RHEUMATOLOGY NURSE
PRACTICE

Inside this Issue

ISSUE **2** | VOLUME **2**

- How does a rheumatoid arthritis (RA) patient's level of pain catastrophizing affect subjective and composite treatment outcomes?
- What evidence supports and refutes the use of opioids for pain management in patients with RA?
- What patient- and practitioner-centered clinical assessment tools are available to gauge and track RA patients' levels of pain?
- What does the ideal multidisciplinary team look like for the RA patient with high levels of chronic pain?

PAIN MANAGEMENT

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Learning Objectives

1. *Discuss the common components of pain in patients with rheumatoid arthritis (RA)*
2. *Assess the clinical applicability of available pain assessment tools for your individual practice*
3. *Review the important components of recent evidence-based guidelines for the use of opioids in patients with chronic pain*
4. *Develop strategies that most appropriately meet the needs of your RA patients reporting chronic pain*

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Pain Management Strategies in Patients with Rheumatoid Arthritis

Pain is the most common complaint for many patients with rheumatoid arthritis (RA) and often the primary reason why they seek medical attention.[1] Over the past 15 years, a paradox in pain management has emerged for RA patients. On the one hand, the advent of effective biologic disease-modifying antirheumatic drugs (DMARDs) has reduced the rate of progressive joint damage and increased the likelihood of achieving clinical remission.[2,3] On the other, despite better control of RA disease activity, long-term observational data indicates that overall pain control is no better today than it was in the pre-biologics era.[3] This underscores the potential role of mechanisms other than inflammation at play in RA patients with residual pain.[3]

Pain management in patients with RA can be especially challenging given heightened national concerns over prescription painkiller use in the general population. Opioid prescriptions in the United States have quadrupled since 1999 and now exceed 259 million prescriptions per year—enough for every adult in the United States to have a bottle.[4] Prescription opioid deaths are also on the rise, with more than 40 adults dying each day from drug overdoses involving opioid pain relievers and heroin.[4] To address this public health crisis, the Centers for Disease Control and Prevention (CDC) launched several new initiatives over the past year that support safe opioid prescribing, including issuing new guidelines for opioid use in chronic pain management.[5]

ACTIVITY SUMMARY

In this issue of Rheumatology Nurse Practice, we will explore the features of RA-related pain, tools for assessing RA-related pain, recommendations for chronic pain management in RA, and additional insights that may impact clinical practice around RA-related pain for rheumatology nurses.

Types of Pain in RA

The pain of RA is a complex, subjective, and highly individualized experience. To begin to understand each patient's unique experience, it is helpful to consider the different components of RA-related pain. One model begins with the underlying physiologic causes of RA-related pain and then considers how the patient experiences pain on a sensory level, on a short-term psychological level (affective component), and on a long-term psychological level (cognitive component) (see Table 1).[6]

Pain assessment tools ask detailed questions about the physiologic, sensory, affective, and cognitive aspects of pain (see **Assessing Pain in the Rheumatology Clinic** section later in this issue).[7] Therefore, it is important to differentiate these components and understand how they relate to each other.

First, the ***physiologic components*** of RA-related pain describe the clinical manifestations of RA disease activity, including joint tenderness and swelling, morning stiffness, and fatigue. The ***sensory components*** describe the physical experience of pain: where, how much, and for how long. Next, the ***affective components*** describe the moment-by-moment psychological experience of pain, ranging from annoyance and distress to short-term fear and anxiety associated with the implications of pain. Lastly, the ***cognitive components*** of pain describe the longer-term, cumulative experience of pain. Depending on the patient's coping skills and support network, the experience of pain can lead to depression and poor quality of life. In general, the cognitive components of pain determine the degree of suffering associated with RA-related pain.[6]

The Intertwining of Pain and Depression

Mood disorders are one of the most common comorbidities of RA. In a recent study of 1,004 RA patients, 55% reported depressive symptoms and 23% met the diagnostic criteria for clinical depression. The presence of chronic pain more than doubled the likelihood of depression (odds ratio, 2.55). Despite the high prevalence of symptoms, depression was undertreated. Among RA patients with depressive symptoms in the study, only 12% were receiving anti-depressant drug therapy.[8]

In another study of 147 patients with early RA (duration ≤1 year), 47% exhibited symptoms of anxiety and depression.[9] Compared with RA patients without mood disorders, patients with anxiety and depression had significantly higher RA disease activity, more severe disability scores, and higher pain scores.[9] These findings underscore the need to identify and manage mood disorders even in the early stages of RA.

Fatigue is also common in RA and shows a complex interaction with mood disorders and pain outcomes. In a study of 542 RA patients, 41% met the diagnostic criteria for severe fatigue.[10] In addition, the presence of psychiatric disorders is associated with higher pain and fatigue scores in RA.[11] Addressing the overlapping symptoms of pain, fatigue, and mood disturbances in patients with RA is important to relieve the heavy symptom burden in these patients.

Catastrophizing Pain

On the far end of the affective/cognitive spectrum, *pain catastrophizing* describes a negative response to

Table 1

Commonly Described Aspects of RA-related pain[6]

PHYSIOLOGICAL	››››››››	››››››››	PSYCHOLOGICAL
Physiologic Components	**Sensory Components**	**Affective Components**	**Cognitive Components**
Morning stiffness	Intensity	Annoyance	Depression
Pain on motion	Duration	Distress	Self-esteem
Joint tenderness	Location	Short-term fear or anxiety	Loss of freedom
Joint swelling	Quality		Impact on life activities
Fatigue			

real or anticipated pain.[12] Although catastrophizing may manifest in different ways, examples include an inability to divert attention away from pain, a tendency to exaggerate the seriousness or perceived threat of pain, and a tendency toward pain-related worry or fear.[12] A high level of pain catastrophizing is a risk factor for poor outcomes of pain treatment.[12] In RA, where pain control is a treatment priority for most patients,[1] the interaction between pain catastrophizing and treatment outcomes is an important consideration.

