

## REVIEW

# Chronic non-malignant musculoskeletal pain in older adults: clinical issues and opioid intervention

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Musculoskeletal pain is common, frequently under-reported, and inadequately treated in the older adult. The objective of this article is to review the management of musculoskeletal pain syndromes in older adults emphasising the potential role of opioid agents in carefully selected patients. Systematic analysis of the relevant literature was done. Even in cognitively impaired patients, assessment of musculoskeletal pain is mandatory. An algorithm for musculoskeletal pain is presented emphasising a stepwise pharmacological approach in combination with an array of non-pharmacological therapies. Comorbid conditions may limit therapeutic choices, particularly in the elderly. Repeated assessment of pain levels as well as functional status is critical for optimal pain management.

developed nations and triple in developing nations.<sup>5</sup> In an aging population, chronic disabling conditions are most common.<sup>6–8</sup> Empirical evidence of the association between the presence of musculoskeletal pain and physical disability has been reported in the older adult.<sup>9</sup>

Despite the ready availability of effective pharmacological and non-pharmacological treatments, inadequate management of pain, particularly in the elderly, is well documented in the United States.<sup>10–12</sup> The most common aetiology of chronic non-malignant pain in older persons is musculoskeletal including arthritis and myofascial pain syndromes. According to the National Council on Aging, the major sources of pain identified in nursing home patients included arthritis (24%) and previous fractures (14%).<sup>13</sup> Similarly, another study concluded the most common causes of pain in nursing home patients to be arthritis (70%) and previous fractures (13%).<sup>14</sup> For example the frequency of symptomatic osteoarthritis of the hip and knee is 9% in persons aged 30 and over.<sup>15</sup> Radiographically, knee osteoarthritis is nearly twice more common in women and increases with increasing age, reaching a prevalence of 19.5% to 25% in women by 65 years of age.<sup>16–18</sup> Approximately one third of the patients with radiographic knee osteoarthritis experience symptoms.<sup>16, 17</sup> Because of the magnitude of the problem, we aim to review the management of musculoskeletal pain syndromes in older adults and emphasise the potential role of opioid agents in carefully selected patients through this article.

Changes in the demographic characteristics of the world population represent a critical challenge to clinicians. The number of adults aged 65 and older continues to grow at an unprecedented rate. The definition of the elderly, according to the United Nations, are those 65 years and more, which constitute the elderly (older persons) and those 80 years or more making up the oldest old.<sup>1</sup> In the United States individuals who had reached their 65th birthday accounted for only 4% of the total population in 1900, but currently number 35 million persons, approximately 13% of the population.<sup>2, 3</sup> Although the number of those aged 85 or older in 1990 accounted for little more than 1% of the population, their representation within the general populace is projected to quadruple by 2050.<sup>2, 4</sup>

The aging of the world's population exhibits similar trends. According to the United Nations,<sup>5</sup> the number of people worldwide aged 60 years or older will increase from one in 10 currently, to one in five by 2050. In some developed countries this proportion will increase from the projected one in five to one in two by the year 2050. The population aged 80 years or older is also projected to increase from 11% of those older than 60 years now to 19% by 2050. The number of centenarians is expected to increase 15-fold to 2.2 million. The rate of aging of the population is greatest in developing countries, a growing challenge for nations with few health care resources. By 2050, the ratio of people 65 years or older to those aged 15–64 years will double in

## MUSCULOSKELETAL PAIN IN THE OLDER ADULT

The increasing role of surgical treatment of musculoskeletal pain in the older adult underlines the magnitude of the problem. In the Medicare population in the United States for example, rates of total joint replacement surgery for patients with severe hip or knee osteoarthritis more than doubled between 1988 and 1997. Over the same time period, rates of spine surgery in Medicare patients increased by 57%.<sup>19</sup>

Other non-rheumatic disorders more common in older patients may also present with musculoskeletal pain. For example symptoms associated with Parkinson's disease include muscle

