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Treatment strategies for anterior cutaneous nerve entrapment syndrome in children: A systematic review☆

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ABSTRACT

Background: Anterior cutaneous nerve entrapment syndrome (ACNES) is a frequently overlooked cause of chronic abdominal pain in children. Currently, both nonsurgical and surgical treatment options are available to treat this disease. The objective was to give insight into the success rate of different treatment strategies for children with ACNES, and provide treatment recommendations for physicians based on the published evidence.
Method: A literature search of PubMed, Embase.com and the Wiley/Cochrane Library was conducted for studies published up to 25 February 2020. Randomized controlled trials, prospective or retrospective cohort studies, meta-analyses and literature reviews describing the outcome of different treatment strategies for children (<18 years old) with ACNES with a follow-up duration of at least four weeks were included.
Results: Six studies, involving 224 patients, were included with an overall quality reported to be between fair and poor. Treatment success of local injections with an anesthetic agent into the trigger point ranged from 38% to 87% with a follow-up ranging from 4 weeks to 39 months. In addition, treatment success of anterior neurectomy ranged from 86% to 100%, with a follow-up duration ranging from 4 weeks to 36 months.
Conclusion: A step-up treatment strategy should be applied when treating pediatric patients with ACNES. This strategy starts with an injection with a local anesthetic agent, reserving surgery (anterior neurectomy) as a viable option in case of persistent pain.
Level of evidence: II.

Contents

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Chronic abdominal pain (CAP) in the pediatric population is common, with an estimated prevalence of 10%–19% [1–5]. The differential diagnosis of CAP is extensive, but pain originating from the abdominal wall is frequently overlooked [6–10]. Recently, anterior cutaneous nerve entrapment syndrome (ACNES) has become increasingly recognized as a possible cause of CAP [7,11–14]. Although the exact pathophysiology of ACNES is unknown, it is postulated that it is the result of mechanical compression on or traction of cutaneous branches from the intercostal nerves (Th7–Th12) [7,11,12]. Data regarding the exact incidence of ACNES in the pediatric population are lacking, although recently ACNES was diagnosed in 13% of children initially diagnosed with functional abdominal pain [15].

The diagnosis of ACNES is based upon patient history and physical examination. Pain is the most dominant symptom. In addition, coughing, body stretching, or any type of movement or more intense use of abdominal muscles may aggravate the pain [11]. At physical examination painful abdominal palpation, positive pinch test and Carnett's sign may be found [11,16]. Furthermore, altered skin sensibility demonstrated by a swab or alcohol-soaked gauze strongly supports to the diagnosis [11,16,17]. In addition, one can inject a local anesthetic into the trigger point. Pain relief for several hours or days confirms the diagnosis [11,17,18].

Currently, nonsurgical and surgical treatment strategies are available for ACNES, with an overall success rate of up to 85% in the adult population [11,17,19–23]. Initially, the preferred nonsurgical treatment is one or multiple injections with a local anesthetic agent (e.g. lidocaine or bupivacaine) into the trigger point, with or without corticosteroids and with or without ultrasound guidance [11,12,16,17,24–27]. Surgical treatment, consisting of a neurectomy, should be considered if multiple injections with a local anesthetic agent are only successful for a short period of time [11,17,19–23,28,29].

Data regarding the outcome of these treatment strategies in the pediatric population are lacking. The aim of this systematic review is to summarize the currently available literature regarding the outcome of the different treatment strategies of ACNES in the pediatric population and to provide treatment recommendations for physicians.

1. Methods

We conducted a systematic literature review (SR) according to the PRISMA statement [30]. The complete protocol was registered at PROSPERO: International prospective register of systematic review with identification number CRD42019117208. PubMed, Embase.com and Wiley/Cochrane Library were searched up to 25 February 2020. The following terms were used (including synonyms and closely related words) as index terms or free-text words: 'ACNES' and 'child' or 'infant' or 'adolescent' (see Appendix A for the full search strategy for each resource). Duplicate articles were excluded. References of identified articles were screened for additional relevant articles. Prior to the selection articles not written in English were excluded.

