

Treatment of chronic pain in pediatric rheumatic disease

Yukiko Kimura* and Gary A Walco

SUMMARY

Pain in children with rheumatic disease is common, and is most often caused by arthritis. Despite the widespread use of effective new biologic agents, pain continues to be a problem in these patients, and it greatly impairs their daily functioning and quality of life. The pathogenesis of pain in children with rheumatic diseases is multifactorial, and disease treatment alone is often not enough to alleviate it. No standard of care or detailed algorithm for managing pain in these patients exists. Specific pain treatments often include acetaminophen, NSAIDs and medications that treat arthritis, such as methotrexate and etanercept. Other approaches should include nonpharmacologic interventions, for example exercise and cognitive-behavioral therapy, as well as the use of analgesics such as opioids in patients whose pain is refractory to standard therapies. The use of systemic corticosteroids to treat pain in children with arthritis should be avoided.

KEYWORDS chronic pain, juvenile idiopathic arthritis, pediatric, rheumatic disease, treatment

REVIEW CRITERIA

A review of the literature was performed by searching MEDLINE and PubMed databases using search terms such as "arthritis", "inflammation" and "pain", and subsequently highlighting pediatrics. Abstracts and full papers published between January 1996 and July 2006 were considered. All papers identified were English-language papers. We relied on major textbooks for background information and references. We also searched the reference lists of identified articles for further papers, which were supplemented with scholarly reviews and books.

CME

Y Kimura is the founder and Chief of the Section of Pediatric Rheumatology at the Joseph M Sanzari Children's Hospital of Hackensack University Medical Center, Hackensack, and Associate Professor of Pediatrics at the University of Medicine and Dentistry, New Jersey. GA Walco is Professor of Pediatrics at the University of Medicine and Dentistry, New Jersey, and Director of the David Center for Children's Pain and Palliative Care at Hackensack University Medical Center, Hackensack, NJ, USA.

Correspondence

*Pediatric Rheumatology, Joseph M Sanzari Children's Hospital, Hackensack University Medical Center, Hackensack, NJ 07601, USA
ykimura@hmed.com

Received 24 July 2006 Accepted 16 January 2007

www.nature.com/clinicalpractice
doi:10.1038/ncprheum0458

Medscape Continuing Medical Education online

Medscape, LLC is pleased to provide online continuing medical education (CME) for this journal article, allowing clinicians the opportunity to earn CME credit. Medscape, LLC is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide CME for physicians. Medscape, LLC designates this educational activity for a maximum of 1.0 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity. All other clinicians completing this activity will be issued a certificate of participation. To receive credit, please go to <http://www.medscape.com/cme/ncp> and complete the post-test.

Learning objectives

Upon completion of this activity, participants should be able to:

- 1 Describe the prevalence of pain in children with rheumatic diseases.
- 2 Identify underlying mechanisms for pain in children with rheumatic diseases.
- 3 Describe the American Pain Society guidelines for pain treatment.
- 4 List pharmacologic approaches to pain management in children with rheumatic diseases.
- 5 Identify nonpharmacologic approaches to pain management in children with rheumatic diseases.

INTRODUCTION

Pain is the most common symptom of rheumatic disease in children;¹ these diseases are characterized by localized or systemic inflammation that is usually autoimmune in origin. Pain can occur in any part of the body where there is inflammation (e.g. the chest in pericarditis, the bowel in ulcerative colitis, or joints in arthritis). In this article, the epidemiology and nature of pain in children with rheumatic disease, as well as approaches to treatment, will be explored. Although there have been other reviews on pain and the treatment of pain in juvenile arthritis and pediatric rheumatic diseases, this paper has a unique focus in that it attempts to bring together both the pediatric rheumatology and pediatric pain literature and perspectives.

ARTHRITIS IS A MAJOR CAUSE OF PAIN IN CHILDREN WITH RHEUMATIC DISEASE

The major symptom of chronic arthritis in children (now called juvenile idiopathic arthritis,

or JIA²) is joint pain. Arthritis is also a common manifestation of many other rheumatic diseases: over 100 different causes of arthritis in children have been identified, and joint pain is the leading cause of disability in patients with these diseases. Children in general experience as much pain as adults,^{3–5} and several studies have shown that many children with arthritis continue to experience pain even after appropriate treatment has been instituted. As many as 40–86% of children with arthritis seen in routine pediatric rheumatology clinic visits reported pain, years after treatment was started.^{1,3} In 2003, Schanberg *et al.*⁶ studied 41 children with JIA who completed daily pain diaries, and found that 70% had considerable pain on 60% of days. In children with rheumatic diseases, pain limits their activities, disrupts school attendance, and contributes to psychosocial distress. In one study, a small decrease in the severity of pain (by a mean of <1 cm on a 10 cm visual analog scale) in these children was shown to have an appreciable effect on their overall well-being.⁷