Researchers recently described the relationship between pain catastrophizing and RA treatment outcomes in a study of 209 RA patients who were starting biologic DMARD therapy.[13] To assess the presence and degree of pain catastrophizing, patients were asked to report on a scale of 0-6 how much they agreed with each of the following statements:

- *"When I have pain, it's terrible and I think it's never going to get any better."*
- *"When I have pain, I feel I can't stand it anymore."*

Based on the mean response to both questions, patients were classified into 2 groups: lower levels of pain catastrophizing (mean score ≤1.5) and higher levels of pain catastrophizing (mean score >1.5). After 12 months of biologic DMARD therapy, all markers of RA disease activity improved significantly for both groups of patients. Despite the overall improvements at 12 months, patients with higher baseline levels of pain catastrophizing had worse disease activity scores than patients with lower baseline levels of pain catastrophizing across all subjective RA measures, including pain visual analog scale (VAS), patient global assessment, and patient-reported functional status and disease burden. Patients with higher levels of baseline pain catastrophizing also had significantly worse scores for measures that required both patient and provider input, such as the total joint count (TJC) and disease activity score with 28 joint count (DAS28). By comparison, there were no differences between patient groups at 12 months in any of the objective measures of RA inflammation, including swollen joint count (SJC), C-reactive protein (CRP), and ultrasound-measured synovitis.[13] These findings demonstrate that pain catastrophizing has a very real impact on subjective and composite treatment outcomes, even when RA treatment is highly effective at controlling inflammatory disease activity. When assessing disease activity in patients with RA, it may be helpful to take into account the degree of pain catastrophizing and to consider interventions aimed at improving coping mechanisms for patients with persistent RA-related pain.

Assessing Pain in the Rheumatoid Clinic

Although several pain assessment tools have been designed with the goal of quantifying RA-related pain, these tools must still rely on patients' subjective experience. Pain assessment tools fall into 2 major categories: self-reported questionnaires that require input from patients only, and combined tools that require input both from patients and healthcare providers. Simple, self-reported pain tools such as the VAS are often used in the routine rheumatology practice setting, while longer and more comprehensive tools are used primarily as endpoints in clinical trials (see Table 2).[7,14]

Rheumatoid Arthritis Pain Scale

The Rheumatoid Arthritis Pain Scale (RAPS) was the first pain-assessment tool developed and validated specifically for RA patients. The RAPS takes approximately 5 minutes to complete and requires input from RA patients and providers. Patients are asked to answer 24 questions describing the presence of pain, pain severity, and the extent that pain interferes with activities of daily living. To get an overall sense of pain, patients are also asked to describe their pain on a 10-point numeric rating scale (NRS). Lastly, the RAPS requires healthcare providers to conduct a total joint count (TJC). The 24 self-reported questions, NRS, and TJC are scored separately.[6] Although the RAPS was validated using physicians to score the TJC, physicians and nurses show high levels of agreement when scoring the TJC in patients with RA.[15]

Patient vs. Provider Global Assessments and the Role of Pain

Global assessments are simple tools for monitoring RA disease activity and response to RA treatment. Global assessments can be patient-reported or provider-reported, and typically involve a single question: "How are you (is the patient) doing?" Responses are marked on a VAS, with scores ranging from 0 to 10. Global assessment scores are rarely used as the sole measure of health status. More commonly, patient- and provider-reported scores are incorporated into composite disease activity measures (e.g. DAS28, clinical disease activity index [CDAI], and simplified disease activity index [SDAI]), which in turn are used to define the thresholds of clinical remission in RA.[16]

The main difference between the patient- and provider-reported global assessment scores involves the assessing respondent: patient-reported domains reflect the patient's subjective experience

of RA, while provider-reported items reflect the provider's perception. Recent studies suggest that provider-reported global assessment scores underestimate the severity and burden of RA-related pain. One study compared patient- and physician-reported global assessment scores among 1,923 RA patients receiving routine care at 3 academic rheumatology centers. The average patient-reported global assessment score was 3.59, indicating significantly worse RA disease activity in the overall study population than the average physician-reported global assessment score of 2.85.[17]

To understand these discrepancies, several other markers of RA disease activity were compared with global assessment scores in the study. On the individual patient level, patient-reported global assessment scores were significantly higher than provider-reported global assessment scores in patients with worse subjective markers of disease activity, including more severe pain and fatigue. Conversely, provider-reported global assessment scores were higher than patient-reported global assessment scores in patients with worse objective or physician-assessed markers of RA disease activity, including higher TJC, higher SJC, and elevated ESR levels.[17]

Another study of 311 patients with RA examined the correlation between patient-reported global assessment scores, provider-reported global assessment scores, markers of RA disease activity, and common RA comorbidities.[18,19] The patient-reported global assessment scores correlated significantly with several objective and subjective

Table 2

Self-Reported Pain Assessment Tools in Rheumatology[7,14]

Tool	Number of Questions	Administration Time	Description
Visual analogue scale (VAS)	1	<1 minute	• Patient describes pain intensity by marking a spot along a 100-mm vertical or horizontal line labelled "no pain" on one end and "worst imaginable pain" on the other • Score range: 0-100
Numeric rating scale	1	<1 minute	• Patient describes pain intensity on a numeric scale ranging from 1 ("no pain") to 10 ("worst imaginable pain") • Can be administered via a written tool or orally • Score range: 1-10
Verbal rating scale	1	<1 minute	• Patient describes pain intensity by selecting from a ranked series of verbal descriptors: no pain, mild pain, moderate pain, severe pain, very severe pain • Score range: 1-5; depends on how many descriptors are offered
Short-Form 36 Bodily Pain Scale (SF-36 BPS)	2	<2 minutes	• Questions assess: 1) pain intensity on a 6-point Likert scale; and 2) impact of pain on normal work on a 5-point Likert scale • Score range: 0-100
Short-form McGill Pain Questionnaire (SF-MPQ)	15 descriptive questions; 2 rating scales	2-5 minutes	• Abbreviated version of the McGill Pain Questionnaire: 11 sensory questions, 4 affective questions, 1 question on pain intensity, 1 pain VAS • Score range: 0-60
West Haven-Yale Multidimensional Pain Inventory (WHYMPI)	49	5-10 minutes	• Subscales evaluate 1) patient's experience with pain, 2) perceived support from spouse or significant other, and 3) extent of participation in daily activities • Identifies 3 coping styles: dysfunctional; interpersonally distressed; and minimizers/adaptive copers • Subscale score rage: 0-6
McGill Pain Questionnaire (MPA)	78	5-10 minutes	• Asks patients to identify words (from a total of 78) that best describe the quality and intensity of pain • Relies on a rich vocabulary of pain descriptors, which may be challenging for low-literacy patients • Score range: 0-78

variables, including pain, fatigue, physical function, anxiety, and SJC.[18] By comparison, the provider-reported global assessment scores correlated only with SJC and CRP levels, showing no correlation with pain.[19] Together, these findings indicate that patients and providers prioritize different aspects of RA disease activity in their global assessments, with patients placing a greater emphasis on pain.[17-19] Management decisions that disregard pain and other subjective features of RA may lead to disappointing treatment outcomes from the patient's perspective

Pain Pathways Beyond Inflammation

Joint inflammation is widely recognized as a common source of RA-related pain. However, patients with RA may experience several types of pain: pain from tissue injury and inflammation (***inflammatory pain***); pain arising from damage to the nervous system (***neuropathic pain***); and pain associated with abnormal central nervous system functioning and/or pain processing (***central pain***).[20] Comorbid pain syndromes are typically overrepresented in patients with RA. The prevalence of fibromyalgia, for instance, is approximately 4.0% among patients with RA, or approximately twice as high as that among persons without RA (1.9%).[2] In an analysis of the 2012 U.S. National Health Interview Survey, which represents 225 million adults, 15.3% of individuals who met the diagnostic criteria for fibromyalgia were also diagnosed with RA.[21] By comparison, the rate of RA in the general U.S. adult population is approximately 1.0%.[22]

Even when inflammatory joint pain is controlled with standard RA medications, other types of pain may remain undiagnosed and undertreated.[23] In one study of 84 patients with RA, 31% had neuropathic pain.[23] Therefore, it is important to consider the presence of neuropathic pain, central pain, and other pain pathways in the assessment and management of pain.