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**Abbreviations:** COX-2, cyclo-oxygenase-2; NSAID, non-steroidal anti-inflammatory drug; TCA, tricyclic antidepressant; TENS, transcutaneous electrical nerve stimulation

cramps or tightness in the neck, back, and legs; a dull pain in the head and neck; painful dystonias especially in the feet; and neuropathic pain consisting of burning pain, tingling, or numbness.<sup>20</sup> Careful evaluation of the elderly with musculoskeletal pain symptoms for such non-rheumatic disorders is mandatory. Not only is musculoskeletal pain a common problem in the elderly, it commonly leads to a decrease in functional ability and quality of life.<sup>21</sup> Chronic pain is a complex phenomenon and requires a multifaceted approach incorporating non-pharmacological and pharmacological modalities. For carefully selected patients, opioids may provide excellent analgesia with a favourable risk: benefit ratio.

### UNIQUE ISSUES IN PAIN MANAGEMENT IN THE OLDER ADULT

Although elders suffer chronic pain more frequently than do other populations,<sup>13 22 23</sup> their pain is often under-reported and under-treated.<sup>13 24 25</sup>

Reasons for under-reporting are the beliefs and expectations about pain as a normal part of aging or concern, poor health education among the elderly, misinterpretation of symptoms because of concomitant disease, and communication problems. The discrepancy between the high prevalence of pain in the elderly and the limited attention paid to this group in the research literature and in medical and nursing texts has also been noted.<sup>26</sup> Of all reports about pain published annually, fewer than 1% focus on pain experience or syndromes in the elderly.<sup>27</sup> The consequences of poorly managed pain, particularly in the elderly, may include depression,<sup>24 25 28-33</sup> social isolation,<sup>24 25</sup> sleep disturbance,<sup>24 25</sup> decreased ambulation,<sup>24 25</sup> and increased healthcare utilisation and cost.<sup>25</sup>

Comorbid medical conditions are typically much more common in an elderly population.<sup>28 34</sup> Many patients over 65 have multiple non-rheumatic disease conditions such as cardiovascular disease, diabetes, hypertension, and renal disease that functionally limit normal activity. These medical problems significantly complicate treatment of musculoskeletal symptoms. Memory and cognitive impairment add to this problem. Cognitive impairment, delirium (common among the acutely ill elderly), and dementia (which occurs in as many as 50% of the institutionalised elderly) pose serious barriers to pain assessment.<sup>35</sup> Patients with cognitive impairment have been the subjects of two significant studies.<sup>14 36</sup> Parmelee *et al* concluded that in patients with mild to moderate cognitive impairment, complaints of pain were no less valid than in patients with normal cognitive function.<sup>36</sup> In a separate study, the investigators found that at least 80% of patients could respond to at least one of the scales and give meaningful and probably reliable information about their pain.<sup>14</sup>

The initial assessment of the older person with musculoskeletal pain should address at least the following primary objectives: distinguish patients with common musculoskeletal causes of pain from those with serious visceral or non-rheumatic spinal pain; identify significant comorbid conditions that may influence the treatment or may even present as musculoskeletal pain; and recognise significant complicating psychosocial issues that may impact on the management of the patient's pain.<sup>28</sup>

### PAIN MANAGEMENT IN THE OLDER PATIENT

The American Geriatrics Society disseminated a clinical practice guideline for the management of chronic pain in older populations in 1998.<sup>25</sup> Since then, important advances in pharmacology and strategies for the assessment and management of pain in the elderly have emerged.<sup>37 38</sup> Unfortunately, pain management strategies for older patients

have not been systematically evaluated, and most approaches have been extrapolated from clinical experience with younger patients and patients with cancer pain. Both non-pharmacological and pharmacological modalities should be considered with treatment individualised as much as possible.

A proposed pain treatment algorithm for chronic non-malignant musculoskeletal pain is shown in fig 1.

### NON-PHARMACOLOGICAL STRATEGIES

Non-pharmacological approaches used alone or in combination with appropriate pharmacological strategies should be an integral part of care plans for most chronic pain patients.<sup>39</sup> These approaches may augment the efficacy of medications, but typically have fewer adverse effects. Non-pharmacological therapies and interventions include physical therapy, occupational therapy, exercise modalities, transcutaneous electrical nerve stimulation (TENS), education, acupuncture, and social support.