EFFECT OF BIOLOGIC AGENTS ON PAIN REDUCTION

The widespread use of extremely effective biologic agents, such as the tumor necrosis factor (TNF) inhibitors, in adults as well as children with arthritis could be expected to eliminate or at least greatly reduce arthritis activity (and, therefore, pain). In Schanberg and colleagues' daily diary study of pain in children with arthritis, however, 66% of patients were taking therapies such as methotrexate, TNF inhibitors, or both, and many still experienced pain.⁶ In a survey conducted by the Arthritis Foundation, 71% of 500 adults with rheumatoid arthritis who were taking methotrexate, biologic therapies (or both) continued to report pain, and 55% of these individuals had to modify their daily household activities because of their pain.⁸ Although biologic agents do reduce and sometimes eliminate disease activity and pain in many patients, these effects are by no means universal; there are many patients in whom disease control and pain control are incomplete. Many other factors besides disease activity contribute to the pain experience in children as well as adults with arthritis.

PAIN MECHANISMS

Current models of pain transmission stem from the gate-control theory of pain, which focuses on several key elements.^{9,10} Primary afferent

neurons have three main functions in nociception: detection of noxious or damaging stimuli (transduction); conveyance of sensory input from the periphery to the spinal cord (conduction); and synaptic transfer of input to neurons within specific laminae of the dorsal horn of the spinal cord (transmission).¹⁰ Conduction of pain sensations usually occurs via A δ fibers—which are myelinated, of small-to-medium diameter (1–5 μ m), and conduct fairly rapidly (5–30 m/s)—and C fibers, which are unmyelinated, of small diameter (0.25–1.5 μ m) and conduct more slowly (0.5–2 m/s). A δ fibers have small receptive fields and react to high-intensity thermal or mechanical input. C fibers have broader receptive fields than A δ fibers, and are activated by thermal, mechanical, and chemical stimuli. In addition, C fibers can be sensitized by mediators of the inflammatory response (e.g. prostaglandin E₂ and bradykinin), and once such sensitization occurs, non-noxious low-level stimulation also elicits neural activity.¹¹ C fibers are, therefore, likely to underlie the persistent secondary pain, hyperalgesia, and hypersensitivity associated with inflamed tissue.

Mechanisms of pain in inflammation

The peripheral sensitization that is associated with inflammatory processes is of particular interest in rheumatic disease. Tissue injury causes the release of inflammatory mediators from damaged cells (e.g. bradykinin); these mediators are central to the initiation of the inflammatory cascade. Tissue injury also causes release of cytokines that have a role in both initiation and maintenance of the inflammatory response. Prostaglandins are synthesized by the constitutively expressed cyclo-oxygenases 1 and 2, which are important mediators of inflammation, fever, and pain.¹⁰ Prostaglandins contribute to pain by direct activation of nociceptors, as well as by sensitization of primary afferent neurons to bradykinin and other mediators.

Most primary nociceptive afferent fibers project to defined areas within the dorsal horn of the spinal cord. Glutamate is the primary neurochemical mediator between afferent nociceptors and dorsal horn cells; glutamate binds to receptors for alpha-amino-3-hydroxy-5-methyl-isoxazole-4 propionic acid and *N*-methyl-D-aspartate. Second-order afferent fibers in the dorsal horn are either wide dynamic range or nociceptive-specific neurons, which project to sites within the brain stem, midbrain,

and thalamus. The unique characteristics of wide dynamic range and nociceptive-specific neurons largely account for the spatial and temporal elements of afferent input, as well as for encoding specific pain qualities (intensity, modality, and localization). Ultimately, projections to the somatosensory cortex yield the ability to localize and discriminate pain, while those to the anterior cingulate gyrus account for the affective component.