Eligible for inclusion were studies that investigated the outcome of different treatment strategies for children (<18 years old) with ACNES and had a follow-up period of at least four weeks. Criteria for ACNES were localized abdominal pain during palpation and a positive Carnett test [11,16]. Eligible study designs were randomized controlled trials (RCTs), prospective or retrospective cohort studies, meta-analyses or literature reviews. Other study designs, such as case series or case reports, were excluded. Study selection, data extraction and quality assessment were done independently by two reviewers. In case of disagreement, a third reviewer was consulted. Data extraction was performed using a standardized electronic data collection sheet (see Appendix B). The Downs & Black checklist was used for quality assessment [31]. Primary outcome for this systematic review was treatment success defined as no pain or less pain after treatment. Data are analyzed descriptively and will be displayed as mentioned in the original manuscript. Additional information regarding the protocol of the SR can be found through PROSPERO #CRD42019117208.

2. Results

The search yielded a total of 149 articles: 39 in PubMed, 105 in Embase.com and 5 in the Wiley/Cochrane Library. Eight articles were selected for full-text assessment. Two articles were excluded because of no diagnostic criteria for ACNES ($N=1$) and no mentioning of a follow up period ($N=1$). Six articles were included in the SR. A flowchart of study identification and selection is provided in Fig. 1.

2.1. General characteristics of included studies

General characteristics of the six included studies are shown in Table 1. Designs of the included studies were prospective cohort studies ($N=4$) and retrospective cohort studies ($N=2$). Methodological quality was assessed as fair for three studies [12,15,29], and as poor for three other studies [24,28,32] (see Appendix B). In total, 224 patients were included in these six studies with a median (range) of 32 (6–85) patients. The follow-up period ranged from 4 weeks to 39 months. One study [12] had a follow-up duration of 2–12 weeks. Three patients from this study were excluded from further analysis owing to a follow-up duration of less than four weeks. Large heterogeneity exists between the included studies regarding (but not limited to) duration of follow-up, diagnostic criteria and type of local anesthetic agents (see Appendix D).

2.2. Excluded studies

Two retrospective articles were excluded. One article described the outcome of neurectomy in nine patients with ACNES but did not report the diagnostic criteria for ACNES. The second article described the outcome of trigger point injections and neurectomy in 12 patients, but data regarding the follow-up period were lacking.

2.3. Outcome of treatment strategies

2.3.1. Outcome of trigger point injections with a local anesthetic agent

Table 2 shows our primary outcome (treatment success) of local injections with an anesthetic agent into the trigger point. A total of 142 patients received trigger point injections. The number of injections per patient ranged from 1 to 7. One study [12] performed ultrasound-