Evidence supporting the effectiveness of physical therapy is well documented, and active exercises, conditioning, and incorporating weight training into an exercise programme is commonly prescribed for patients with chronic musculoskeletal pain.<sup>40 41</sup> Although comorbid medical conditions and the general frailty of elderly patients often raise concerns about safety of an exercise oriented approach, published trials of non-medicinal and non-invasive therapies for hip and knee osteoarthritis have shown beneficial effects in older persons participating in exercises.<sup>42 43</sup> Occupational therapy interventions that focus on everyday practices of the older adult can make a significant difference to a patient's independence and reduce hazards. Minor modifications should be made, if appropriate, like installation of handrails, raised seats, and improved lighting within the home.

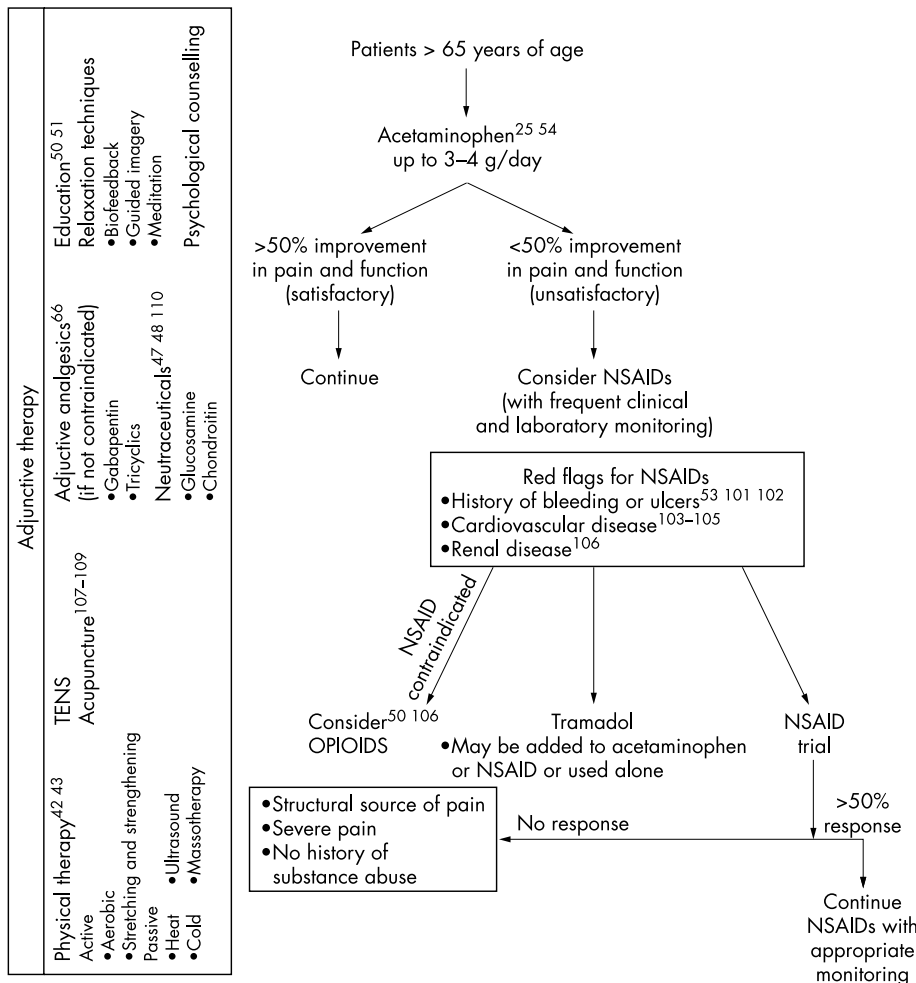
Controlled trials<sup>44</sup> and more recent meta-analysis<sup>45 46</sup> have concluded that TENS is not effective in the treatment of chronic low back pain. Despite this evidence, TENS is widely used to treat chronic musculoskeletal pain in elderly patients. So called passive modalities such as massage, ultrasound, heat, or ice may provide temporary symptomatic relief with the advantage of minimising transport of the older patient and low cost treatment. A recent assessment of nutraceuticals (foods or naturally occurring food supplements thought to have a beneficial effect on human health such as glucosamine) as therapeutic agents in osteoarthritis has suggested a beneficial effect on chronic musculoskeletal symptoms ranging from moderate to large.<sup>47 48</sup>