Central pain mechanisms

Neural activity is not unidirectional, and pain-modulating systems within the central nervous system also have a major role. Pain modulation can occur through local interneuron circuits within the dorsal horn that act on primary A δ and C-fiber afferent fibers, as well as wide dynamic range and nociceptive-specific neurons. These neurons inhibit release of the endogenous opioid peptides dynorphin and enkephalin, as well as γ -aminobutyric acid. Within the rostral medulla, 'on' and 'off' neurons function to modulate pain principally through serotonin and norepinephrine. Perhaps the most significant site of pain modulation seems to be the midbrain periaqueductal gray matter, with efferent projections from the cingulate gyrus, limbic system, and hypothalamus. Cortical processes have been shown to have a major role in the mediation of pain processing that includes elements of cognition, arousal state, attention, and expectation.

Pain in arthritis is multifactorial

Chronic or recurrent pain in children with rheumatic disease is the result of an integration of biological processes, psychological factors, and sociocultural contexts, all of which must be considered within a developmental framework.¹² In relation to chronicity of pain, there are qualitative and not simply quantitative shifts in the severity, characteristics, and regularity of pain with time. Ongoing pain can result in sensitization of the peripheral and central nervous systems, which produce neurophysiological, neurochemical and neuroanatomical changes.¹³ In addition, the extent of disability associated with chronic pain can vary from none to severe, and pain can continue in the absence of tissue damage.¹⁴

In this context, it is not surprising that the activity and severity of arthritis are predictive of only a small proportion of the variance in pain reported by patients with JIA. For example,

arthritis subtype predicted only 8%,¹⁵ and the presence of joint inflammation predicted only 10% of the variance in reported pain.¹⁶ Schanberg *et al.*⁴ and Malleson *et al.*¹⁷ found that disease activity itself predicted 28% and 6.5% of the variance in reported pain, respectively. Pain perception is multifactorial; therefore, a biopsychosocial model that includes the individual's age and developmental status, coping ability, mood, stress levels, and environmental and family factors, in addition to disease status and severity, is required.^{12,18}

PAIN ASSESSMENT

As previously mentioned, an evaluation of chronic inflammatory pain should include assessment of biological, psychological and sociocultural factors in a developmental context.¹² Evaluation should begin with a history of the problem, including a detailed description of the sensory nature of the pain in terms of its intensity, quality, location, duration, variability, predictability, exacerbating and alleviating factors, and impact on daily life (for example its effects on sleeping, eating, school, social and physical activities, family and peer interactions). Details of the onset and development, evaluation and treatment of pain should be obtained. Information about the level of distress (for the child and family) that can be attributed to the pain and the impact of the pain on cognitive functioning, anxiety, depression, and feelings of hopelessness should be included. Information should also be solicited on the child's and family's perception of the cause of the current pain problem, with details of any past pain problems and how they were resolved.¹⁹ Additionally, a 'pain history' should include a history of surgeries and hospitalizations, birth and early childhood history, developmental milestones, social history including school, social life, activities, and family medical and social history. In contrast to assessments of acute pain, the evaluation of recurrent or chronic pain should also include contextual factors (Box 1). Over the past several years there has been a blossoming of literature that begins to address these issues, but by and large this field is still in its infancy.

CURRENT TREATMENT GUIDELINES AND PRACTICE FOR PAIN DUE TO ARTHRITIS

Since pain perception is multifactorial, an interdisciplinary pain-management plan seems to be the best strategy for effective pain control in

children with arthritis. There are currently no established, detailed guidelines for pain management in children with JIA and other rheumatic diseases. An algorithm for pain treatment was published by the American Pain Society in 2002,²⁰ but it discusses pain management only in very general terms: these guidelines state that the mainstays of pharmacologic treatment are NSAIDs and acetaminophen, but opioids should be considered if these agents are insufficient; systemic corticosteroids should be avoided; and nonpharmacologic modalities should be used as much as possible.

A survey of pediatric rheumatologists who belong to the Childhood Arthritis and Rheumatology Research Alliance (CARRA, a research network in North America) was conducted in order to assess current pain treatment practices.²¹ Although 77% of pediatric rheumatologists acknowledged that children with arthritis continue to have pain despite adequate treatment for their arthritis, 60% disagreed with the use of opioids to treat this residual pain. Interestingly, 87% had used opioids in the past year to treat pain in their patients (this proportion included 68% of the respondents who disagreed with opioid use), and 27% had used systemic corticosteroids to treat pain. Opioid side effects and addiction or dependence were cited as the main concerns that prevented the use of opioids to treat residual pain (55% and 38% respectively).

