, followed by tourniquet inflation and administration of ketorolac (0.5 mg/kg) and lidocaine (2 mg/kg) [21]. Studies reported variable response patterns, in one case the initial IVRA reduced the VAS score from 8/10 to 0/10, but pain gradually returned to baseline (VAS 8/10) over two weeks, necessitating a second IVRA treatment [19]. On the other hand, a patient achieved complete symptom resolution following IVRA, the durability and consistency of response varied across cases. Combinations of interventions have been investigated, with highly heterogenous protocols and study designs. The combination of continuous sciatic peripheral nerve block and parenteral ketamine reduced VAS scores from 8/10 to 1/10 [26]. High-dose ketamine infusions as part of comprehensive multimodal therapy have shown promise in treating refractory CRPS cases [29]. The protocol involved ketamine administration at gradually increasing doses (3–5 mg/kg/h) combined with midazolam over a 5-day period. These infusions were implemented within a comprehensive treatment approach, targeting multiple pain mechanisms in patients who had failed conventional therapies [29].

3.1.4. Spinal cord stimulation

Spinal cord stimulation (SCS) is reserved for severe cases of chronic pain when other treatment approaches have been appropriately employed without success. The expected benefit of SCS is grounded in Melzack and Wall's 1965 gate control theory, suggesting that pain control is achieved by stimulating nerve fibers in the spinal cord, inhibiting pain signal conduction to the brain [41]. Other mechanisms suggest that SCS produces a direct inhibition of wide dynamic range neurons modulating pain signaling [42] and decreasing the expression of anti- and proinflammatory cytokines in both the CRPS-affected limb and the contralateral limb after treatment [43].

A case report showed positive pain reduction after the implantation of SCS in a teenager with CRPS of the right lower extremity. After the patient failed to respond to ketamine infusion, physical rehabilitation, and other conservative methods, SCS was trialed and reduced pain from a previous level of 10/10 to 4/10 [32]. A case series was conducted on 7 patients who failed conservative medical management and sympathetic blocks using guanethidine. The placement of SCS showed positive results for pain reduction in most individuals [33]. A previously discussed case series of 10 patients showed that two individuals experienced inadequate symptom control with epidural catheters. Consequently, these patients underwent SCS placement, resulting in complete control and resolution of CRPS symptoms [17]. These positive results support using SCS as a viable option for treating intractable pain in pediatric CRPS [44]. The mean age of patients in these studies was 11.6 years, with the youngest reported patient being 8 years old [2,33,44]. Currently, there is no specified age cutoff for SCS use in pediatric populations, though careful patient selection and risk-benefit assessment remain crucial for this intervention.

3.2. CRPS diagnosis and classification

Only 22.4 % of our included studies used clear diagnostic criteria to classify CRPS, with type 1 being the most common diagnosis [6,9,13,18,19,21,24–30,32,33]. From those studies, 64.5% used the Budapest Criteria [6,11,16–18,26,29,31] aligning with the reports of previous studies [7,45]. Clinical suspicion based on symptoms, laboratory workup, meticulous physical and history examination, and exclusion of other conditions still hold the most valuable information for diagnosing CRPS in children. Although the Budapest and IASP criteria can assist in diagnosis, they have yet to be validated for pediatric CRPS.

3.3. Trauma onset of CRPS vs. spontaneous onset of CRPS

While the epidemiology studies show that the incidence in children is rare around 1.14–1.2/100.000/year whereas in adults there is a range from 5.5 to 26.2/100.000/year [46,47]. Our study reveals a notable finding of 15.30% of pediatric CRPS cases presented with a spontaneous onset, a proportion that is markedly higher than typically observed in adult populations where is relatively close to 7% reported in recent studies [48]. The absence of a clear precipitating event in a significant portion of pediatric cases implies that factors beyond physical trauma may play a crucial role in the development of CRPS in children [49]. This distinction could potentially explain the varied responses to interventions observed between pediatric and adult populations. The unique characteristics of pediatric CRPS, particularly the higher prevalence of spontaneous onset, warrant further investigation into age-specific pathophysiological processes and may necessitate tailored therapeutic approaches for this younger demographic.

3.4. Challenges and limitations

Most of our included studies provide low-quality evidence supporting the efficacy of interventions in treating pediatric CRPS, as identified studies included case-control studies, case series, and retrospective studies. Our included studies revealed a lack of consensus regarding diagnostic criteria, treatment protocols, and assessment methods. Data search was limited to English publications, which may have overlooked relevant literature and cultural differences in the presentation and management of this rare condition. Little progress has been made in generating high-quality evidence to clarify the role of interventional treatments for pediatric CRPS. This is consistent with other studies involving invasive procedures in pediatric patients, considering the methodological complexities and ethical challenges of exploring research initiatives with the pediatric population and invasive interventions [50]. This review is limited in its ability to provide definitive clinical guidelines for the utilization of interventional techniques, but does summarize interventions that have been documented as successful and safe in the literature. All things considered, readers should be aware of the high risk of bias in the included studies, given the inherent methodological limitations, as well as the tendency for case reports to present promising results that may not accurately represent the full extent of an intervention's benefit.

4. Conclusions

This review summarizes the different interventional pain management methods utilized to treat pediatric CRPS. While techniques such as continuous epidural anesthesia, lumbar sympathetic blocks, peripheral procedures, and spinal cord stimulation have been safely and successfully used as part of a multimodal treatment strategy, the lack of high-quality evidence and specific protocols for CRPS diagnosis and management in pediatric patients calls for further research.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Christine Hunt reports a relationship with Nevro Corp that includes: funding grants, not related to this study. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.inpm.2024.100532.

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