Additional research has shown that simply providing a supportive environment helps to control pain.<sup>49</sup> Providing patients and families accurate and understandable information about pain, pain assessment, and the use of drugs and other methods of pain relief, as well as emphasising that almost all pain can be effectively managed, improves outcome. Patient education should also address major barriers to effective pain management, namely, patients' reluctance to talk about their pain with their care providers, their fears about becoming addicted to opioids, and that the pain cannot be effectively controlled without unacceptable consequences. Other misconceptions, such as the thought that pain medication should be saved for when pain is severe or else it might not be effective, should be addressed.<sup>50</sup>

Patients who receive medication related education have a higher rate of compliance with analgesic prescriptions, fewer concerns about taking opioid analgesics, and lower pain levels than do patients not given such information.<sup>51</sup>

### PHARMACOLOGICAL INTERVENTION

Available analgesics include non-opioids such as acetaminophen (paracetamol in the UK)<sup>52</sup> non-steroidal anti-inflammatory drugs (NSAIDs),<sup>53</sup> cyclo-oxygenase-2 (COX-2)



**Figure 1** Proposed pain treatment algorithm for chronic non-malignant musculoskeletal pain (NSAID, non-steroidal anti-inflammatory; TENS, transcutaneous electrical nerve stimulation).

specific NSAIDs; weak opioids such as codeine and tramadol,<sup>54</sup> and opioids such as oxycodone and morphine. As noted in the American Geriatrics Society 2002 guidelines, the higher risk of adverse effects of some effective analgesics limits their use in the older patient.<sup>37</sup> The American Geriatrics Society clinical practice guideline 2002<sup>37</sup> and the American College of Rheumatology<sup>52,55,56</sup> both recommend acetaminophen as the first line agent in the treatment of mild to moderate pain of musculoskeletal origin.

Studies comparing acetaminophen and ibuprofen or naproxen in osteoarthritis of the knee have demonstrated comparable efficacy in outcomes. NSAID toxicity both renal and gastrointestinal is increased in older patients.<sup>56,57</sup> The risk of serious complications associated with NSAIDs increases by 4% for each one year increase in age after 65 years.<sup>57</sup> Elderly patients with reduced renal perfusion or cardiovascular disease are more dependent on renal prostaglandin synthesis to maintain renal blood flow. NSAID therapy may precipitate renal failure and increase the risk of hospitalisation for congestive heart failure in patients with cardiovascular disease by 10-fold. COX-2 selective NSAIDs offer improved gastrointestinal tolerance but pose similar risk to renal function. The elderly are more sensitive to the side effects of drugs such as the NSAIDs described and this can be compounded by other drugs, for example, steroids. This is an important consideration in elderly patients with concomitant disease who may be on numerous drugs and may be an influencing factor in prescribing analgesics.

Tramadol, with its indication for moderate to moderately severe pain, can be considered a suitable choice for

osteoarthritis pain unrelieved by acetaminophen.<sup>58</sup> Tramadol is a centrally acting analgesic with weak affinity for  $\mu$ -opioid receptors as an agonist, which possibly allows its efficacy to stretch over a wider range of painful pathologies than the other opioids.<sup>59,60</sup> Owing to its pharmacological properties, it is more appropriate for patients suffering from gastrointestinal (constipation) and renal problems,<sup>61</sup> combined with low dependence potential,<sup>62</sup> which proves to be a significant advantage over the other agents, especially in the elderly.

