Statement regarding the use of opioid analgesics in patients with chronic non-cancer pain

Preamble

A. 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 for potential harm.

B. The FPM recognises that opioids are widely and often inappropriately prescribed for CNCP despite the lack of clear evidence of efficacy.

C. The FPM also recognises the changed regulatory environment introduced in Australia by the TGA[1] in 2020, specifically[2]:

"[Modified-release opioid product] is indicated for the management of severe pain where
- other treatment options have failed, are contraindicated, not tolerated or are otherwise inappropriate to provide sufficient management of pain, and
- the pain is opioid-responsive, and
- requires daily, continuous, long term treatment.

"[Modified-release opioid product] is not indicated for use in chronic non-cancer pain other than in exceptional circumstances."

D. The FPM interprets "exceptional circumstances" in this context to denote:
- Severe pain,
  - for which other treatment options have failed, are contraindicated, not tolerated or are otherwise inappropriate to provide sufficient management, *and*
  - which has been shown to be opioid-responsive

E. In New Zealand, Medsafe has not taken an overarching regulatory approach. The indications for each drug are listed in its data sheet.[3] Some but not all products mention criteria such as opioid-responsiveness, failure of conservative methods of analgesia, and absence of psychological contraindication, drug-seeking behaviour or history of drug misuse. CNCP is not necessarily specified.

F. This document describes the current position of the FPM regarding the prescription of opioids in CNCP, presented as a series of principles and a synopsis of the evidence and reasoning on which they are based.

[1] Therapeutic Goods Administration, Department of Health, Commonwealth of Australia
[2] Therapeutics Good Administration. Prescription opioids hub: Upcoming changes to reduce harm. https://www.tga.gov.au/node/877210: TGA, 2020. Accessed 11/3/2020.
[3] https://www.medsafe.govt.nz/Profs/Datasheet/[product] Accessed 31/3/2020.

PRINCIPLES

1. GENERAL PRINCIPLES INFORMING THE MANAGEMENT OF PATIENTS WITH CHRONIC NON-CANCER PAIN

1.1 Careful assessment of the social, psychological and biomedical contributors[4] to the person's presentation should be undertaken to inform a management plan for people with CNCP.

1.2 The first line of therapy for CNCP involves engaging the person to develop pain self-management skills[5].

1.3 Second line therapies in CNCP include drug treatment which, while not a core component of a management plan, may play a role in facilitating functional goals and maintaining social roles including employment.

1.4 Drug treatment for the patient with CNCP is only ever part of a multimodal plan towards self-management and should be prescribed on a time-limited basis.

1.5 Drug treatment with opioids in patients with CNCP may be considered in the exceptional circumstances described in Preamble point D above.

2. PRINCIPLES INFORMING THE PRESCRIPTION OF OPIOIDS TO PATIENTS WITH CHRONIC NON-CANCER PAIN

2.1 General

2.1.1 Opioid treatment in CNCP is always an ongoing individual trial of therapy. Prescription of opioids, in the context of Principle 1.5 above, is contingent upon:

- demonstration of benefit;
- active surveillance for harms; and
- periodic attempts at dose minimisation.

2.1.2 It is the responsibility of each prescriber to be thoroughly acquainted with:

- the clinical pharmacology of the opioid(s) to be prescribed;
- the efficacy and harms of those opioids;
- the interactions of opioids with other drugs; and
- the regulatory requirements imposed by the jurisdiction in which they practise.

2.1.3 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 clear articulation of the goals of the trial, including an agreement that if the goals are not met, then this treatment will be withdrawn.[6]

Such goals extend beyond pain relief alone, to include improvement in activity and participation.[7] Goals need to be negotiated according to the individual's wishes and capability.

2.1.4 Opioid treatment requires regular, documented assessment that addresses the "5As":

- analgesia
- activity
- adverse effects
- affect
- aberrant behaviour

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[4] Sociopsychobiomedical Assessment. Faculty of Pain Medicine, ANZCA, Curriculum 2015-. http://fpm.anzca.edu.au/training/2015-training-program. 2015.