RA-related pain Management Guidelines

Historically, rheumatology providers have had little formal guidance on RA-related pain management. In 2012, however, an international consortium of 453 rheumatologists developed 11 key principles to guide pharmacologic pain management in patients with RA (see Table 3).[24] At present, these recommendations stand as the most detailed framework for the treatment of pain in patients with RA. Neither of the most recent RA treatment guidelines from the American College of Rheumatology (ACR) or the European League Against Rheumatism (EULAR) mentions the assessment or treatment of RA-related pain.[25,26]

Opioid Use and Misuse: A Growing Epidemic

When discussing the role of opioid therapy, pain is generally classified in 2 major ways.

First, pain is described as acute or chronic. Acute pain can include medical pain (e.g., passing a kidney stone), traumatic pain (e.g., a fracture or blunt force trauma), or postoperative pain. Acute pain is expected to resolve within a normal recovery period. Chronic pain is generally recognized as pain that lasts longer than 3 months or the expected timeframe of normal tissue healing. Approximately 14.6% of the general population has chronic pain, although the prevalence is higher in patients with musculoskeletal pain conditions such as RA, chronic low back pain, and severe headaches.[4]

Second, pain is described as cancer pain or non-cancer pain. Pain from a terminal illness generally follows the guidelines for cancer pain.

Within that framework, current clinical evidence supports the use of opioid analgesics in 3 specific scenarios:

- Short-term use for acute non-cancer pain
- Chronic use for cancer-related pain
- Palliative care and end-of-life pain management

Despite these narrow indications, prescriptions for opioid pain relievers have risen dramatically in recent years.[4] The largest area of growth in opioid prescriptions is for chronic non-cancer pain, even though the analgesic effects of opioids do not persist beyond 8 weeks in patients without cancer or a terminal illness.[27] Nonetheless, 20% of patients who present to healthcare providers with non-cancer pain are given an opioid prescription.[4]

The reasons for the increased use of opioids within the general population are complex. Some experts point to mandates from the Joint Commission and the Centers for Medicare and Medicaid Services for healthcare providers to document pain as the "fifth vital sign" at every patient encounter.[28] As a result, patients have higher expectations for better pain management, with some patients unrealistically seeking complete control of all pain. This is compounded by the growing reliance on patient satisfaction surveys that are tied to hospital reimbursement rates, as well as growing acceptance and decreasing stigma around opioid use.[2,28] In response to these pressures, clinicians wrote 259 million prescriptions for opioid pain relievers in 2012—enough for every adult in the United States to have a bottle.[5]

Consequences of Abuse: Opioid and Heroin Overdoses

Individuals with RA, as with the general population, are susceptible to addiction. Although no studies have been conducted on the incidence of heroin use specifically in patients with RA, some generalizations can serve as a backdrop for a discussion about the connection between opioid use and heroin. In addition, it is helpful to understand why a recent spike in heroin overdoses has led to public health campaigns focused on prescription opioid misuse.

Patients who develop a dependence on prescription opioid analgesics are at risk for initiating heroin. Past misuse of prescription opioid pain relievers is the strongest predictor of future heroin use. Additional factors such as the increased availability of heroin, its lower cost relative to prescription opioids, and its high purity have contributed to increased heroin usage, overdoes, and death. Between 1999 and 2014, more than 165,000 adults in the U.S. died from a prescription opioid overdose. In the last year, the rate of heroin deaths alone increased by more than 25%.

In 2015, the CDC issued a call to action to curb the opioid epidemic in the United States. To

Table 3

General Principles for the Pharmacologic Management of RA-related pain[24]

Recommendation 1: Pain assessment	• Measure pain routinely using one of the following validated scales: VAS, NRS or VRS • Consider multi-dimensional measures or site-specific tools as needed
Recommendation 2: First-line pain therapy	• Acetaminophen is recommended for the treatment of persistent pain
Recommendation 3: Glucocorticoids	• Systemic glucocorticoids are not recommended for routine pain management in the absence of signs and symptoms of inflammation
Recommendation 4: Antidepressants	• Consider adjuvant treatment with tricyclic antidepressants and neuromodulators • Muscle relaxants and benzodiazepines are not recommended
Recommendation 5: Opioids	• Weak opioids may be used for short-term treatment of pain when other therapies have failed or are contraindicated; long-term use may be considered and should be regularly reviewed • Strong opioids should only be used in exceptional cases
Recommendation 6: Intensifying therapy	• In patients with an inadequate response to acetaminophen or NSAID monotherapy, consider adding a drug with a different mode of action • Combinations of two or more NSAIDs should not be used
Recommendation 7: NSAID dosing	• NSAIDs should be used at the lowest effective dose, either continuously or on demand, according to clinical circumstances
Recommendation 8: Pregnancy	• Apply existing guidance regarding the safety of pain pharmacotherapies during pre-conception, pregnancy, and lactation
Recommendation 9: Methotrexate	• Methotrexate can be used safely in combination with standard doses of acetaminophen and/or NSAIDs (excluding anti-inflammatory doses of aspirin)
Recommendation 10: Gastrointestinal comorbidities	• In patients with gastrointestinal comorbidities, acetaminophen should be considered first • Non-selective NSAIDs in combination with PPI, or COX-2 selective inhibitors ± PPI, may be used with caution • In the presence of liver disease, standard precautions for use of NSAIDs and other analgesics should be applied
Recommendation 11: Cardiovascular and renal comorbidities	• In patients with pre-existing hypertension, cardiovascular or renal disease, acetaminophen should be used first • Use NSAIDs, including COX-2 selective inhibitors, with caution

COX-2, cyclooxygenase-2; NRS, numeric rating scale; NSAID, nonsteroidal antiinflammatory drug; PPI, proton pump inhibitor; VAS, visual analogue scale; VRS, verbal rating scale.

edge toward its goal, the CDC outlined a 4-step strategy to prevent deaths due to opioid and heroin overdoses:

- **Limit opioid misuse and addiction:** Reduce the over-prescribing of opioids and facilitate safe opioid prescribing practices with clinician support tools such as updated clinical guidelines (see next section: 2016 CDC Guideline on Opioid Use).
- **Expand access to substance-abuse treatment:** Provide greater access to treatment options for opioid use disorder, including access to medication-assisted treatment strategies that combine the use of medication and behavioral therapies.
- **Expand access to naloxone:** Increase access and use of naloxone, the opiate antagonist that blocks the effects of opioids, reverses the life-threatening symptoms of an opioid overdose, and prevents overdose deaths.
- **Improve detection and response to outbreaks:** Collaboration among state and local public health agencies, law enforcement, and medical examiners is needed to improve response times to outbreaks of illicit opioid overdoses due to tainted street drugs.

