Faculty of Pain Medicine
Australian and New Zealand College of Anaesthetists

Recommendations regarding the use of Opioid Analgesics in patients with chronic Non-Cancer Pain

PURPOSE

The Faculty of Pain Medicine (FPM) recognises the lack of definitive evidence supporting the long-term effectiveness of opioid analgesics in people experiencing chronic non-cancer pain (CNCP) and the substantial evidence of potential harm. This document outlines the current position of the FPM regarding opioid use in CNCP. It is anticipated that this position will evolve as the evidence base develops.

CURRENT EVIDENCE

The efficacy of opioid therapy is supported by strong evidence from randomised controlled trials in acute pain [1] and from systematic reviews in cancer pain [2,3], palliative care [4] and opioid dependency/addiction [5]. In CNCP systematic reviews report modest short term analgesic benefit [6,7]. However the duration of the RCTs reviewed (up to 4 months) was too short to adequately inform the long term role of opioid treatment in CNCP.

A recent systematic review that examined the evidence of long term opioid efficacy and risk [8] concluded that “evidence is insufficient to determine the effectiveness of long term opioid therapy for improving chronic pain and function”. There is also a dose-dependent risk of serious harms especially when opioids are combined with other psycho-active agents including alcohol.

Tolerance [9,10] and other adverse effects are potential limiting factors with long term opioid use. A systematic review of opioid response after 6 months of therapy in 25 non-randomised case series showed weak evidence of modest analgesic benefit and inconclusive data in regard to improvement in physical function and quality of life [11]. Population studies show that people maintained on long term opioid therapy for CNCP describe more troublesome pain and greater functional interference than people not on opioids [12]. A recent Australian population study examined a cohort of patients on long term opioid therapy and found that two-thirds were unemployed or receiving a government benefit and almost half had low income [13]. In addition, 80% of the cohort reported multiple pain conditions, 50% significant depression, 50% suicidal ideation, over 50% a history of childhood abuse or neglect and over 30% had a lifetime alcohol use disorder. Such associations illustrate the complexity of the phenotype of CNCP and highlight the need for multidisciplinary assessment and management.

Clinical experience and multiple studies have indicated that the use of high pain severity ratings is a poor basis for selection of patients for opioid prescription. Pain ratings are well-known to be influenced by multiple psychological and contextual factors [14,15]. Patients with mental health and substance abuse problems are more likely to be prescribed chronic opioid therapy (“adverse selection”) and at higher doses than people without those risk factors [16]. Once established, dependence on opioids makes it hard to wean and cease them despite lack of analgesic benefit [17].

Accumulating evidence highlights the adverse effects of opioid therapy. Falls, cognitive impairment and gastrointestinal problems are well recognised clinically but have not been well studied over the long term [8]. Better documented risks include opioid misuse and addiction [18,19], overdose and death [20,21,22], sleep apnoea [23,24,25], sexual and other endocrine dysfunction [26,27,28], driving impairment [29,30,31,32] and opioid prescription to manage psychological distress (the “chemical coper”) [33]. An additional concern is that many patients on long term opioid therapy are co-prescribed benzodiazepines and the combination of these, potentially with other sedatives and alcohol, is associated with a further increased risk of apnoea and death [20, 34].
Screening for opioid risk has been recommended but at this point evidence of effectiveness is lacking. Screening for high risk patients, treatment agreements and urine testing have not been shown to reduce overall rates of opioid prescribing, misuse, or overdose [35]. Newer strategies aimed at reducing the risk of opioid misuse require evaluation. These include more selective prescription of opioids, avoidance of additional sedative hypnotics, prescription of lower doses, tamper resistant formulations [36,37] and prescription monitoring programs [35].

It is clear that opioid pharmacotherapy cannot be considered to be a core component of the management of CNCP. Furthermore, issues of patient selection and duration of opioid therapy require further definition.

A focus on pain relief alone via the passive receipt of opioid therapy can distract both patient and prescriber from active self-management strategies. This raises the question of suitable therapeutic alternatives, an issue that remains only partially resolved given the modest gains reported from cognitive behavioural approaches [38,39]. Clearly there are challenges in systematically reviewing studies with different treatment components and methodologies. Not all cognitive behavioural programs are the same. Hence the content and quality of multidisciplinary programs need further examination. Nevertheless, the benefits of the multidisciplinary approach are highlighted by studies showing improvement in pain and physical and emotional functioning after opioid cessation in a cognitive behavioural pain management program [40,41]. Strategies showing promise as components of the evolving multidisciplinary approach include neuroscience education [42,43], physical activity [44,45], nutrition [46], social engagement [47,48], mindfulness [49,50,51] and other psychotherapies [52,53].

The FPM endorses the need for further research to examine the efficacy and safety of long term opioid therapy in CNCP. There is a particular need to determine whether any sub-groups of patients experiencing CNCP have greater likelihood of ongoing therapeutic benefit and lesser likelihood of harm. Alternative research methodologies such as n-of-1 trials and benchmarking studies are required, given the impracticality of conducting randomised controlled trials over a time frame relevant to chronic pain.