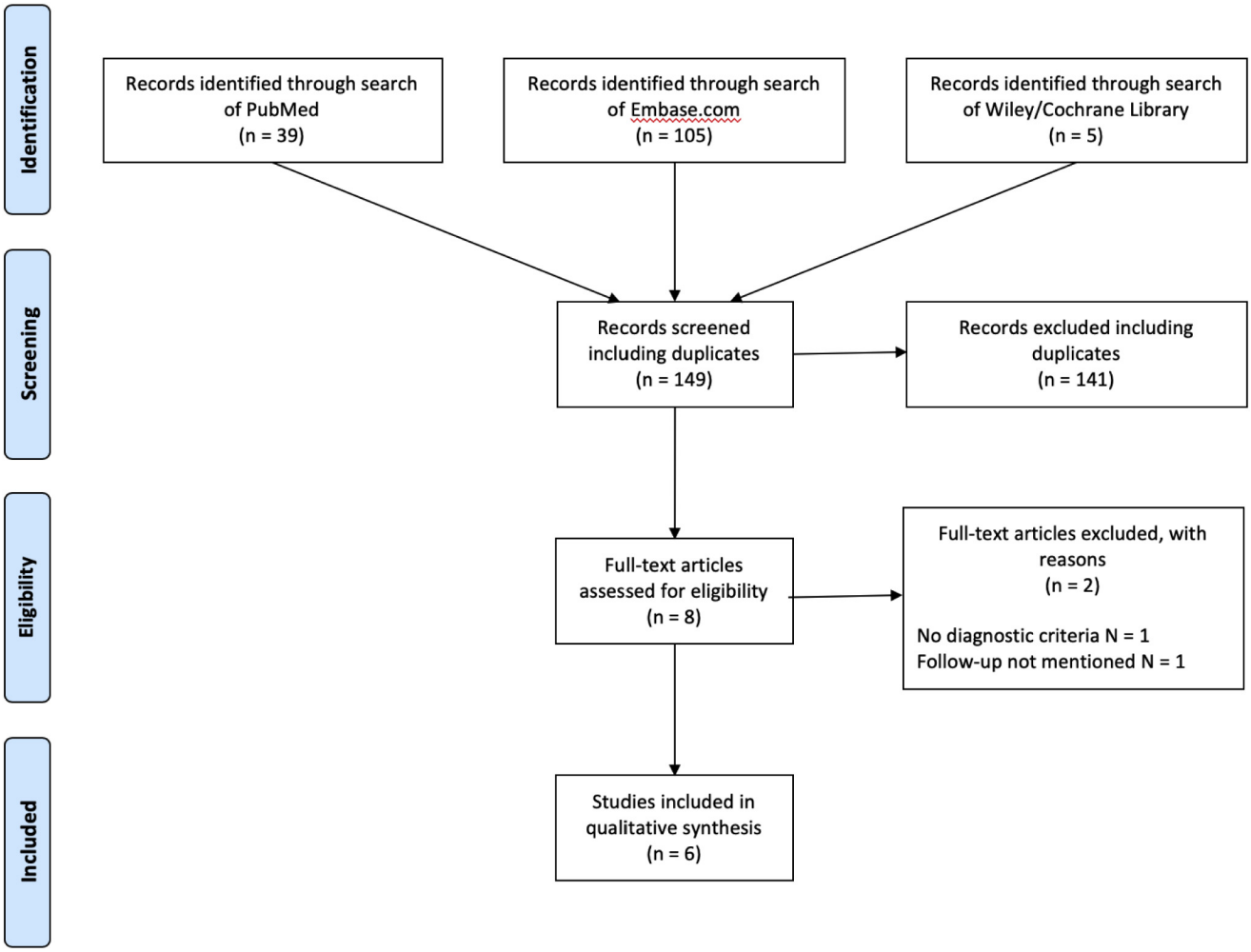

Fig. 1. Flowchart of study identification, inclusion and selection.

guided subfascial injections with 40 mg 1% lidocaine and 4 mg dexamethasone, whereas the other two studies [15,24] initially performed injections with 5 ml 1% lidocaine using the free hand technique and added 40 mg methylprednisolone if further treatment was needed. Treatment success ranged from 38% to 87%, with a follow-up duration ranging from 4 weeks to 39 months. One study [24] mentioned a short-term pain reduction of at least 50% in 83 (98%) patients. Two studies [12,15] performed an anterior neurectomy if initial trigger point injections were not successful.

2.3.2. Outcome of anterior neurectomy

Table 3 shows the primary outcome for treatment success of anterior neurectomy and the number of patients that underwent anterior neurectomy per study. A total of 104 patients underwent anterior neurectomy. Treatment success ranged from 86% to 100%, with a follow-up duration of 4 weeks to 36 months. One prospective study [29] ($N = 60$) mentioned that 78% of the patients gained pain relief after anterior neurectomy, but occasionally experienced some pain during physical exertion.

Table 1
Patient characteristics.

	Kifer [12]	Siawash [15]	Siawash [24]	Scheltinga [28]	Siawash [29]	Armstrong [32]
General						
Year published	2018	2016	2017	2011	2017	2017
Design	Prospective cohort	Retrospective cohort	Prospective cohort	Prospective cohort	Prospective cohort	Retrospective cohort
Patient characteristics						
No. of patients included	38	12[d]	85	6	60	26
Age (years)	15 (9–17)	15 (2)[a]	15 (8–17)	15 (9–16)	15 (2)[a]	15 (13·8–17·3)
Female, *no.* (%)	28 (74)	11 (92)	66 (78)	Unknown	48 (80)	21 (81)
Previous surgeries, *no. (%)*	3 (8)	Unknown	Unknown	Unknown	0 (0)	4 (15)
Duration of follow-up	1.7 years (1–2.7 years)	2–12 weeks[c]	17 months (4–39)	17 months (4–39)	4–6 weeks[c]	25.5 months (15–36)
Pain score prior to treatment	Unknown	7 (5–9)[b]	8 (6–9)	Unknown	6–9[c]	9·4 (6–10)[b]

Data displayed as median (range), unless stated otherwise.
[a] Data displayed as mean (SD).
[b] Data displayed as mean (range).
[c] Data displayed as range.
[d] Three patients will be excluded from further analysis.

Table 2
Primary outcome: treatment success of trigger point injections.