These strategies complement 2 existing national Risk Evaluation and Mitigation Strategy (REMS) programs specific to extended-release and long-acting opioids and transmucosal immediate-release fentanyl products, respectively.[27] These opioid REMS programs feature prescriber education, patient education, and patient-prescriber agreements that outline each party's responsibilities for safe opioid use.[27]

Individual states and healthcare systems have launched their own opioid harm-reduction programs. The Michigan Automated Prescription System (MAPS) functions as a centralized database of all prescriptions of Schedule 2-5 substances dispensed by pharmacies and healthcare professionals in the state. The MAPS database provides healthcare professionals with patient-specific prescription records, allowing clinicians to determine if patients are "doctor shopping" for multiple concurrent prescriptions.[29]

Data from the Ohio Automated Rx Reporting System (OARRS) shows a reduction in the rate of "doctor shopping" for opioid prescriptions by approximately 50% since its launch in 2007.[30] On July 1, 2016, California launched the Controlled Substance Utilization Review and Evaluation System (CURES) database to address prescription drug abuse and diversion.[31] Best practices from the REMS, MAPS, OARRS, and CURES programs may serve as a framework for addressing opioid misuse on a national level.

New Guidelines for Opioid Use for Chronic Pain

Part of the strategy to minimize the morbidity and mortality associated with opioid overdose involves better guidance on safe opioid use. In March 2016, the CDC published new evidence-based guidelines for the use of opioids in patients with chronic pain.[5] The guidelines include 12 recommendations (cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm) centered around the following 3 basic principles:

- **Limit opioid use:** Select non-opioid therapy as the preferred choice for treating chronic pain outside the settings of active cancer, palliative care, and end-of life care.
- **Limit opioid dosing:** When opioids are used, select the lowest possible dose for the shortest possible duration to minimize the risk of opioid use disorder and overdose.
- **Monitor patients closely:** In addition to exercising caution when prescribing opioids, providers should monitor all patients closely for signs of opioid use disorder.

The CDC website offers patient education materials and other tools to support clinicians in implementing the new opioid recommendations (cdc.gov/drugoverdose/prescribing/resources.html). The resources include a downloadable checklist for prescribing opioids for chronic pain (cdc.gov/drugoverdose/pdf/pdo_checklist-a.pdf).

What is the Evidence for Opioid Use in RA?

There is little evidence to support chronic opioid use in patients with RA. A recent Cochrane Review examined data from 11 studies of opioid use in 672 RA patients with pain.[32,33] The studies focused on 6 weak oral opioids (defined as dextropropoxyphene, codeine, tramadol, tilidine, pentazocine, and morphine) taken alone or in combination with other non-opioid analgesics for no more than 6 weeks, as well as 1 strong opioid (controlled-release morphine sulfate). Given that only 20 patients (2.9%) received morphine sulfate, the study findings focus primarily on the role of weak opioids in patients with RA. Patients treated with opioids were 44% more likely than those receiving placebo to report an improvement of at least 30% in global impression of pain control. However, 18.6% of patients treated with opioids decided to discontinue treatment due to inadequate

analgesic effects. A similar proportion of patients in the placebo group discontinued treatment. In practical terms, this translates into needing to treat 6 patients with opioids for 1 patient to achieve a benefit rated as "good" or "very good" within the first 6 weeks of treatment.

Patients treated with opioids were nearly 4 times more likely than those receiving placebo to report side effects, including nausea, vomiting, dizziness, and constipation (odds ratio, 3.90). The number needed to treat is 4, meaning that 4 patients will need to be treated with a opioid to result in 1 extra adverse event within the first 6 weeks of therapy. Overall, the review found limited evidence that oral opioids can improve RA-related pain control when taken for up to 6 weeks, but that the risk of adverse effects outweighs the benefits of treatment for most patients. To date, there is not enough evidence in RA patients to draw conclusions about the use of weak opioids for longer than 6 weeks, or the role of strong opioids for managing RA-related pain.[32,33]

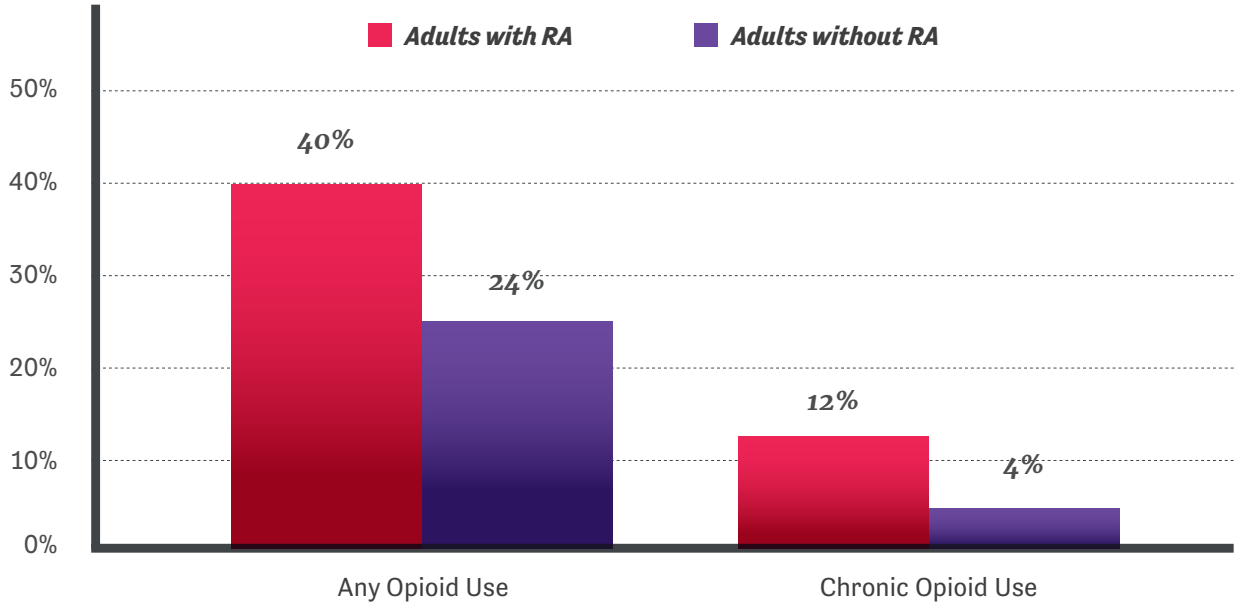
Another recent study highlighted the safety issues associated with prescription opioid use in patients with chronic noncancer pain, which may be relevant when weighing the potential risks and benefits of opioid therapy in patients with RA.[34] The 12-year study compared outcomes following 22,912 new prescriptions for long-acting opioids and other control medications (analgesic anticonvulsants or low-dose cyclic antidepressants) in patients being treated for back pain (75%), other musculoskeletal pain (63%), and/or abdominal pain (18%). Compared with patients treated with control medications, those treated with long-acting opioids had a 64% increase in the risk of death for any reason. More than two-thirds of the excess deaths in the opioid group were attributed to causes other than unintentional overdose. In particular, patients treated with opioids had a 65% increase in the risk of cardiovascular death compared with those treated with anticonvulsants or antidepressants.[34]