Tricyclic antidepressants (TCAs) have long been used for the treatment of chronic neuropathic pain and strong evidence from systematic reviews of randomised trials showing their effectiveness has been reported.<sup>63-65</sup> There may be a role for TCAs among selected elderly, who are likely to suffer from chronic painful conditions.<sup>66</sup> The analgesic effects of TCAs appear to be independent of any antidepressant effect, as TCAs have been shown to be effective in patients with chronic pain who do not have comorbid depression.<sup>67</sup> The risk of cardiovascular toxicity of TCAs must be considered in an elderly population. Although gabapentin has been widely employed in various types of chronic neuropathic pain, little evidence for efficacy in musculoskeletal pain is available. Other anticonvulsants such as carbamazepine, phenytoin, and sodium valproate are also used in the treatment of patients with neuropathic pain.<sup>68</sup>

The three step analgesic ladder, originally proposed for cancer pain relief by the World Health Organisation,<sup>69</sup> is useful and now widely employed for all types of pain, including the chronic pain of musculoskeletal disease.

The possibility of controlling otherwise intractable pain by the relatively brief application of a neurolytic agent or a local anaesthetic makes neural blockade an attractive approach in selected patients. Studies have concluded that treatment with nerve blocks alone is not very effective as a long term treatment for chronic pain.<sup>70</sup> Interpretation of these procedures has received much criticism as scientific studies validating their results are still wanting.<sup>71–73</sup>

## OPIOID INTERVENTION

For carefully selected elderly patients, opioid analgesics may represent the optimal approaches to pain control and hopefully improved function. For significant pain inadequately relieved by acetaminophen or tramadol, opioids may pose less risk of major toxicity than NSAIDs as outlined above.

Since Portenoy and Foley's landmark paper in 1986,<sup>74</sup> multiple studies, many flawed, have suggested that long term opioid therapy (treatment for four or more years) effectively relieves pain in patients with non-malignant pain. Much less clear, however, is whether improvement in social or physical function—employment, recreational activities, even self care—accompanies pain reduction. Portenoy's retrospective review of 38 patients with non-malignant pain (14 with chronic back pain), most treated for more than four years with long term opioids, found that 24 patients noted partial or full relief of pain. However, no significant improvement in social function or employment was demonstrable. No toxicity was reported, though two of the patients with a prior history of substance abuse became "management problems". In a population of 112 patients treated with long term opioids for a mean of two years, Jamison *et al* reported that 83% of patients found the opioids "moderately beneficial" in relieving their pain<sup>75</sup>; 45% of these patients had chronic low back pain. In this retrospective analysis, no attempt to assess effect on functional status was possible. In a recent subsequent study,<sup>76</sup> the same author compared sustained released morphine with naproxen and set dose oxycodone in 36 patients with chronic low back pain in a randomised, open trial. Though the opioid treated patients demonstrated superior pain relief and less emotional distress, no difference was found in activity level or hours of sleep. Similarly, Moulin *et al*, in a randomised, double blind crossover study of 46 patients, most of whom had regional myofascial pain syndromes,<sup>77</sup> were treated with long acting morphine (MS Contin) and found significant improvement in pain control but no difference in physical or psychosocial function as assessed by the Sickness Impact Profile instrument.<sup>78</sup> Conversely, in a study of 100 patients treated with long term opioid therapy,<sup>79</sup> Zenz *et al* found that 79% of patients experienced good or partial pain relief and that significant improvement in the Karnofsky performance scale<sup>80</sup> and was seen in patients with at least a 50% improvement in pain level. The Karnofsky Performance Scale Index allows patients to be classified as to their functional impairment. This can be used to compare effectiveness of different therapies and to assess the prognosis in individual patients. The lower the Karnofsky score, the worse the survival for most serious illnesses.