	Kifer [12] N = 38	Siawash [15] N = 9	Siawash [24] N = 85
Used treatment	Ultrasound-guided subfascial injection of 40 mg 1% lidocaine and 4 mg dexamethasone	1st treatment: injection with 5 ml 1% lidocaine using the free-hand technique Consecutive treatment: injection with 4 ml 1% lidocaine and 1 ml methylprednisolone (40 mg) using the free-hand technique	1st treatment: injection with 5 ml 1% lidocaine using the free-hand technique Consecutive treatment: injection with 4 ml 1% lidocaine and 1 ml methylprednisolone (40 mg) using the free-hand technique
No. of injections per patient	2 (1–7)	2–4[a]	1–4[a]
Results after injection, *no. (%)*			
Pain free	33 (87)	2 (42)	32 (38)
No change	5 (13)	7 (58)	53 (62)

Data displayed as median (range) unless stated otherwise.
[a] Data displayed as range.

Two prospective studies ($N = 6$ and $N = 60$) and one retrospective study ($N = 26$) mentioned no perioperative or postoperative complications for those children that underwent an anterior neurectomy, indicating that complications were absent [28,29,32].

2.3.3. Length of hospital stay

One prospective study ($N = 6$) and one retrospective study ($N = 26$) showed that all patients were discharged at the day of surgery (anterior neurectomy) [28,32].

2.3.4. Recurrence rate of ACNES after anterior neurectomy

Only one prospective ($N = 38$) study and one retrospective study ($N = 26$) mentioned the recurrence rate. The prospective study showed new onset (i.e. pain in a different location) of ACNES in 3 patients (8%) within the follow-up period of (median (range)) 1.7 (1–2.7) years [12]. The retrospective study ($N = 26$) showed a recurrence of ACNES in 11 patients (42%) with a median time until recurrence of 3 (1–20) months [32]. The authors of the latter study do not specify whether the pain recurred in the same location or in a different location (i.e. new onset).

2.3.5. Hindrance during sports and school activities

One prospective study ($N = 85$) mentioned that 76 (89%) patients had significant hindrance during sports and school activities before treatment. Posttreatment hindrance was not specified [24].

2.3.6. Absence from school

Only one prospective study ($N = 6$) mentioned that the mean (range) number of days patients were absent from school before treatment was 25 (10–31) [28].

3. Discussion

Data regarding the outcome of nonsurgical and surgical treatment of ACNES in the pediatric population are scarce, and even more high-quality data, such as RCTs, are lacking. Based upon the low quality of data identified, we carefully conclude that nonsurgical treatment of ACNES in the form of injections with a local anesthetic agent is a viable first treatment strategy with success rates reported between 38% and 87%. In case of failure, an anterior neurectomy can be performed with an expected success rate of 86% to 100%. Overall, the reported success rates are high, but this systematic review points out the necessity of high-quality data regarding the treatment outcomes for this disease in the pediatric population.

Initially, nonsurgical treatment options for ACNES should be considered. In particular an injection with a local anesthetic agent should be undertaken owing to both its diagnostic and therapeutic nature. It strengthens the diagnosis of ACNES if the patient experiences pain relief after an injection with a local anesthetic agent [11,17,18]. In our opinion, this is an office procedure that can safely be executed in an outpatient environment. As mentioned in the pediatric population, injections with local anesthetic agents are reported to be effective in 38% to 87% of the children with ACNES. This is in large contrast to the reported effectiveness of this treatment strategy in the adult population of only 33% [17,19,33]. Explanations for these differences in reported success rates of this treatment might be the use of different anesthetic agents, with or without corticosteroids (see Appendix D). However, a recent RCT in adults showed that adding methylprednisolone had no significant effect on the treatment outcome [33]. Another explanation might be the use of ultrasound-guided injections instead of free-hand technique. An ultrasound-guided technique allows for a more accurate injection of the anesthetic agent, although short-term and long-term pain relief in adults did not differ between both techniques in low-quality studies [19,25,34–36]. However, the ultrasound-guided technique might be useful to use in the pediatric population. In general, children have less abdominal fat than adults, increasing the accuracy of the ultrasound and making it easier to visualize the needle during the procedure [37–39]. But still based upon the relatively high treatment success of injections and their diagnostic capabilities, we opt for a step-up approach starting with the least invasive (injection) and reserving the most invasive (surgery) for those not responding or with temporary effect. Avoiding surgery in the pediatric population should always be attempted as a recent systematic review concluded that the effects of general anesthesia on neurocognitive development in children older than 4 years have been investigated scarcely [40]. Since the effects of general anesthesia in children older than 4 years are largely unknown, treatment options without the need to use general anesthesia should be considered first.