Trends in Opioid Use in RA

Despite the lack of evidence to support opioid use in RA, there is a high rate of prescription opioid analgesic use among RA patients. Patients with RA are more likely than individuals without RA to use opioids, even after controlling for traditional risk factors for opioid use such as smoking, educational level, depression, other pain syndromes, and comorbidity burden (see Figure 1).[2] Although opioid prescriptions are an imperfect approximation of actual opioid use, prescription rates are one of the best tools for understanding utilization trends in different patient populations.

One recent retrospective study analyzed opioid prescription use between 2005 and 2014 among 501 patients with RA and 532 age- and sex-matched individuals without RA. In general, patients with RA were 1.5 times more likely to use opioids than individuals without RA, and twice as likely to use these medications chronically. The prevalence

Figure 1
Opioid Use in Adults With or Without RA, 2014[2]



"Any opioid use" is defined as having one or more opioid prescriptions for any period of time. "Chronic opioid use" is defined as having a prescription for any opioid at the usual dose and schedule for 60 days or more within a 6-month period, or use of fentanyl, methadone, and/or controlled/extended-release oxycodone.

of opioid use increased in both groups by 19% during each year of the 10-year follow-up period, matching upward trends in opioid use in the general population. By 2014, 40% of patients with RA reported any opioid use, compared with 24% of individuals without RA. This included chronic opioid use in 12% of RA patients and 4% of persons without RA. The most commonly prescribed opioids were oxycodone (39%), hydrocodone (18%), tramadol (22%), fentanyl (6%), codeine (5%), propoxyphene (4%), and morphine (3%).[2]

Among RA patients, there was no correlation between opioid use and standard markers of RA disease severity, including rheumatoid factor (RF) or anti-citrullinated protein antibody (ACPA) positivity, elevated erythrocyte sedimentation rate (ESR), the presence of rheumatoid nodules or erosive changes on radiographs, or treatment with biologic therapy.[2] This suggests the importance of another pain pathway related to chronic inflammation that may be activated in some patients with RA.

Non-Opioid Pain Medication in RA

Non-opioid analgesics form the cornerstone of pain therapy for patients with RA-related pain despite adequate control of RA inflammatory disease activity. First-line treatment with acetaminophen or NSAID monotherapy is recommended for RA patients with persistent pain (see Table 3 on page 8). Standard precautions around acetaminophen and NSAID use should be considered for special patient populations, including patients who are pregnant and those with comorbid gastrointestinal, cardiovascular, or renal disease. Glucocorticoids are not recommended for RA-related pain management in the absence of uncontrolled inflammation.[24]

The potential analgesic effects of antidepressants have been examined in patients with RA, including those with and without comorbid depression.[35,36] The benefits of tricyclic antidepressants and selective serotonin-uptake inhibitors are limited, although most studies in RA patients have been small and involved short treatment durations.[35,36] In general, antidepressants are not recommended as the sole treatment strategy for RA-related pain management, but they may be useful as part of a comprehensive analgesic approach in select patients.[32] It may be appropriate to consider newer antidepressant classes in patients with pain from RA and comorbid depressive symptoms.[24]

Cannabinoids have also been evaluated for the management of chronic pain in patients with rheumatic disease, although to date, there is not enough evidence to support the use of cannabinoid preparations to manage RA-related pain.[37]

Role of Early RA Treatment in Pain Management

Patients with early RA may have a unique window of opportunity for controlling pain from RA. One recent study examined trends in RA-related pain control during the first 2 years of DMARD treatment in 205 patients with early RA. Prior to starting DMARD therapy, 20% of patients had low RA disease activity, 47% had moderate disease activity, and 33% had high RA disease activity. The mean pain VAS was 45 mm. Patients started intensive DMARD therapy according to the Treat to Target (T2T) guidelines, with the goal of achieving clinical remission. The mean pain VAS decreased to 12 mm after 1 month of DMARD therapy and 6 mm after 1 year. Patients maintained a mean pain VAS of 7 mm through the second year of DMARD therapy, with 87% of patients reporting no pain or mild pain. These results show that early RA treatment, initiated with the aggressive T2T goal of clinical remission, leads to a rapid, substantial, and sustained decrease in the burden of RA-related pain.[38]

Alternatives to Pain Medications

Nonpharmacologic strategies for managing RA-related pain include physical activity and cognitive behavioral therapy.[5] Multimodal exercise programs that incorporate aerobic activity, resistance training, and flexibility exercises have been shown to reduce pain in patients with RA, osteoarthritis, fibromyalgia, and chronic low back pain. Evidence also supports the benefits of specific activities such as low/moderate-intensity pool exercises and mind-body exercise programs such as yoga and Tai Chi. Across several studies, the analgesic effects of physical activity are largely comparable to those of simple NSAIDs for controlling RA-related pain.[39]

Fear of pain, depression, anxiety, poor sleep, and other barriers may negatively impact a patient's motivation to exercise. To address these physical and emotional barriers, exercise recommendations should be tailored to meet the specific needs and limitations of patients with chronic pain. Over time, routine physical activity will improve physical function, sleep, fatigue, depression, and anxiety in patients with RA and other rheumatic diseases. Combining exercise with cognitive behavioral therapy, self-management education, and other nonpharmacologic interventions can further improve overall RA-related pain management.[39]