PRINCIPLES OF OPIOID PRESCRIBING

The FPM recognises that at the present time opioids are widely prescribed for CNCP despite the lack of clear evidence of efficacy. Given this reality, the following principles are offered to guide their prescription.

1. **Comprehensive assessment**

The Faculty strongly endorses the sociopsychobiomedical framework for assessment and management of people experiencing CNCP [54]. This is not to ignore biomedical (somatic) contributions, where a confident diagnosis should be made if possible.

Sociological assessment identifies factors in the patient’s environment related to family and other relationships, work, life events, housing, sleep, activity and nutrition. A bidirectional link to the experience of pain is recognised whereby such factors can worsen pain whilst the pain can also negatively impact on each of these areas.

Psychological assessment explores the patient’s beliefs, mood state, behaviours and responses that may contribute to the experience of pain and treatment outcome. Relevant beliefs include understanding of diagnosis and prognosis, and expectations about treatment, including willingness to be an active participant. As the experience of chronic pain is commonly accompanied and influenced by mood and anxiety disorders, these should be evaluated through interview or questionnaire, as an indicator for further professional input. Behavioural responses to pain can include avoidance of activities likely to aggravate pain or overdoing these same activities after taking analgesics. Cognitive impairment, personality traits and disorders should also be considered.

Comprehensive assessment also addresses the risk of opioid misuse [18,55]. In broad terms, the potential for problematic opioid use, including addiction, is higher in younger patients, those without a confident biomedical diagnosis, those in contact with users of non-prescribed medication, those with active substance abuse problems or patients with co-morbid psychiatric disorders. Such considerations need not necessarily preclude opioid therapy but act as alerts to guide close monitoring.
2. Multimodal therapy

Pharmacotherapy for the patient experiencing pain is only ever one part of a multimodal plan towards self-management [56] and should be prescribed on a time-limited basis.

Non-drug therapies include education, pacing of activity including use of the painful part, addressing postural components, structured exercise programs, sleep hygiene and psychological therapies, with input where required from nurse educator, physical therapist, psychologist, occupational therapist, social worker, rehabilitation counsellor or dietitian.

Drug therapy for patients in pain is mainly for symptom control. In some situations where the mechanism of pain can be confidently determined, such as inflammatory or neuropathic conditions, anti-inflammatory or anti-neuropathic agents respectively may be helpful in modifying pathogenesis. However in most cases, symptom control itself is important, not only for reduction in distress but also as an adjunct to non-drug approaches towards an improved quality of life.

Paracetamol has been recommended as first-line drug therapy for CNCP; however this has been challenged by a recent systematic review [57]. Non-steroidal anti-inflammatory drugs (NSAIDs) offer little advantage over paracetamol [58], especially in the most common situations when inflammation is not the relevant mechanism.

Non-opioid adjuvant analgesic agents can be considered before opioids, especially for treatment of neuropathic pain. These include tricyclic antidepressant drugs (amitriptyline, nortriptyline), serotonin-noradrenaline reuptake inhibitors (venlafaxine, desvenlafaxine, duloxetine) and anticonvulsants (gabapentin, pregabalin). Co-morbid anxiety or depression should be treated by psychological approaches and/or appropriate medications.

Invasive medical procedures (injections, implants) may be considered in selected cases to support active self-management, in parallel with the above approaches. However the evidence for long term benefit is weak and there is significant risk of harm.

3. Opioid therapy

If after comprehensive assessment, opioid therapy is thought warranted as part of a multimodal plan facilitating self-management, there are several important aspects of prescribing to consider:

i. Agreement regarding an opioid trial
ii. Conduct of an opioid trial
iii. Response to difficulty in achieving or maintaining therapeutic goals
iv. Understanding of appropriate weaning strategies

The FPM emphasises that it is the responsibility of each prescriber to be thoroughly acquainted with not only the clinical pharmacology of the various opioids and their interactions with other drugs but also the regulatory requirements imposed by the jurisdiction in which they practise.

I. AGREEMENT REGARDING AN OPIOID TRIAL

The aim of an opioid analgesic trial is to discover the individual’s responsiveness to this therapy in terms of improved quality of life. This requires frank articulation of the goals of the trial, including an agreement that if the goals are not met, then the treatment will be discontinued. The goals are beyond pain relief alone and emphasise improvement in physical, emotional and mental functioning, including an increase in activity. These goals can be negotiated according to the individual’s wishes and capacity.