An alternative, relatively painless, nonsurgical treatment option is pulsed radiofrequency (PRF), which, in adults, has a short-term treatment success of 38% to 50% 6–8 weeks after PRF [41,42]. Treatment success in these studies was defined as decrease in pain of more than 50%. PRF has a long-term treatment success (up to 15 months post-PRF) ranging

Table 3
Primary outcome: treatment success of anterior neurectomy.

	Kifer [12] N = 5	Siawash [15] N = 7	Scheltinga [28] N = 6	Siawash [29] N = 60	Armstrong [32] N = 26
Results after neurectomy, *no.* (%)					
Pain free	5 (100)	6 (86)	6 (100)	47 (78)	23 (88)

from 8% to 42% [41–43]. A recent RCT compared the effect of PRF treatment and neurectomy in adult patients with ACNES. They showed that a higher proportion of treatment success (8 weeks post-treatment) was detected in the group that underwent neurectomy compared to the group that underwent PRF (61% vs 38%); however this was not statistically significant [42]. In addition, long-term treatment success (6 months post-treatment) was significantly higher in the group undergoing a neurectomy compared to PRF (50% vs 13%) [42]. Based on the results in the recent RCT, PRF might be a viable treatment prior to surgery in children with ACNES. However, at the time of this review, no studies were available regarding the effect of PRF in the pediatric population.

Anterior neurectomy for ACNES is a viable option in case of persistent pain after injection of local anesthetics. In the adult population, a success rate is reported of +/− 85% which is comparable to the success rate identified by this review for the pediatric population [11,17,20–23]. Postoperative complications include hematoma/seroma formation and wound infection [17,22,23]. The exact incidence of these postoperative complications is unknown. However, they are rare and as mentioned above did not occur in the children that underwent neurectomy in the included studies of this review. As described above, the recurrence rate of ACNES in children after anterior neurectomy ranges from 8% to 42%, whereas the recurrence rate of ACNES after anterior neurectomy in adults ranges from 10% to 16% [11,22,23]. The difference in recurrence rate could be explained by several factors. First, it is unclear whether recurrence is defined as recurrence of pain in the same location as before treatment or as residual disease, or if pain occurred in a different location (i.e. new onset). Secondly, it is known that nerve regeneration decreases with age and that aged nerves are less likely to take over the innervation of the resected nerve [44,45]. This means that other nerves in children might be more likely to take over the innervation of the resected nerve. Thirdly, the follow-up duration greatly differs between these studies, ranging from 3 months to 93 months. Some patients might experience recurrence of ACNES after the follow-up period. Finally, it is unclear if the included patients had any risk factors associated with the development or recurrence of ACNES, like surgery within the abdominal area or blunt force abdominal trauma [11,17,22,28,46–48]. If there is recurrence of pain, a posterior neurectomy could be performed. This has a success rate of 71% in the adult population, whereas a secondary anterior neurectomy has a success rate of only 30% [23]. However, this is based on a small retrospective observational cohort study. High-quality studies should indicate if posterior neurectomy is superior compared to anterior neurectomy in patients with recurrent pain.

To our knowledge, this is the first systematic review reporting the outcome of treatment options for ACNES in the pediatric population. Still several limitations are present. A major limitation of this review is the large heterogeneity between the included studies. It is possible that the duration of follow-up, type of anesthetic agent and difference in diagnostic criteria are of influence on the outcome of the treatment options for ACNES and thus are of influence on the results of this review. Therefore, a proper meta-analysis could not be performed. Secondly, only cohort studies with a small number of patients and without a control arm were available, and two potential studies had to be excluded since important data were missing. Thirdly, we chose a follow up period of at least 4 weeks. This might be considered as too short-term. It will be of more interest whether or not recurrence will occur on long-term follow-up.

4. Conclusion

Overall, this systematic review shows that high quality data regarding the outcome of treatment options for ACNES in the pediatric population are lacking and points out the necessity of well-designed RCTs. Based upon the available data we (carefully) conclude that a step-up approach should be applied starting with injections with a local anesthetic agent reserving neurectomy for those with limited effect of these injections.