## Addiction

Fear of addiction has been a major barrier to long term opioid treatment in chronic non-malignant pain, particularly by physicians who may confuse physical dependence with addictive behaviour. Pseudoaddictive drug seeking by patients with poorly managed chronic pain may further discourage opioid treatment. A number of reports demonstrate minimal risk of addiction in patients treated with long term opioids who do not have a prior history of substance

## Box 1: Suggested guidelines for long term opioid use

1. Patients considered for long term opioids should have a well defined structural source of pain.
2. Patients with non-specific musculoskeletal syndromes are poor candidates for long term opioids particularly if self assessed disability is inconsistent with underlying structural disease.
3. In many patients, a pre-therapy psychosocial assessment by an experienced pain psychologist or psychiatrist should be performed.
4. Patients with current or previous substance abuse should be considered for long term opioids only rarely and after careful psychological assessment and with meticulous follow up. In these patients, an opioid contract is mandatory.
5. In all patients with chronic non-malignant pain treated with opioids, regular assessment of efficacy of treatment should include pain and functional status. Functional measures may include pain disability index.
6. If treatment is ineffective as assessed by these parameters, it should be terminated.

abuse.<sup>75–77 79 81</sup> Moulin *et al* reviewed three studies including almost 25 000 patients treated with long term opioids without a history of drug dependence and found only seven cases of iatrogenic addiction.<sup>77</sup> Whether or not patients with a history of prior substance abuse but with an appropriate indication for long term opioids should ever be considered for such treatment is controversial. Dunbar and Katz retrospectively studied 20 patients with a history of chronic non-malignant pain and substance abuse treated with chronic opioids for more than one year.<sup>82</sup> Eleven of the 20 patients demonstrated no evidence of abuse. One of the factors associated with less risk of abuse was that these patients were more likely to have a stable family. In addition, they were active members of Alcoholics Anonymous, and had abused alcohol alone rather than multiple substances. Again, these studies did not specifically assess these issues in the older population.

## Tolerance

The available clinical studies provide few data to answer the question of clinical tolerance. The retrospective analysis by Jamison *et al* of 112 patients found that 25% of patients reported the opioid had not lost its ability to relieve the pain over time and 35% of patients reported no need to increase the dose of their medication.<sup>75</sup> In general, our anecdotal clinical experience suggests that tolerance is not a significant clinical problem in older adults.

## Cognitive function

Haythornthwaite *et al* studied 19 patients receiving long acting, oral opioid medications in comparison with 10 patients receiving usual care.<sup>83</sup> Multiple tools assessing cognitive function were prospectively administered to both groups. No declines in cognitive function were associated with the long acting opioid medications and these patients actually showed significant improvement in measures of psychomotor speed and sustained attention. After reviewing the literature, Zacny concluded that morphine-like opioids do not appear to disrupt performance related to driving.<sup>84</sup> These studies to date suggest that people taking opioids at a

stabilised dose for medically approved reasons should be allowed to work.<sup>83, 84</sup> Further studies specifically in older patients who may have less "cognitive reserve" are required.

### Regulatory issues

The roles of both health professionals and law enforcement personnel in maintaining the essential balance between patient care and diversion prevention is critical. Fears of regulatory sanctions, abuse, and side effects can lead to reluctance to prescribe opioids for non-cancer pain. Regulatory concerns are best addressed by careful, repeated assessment of the "four As": analgesia, activities of daily living, adverse effects, and aberrant behaviour.<sup>85</sup> "Affect" could be a fifth addition to show the monitoring of the emotional side of pain. Failure to treat intractable pain is rapidly emerging as an important liability issue for physicians.<sup>81</sup> The British Geriatrics Society compendium of good practice and the American Bar Association advocates a serious look at pain management and the rights of patients with pain.