In this respect, a therapeutic contract is established, which can be made explicit verbally, through entries in notes or in a formal written agreement. This contract reflects the seriousness of the undertaking between prescriber and patient. There should be only one prescriber of a patient’s opioids, with adequate back-up provision should that prescriber be unavailable. Ideally, the one pharmacy should dispense the opioid. Once opioid-responsiveness is established and adverse-effect profile addressed, the contract can be extended, with caveats such as no early repeats, no replacements for loss and an option for random urine monitoring (where appropriate) until a stable dose regimen is established. The contract may include an option for a time-limited maintenance period before staged withdrawal of opioid therapy.
II. CONDUCT OF AN OPIOID TRIAL (Appendix 1)

Chronic pain should not be treated with short-acting drugs (oral, transmucosal or parenteral), as the more rapid onset of effect increases the potential for positive reinforcement of drug-taking. For this reason avoidance of or weaning from short-acting preparations is suggested, in favour of a trial of long-acting or sustained-release preparations (oral or transdermal).

The use of opioid analgesics in the management of pain is an ongoing individual trial of therapy. Regular assessment addresses and documents “5As”:

• Analgesia
• Activity
• Adverse effects
• Affect
• Aberrant behaviour

Titration of dose according to this “5A” assessment need not be rapid: such a trial may take several weeks. An improvement in overall well-being in the opioid-responsive patient may incur “incident” pain, which can be addressed pharmacologically by a modification of the long-acting opioid dose rather than by adding a short-acting agent. The question of a “ceiling dose” has not been settled. Caution is warranted at oral morphine equivalent daily doses (oMEDD) >40mg [20,21,59,60,61] and doses above oMEDD of 100 mg [61] should prompt reassessment and specialist advice (Appendix B). Particular caution is required in prescribing transdermal fentanyl patches, as the lowest available dose (12mcg/hr) is close to the oMEDD 40mg threshold.

Once opioid-responsiveness and stability of dose have been achieved, regular review should be undertaken, with repeat prescriptions contingent on ongoing satisfactory “5A” assessment. At least annual peer or specialist review is recommended.

III. RESPONSE TO DIFFICULTY IN ACHIEVING OR MAINTAINING THERAPEUTIC GOALS

Difficulty in achieving satisfactory “5A” assessments in the context of the individually tailored goals of an opioid trial may be attributable to pharmacodynamic, pharmacokinetic or behavioural factors. Pharmacodynamic factors, such as non-responsiveness of distress or development of intolerable adverse effects, and pharmacokinetic factors, such as insufficient (or excessive) duration of effect, may respond to change in opioid preparation or change in dosing regimen. Behavioural factors, such as poor activity pacing, may respond to specific attention to those aspects.

Variations in stability of dose and responsiveness over time, including apparent increase in dose requirements (other than for incident pain), may reflect change in the underlying biomedical (somatic) contribution, development of tolerance (pharmacological, psychological or increased sensitivity to stimuli), change in mood, social circumstances or other stressors, or development of aberrant drug-taking behaviour. Such situations require comprehensive reassessment.

Actions arising out of such re-assessment may include recalibration of goals of therapy, reconsideration of other modes of therapy, consultation with colleague(s) and opioid reduction, to the minimum effective dose or cessation.

IV. UNDERSTANDING OF APPROPRIATE WEANING STRATEGIES

A clear understanding of pragmatic exit strategies is required for any doctor prescribing opioids. The involvement of Addiction Medicine services can often be helpful in considering prescribing boundaries and therapeutic pathways. Specific weaning strategies in the context of transition to self-management include:

1. If opioids are commenced for the pain of acute nociception, there is a need to give clear direction about the anticipated duration of therapy. Typically opioids should be weaned and ceased as the acute injury heals. Even in complex cases this should be within 90 days.
2. In situations where long term opioid therapy has been maintained (at times for many years) without meaningful improvement in function, the desired outcome is weaning to cessation if possible. One practical strategy is to reduce the daily opioid dose each month by 10-25% of the starting dose. This brings cessation in 3-9 months.

3. If weaning is required after a shorter period of opioid therapy, such as after failure to achieve the goals of an opioid trial, or after a negotiated treatment phase for acute pain, then a faster rate of weaning is generally appropriate. One option is a step-wise reduction of the daily opioid dose each week by 10-25% of the starting dose.

4. If weaning is required in response to significant adverse effects or opioid misuse, then daily step-wise reduction may be more appropriate. Alternatively, immediate opioid cessation and pharmacological treatment of withdrawal symptoms can be considered.

5. If a previous attempt at opioid weaning has proven unsuccessful, then the rate can be slowed. This can be achieved by reducing the size of the dose reduction each month and/or by increasing the time spent at each dose level (eg. 2 or 3 months between reductions).

6. In some cases it may become apparent during weaning that the primary problem is opioid dependency rather than pain. If so, referral to an Addiction Medicine service is recommended.

REFERENCES


35. Deyo RA, Von Korff M, Duhrkoop D. Opioids for low back pain. BMJ. 2015 Jan 5;350:g6380. doi: 10.1136/bmj.g6380


54. FPM revised curriculum (need website link)


FURTHER READING


• Cohen ML, Wodak AD. The judicious use of opioids in managing chronic noncancer pain. Medicine Today 2010, 11(2) (February):10-18


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