Acknowledgment

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Appendix A. Search strategies

A.1. Search strategy for PubMed (25 February 2020)

Search	Query	Items found
#11	(#8 AND #10)	**39**
#10	child*[tw] OR schoolchild*[tw] OR infan*[tw] OR adolescen*[tw] OR pediatri*[tw] OR paediatr*[tw] OR neonat*[tw] OR boy[tw] OR boys[tw] OR boyhood[tw] OR girl[tw] OR girls[tw] OR girlhood[tw] OR youth[tw] OR youths[tw] OR baby[tw] OR babies[tw] OR toddler*[tw] OR teen[tw] OR teens[tw] OR teenager*[tw] OR newborn*[tw] OR postneonat*[tw] OR postnat*[tw] OR perinat*[tw] OR puberty[tw] OR preschool*[tw] OR suckling*[tw] OR picu[tw] OR nicu[tw] OR "Arthritis, Juvenile"[Mesh] OR "Myoclonic Epilepsy, Juvenile"[Mesh] OR "Leukemia, Myelomonocytic, Juvenile"[Mesh] OR "Xanthogranuloma, Juvenile"[Mesh] OR "Juvenile Delinquency"[Mesh] OR "Corneal Dystrophy, Juvenile Epithelial of Meesmann"[Mesh]	**4,251,854**
#8	abdominal wall pain[tiab] OR abdominal cutaneous nerve entrapment syndrome*[tiab] OR anterior cutaneous nerve entrapment syndrome*[tiab] OR anterior abdominal nerve entrapment syndrome*[tiab] OR ("Abdominal Wall"[MeSH Terms] AND "Nerve Compression Syndromes"[MeSH Terms])	**182**

A.2. Search strategy for Wiley/Cochrane Library (25 February 2020)

ID	Search	Hits
#1	("abdominal wall pain" OR "abdominal cutaneous nerve entrapment syndrome*" OR "anterior cutaneous nerve entrapment syndrome*" OR "anterior abdominal nerve entrapment syndrome*"):ti,ab,kw	**31**
#2	(infan* or child* or adolescen* or pediatric* or paediatric* or pube* or juvenil* or school* or newborn* or "new-born*" or "neo-nat*" or neonat* or premature* or postmature* or "pre-mature*" or "post-mature*" or preterm* or "pre-term*" or baby or babies or toddler* or youngster* or preschool* or kindergart* or kid or kids or playgroup* or "play-group*" or playschool* or prepube* or preadolescen* or "junior high*" or highschool* or "senior high" or "young people*" or minors):ti,ab,kw	**289,490**
#3	#1 AND #2	**5**

CENTRAL: 5

A.3. Search strategy for Embase.com (25 February 2020)

No.	Query	Results
#3	#1 AND #2	**105**
#2	adolescen*:ti,ab,kw OR 'adolescence'/exp OR 'adolescent coping orientation for problem experiences'/exp OR 'adolescent development'/exp OR 'adolescent disease'/exp OR 'adolescent health'/exp OR 'adolescent parent'/exp OR 'adolescent pregnancy'/exp OR 'adolescent smoking'/exp OR 'adolescent'/exp OR 'adolescent-family inventory of life events and changes'/exp OR babies:ti,ab,kw OR baby:ti,ab,kw OR 'birth weight'/exp OR boy:ti,ab,kw OR boyhood:ti,ab,kw OR boys:ti,ab,kw OR 'brazelton neonatal behavioral assessment scale'/exp OR 'child abuse'/exp OR 'child advocacy'/exp OR 'child behavior checklist'/exp OR 'child behavior'/exp OR 'child care'/exp OR 'child death'/exp OR 'child health care'/exp OR 'child health'/exp OR 'child nutrition'/exp OR 'child parent relation'/exp OR 'child psychology'/exp OR	**5,503,926**

(continued on next page)

(continued)