PHARMACOLOGIC APPROACHES

Reduction of disease activity is the ultimate goal of treatment for most diseases; in arthritis, reduction of disease activity has been shown to be associated with improved radiographic outcomes, functional capability and reduced pain. Treatment depends on the type and severity of the arthritis, and can include NSAIDs, disease-modifying agents such as methotrexate, sulfasalazine, hydroxychloroquine, leflunomide and ciclosporin, biologic agents such as the TNF inhibitors, anti-interleukin-1 agents, inhibitors of T-cell co-stimulation, and anti-B cell agents.^{22,23} Intra-articular injection of long-acting corticosteroids can be a highly effective means of immediately reducing joint inflammation and pain. By contrast, the use of systemic corticosteroids to reduce disease activity and pain should be actively discouraged, except in cases where there is severe, life-threatening, uncontrollable systemic disease, or when

Box 1 Contextual factors that can influence a child's pain experience.

The following issues and questions, which highlight the complexity of factors that can influence a child's pain experience, should be considered.

- The relationship between the nature and severity of the underlying pathophysiology, and the child's pain experience
- Experimental indices, such as pain threshold, pain tolerance, pain responsiveness, and how these relate to clinical pain experiences
- The relationship between physiological maturation and pain, especially around specific periods in development such as infancy and puberty
- The relationship of gender to pain: to what degree are gender-related factors genetically versus environmentally based, and how do gender-related factors interact with other developmental processes?
- The relationship between temperament, personality development, and pain
- The relationship between affective state and pain in the context of emotional development, including increasing differentiation or integration of affect
- Cognitive developmental factors are important, including the development of a concept of pain
- Factors of social development that have a role in children's pain experiences
- Note important pain behaviors, what are the consequences of these behaviors, and appreciate that social learning interacts with developmental factors
- Consider the relationship between academic achievement and pain. For example, is there an over-representation of children with learning deficits among those who experience chronic pain?
- Family factors might precede or maintain pain syndromes; how does the persistent pain in a child reciprocally affect the family system?
- Sociocultural factors can affect pain experience and pain behavior in children
- The role that health-care providers have in facilitating the development or maintenance of recurrent and chronic pain syndromes in children and adolescents

Table 1 NSAIDs approved by the US FDA for use in children.

Name of drug	Brand name	Maximum daily dose (mg)	Pediatric daily dose	Available forms
Aspirin ^a	NS	4,000	80–100 mg/kg, divided TID	81 mg chewable tablet 325, 600 mg tablets 800 mg sustained release
Ibuprofen	NS	2,400	40 mg/kg divided TID	100 mg chewable tablet 200 mg tablet 100 mg (5 ml) suspension
Naproxen	Naprosyn [®] Naprelan [®]	1,100	15–20 mg/kg divided BID	250, 375, 500 mg tablets 125 mg (5 ml) suspension
Oxaprozin	Daypro [®]	1,200	10–20 mg/kg once daily	600 mg tablet
Etodolac SR	Lodine [®] SR	1,200	20–30 mg/kg once a day	400, 500, 600 mg tablets
Meloxicam	Mobic [®]	15	0.125–0.25 mg/kg once daily	7.5 mg (5 ml) suspension
Indomethacin	Indocin [®]	200	2–4 mg/kg divided TID, or divided BID if using extended-release formulation	25, 50 mg capsules 25 mg (5 ml) suspension 75 mg sustained release
Celecoxib	Celebrex [®]	400	50 mg BID (for children of 10–25 kg) 100 mg BID (for children >25 kg)	100, 200 mg capsules

^aAspirin use in children has been associated with a possible increased risk of Reye syndrome. Abbreviations: BID, twice a day; NS, not specified; TID, three times a day.

arthritis is so severe that the child will otherwise become bedridden or wheelchair-bound. Chronic use of systemic corticosteroids have many deleterious side effects (e.g. growth retardation, osteoporosis, avascular necrosis, cataracts and immunosuppression), which can be especially devastating for children. Interestingly, however, 27% of pediatric rheumatologists in the CARRA survey of pain treatment preferred to use systemic corticosteroids rather than to treat residual pain specifically with analgesics in children with arthritis.²¹ This might be because corticosteroids have traditionally been used to reduce pain in rheumatic disease. As one of the oldest and most potent anti-inflammatory medications available, these agents can reduce inflammation and secondarily pain with an immediate and substantial effect. Medications such as opioids have not traditionally been used to reduce pain in rheumatology, however, owing to fears and misconceptions about side effects and potential drug-dependency problems.