Placebo Effect in Pain Management

The placebo effect occurs when patients experience pain relief simply because they anticipate an

analgesic benefit, even when no active treatment is given.[40] Placebos are often administered as sham medications (i.e., sugar pills), but also come in the form of verbal instructions, visual cues, and cognitive conditioning.[40] Remarkably, the placebo effect is not all in the patient's mind. Placebos can trigger the endogenous release of natural opioids, with onsets of action that mimic those of prescription drugs.[40] In some patients, the magnitude of the placebo response can match or surpass the analgesic effects of active treatment with NSAIDs.[41]

The opposite of the placebo response is the nocebo response: when patients experience new negative symptoms due to expectation or apprehension of side effects, even when an inert treatment is given.[41] Although both the placebo and nocebo responses influence the patient's symptom burden, they typically have no effects on the underlying disease process. Research is now underway to harness the placebo response as part of a comprehensive strategy for chronic pain management.[40,41]

Multidisciplinary Pain Management Clinics

In general, RA patients with persistent pain may benefit from specialty care in one of two types of clinic environments. The first is a multidisciplinary rheumatology clinic that focuses on patients with rheumatic diseases and provides a range of pharmacologic and nonpharmacologic interventions, with competence in RA-related pain management. The second is a specialized pain clinic that serves patients across a spectrum of diagnoses that involve chronic pain. There are benefits and limitations to both treatment settings. Multidisciplinary rheumatology clinics often have a better understanding of the nuances of rheumatic diseases, but may have less experience managing chronic pain. Conversely, pain clinics may offer a wider variety of pain interventions, but often lack expertise in RA care.[42] Multidisciplinary rheumatology clinics may be more appropriate for patients with complex pain syndromes, such as patients with comorbid RA and fibromyalgia.[43]

Regardless of the setting, the ideal multidisciplinary team involves a physician specializing in pain management (general practitioner or anesthesiologist), a mental health specialist (psychiatrist and/or psychologist), a physical therapist, and a nurse.[42] Some teams also involve occupational therapists, vocational rehabilitation experts, and social workers.[43] Pain clinics are diverse in their offerings, but the types of interventions may include:[42,43]

- Cognitive-behavioral therapy
- Supervised exercise programs
- Specialized procedures such as nerve blocks
- Massage, meditation, and other stress reduction therapies
- Self-management education
- Psychological counseling to build coping skills and address pain catastrophizing, if needed

Most rheumatology patients who are referred to a specialty pain clinic will be under the care of a rheumatology practice and have a defined diagnosis, such as RA.[42] Outpatient specialty pain programs typically last several weeks, during which time patients and providers identify a pain reduction regimen that meets the patient's specific medical and psychological needs.[42,43] Pain management plans should be developed in collaboration with the patient's rheumatologist or primary care provider. The goal is to empower the patient to return to his or her regular treatment environment with better self-management and coping skills.[42,43] In a study of patients with fibromyalgia, attending a nurse-led chronic musculoskeletal pain clinic significantly reduced the number of subsequent office visits to primary care physicians, indicating a significant improvement in pain self-management.[44]

Summary

Pain is common in RA and does not necessarily correlate with RA disease activity, suggesting the need for a comprehensive approach to pain management that goes beyond targeting inflammation. For most patients with RA, the potential short-term benefits of opioid therapy outweigh the risks. Instead, non-opioid analgesics are recommended for the first-line treatment of RA-related pain. Depression, anxiety, fatigue, and pain catastrophizing predict worse pain outcomes, and should be addressed with referrals for cognitive behavior therapy, adjunctive antidepressant therapy, and other individualized interventions. Rheumatology providers should consider referring RA patients with residual pain to a multidisciplinary rheumatology clinic or to a specialty pain center for improved pain control.

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Providing Protection for Our Patients in Pain

by Jacqueline Fritz, RN, MSN, CNS, RNBC

P *— Protect* ***A*** *— Anyone* ***I*** *— In* ***N*** *— Nociceptive Pain*

According to the American Pain Society, patients in pain are the largest group of Americans that receive suboptimal care.[1] A 2015 study by the National Institutes of Health further illustrated this epidemic, stating that 11.2% of our population has chronic pain daily.[2] Quite simply, pain has become a silent epidemic of distress, disability, and danger in the United States.

As rheumatology nurses, we see nociceptive pain perhaps more commonly than any other type. Nociceptive pain is a chronic condition detected by nerve endings (called nociceptors) that are found in the skin, internal surfaces of the bone, and joint surfaces. There are so many ways to treat chronic pain (either nociceptive or neuropathic), and we are often faced with difficult risk vs. benefit decisions when determining the most appropriate route for our patients.

S.B. is a patient of mine being treated for RA and reflex sympathetic dystrophy. Managing her pain, to put it mildly, has been a challenge. Her chart is complex—acute phase reactants are never elevated, but she always has numerous tender and swollen joints. Her Vectra DA score hovers around 59, indicating a high level of disease activity.

Her medication history is just as dizzying—she has tried GABA receptor antagonists, NSAIDs, SNRIs, tricyclics, sedatives, antispasmodics, benzodiazepines, and all the nonbiologic DMARDs typically used to manage RA. She's also cycled through numerous opioids—both oral and transdermal—with minimal success.

Steroids help, but we are limited in their use due to S.B.'s diabetes. Her insurance will not cover a corticotropin injection or prednisone delayed release tablets. Biologics are out since S.B. has frequent allergic reactions, difficulty tolerating medications, or simply has not responded to previous efforts.

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Jacqueline Fritz, RN, MSN, CNS, RNBC, is Owner and Coordinator of Education at the Medical Advancement Center in Cypress, CA. Her primary responsibility is working as an advanced practice nurse for a large rheumatology practice where she is involved in patient visits, research programs, and infusion center coordination. In addition, she enjoys speaking, teaching, and learning about immunology.

With each medication failure and exacerbation of her nociceptive pain, S.B.'s depression grew worse. For years, I watched her will to live being sucked out of her every month. It has been heartbreaking. Every time she had an appointment, we would go over additional alternative therapies we could try. Her electronic medical record of failed therapies grew lengthy, and certainly demonstrated our concentrated efforts to find a solution.

Out of desperation, I called a device manufacturer a few months ago to see if S.B. would qualify for an intrathecal pain pump (she did). This was one of those complex risk vs. benefit determinations—there are many contraindications to intrathecal pain pumps such as infection, bleeding and cerebral spinal fluid leaks, especially for patients with immunosuppression.[3]

Intrathecal pain pumps are typically usually used for cancer patients or patients where conservative treatments for pain management have failed. The tip of catheter is placed in the intrathecal space surrounding the spinal cord. A trial of medication is connected to a temporary pump to determine if the system will help. Again, for S.B., even a small incision was worrisome, but we had reached the point where this seemed to be best option.