[5] Pain self-management skills development is a process where a person to learns ways to manage their symptoms and achieve goals (Nicholas & Blyth. Pain Management, 2016;6(1):75-88).

[6] This could be incorporated into an "opioid contract".

[7] The International Classification of Functioning Disability and Health model (ICF) describes body functions, activities and participation.

2.1.5 The criteria for "opioid-responsiveness" may include but are not limited to:

a. increase in function, as determined by an agreed activity or set of activities, assisted by instruments such as BPI[8] or PEG[9]
b. absence of limiting side-effects, especially those that might interfere with sleep, learning and active self-management
c. reduction in pain, quantified by instruments such as BPI, PEG, VAS[10], NRS[11]
d. sustained response over time, not requiring dose escalation

2.1.6 If goals are met during a trial, then it is important to determine the lowest dose of opioid that is associated with sustained benefit. This dose may not be zero.

2.1.7 If the opioid trial goals are not met, then a process of weaning should be commenced. Specific weaning strategies in the context of transition to self-management include:

2.1.7.1 In situations where opioid therapy has been maintained for a long time 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%.

2.1.7.2 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%.

2.1.7.3 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.

2.1.7.4 If an 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 and/or by increasing the time spent at each dose level (e.g. 2 or 3 months between reductions).

2.1.7.5 In cases where it becomes apparent during weaning that the primary problem is opioid dependence rather than pain, involvement of an Addiction Medicine service is recommended.

2.1.7.6 Use of complex pharmacological treatments to assist weaning should be undertaken only by practitioners accredited in such treatment modalities.

2.1.8 During the period of opioid weaning,

- ongoing attempts to develop pain self-management skills remain important
- compliance with regulatory requirements remains essential
- limited dispensing and urine drug screening may be considered.

2.2 Additional principles underpinning management of the patient already established on opioids (the "inherited" or "legacy" patient)

2.2.1 Reassessment of the social, psychological and biomedical contributors to the person's presentation should be performed and repeated over time.

2.2.2 Consolidation of all opioid formulations to one opioid formulation should be undertaken, guided by contemporary equianalgesic tables.[12]

[8] BPI: Brief Pain Inventory (Tai G, Jensen MP, Thornberg JI, Shouti BF. Validation of the Brief Pain Inventory for chronic non-malignant pain. J Pain 2004(2); 5:133-137.)

[9] PEG Pain-Enjoyment-General Activity scale of pain intensity and interference (Krebs EE, Lorenz KA, Bair MJ, et al. Development and Initial Validation of the PEG, a Three-item scale Assessing Pain Intensity and Interference. J Gen Intern Med 2009; 24(6): 733- 738.)

[10] VAS: visual analogue (pain) scale

[11] NRS: numerical rating (pain) scale

[12] As per FPM Opioid Calculator app v 2.7.1 and document [www.fpm.anzca.edu.au/documents/opioid-dose-equivalence.pdf]

2.3 Additional principles underpinning initiating a trial in an opioid-naïve patient

2.3.1 A trial of opioid drug treatment may be considered after comprehensive assessment and trials of non-drug therapy and non-opioid drug treatment, as part of a multimodal plan facilitating self-management, according to principles 1.5 and 2.1.1 above.

2.3.2 Although short-acting opioids may be useful in determining initial opioid-responsiveness in CNCP, as in 2.1.5 above, they should not be prescribed over the longer term, out of consideration for the development of tolerance and the potential for positive reinforcement of drug-taking behaviour. A definitive trial should be determined using long-acting or modified-release opioid preparations.

2.3.3 Transdermal fentanyl should not be initiated in CNCP.

2.3.4 Ascertainment of opioid-responsiveness by titration of dose should be achievable within two months of initiation.

2.3.5 Opioid-responsiveness should be evident at oral morphine equivalent (OME) doses ≤ 60mg per day.[13,14] If doses exceed this, specialist consultation should be sought.