Nonsteroidal anti-inflammatory drugs

NSAIDs are the mainstay of pain treatment in pediatric patients with rheumatic diseases (Table 1); they provide rapid and effective analgesia, and have the advantage of an oral route of administration. NSAIDs inhibit cyclo-oxygenase enzymes, which reduce prostaglandin production

and, subsequently, pain. The analgesia provided by NSAIDs is additive to that of opioids and anticonvulsants. NSAIDs, however, have a ceiling effect (i.e. there is a limit beyond which increased doses have no effect), and there are significant potential adverse effects such as gastrointestinal toxicity (abdominal pain, gastritis, ulcers and diarrhea), renal toxicity, hepatotoxicity, and possible cardiovascular toxicity. Platelet inhibition occurs with most NSAIDs, and might need to be considered in patients with a coexisting bleeding diathesis or when a surgical procedure is contemplated. Some NSAIDs have also been associated with pseudoporphyria, which can cause significant scarring.²⁴

Acetaminophen

Acetaminophen is an excellent analgesic for mild pain that can be used in combination with NSAIDs. Patients must be cautioned not to take more than the recommended dosage (10–15 mg/kg every 4–6 h, maximum of 4 g in 24 h). Larger doses, especially taken chronically, can cause significant hepatotoxicity and are an important cause of liver failure. In view of this fact, it is important to remember that many analgesics contain acetaminophen as well as the principal analgesic (e.g. Percocet[®] contains acetaminophen in addition to oxycodone), in order to avoid unknowingly overdosing patients with

Table 2 Common trade names of opioids used for chronic or acute pain.

Generic drug name	Brand names	Other constituents
Codeine	None	Acetaminophen
Oxycodone	Oxycontin [®] , Oxydose [®] , Oxyfast [®] Percocet [®] , Tylox [®] , Roxicet [®] , Endocet [®] , Roxilox [®] Percodan [®] , Endodan [®] Combunox [®]	None Acetaminophen Aspirin Ibuprofen
Hydrocodone ^a	Lortab [®] , Vicodin [®] , Anexia [®] Lorcet [®] Reprexain [®] , Vicoprofen [®]	None Acetaminophen Ibuprofen
Morphine	MS Contin [®] , Avinza [®] , Kadian [®] , MSIR [®]	None
Methadone	Dolophine [®] , Methadose [®]	None
Hydromorphone	Dilaudid [®] , Hydromorph Contin [®]	None

^aHydrocodone generally comes in tablets for adult dosing only.

acetaminophen. Table 2 lists some brand names for combinations of opioids, acetaminophen and other analgesics.

Other analgesics

The use of opioids—which act as agonists that block principally μ and less commonly κ receptors in the central nervous system—to treat chronic, nonmalignant pain is gaining acceptance.^{25,26} Randomized, controlled studies of various opioids have been performed in adults with arthritis and other causes of chronic pain, and have demonstrated their efficacy and safety.^{27–29} Opioids are safe, can be beneficial, and are better tolerated than more aggressive medical and surgical approaches to pain management (Table 2 lists commonly used opioid preparations). The use of these agents in pediatric rheumatic diseases has been limited, and they have not typically been part of a treatment plan for continued residual pain.²¹ Tramadol is a weak opioid that has been found to provide fairly effective relief of mild to moderate pain when NSAIDs and acetaminophen have failed,³⁰ but it has not been studied specifically in children with arthritis. Other, more effective choices include oxycodone preparations for acute pain, and long-acting preparations such as methadone (which has the additional benefit of acting as an antagonist of *N*-methyl-D-aspartate receptors), for long-term pain management. Although data are sparse in children, there is intriguing evidence that opioids have significant anti-inflammatory effects, which might be of benefit in inflammatory diseases.³¹ Finally, tricyclic antidepressants and anticonvulsants (e.g. gabapentin) can be useful, especially

when there is coexisting centrally mediated or neuropathic pain.

NONPHARMACOLOGIC APPROACHES

Cognitive-behavioral therapy

Two major behavioral modalities can be invoked in the context of chronic or recurrent pain: regulation of pain perception, using specific cognitive-behavioral or self-regulatory strategies that facilitate coping with pain or modify the patient's subjective pain experience; and pain-behavior modulation, which focuses on operant paradigms that are intended to increase adaptive behavior and minimize pain-related or 'sick' role behavior.³² In addition, if there are concerns about major contextual factors, those too must be addressed.