### Side effects

Opioids share a common mechanism of action, and common side effect profiles in the elderly. Their impact on the central nervous system, gastrointestinal function, and respiration may be clear, with less obvious effects on other systems including cardiovascular, urinary, skin, and others. Side effects may be related to a specific drug or combination of drugs, the total daily opioid dose, starting a drug or increasing the amount taken, drug by-products, and to the patient's age and concurrent medical condition. Recognising the side effects and treating them is important. Side effects can be avoided by using lower doses of the drug or administering less frequently (for example, eight hourly instead of four hourly). Because of age related declines in renal function,<sup>86</sup> the elderly are theoretically more prone to adverse effects like agitation, myoclonus, and seizures than younger adults. Ultra-long acting opioids, such as methadone, should be used with extreme caution. Methadone is partly excreted unchanged in the urine and its half life outlasts its duration of analgesic action, making titration difficult. The drug can accumulate, and delayed toxicity can occur, especially in the elderly.<sup>87</sup> Hence, initial and incremental doses of morphine and other opioid analgesics should generally be smaller for frail elderly patients because of age related pharmacodynamic and pharmacokinetic factors.<sup>88</sup>

Respiratory depression, sedation, constipation, nausea, vomiting, and itching are the other side effects of opioids encountered in practice. It is important to discuss these potential side effects with patients before and during the use of the medications. Health care professionals fear respiratory depression with the use of opioids. It is often a reason for under-dosing or limited use of opioids.<sup>89-91</sup> Tolerance to the respiratory depressant effect of opioids occurs rapidly. Therefore, the risk is greater in the treatment of acute pain or with increased dose adjustments of opioids than with chronic treatments.<sup>92</sup> All patients should be observed closely during times of peak analgesic blood concentrations and for respiratory depression. Most patients who have been receiving opioids will tolerate graduate increments in medication with little or no problem. However, because opioids can lead to hypotension and respiratory depression, caution is required in frail patients with haemodynamic instability or respiratory decompensation. If respiratory depression occurs, it should be treated cautiously with an antagonist such as naloxone.<sup>93</sup>

Sedation is a common complaint in opioid naive patients. This usually settles in 2-3 days. Sometimes a slight dose adjustment will decrease sedation but not increase pain. Switching to another analgesic with an equianalgesic dose is

another option.<sup>94</sup> From a patient's standpoint, constipation is often the most troublesome consequence of opioid therapy.<sup>25, 95, 96</sup> Do not wait until constipation occurs. Particularly in older patients using opioids regularly, prevention of constipation with stool softeners, adequate fluid intake, and non-bulk forming laxatives is advisable.

Equally nausea and vomiting are often transient and settle after 2-3 days. Systematic use of metoclopramide with opioid therapy for non-malignant pain decreases the risk of nausea and vomiting.<sup>97</sup> If nausea and vomiting are persistent, switching to an equianalgesic dose of another opioid may relieve the symptoms. Allergic reactions to opioids are rare. A higher incidence of pruritus occurs with intraspinal use of opioids.<sup>98, 99</sup> An assessment is necessary. Opioid induced histamine release from mast cells resulting in urticaria, pruritus, bronchospasm, and hypotension doesn't usually demonstrate a typical anaphylactic reaction cascade but nevertheless can in severe cases elicit the clinical picture of an anaphylactic shock. Opioid induced pruritus can be caused either centrally or peripherally by histamine liberation. The mechanism of centrally elicited pruritus is poorly understood. The opioid induced central pruritus can be reversed by naloxone and is probably caused by a change in neurotransmitter release in spinal and supraspinal centres.<sup>100</sup>

### CONCLUSION

Musculoskeletal pain is common and under-treated in the elderly. Unfortunately, older patients are often excluded from studies assessing various medication effects in pain reduction. Often, an attempt is made in clinical trials to avoid the influences of other medical conditions or drug interactions with coadministered medications. As a result, most of the literature derived from studies employing pharmacological and non-pharmacological approaches has largely focused on diverse patient populations, not exclusively the elderly. Most new analgesics recently approved by the Food and Drug Administration have few data available on their use in patients over the age of 80 years or in those with multiple medical problems. Limited data are available to describe potential drug interactions.

As a result of physiological age related changes in drug metabolic pathways and comorbid disease, the elderly may be more sensitive to analgesic drug effect and or greater risk of toxicity. Despite potential risks, the need for improved pain management in the older population for greater function and quality of life mandates long term care. Controlled trials of opioid analgesia in this population to guide rational therapy are critically needed.

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