Two weeks after the insertion of the pain pump, S.B returned to our office with a smile on her face. The intrathecal pump had helped immensely, reducing her pain by approximately 50% and decreasing the number of tender joints. While there were big smiles and hugs for everyone, I reminded S.B. that there were still hurdles to overcome before we could celebrate. She'll soon need surgery to place the pump permanently, a procedure that carries risks of general anesthesia and infection. Still, hearing S.B. talk about the condo she is going to buy near the beach instead of suicide has been a major pick-me-up.

The best approach for rheumatology nurses continues to be identifying patients with rheumatic disease and taking an appropriate stepwise approach to treating to a predetermined target. With some patients, this is easy; with others like S.B., it can be much more challenging. The rewards, however, are great when we achieve a measure of success in our most frustrated patients.

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Keeping It Simple: Patient Education for Opioid Use

by Elizabeth Kirchner, CNP

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Patients with rheumatoid arthritis (RA) and chronic pain often have complex problems. These problems can run the gamut from permanent joint damage to soft tissue pain to daily headaches to psychological suffering. The pharmacologic and non-pharmacologic approaches to treating pain can also be complex and require a multi-disciplinary team to manage properly.

However, one component of pain management that does not need to be complex is patient education. And as rheumatology nurses, this is a particular area where we can have a real impact on our patients' lives.

My first step in educating patients about pain management is to talk to them about the many options available for treating chronic pain. If the conversation turns to opioid analgesics, I try to give a fair and balanced view of the potential risks and benefits associated with this class of drugs. Just to be clear—in some patients, opioids may be a viable option. However, responsible healthcare providers are aware that there are many misconceptions and opportunities for problems surrounding this class of drugs.

When we're educating our patients about opioids—just as with any other subject—there are many opportunities to connect with them in a way that they will understand and that will have meaning. There is often something in the patient's history that guides me toward one particular angle during discussions of possible opioid use. For example,

"...one component of pain management that does not need to be complex is patient education. And as rheumatology nurses, this is a particular area where we can have a real impact..."

in a patient who has proven to be an avid researcher about medications in the past, I focus my attention on clinical trials and post-marketing safety data. For patients who have small children or teenagers in the house, I may focus on household and community safety and statistics.

Regardless of the patient, here are the baseline opioid-related topics I make sure to always address.

1. **Long-term opioid safety studies in autoimmune diseases**

   Basically, as I explain to my patients, there aren't any. I ask them how they would feel about taking any of their other medications (methotrexate, for example, or even a cholesterol or blood pressure medicine) if that medication hadn't been studied in a randomized, double-blind, placebo-controlled fashion in patients with a condition similar to theirs. Most of the time, my patients tell me they would not be comfortable taking that medication under those circumstances.

   I then tell them that there are no studies of the long-term effects of opioids in patients with autoimmune inflammatory disease. None. Zero. We basically have no idea what to tell patients to expect if they take opioids for longer than 6 weeks.

2. **Efficacy**

   There are many misconceptions about how effective opioids are at relieving pain. Patients frequently tell me that their pain medicine only "takes the edge off," which is when I remind them that that's often about all they can expect. Opioids aren't miracle drugs; they will not give patients a 100% pain-free existence. The pain management experts at our hospital tell patients that opioids alone will control about 30% of their pain. Taking more opioids won't increase that percentage; it will only increase the chances of adverse effects.

   In patients who need opioids for chronic pain, we're looking for a measurable increase in functionality. Here is an example: A patient tells me her pain rates "a 7 out of 10," and she is in too much pain to do more than the very basics. Yoga, physical therapy, and acetaminophen have helped, but only slightly. After a 1-month trial of opioids, she returns to clinic reporting that her pain is still "a 6 or 7," but now she walks the dog, visits with friends, does more around the house, and is thinking about returning to work part time. We would define her case as a success.

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3. **Known risks of opioid analgesics**

   These include constipation, nausea, drowsiness, dry mouth, loss of appetite, impaired concentration, impaired memory, urinary retention, mood swings, erectile dysfunction, anorgasmia, hormonal imbalances, itching, swelling, hyperalgesia, respiratory depression, low blood pressure, dizziness, nervousness, seizures, and weight gain… just to name a few.

4. **Drug-drug interactions**

   Many patients who take opioids for pain are also prescribed benzodiazepines such as zolpidem for sleep or lorazepam for anxiety. There are more and more studies coming out concluding that the combination of opioids and benzodiazepines can be harmful, leading to an increased incidence of respiratory depression and even accidental overdose.[1] Since patients with RA are often on multiple medications, these and other potential drug-drug interactions may be significant.

5. **Risks to self**

   Opioids frequently cause sedation. Patients who take opioids should be cautioned against driving or operating any heavy machinery.

6. **Risks to family/friends**

   Unfortunately, we have all heard stories of children, teenagers, or young adults accidentally or intentionally taking their parents' or grandparents' pain medication. Sadly, some of these stories end in death. It doesn't really matter if the patient promises to keep their medication hidden or locked up. All it takes is one time forgetting to put it away and one of their loved ones can be seriously hurt or killed.

7. **Addiction**

   We cannot predict who will become addicted to pain medication, but it is a fact that some patients do. Patients deserve to know that there is a risk of addiction if they take opioids.

8. **Legal issues**

   Many patients are unaware that if they are involved in a legal dispute and it is deemed relevant by the courts, their prescription history can be subpoenaed. In the state where I practice (Ohio), law enforcement officials can legally access a controlled-substance database for any active investigation without a court order.

Every time a nurse counsels a patient about his or her medications, it is essential to make sure that the patient is educated about the potential risks. This is just as true for something as seemingly innocuous as acetaminophen (which we all know is not as innocuous as many believe) as it is for the big guns like biologic agents, chemotherapy, and antibiotics.

Educating patients about opioids is complicated by legal, political, and social issues. These can make the patient discussion about risks and benefits more difficult and time consuming than it might for other types of medications. Patients, however, deserve to know the facts, and it's our job to give them an unbiased and comprehensive review of the key issues to consider.

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Cycling Through a Lifetime of Pain Management

by Iris Zink, MSN, NP

J.G. is a 66-year-old patient of mine who lives with rheumatoid arthritis (diagnosed at age 31), osteoarthritis of her entire spine, gouty arthritis, and osteopenia. Of course, she struggles with the chronic pain associated with these diseases and has for decades.

We have tried nearly every medication available to try to get J.G.'s disease under control and relieve her symptoms. For many years she was managed with intramuscular gold, oral and injectable steroids, and aspirin. She was eventually moved up to a triple cocktail of methotrexate, sulfasalazine, and hydroxychloroquine in addition to the gold therapy.