A systematic review of controlled trials of psychological therapy for chronic pain³³ concluded that there is evidence to support the use of cognitive-behavioral therapy to treat headaches, and encouraged controlled randomized trials to investigate its efficacy in other types of recurrent and chronic pain. In a review of empirically supported treatments for disease-related pain in children, Walco *et al.*³⁴ specifically focused on pain associated with arthritis in children. These authors determined that the available studies showed promise for these interventions, but concluded that additional systematic, randomized trials were needed. They cited two studies that were essentially clinical series, both of which implemented cognitive-behavioral therapy with significant improvements in pain intensity and function in children with JIA.^{35,36}

Physical therapy and exercise

Physical therapy and exercise programs can help to reduce pain in children with arthritis and should, therefore, be encouraged, especially since children with arthritis tend to be less physically active than their peers and might become deconditioned.^{37,38} Klepper *et al.*³⁹ studied the effect of an exercise regimen in 25 children with arthritis; they showed that improved aerobic conditioning could be achieved, and that this benefit was associated with some improvement in pain and did not exacerbate disease. Several studies have shown that exercise therapy was associated with decreases in affected joint count and disease severity.⁴⁰

Surgical approaches to pain in arthritis

In patients with severe, unremitting pain, deformity and functional limitation, surgical interventions such as synovectomy can be helpful and can reduce pain.⁴¹ Arthroplasty is another option for a joint destroyed by arthritis, but such surgery should be delayed for as long as possible in a child. Results of arthroplasty from highly specialized, tertiary-care centers report effective pain relief and improved function in treated patients, many of whom were wheelchair-bound before surgery.^{42–44} With early and aggressive use of new, highly effective biologic treatments that greatly improve radiographic outcomes (and very likely long-term outcomes as well),⁴⁵ however, surgical treatment for JIA will hopefully become a rare occurrence.

Other approaches

There are descriptive studies that show a potential role for massage therapy and orthotics in reducing pain due to arthritis in children.^{46,47} Further controlled studies on these and other integrative interventions are required before any conclusions relating to the effectiveness of these approaches can be reached. An evidence-based review of nonpharmacologic treatments for adults with rheumatoid arthritis found that physical exercise, sports and muscle-strength exercises were advisable, as were orthotics when foot pain or foot alignment abnormalities existed; however, there was little evidence that dietary measures, nutritional supplements and elimination diets were effective.⁴⁸

PROCEDURAL PAIN CONTROL

Medical procedures such as phlebotomy, injections of medications, intravenous catheter insertions, and intra-articular injections are a

cause of significant pain in children with JIA and other rheumatic diseases. A survey of pediatric rheumatologists in North America revealed that there is no standard of care in relation to methods of local anesthesia before intra-articular injections.⁴⁹ The most popular agent was an anesthetic cream called EMLA (Eutetic Mixture of Local Anesthetics) and/or subcutaneous lidocaine, but others used ethyl chloride spray, lidocaine iontophoresis, and midazolam. Optimal approaches to pain management during such procedures need to be systemically studied in this population.

CONCLUSIONS

Although arthritis is a common cause of pain in children with rheumatic diseases, inflammation in other organs can also be a source of pain. Noninflammatory pain such as that caused by centrally mediated pain syndromes can coexist with arthritic pain in these patients. Considerable pain has been documented to exist in most patients, even when disease management has been optimized. Consideration should be given to the use of analgesic medications, especially opioids, in children who continue to have significant chronic pain. The epidemiology, character and treatment of chronic pain in children with rheumatic diseases need to be studied systematically in large numbers of patients.

KEY POINTS

- Pain continues to be common in children with rheumatic diseases, despite advances in arthritis treatment
- The pathogenesis of pain in children with rheumatic diseases is multifactorial
- Pain management should be interdisciplinary and consist of nonpharmacologic as well as pharmacologic interventions
- There are no current detailed treatment guidelines for treatment of pain in children with rheumatic diseases
- More aggressive pain treatments should be considered in those patients who continue to have significant residual pain

References

- 1 Lovell D and Walco GA (1989) Pain associated with juvenile rheumatoid arthritis. *Pediatr Clin North Am* **36**: 1015–1027
- 2 Petty RE *et al.* (2004) International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. *J Rheumatol* **31**: 390–392