No.	Query	Results
	'child restraint system'/exp OR 'child safety'/exp OR 'child welfare'/exp OR child*:ti,ab,kw OR 'child'/exp OR 'childhood disease'/exp OR 'childhood mortality'/exp OR 'childhood'/exp OR girl:ti,ab,kw OR girlhood:ti,ab,kw OR girls:ti,ab,kw OR 'high risk infant'/exp OR infan*:ti,ab,kw OR 'infant disease'/exp OR 'infant mortality'/exp OR 'infant nutrition'/exp OR 'infant welfare'/exp OR 'infanticide'/exp OR 'infantile diarrhea'/exp OR 'infantile hypotonia'/exp OR 'juvenile delinquency'/exp OR neonat*:ti,ab,kw OR 'neonatal weight loss'/exp OR 'newborn disease'/exp OR 'newborn morbidity'/exp OR 'newborn period'/exp OR newborn*:ti,ab,kw OR 'newborn'/exp OR nicu:ti,ab,kw OR 'only child'/exp OR paediatr*:ti,ab,kw OR pediatri*:de,ab,ti OR 'pediatric advanced life support'/exp OR 'pediatric anesthesia'/exp OR 'pediatric cardiology'/exp OR 'pediatric hospital'/exp OR 'pediatric intensive care nursing'/exp OR 'pediatric nurse practitioner'/exp OR 'pediatric nursing'/exp OR 'pediatric rehabilitation'/exp OR 'pediatric surgery'/exp OR 'newborn hypoxia'/exp OR 'pediatric ward'/exp OR 'pediatrics'/exp OR perinat*:ti,ab,kw OR 'perinatal development'/exp OR 'perinatal period'/exp OR 'persistent hyperinsulinemic hypoglycemia of infancy'/exp OR picu:ti,ab,kw OR postnat*:ti,ab,kw OR 'postnatal care'/exp OR 'postnatal development'/exp OR 'postnatal growth'/exp OR postneonat*:ti,ab,kw OR preschool*:ti,ab,kw OR puberty:ti,ab,kw OR 'runaway behavior'/exp OR 'school child':ti,ab,kw OR schoolchild*:ti,ab,kw OR 'severe myoclonic epilepsy in infancy'/exp OR suckling*:ti,ab,kw OR teen:ti,ab,kw OR teenager*:ti,ab,kw OR teens:ti,ab,kw OR toddler*:ti,ab,kw OR 'transient hypogammaglobulinemia of infancy'/exp OR youth:ti,ab,kw OR youths:ti,ab,kw	
#1	'abdominal wall'/exp AND 'nerve compression'/exp OR 'anterior cutaneous nerve entrapment syndrome'/exp OR 'abdominal wall pain':ti,ab,kw OR 'abdominal cutaneous nerve entrapment syndrome*':ti,ab,kw OR 'anterior cutaneous nerve entrapment syndrome*':ti,ab,kw OR 'anterior abdominal nerve entrapment syndrome*':ti,ab,kw	**337**

Appendix B. Data-extraction form

B.1. General information

Date form completed

(dd/mm/yyyy)

Name of person extracting data

Report title

(Title of paper, author and year of publication)

Additional features

(Country of origin, source of funding)

Publication type

(e.g. full report / abstract / letter)

Start date and end date

Notes:

B.2. Methods

	Description	Location in text *(page & fig/table)*
Aim/objectives of study		
Study design		
Study Inclusion criteria		
Study exclusion criteria		
Diagnostic criteria		
Treatment options		
Duration of follow-up		
Notes:		

B.3. Participant characteristics

	Description	Location in text *(page & fig/table)*
Number of patients included		
Number of patients lost-to follow-up		
Missing data		
Age		
Gender		
Ethnicity		
Medical history		
Diagnostic delay		
Location of abdominal pain		
Previous surgeries		

B.4. Outcome and results

4A Primary outcomes:

	Description as stated in report/paper	Location in text *(pg & ¶/fig/table)*
Outcome name		
Outcome definition *(with diagnostic criteria if relevant)*		
Tool and/or Unit of measurement *(if relevant)*		
Imputation of missing data *(e.g. assumptions made for ITT analysis)*		
Assumed risk estimate (*e.g. baseline or population risk noted in Background)*		
Pretreatment pain score (e.g. VAS, NRS) (if applicable)		
Used treatment		
Number of injections (if relevant)		
Results after treatment (i.e. pain free, less pain or no change)		
Appropriateness of statistical methods		
Reanalysis possible		
Notes:		

4B Secondary outcomes:

	Definition used in study
Reference standard	
Statistical techniques used	
Measurement tool or method used	
Unit of measurement	
Number of patients *(if relevant)*	
Results (e.g. site of recurrence, complications) (if relevant)	
Median	
Mean	
Range	

Appendix C. Quality assessment of the included nonrandomized studies using the Downs & Black checklist.[1]