In June 2001, J.G. was put on etanercept for her worsening rheumatoid arthritis (RA). Shortly thereafter, she was hospitalized for an upper respiratory infection that progressed to pneumonia, and the etanercept was discontinued.

Over the course of the next few years, J.G.'s condition continued to worsen. She developed chronic kidney disease that required multiple blood transfusions, had cervical spinal stenosis surgery that left residual numbness in her hands, and complained regularly of lumbar spinal issues. It wasn't until we transitioned J.G. to abatacept in 2010 that we finally started to see some improvement in her health, with

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improvements in her kidney disease, anemia, and near-elimination of the need for blood transfusions.

As with many of our patients who struggle to get their disease under control and suffer through many bad days, J.G. tried a variety of approaches to manage her pain, including tramadol hydrochloride/acetaminophen, hydrocodone, and acetaminophen with codeine. At the height of her pain in 2003, J.G. began taking controlled-release morphine.

Unfortunately, like clockwork, every two weeks J.G. would have one bad day of vomiting due to the morphine, likely due to her poor renal function. Two days after each vomiting episode, J.G. was able to resume taking morphine again and would be fine until the cycle repeated 2 weeks later.

This pattern continued for many years despite our efforts to make minor tweaks to the regimen. In 2011, J.G. was finally able to wean herself off of morphine after receiving a prescription for medical marijuana from another physician.

The use of medical marijuana is clearly a controversial issue across the country, and in our clinic, we do not sign for medical marijuana dispensing cards despite the 2008 passage of a statewide referendum in Michigan legalizing use of the drug in patients with debilitating medical conditions. J.G. currently smokes 2-3 joints of medical-grade marijuana each day to help with pain control and reports that it positively impacts her day-to-day activities. There is some preclinical evidence showing that inflammatory cytokines are dampened down by cannabinoid receptors present on lipocytes, though more research is clearly needed.[1]

As I think about J.G., there are many questions that run through my mind. If her RA had been better controlled earlier in her life, would she have required fewer pain medications? If she had been less reliant on steroids and narcotics, would she still have developed chronic kidney disease? Did her kidneys improve when she was able to wean herself off of morphine? What side effects might long-term use of medical marijuana cause in her future?

There are no right answers when it comes to the management of chronic pain. As nurses, we are passionate about helping our patients, and while we may not always agree with their choices, it is important that we listen and empathize with them to try to maximize their quality of life.

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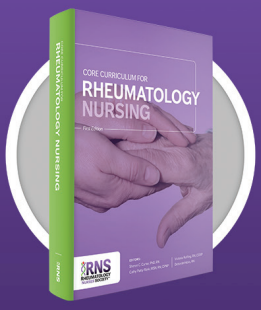

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Making Better Informed Decisions About Opioid Use

by Sheree C. Carter, PhD, RN

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It seems as though once direct-to-consumer advertising appeared for the treatment for opioid-induced constipation, there was an upsurge in the practice of prescribing and treating chronic pain with opioids. Being rheumatology nurses, we are all very familiar with chronic pain and the struggles of our patients to function despite their inflammatory disease. Part of our decision to dedicate this issue of *Rheumatology Nurse Practice* to pain management is to provide evidence-based information and credible resources in order to educate providers in an informed, unbiased, and respectful manner.

Recently, I had the pleasure of attending a Substance Abuse and Mental Health Services Administration (SAMHSA) seminar on clinical challenges in opioid management. During this seminar, SAMHSA speakers reported data from a review by Vowles et al that looked at problematic opioid use in chronic pain.[1]

In the author's review of 38 studies involving chronic pain patients treated with opioids between January 2000 and December 2013, only 8-10% of all cases ended in addiction and only 20-30% resulted in opioid misuse or abuse. Areas of misuse and abuse were categorized as "underuse," "erratic or off the written prescription" (more than one prescribed pill or less hours between doses), "inappropriate use for symptoms other than for which the opioid was prescribed" (stress, anxiety management), or "used with alcohol, benzodiazepines, or illegal substances."[1]

The takeaway from this study is that opioid misuse can be relatively common, but actual abuse or addiction is generally uncommon. Not prescribing an opiate for severe chronic pain due to fear of turning the patient into an addict is markedly at the forefront of the prescriber's thoughts for pain management, especially in today's news cycle. However, there is no substitute for a thorough assessment of the patient for the probability of potential opioid misuse or abuse.

As we age, pain is a part of life. Everyone experiences pain differently, in both a sensory and emotional form. The ultimate goal in managing chronic, non-malignant pain must be to improve patient functioning, increase physical activity, and identify, eliminate, or reduce pain reinforcers. The outcome goal should **never** be total eradication of pain.

The first goal in treating patients with chronic pain is to establish the type of pain the patient is experiencing. In rheumatology, we are most familiar with inflammatory pain and often treat to reduce inflammation that causes pain. Opiates are not typically the best choice for that type of pain.

When the symptom of pain becomes a disease of pain (ie, chronic pain), an opiate is a more viable option. At the recent SAMHSA seminar, speakers suggested tying opioid pain relief to an objective marker, such as functional improvement.[2] The validated Diagnosis, Intractability, Risk, Efficiency (DIRE) tool is a simple assessment that takes less than 2 minutes to complete and may help identify patients at risk of opioid abuse, misuse, or addiction. It is available both in paper format and as an iPhone app.[3] There are many other suitable tools—I encourage you to do research to select one that meets your needs.

"The ultimate goal in managing chronic, non-malignant pain must be to improve patient functioning, increase physical activity, and identify, eliminate, or reduce pain reinforcers. The outcome goal should never be total eradication of pain."

There were several online courses recommended during the SAMSHA meeting for anyone interested in additional information as well as AMA PRA Category 1 Credits™. SAMHSA has a free, 6-module online course available at www.opioidprescribing.com. The Office of Disease Prevention and Health Promotion (ODPHP) has a web-based training course that allows the learner to assume the character of a nurse, pharmacist, patient, and/or primary care physician located at health.gov/hcq/training-pathways.asp.

Lastly, a good resource for current guidelines and checklists specific to opioid prescriptions for chronic pain is provided by the Centers for Disease Control and Prevention (CDC) and can be found at cdc.gov/drugoverdose/prescribing/guideline.html.

As you think about the treatment of chronic pain, keep in mind that the frequency of opioid misuse, abuse, and addiction may be lower than you think. It is estimated that 1 of every 5 individuals with chronic pain are prescribed an opioid, so the risk is real, but so are the potential benefits.[4]

As rheumatology nurses, it is first important to understand the type of pain you are treating. Fully assess your patients risk for potential misuse, abuse, or addiction. Tie prescriptions to functional improvement and monitor patients frequently. Finally, educate yourself on use and guidelines associated with opioids. By taking these steps, you can be an informed and responsible provider for your patients.

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