- 3 Sherry D *et al.* (1990) Painless juvenile rheumatoid arthritis. *J Pediatr* **116**: 921–923
- 4 Schanberg L *et al.* (1997) Pain coping and the pain experience in children with juvenile chronic arthritis. *Pain* **73**: 181–189
- 5 Hagglund K *et al.* (1995) Predicting pain among children with juvenile rheumatoid arthritis. *Arthritis Care Res* **8**: 36–42
- 6 Schanberg L *et al.* (2003) Daily pain and symptoms in children with polyarticular arthritis. *Arthritis Rheum* **48**: 1390–1397
- 7 Dhanani S *et al.* (2002) Minimal difference in pain associated with change in quality of life in children with rheumatic disease. *Arthritis Rheum* **47**: 501–505
- 8 Gruver D (2004) Living with rheumatoid arthritis: unmet needs [http://www.arthritis.org/conditions/diseasecenter/RA/RASurvey/WhitePaperFinal.pdf] (accessed 9 February 2007)
- 9 Merkel S *et al.* (1997) The FLACC: a behavioral scale for scoring postoperative pain in young children. *Pediatr Nursing* **23**: 293–297
- 10 Kidd BL and Urban LA (2001) Mechanisms of inflammatory pain. *Br J Anaesth* **87**: 3–11
- 11 Giordano J (2006) The neuroscience of pain and analgesia. In *Weiner's Pain Management: A Practical Guide for Clinicians* (Eds Boswell MV and Cole BE) Boca Raton: Taylor & Francis
- 12 Zeltzer L *et al.* (1997) Pain responsiveness and chronic pain: a psychobiological perspective. *J Develop Behav Pediatr* **18**: 13–22
- 13 Woolf CJ and Salter MW (2000) Neuronal plasticity: increasing the gain in pain. *Science* **288**: 1965–1969
- 14 Pediatric chronic pain: a position statement from the American Pain Society [http://www.ampainsoc.org/advocacy/pediatric.htm] (accessed 9 February 2007)
- 15 Thompson K *et al.* (1987) Comprehensive assessment of pain in juvenile rheumatoid arthritis: an empirical model. *J Pediatr Psychol* **12**: 241–255
- 16 Ilowite N *et al.* (1992) Assessment of pain in patients with juvenile rheumatoid arthritis: relation between pain intensity and degree of joint inflammation. *Ann Rheum Dis* **51**: 343–346
- 17 Malleson P *et al.* (2004) Predictors of pain in children with established juvenile rheumatoid arthritis. *Arthritis Rheum* **51**: 222–227
- 18 Rapoff MA and Lindsley CB (2000) The pain puzzle: a visual and conceptual metaphor for understanding and treating pain in pediatric rheumatic disease. *J Rheumatol Suppl* **58**: 29–33
- 19 Zeltzer L *et al.* (1997) A psychobiologic approach to pediatric pain: Part II. Prevention and treatment. *Curr Prob Pediatr* **27**: 264–284
- 20 Anonymous (2002) Guideline for the management of pain in osteoarthritis, rheumatoid arthritis and juvenile chronic arthritis. Glenview: American Pain Society
- 21 Kimura Y *et al.* (2006) Treatment of pain in juvenile idiopathic arthritis: a survey of pediatric rheumatologists. *Arthritis Rheum* **55**: 81–85
- 22 Hashkes PJ and Laxer RM (2005) Medical treatment of juvenile idiopathic arthritis. *JAMA* **294**: 1671–1684
- 23 Weiss J and Ilowite NT (2005) Juvenile idiopathic arthritis. *Pediatr Clin North Am* **52**: 413–442
- 24 Lang B and Finlayson LA (1994) Naproxen-induced pseudoporphyria in patients with juvenile rheumatoid arthritis. *J Pediatr* **124**: 639–642
- 25 Dominick K *et al.* (2004) Patterns of opioid analgesic prescription among patients with osteoarthritis. *J Pain Palliat Care Pharmacother* **18**: 31–46
- 26 Kalso E *et al.* (2004) Opioids in chronic non-cancer pain: systematic review of efficacy and safety. *Pain* **112**: 372–380
- 27 Cowan D *et al.* (2005) A randomized, double-blind, placebo-controlled, cross-over pilot study to assess the effects of long-term opioid drug consumption and subsequent abstinence in chronic noncancer pain patients receiving controlled-release morphine. *Pain Med* **6**: 113–121
- 28 Caldwell J *et al.* (1999) Treatment of osteoarthritis pain with controlled release oxycodone or fixed combination oxycodone plus acetaminophen added to nonsteroidal antiinflammatory drugs: a double blind, randomized, multicenter, placebo controlled trial. *J Rheumatol* **26**: 862–869
- 29 Furlan AD *et al.* (2006) Opioids for chronic noncancer pain: a meta-analysis of effectiveness and side effects. *CMAJ* **174**: 1589–1594
- 30 Malonne H *et al.* (2004) Efficacy and tolerability of sustained-release tramadol in the treatment of symptomatic osteoarthritis of the hip or knee: a multicenter, randomized, double-blind, placebo-controlled study. *Clin Ther* **26**: 1774–1782
- 31 Walker JS (2003) Anti-inflammatory effects of opioids. *Adv Exp Med Biol* **521**: 148–160
- 32 Varni JW *et al.* (1990) Cognitive-behavioral assessment and treatment of pediatric pain. In *Handbook of Clinical Behavioral Pediatrics*, 83–97 (eds Gross AM and Drabman RS) New York: Plenum Press
- 33 Eccleston C *et al.* (2002) Systematic review of randomised controlled trials of psychological therapy for chronic pain in children and adolescents, with a subset meta-analysis of pain relief. *Pain* **99**: 157–165
- 34 Walco G *et al.* (1999) Empirically supported treatments in pediatric psychology: disease related pain. *J Pediatr Psychol* **24**: 155–167
- 35 Lavigne J *et al.* (1992) Evaluation of a psychological treatment package for treating pain in juvenile rheumatoid arthritis. *Arthritis Care Res* **5**: 101–110
- 36 Walco G *et al.* (1992) Cognitive-behavioral pain management in children with juvenile rheumatoid arthritis. *Pediatrics* **89**: 1075–1079
- 37 Takken T *et al.* (2003) Relationship between functional ability and physical fitness in juvenile idiopathic arthritis patients. *Scand J Rheumatol* **32**: 174–178
- 38 Takken T *et al.* (2002) Aerobic fitness in children with juvenile idiopathic arthritis: a systematic review. *J Rheumatol* **29**: 2643–2637
- 39 Klepper S (1999) Effects of an eight-week physical conditioning program on disease signs and symptoms in children with chronic arthritis. *Arthritis Care Res* **12**: 52–60
- 40 Singh-Grewal D *et al.* (2006) Pilot study of fitness training and exercise testing in polyarticular childhood arthritis. *Arthritis Rheum* **55**: 364–372
- 41 Maenpaa H *et al.* (2003) Elbow synovectomy on patients with juvenile rheumatoid arthritis. *Clin Orthop Rel Res* **412**: 65–70