2.4 Response to difficulty achieving or maintaining therapeutic goals in an opioid trial

2.4.1 Difficulty in establishing opioid-responsiveness in the context of the individually tailored goals of an opioid trial, as defined above, 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 reinforcement of pain self-management skills.

2.4.2 Variations in stability of dose and responsiveness over time, including apparent increase in dose requirements may reflect change in the underlying biomedical contribution, development of tolerance, changes in mood, social circumstances or other stressors, or development of aberrant drug-taking behaviour. Such situations require comprehensive reassessment.

2.4.3 Actions arising out of such reassessment may include:

- recalibration of goals of therapy
- reconsideration of other modes of therapy
- consultation with colleague(s)
- opioid reduction to the minimum effective dose or cessation

[13] NSW Therapeutic Advisory Group Inc., Preventing and managing problems with opioid prescribing for chronic non-cancer pain. NSW TAG: Sydney, 2015
[14] http://www.aci.health.nsw.gov.au/chronic-pain/health-professionals/quick_steps_through_opioid_management

SYNOPSIS OF CURRENT EVIDENCE (2020)

Complex phenotype of CNCP
The complexity of the phenotype of CNCP needs to be appreciated in understanding what is the role effectiveness of opioid therapy. A recent Australian population study[15] found, in a cohort of patients with CNCP who were taking long term opioid therapy, that two-thirds were unemployed or in receipt of a government benefit and almost half had low income. Furthermore, 80% of the cohort reported multiple pain conditions, 50% significant depression, 50% suicidal ideation, and more than 50% had a history of childhood abuse or neglect and over 30% had a lifetime alcohol use disorder. This is reflected in population studies that show that people maintained on long term opioid therapy for CNCP describe more troublesome pain and greater functional interference than people not on opioids. Such associations underline the need for comprehensive multidisciplinary assessment of people with CNCP.

Efficacy of opioids in CNCP
The efficacy of opioid therapy is supported by strong evidence from randomised controlled trials in acute pain and from systematic reviews in cancer pain, palliative care and opioid dependency/addiction. By contrast, recent systematic reviews in CNCP have concluded that, despite modest analgesic benefit in the short term, there is insufficient evidence to determine the effectiveness of long term opioid therapy in terms of improving pain and function. The duration of the RCTs reviewed was less than four months, which is insufficient to adequately inform the long term role of opioid treatment in CNCP.

Adverse effects of opioids in CNCP
Tolerance and other adverse effects are potential limiting factors with long term opioid use. There is also a dose-dependent risk of serious harms, especially when opioids are combined with other psycho-active agents including alcohol. Falls, cognitive impairment and gastrointestinal problems are well recognised clinically but have not been well studied over the long term. Better documented risks include opioid misuse and addiction, overdose and death, sleep apnoea, sexual and other endocrine dysfunction, driving impairment and opioid prescription to manage psychological distress (the “chemical coper”). 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.

Responsible prescription of opioids in CNCP
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. Patients with mental health and substance abuse problems are more likely to be prescribed chronic opioid therapy (See ‘Complex phenotype of CNCP’ above) and at higher doses than people without those risk factors. Once established, dependence on opioids makes it hard to wean and cease them despite lack of analgesic benefit.

Screening for opioid risk
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. 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 and prescription monitoring programs.

Place of opioid use in CNCP
It is clear that opioid pharmacotherapy is not a core component of the management of patients with 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. 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. Strategies showing promise as

[15] (Campbell et al, 2015)

components of the evolving multidisciplinary approach include neuroscience education, physical activity, nutrition, social engagement, mindfulness and other psychotherapies.

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Faculty of Pain Medicine Professional Documents

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STATEMENT – A document that describes where the college stands on a particular issue. This may include areas that lack clarity or where opinions vary. A statement is not prescriptive.

GUIDELINE – A document that offers advice on a particular subject, ideally based on best practice recommendations and information, available evidence and/or expert consensus. A guideline is not prescriptive.

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