	Kifer et al.[2]	Siawash et al.[3]	Siawash et al.[4]	Scheltinga et al.[5]	Siawash et al.[6]	Armstrong et al.[7]
Q1: Aim clearly described?	Yes	Yes	Yes	Yes	Yes	Yes
Q2: Outcomes clearly described?	Yes	Yes	Yes	No	Yes	No
Q3: Patients characteristics clearly described?	Yes	Yes	Yes	Yes	Yes	Yes
Q4: Interventions clearly described?	Yes	Yes	Yes	Yes	Yes	Yes
Q5: Principal confounders clearly described?	No	No	No	No	No	No
Q6: Main findings clearly described?	Yes	Yes	Yes	Yes	Yes	Yes
Q7: Random variability for main outcome provided?	Yes	Yes	Yes	No	Yes	Yes
Q8: Adverse events reported?	No	No	No	No	No	No
Q9: Loss-to-follow up reported?	Yes	Yes	Yes	Yes	Yes	Yes
Q10: Actual p-value reported?	Yes	No	No	No	Yes	No
Q11: Sample asked to participate representative of the population?	Yes	Yes	Yes	Unable to determine	Unable to determine	Unable to determine
Q12: Sample agreed to participate representative of the population?	Unable to determine	Yes	No	Unable to determine	Unable to determine	Unable to determine
Q13: Staff participating representative of the patients' environment?	Yes	Yes	No	No	No	Yes
Q14: Attempt to blind participants?	No	No	No	No	No	No
Q15: Attempt to blind assessors?	No	No	No	No	No	No
Q16: Data dredging results stated clearly?	Yes	Yes	Yes	Yes	Yes	Yes
Q17: Analysis adjusted for length of follow up?	Unable to determine	Unable to determine	Yes	Yes	No	No
Q18: Appropriate statistics?	Yes	Yes	Yes	Yes	Yes	Yes
Q19: Reliable compliance?	Yes	Yes	Yes	Yes	Unable to determine	Yes
Q20: Accurate outcome measures?	Yes	Yes	Yes	Yes	Yes	Yes
Q21: Same population?	No	No	No	No	No	No
Q22: Participants recruited at the same time?	Yes	Yes	Yes	Yes	Yes	Yes
Q23: Randomized?	No	No	No	No	No	No
Q24: Adequate allocation concealment?	No	No	No	No	No	No
Q25: Adequate adjustment for confounders?	No	No	Yes	Unable to determine	Yes	No
Q26: Loss of follow up reported?	Yes	Yes	Yes	Yes	Yes	Yes
Q27: Power calculation?	Unable to determine	No	No	No	No	No

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Appendix D. Additional information regarding the included studies

Additional information on general characteristics: diagnostic criteria and interventions	
Kifer et al.[1]	
Diagnostic criteria	Physical examination Positive Carnett's sign
Nonsurgical treatment	Ultrasound-guided subfascial injection of 40 mg 1% lidocaine and 4 mg dexamethasone into the rectus abdominis muscle at the trigger point
Surgical treatment	Anterior neurectomy
Siawash[2]	
Diagnostic criteria	Localized pain at the lateral border of the rectus abdominis muscle Most intense pain at an area as large as one fingertip Positive Carnett's sign Positive pinch test and/or altered skin perception to light touch and/or cold temperature at the area of most intense pain Normal diagnostics (blood/urine/imaging) ≥50% pain reduction +/− 15 min after abdominal wall injection using a local anesthetic
Nonsurgical treatment	1st treatment: Subfascial injection of 5 ml 1% lidocaine using the free-hand technique ≥2 treatment: Subfascial injection with 4 ml 1% lidocaine and 1 ml methylprednisolone (40 mg) using the free-hand technique (max. 3 subfascial injections)
Surgical treatment	Anterior neurectomy
Siawash et al.[3]	
Diagnostic criteria	Presence of local pain spot in anterior portions of the abdomen Positive Carnett's test Positive pinch test Somatosensory alterations of skin overlying the pain spot Absence of visceral disease as suggested by history taking, normal routine blood/urine analysis, and/or medical imaging
Nonsurgical treatment	Subfascial injection of 5 ml 1% lidocaine using the free-hand technique
Scheltinga et al.[4]	
Diagnostic criteria	Presence of localized pain in the abdominal area Positive Carnett's sign Absence of abnormal blood and urine tests Normal abdominal ultrasound or CT-scan
Nonsurgical treatment	1st injection: Subfascial injection of 5 ml 1% lidocaine 2nd injection: Subfascial injection of 4ml 1% lidocaine and 1 ml methylprednisolone
Surgical treatment	Anterior neurectomy
Siawash et al.[5]	
Diagnostic criteria	Localized abdominal pain Positive Carnett's sign Positive pinch test
Surgical treatment	Anterior neurectomy
Armstrong et al.[6]	
Diagnostic criteria	Localized cutaneous hypersensitivity, percussion and palpation tenderness and positive Carnett's sign
Surgical treatment	Anterior neurectomy

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