Competing interests

The authors have declared associations with the following companies/organizations: Amgen, Cephalon, Endo Pharmaceuticals, National Institutes of Health, and Regeneron. See the article online for full details of the relationship.

- 42 Iesaka K *et al.* (2006) Orthopedic surgical management of hip and knee involvement in patients with juvenile rheumatoid arthritis. *Am J Orthop* **35**: 67–73
- 43 Kitsoulis P *et al.* (2006) Total hip arthroplasty in children with juvenile chronic arthritis: long-term results. *J Pediatr Orthop* **26**: 8–12
- 44 Palmer D *et al.* (2005) Total knee arthroplasty in juvenile rheumatoid arthritis. *J Bone Joint Surg Am* **87**: 1510–1514
- 45 van der Heijde D *et al.* (2006) Comparison of etanercept and methotrexate, alone and combined, in the treatment of rheumatoid arthritis: two-year clinical and radiographic results from the TEMPO study: a double-blind, randomized trial. *Arthritis Rheum* **54**: 1063–1074
- 46 Field T *et al.* (1997) Juvenile rheumatoid arthritis: benefits from massage therapy. *J Pediatr Psych* **22**: 607–617
- 47 Powell M *et al.* (2005) Efficacy of custom foot orthotics in improving pain and functional status in children with juvenile idiopathic arthritis: a randomized trial. *J Rheumatol* **32**: 943–950
- 48 Gossec L *et al.* (2006) Nonpharmacological treatments in early rheumatoid arthritis: clinical practice guidelines based on published evidence and expert opinion. *Joint Bone Spine* **73**: 396–402
- 49 Weiss JE *et al.* (2006) Analgesia for intra-articular corticosteroid injections in juvenile idiopathic arthritis (JIA): a survey of pediatric rheumatologists [abstract]. *Arthritis Rheum* **54 (Suppl)**: S171